The Abstracts of the 5th European Congress on Tropical Medicine and International Health
24–28 May 2007
Amsterdam, the Netherlands
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Access to Essential Medicine

INV 01
Diagnostics for neglected parasitic diseases
D. Mabey1
1LSHTM, Infectious and Tropical Diseases, London, UK

OBJECTIVES To review the literature on recent advances in diagnostics for neglected parasitic diseases.

METHODS Literature review.

RESULTS Better diagnostics tests for parasitic diseases are needed for two main reasons: to improve case management, and to improve disease surveillance. When treatment is expensive or toxic, as in the case of African trypanosomiasis or visceral leishmaniasis, better tests are needed to guide case management. In the case of diseases that can be treated presumptively with cheap and safe drugs, such as onchocerciasis, schistosomiasis or geohelminth infections, there is a need for better tests to monitor the impact of disease control programmes and, potentially, to certify that elimination targets have been achieved. Diagnostic tests to guide case management should ideally be performed at the point of care and, since this is often a remote rural health facility, they should be simple to perform and should not require electricity or sophisticated equipment. Tests for surveillance need not necessarily be performed on site.

CONCLUSION This talk will review recent advances in the diagnosis of neglected parasitic diseases, and identify areas where further research is needed.

Aid Architecture

INV 02
North (EU)–South research collaboration: experiences and expectations
Y. Berhane1
1Addis Continental Institute of Public Health, Addis Ababa, Ethiopia

The section of the plenary dealing with North–South research collaboration is planned to share experiences of the speaker in collaborating with a number of European research teams over many years. Although research collaborations are in most instances based on the problems of the host country; lack of technical, administrative and logistical resources limited full exploitation of the benefits of research collaborations. Research projects often produced very useful findings that were otherwise unavailable. Emphasis on research training and capacity building has produced remarkable success in creating critical mass of researchers in host institutions. However, lack of motivating and retention mechanisms at host institutions seriously constrained sustainable capacity building efforts. Cultural mismatch in research collaboration are serious challenges in making research collaboration a pleasant experience for both sides. Often expectations to utilize research results for improving the health of populations by the host country researchers are not achieved. Expectations of the community to immediately benefit from the research findings also remained unmet due to failure to follow research with interventions. Thus, the values of research remained low outside the academic circle and host government refrain or do little to allocate resources for sustainable research activities. Future collaborative efforts need to emphasis thinking throughout the research cycle, a holistic approach—from researching to intervening in order to bring about better health conditions for the poor.

Amoebiasis

INV 03
Amoebiasis
E. Tannich1
1Bernhard Nocht Institute for Tropical Medicine, Molecular Parasitology, Hamburg, Germany

Amoebiasis has been considered as a classical human parasitic disease of the tropics but it also occurs in areas of moderate climate. In Western Europe amoebiasis plays a role primarily as imported infection of travellers but in addition, autochtonous cases have been repeatedly observed. Recent advances in the diagnosis of Entamoeba histolytica infections have considerably improved the detection of the parasite, which enabled more sophisticated studies on the epidemiology and treatment of amoebiasis. Sequencing of the amoeba genome and the use of new animal models have identified new mechanisms responsible for E. histolytica pathogenicity.

Antibiotic Resistance

INV 04
Antibiotic resistance in low-resource countries
A. Bartoloni1
1Department of Critical Care Medicine and Surgery, Infectious Diseases Unit, University of Florence, Florence, Italy

Bacterial resistance to antimicrobial agents represents a global public health problem. In low-resource countries the extent and the impact of the phenomenon tend to be even larger than in industrialized countries. The high antimicrobial drug resistance rates observed in low-resource countries are likely due to a combination of several factors, among which irrational antimicrobial drug usage and conditions of poor sanitation are thought to play a major role, even if the relative importance of additional factors remains unclear. Surveillance of antimicrobial susceptibility is a key element to provide updated information on the magnitude and trends in resistance, and to plan and monitor intervention strategies aimed at preserving the therapeutic efficacy of antimicrobial agents. In low-resource countries, effective surveillance programmes are difficult to implement for a number of reasons, including scarce financial resources, lack of laboratory facilities and, where laboratories do exist, lack of quality control, reliable reagents and adequate supervision. The limited information based on reliable data on antimicrobial resistance for low-resource countries is mostly from studies conducted on pathogens isolated during disease outbreaks or from community- or hospital-acquired infections observed in the few health centres where high-quality laboratories are available. There is an increasing agreement about the importance of extending the surveillance of antimicrobial resistance to the commensal microbiota of humans and animals. This bacterial population, although not being a specific target, is continuously exposed to the selective pressure generated by antimicrobial chemotherapy and may become a potential reservoir of resistant strains that can cause infections, and of resistance determinants that can be transferred to pathogenic bacteria. Therefore, surveillance of antimicrobial-resistant bacteria

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carried by healthy individuals is considered an indicator of the spread of antimicrobial resistance that could also be useful to predict the emergence of resistance in pathogenic bacteria. The prevention and control of drug resistant infections requires measure to promote the appropriate use of antimicrobial drugs, through a public health education campaign, and to prevent the transmission of infections, through public health campaigns that promote vaccination and hygienic practices. In this perspective, governments have a critical role and should address the problem within the wider priorities of strengthening health systems and diseases controls and prevention programs. Considering the difficulties of many low-resource countries, there is an urgent need of international significant financial and technical support.

**ART Pharmacology and Interactions**

**INV 05**

Antiretroviral pharmacology and interactions

G. Maartens

Continuing efforts to scale up antiretroviral (ARV) therapy in resource-limited settings have resulted in millions of patients being treated globally. Cohort studies have shown good outcomes, and the public health approach has resulted in adherence being better than in industrialised countries. However, the patient populations concerned have been under-represented in the pivotal clinical trials: notably there is a much higher proportion of women and children, and there are important pharmacogenetic differences among South East Asians and Africans that affect the metabolism and safety of ARVs. A limited repertoire of antiretroviral agents is used, and cheaper agents that are more toxic are widely used. Facilities for laboratory monitoring of toxicity are very limited. These factors may result in an increased risk of adverse drug reactions or novel toxicities. Pharmacovigilance infrastructure requires strengthening and there is a need for cohort studies focussing on safety, particularly evaluating long term toxicity. Co-morbidities occur more frequently in resource-limited settings, particularly tuberculosis and malaria. ARVs are involved in a large number of clinically important drug interactions, but there is limited data on interactions with the relevant drugs and populations involved. In addition there is a limited number of drugs available for treating important co-morbidities (e.g. anticonvulsants, rifampicins), so clinicians often need to use drugs that may significantly interact with ARVs rather than substitute non-interacting drugs. There is an urgent need to assess ARV-antimalarial interactions, and more data is necessary on ARV-rifampicin interactions.

**Buruli Ulcer**

**INV 06**

Managing neglected diseases with limited resources: lessons from Buruli ulcer care in amasaman


Clinical Pharmacology, University of Cape Town, Cape Town, South Africa

Swiss Tropical Institute, Molecular Immunology, Basle, Switzerland

Ghana Health Service, Tema Municipal Health Directorate, Tema, Ghana

Noguchi Memorial Institute for Medical Research, Bacteriology, Accra, Ghana

Swiss Tropical Institute, Molecular Immunology, Basle, Switzerland

Ghana Health Service, Amasaman Health Centre, Amasaman, Ghana

Ghana Health Service, Tema General Hospital, Tema, Ghana

University of Heidelberg, Heidelberg, Germany

OBJECTIVES To assess the quality and effectiveness of an in-country intervention programme for management and control of Buruli ulcer disease (BUD) in the context of limited resources.

METHODS Patient and lesion characteristics, and treatment procedures for all BUD cases managed at Amasaman Health Centre, Ga West District, Ghana, from August 1999 through July 2004 were reviewed. Quality of treatment strategies and procedures, and outcomes were evaluated. Resource inputs (human, equipment, infrastructural) were assessed.

RESULTS A locally-initiated, comprehensive and integrated BUD management programme established. Components: community education, surveillance, clinical diagnosis, surgical treatment (functional improvised surgical unit), aseptic intensive wound care, in-patient care facilities (space for 40 beds) rehabilitation (including school), follow-up and extensive improvisation for missing resources (human, equipment, utilities etc.). A total of 222 cases, aged 2–75 years were clinically diagnosed and treated in the study period. Majority, 97.5%, lived in endemic communities in the Densu River basin in the district. Clinical diagnostic accuracy was 94%: among 83 cases for whom post-treatment testing (microscopy, culture and PCR) of excised tissues feasible, 78 had at least one test positive. Early case detection rate was 48.9% (pre-ulcerative cases). Altogether, 391 surgeries were performed. Six (2.7%) and 31 (14.0%) cases respectively, were treated with limited excision with partial or complete suture. The rest had wide excision only or wide excision with skin grafting. Skin graft success rate (take) was 95.8% (115/120). No cases were amputated: severely affected limbs in a number of patients were salvaged. Fifteen patients (6.7%) developed recurrence and needed re-excision. At discharge, no severe deformity sequelae were recorded. Facilities developed also in use for managing other conditions such as caesarian sections.

CONCLUSION The findings of this evaluation show that a local response initiative successfully provided adequate care for BUD at basic level. To date, there are no effective preventive remedies, and control of this neglected disease, relies on early diagnosis/treatment. Although antibiotics have now been shown to eliminate the need for surgery or reduce its extent, many cases still require surgical intervention to achieve a cure. Yet, health systems of developing countries, especially in West Africa, with the heaviest disease burden, lack the resources to provide effective surgical care at basic level, close to remote endemic areas. In the face of persisting resource shortfall to fight BUD in poor countries, we recommend that similar, low-cost locally-appropriate interventions be promoted to address the problem in these countries.

**Child Health**

**INV 07**

Where are we (in international child health)?

M. English

KEMRI/Wellcome Trust Research Programme, Nairobi, Kenya

Child mortality rates in by far the majority of low and middle income countries declined steadily from 1960 to the end of the 1980’s, in many the early period post-independence. In a few survival gains have been sustained and dramatic. However, for many countries the period marked by demographic and health surveys since the 1990’s has seen stagnation or even worsening of child survival even in the absence of major armed conflict. The reasons for this are many and varied and span the arenas of international and national politics, macro and micro economics and social change as well as the more obvious provision of health care. In response to this current crisis of child and newborn survival, born of the realization that we should be doing so much better, efforts are being made to resuscitate their international profile as key global health and development issues. But as practitioners interested in or involved with international health
Clinical AIDS

INV 09
Clinical HIV/AIDS in sub-saharan Africa: new findings in a time of transition
J. A. Bartlett
1Duke University/Kilimanjaro Christian Medical Centre, Medicinal Infections Diseases, Moshi, United Republic of Tanzania

OBJECTIVE To provide an update on clinical HIV/AIDS in sub-Saharan Africa (SSA).

METHODS Three areas will be discussed; opportunistic infections focusing on antimicrobial resistance in MTB and Cryptococcus, expansion of antiretroviral drugs in clinical care (ARV’s), and vulnerabilities of currently employed ARV’s.

RESULTS MTB incidence rates remain high in SSA, and diagnosis is very challenging with the severe limitations of currently available laboratory infrastructure. A recent outbreak of extremely drug-resistant (XDR) TB has forced re-examination of current diagnostic and treatment paradigms, and infection control procedures in SSA. Interventions are urgently needed to prevent expansion of this outbreak. Cryptococcal meningitis treatment failures with oral fluconazole are common, perhaps related to inadequate dosing and drug interactions which lead to fluconazole resistance. Increasing use of ARV’s is changing clinical HIV/AIDS care in SSA. Treated persons have fewer HIV-related morbidities and prolonged survival. However, complications of ARV use are increasing, (lipodystrophy, lipoaccumulation and peripheral neuropathy). Currently employed regimens, which frequently include stavudine in a fixed dose combination with lamivudine/nevirapine, increase the likelihood of these complications. Furthermore, nevirapine- and lamivudine-containing regimens are vulnerable to failure because of low genetic barriers to non-nucleoside reverse transcriptase inhibitor (NNRTI) and lamivudine resistance. NNRTI resistance may also occur as a result of strategies which employ single dose nevirapine to prevent mother to child HIV transmission. Surveillance studies do not yet suggest NNRTI and lamivudine-resistant viruses are commonly identified in treatment-naive HIV-infected persons in SSA, but resistance to these agents has been observed in North American and European cohorts.

Although adherence rates to ARV’s are high in SSA over the short term, issues such as ARV cost, drug supply, transport to clinical services, and stigma/disclosure may limit be much more important objectives funders alike to respect Article 3 of the same Convention that ‘development’; they also challenged policymakers, treasuries and funders alike to respect Article 3 of the same Convention that ‘… in all actions concerning children the best interests of the child shall be a primary consideration.’ Yet the HIV epidemic has critically influenced, and in some regions fundamentally crippled efforts to achieve these goals. Globally, HIV/AIDS accounts for only about 2–3% of child deaths; yet in the African region, HIV is directly or indirectly responsible for 20–30% of under-5 year deaths. In high prevalence areas such as South Africa, HIV accounts for at least 40% of all childhood deaths. According to the 2006 World Health Report, child mortality rates in most countries are falling. There are, however, nine countries in which rates are increasing and of these, five (Botswana, Swaziland, Zimbabwe, Kenya and South Africa) are in East and Southern Africa where HIV prevalence rates are exceptionally high. Africa is also the only region where rates of childhood malnutrition are increasing. By comparison, in the USA, with a population of around 300 million, <100 children are infected with HIV each year. Highly effective interventions almost guarantee that infants born to HIV-infected mothers are uninfected, survive and remain uninfected through their lives. In southern Africa the situation is shamefully different. Less than 10% of HIV infected women receive any drug prophylaxis to reduce transmission and hundreds of thousands of infants become infected and die each year from an essentially preventable infection. Health systems have reached a point of PMTCT fatigue and are switching their finances and human resource investments to antiretroviral treatment in an effort to infuse some hope and pride into otherwise beleaguered systems. With this backdrop, the process of prioritising interventions to have maximum impact on child mortality must reflect the main causes of death, the system of health care delivery, the opportunities to gain synergy between programmes and the need to achieve sustainability.
METHODS Literature review of the current state of affairs from peer reviewed and institutional documents.

CONCLUSION As a parasitic infection of the poorest nations, malaria represents an important global public health hazard with an economic toll far beyond the resolve of the very nations in Africa it affects. From the eradication programs in the late 50s and early 60s, to roll back malaria in 1998, efforts have been largely supported through International donor funds and to an extent by country control programs. The RBM revised goals for 2010, require that 80% of people at risk from malaria are protected by ITNs and IRS; 80% of malaria patients diagnosed and treated with effective anti-malarial medicines within one day of the onset of illness in areas where transmission is stable, 80% of pregnant women receive IPT and that the malaria burden is reduced by 50% compared with 2000 levels. Except for Guinea Bissau, Sao Tome & Principe and the Gambia which between 1999 and 2003 had ITN distribution above 40%, most countries were still below 20% coverage. This has risen to 60% to 80% coverage through integration with Expanded Program on Immunization(EPI). A number of countries now flirt with the idea of reintroducing DDT which has shown dramatic reduction in burden of malaria for the Southern African States of Swaziland, Mozambique and South Africa. With the widespread resistance to aminoquinolines (20% to >65%), sulfadoxine-pyrimethamine [SP:(15–40%)] and under the advice of the WHO in 2001, countries have opted for the use of ACTs even ahead of their country’s baseline data on efficacies. The lack of fixed-dose ACTs in some countries, 3 years after such a policy went into force has made ACT implementation difficult. Assisted by the Global Fund against AIDS, Malaria and TB, in 2006 some 150 million doses are deployed. Since 80% of the cases are treated at home, home management is the recent drive for effective malaria management, requiring investments on education, training of community health workers and shop-keepers; supply of pre-packaged good quality medicines. Intermittent preventive therapy for mothers (IPTp) is being implemented in some 30 countries. IPT for infants (IPTi) is being integrated into EPI. However, 9 years after RBM launch, we still observe weak health systems and challenges in delivery of care to the poor and displaced populations.

INV 11
The Beijing genotype of Mycobacterium tuberculosis has a major influence on the current worldwide tuberculosis epidemic
D. van Soolingen1, J. Glynn2, F. Cobelens3 and L. Kremer1
1National Institute for Public Health and the Environment (RIVM), Tuberculosis Reference Laboratory, Bilthoven, Netherlands; 2National Institute for Public Health and the Environment (RIVM), Tuberculosis Reference Laboratory, Bilthoven, Netherlands; London School of Hygiene and Tropical Medicine, London, UK; 3KNCV Tuberculosis Association, Research Unit, The Hague, Netherlands

OBJECTIVES Findings and ongoing research on the spread of Beijing genotype strains of M. tuberculosis.

METHODS Molecular epidemiology.

RESULTS It has been noticed in the past decade that in geographic areas with a high prevalence of tuberculosis particular, clonal genotypes of Mycobacterium tuberculosis are spreading. For instance in Africa the degree of DNA polymorphism among M. tuberculosis isolates is much lower than in countries in Europe. The rate of conservation among M. tuberculosis strains in Asia was found to be extremely high and therefore the respective genotype has been designated the Beijing genotype. In a worldwide survey published in 2006 in EID it was found that the Beijing genotype is emerging in Vietnam, South Africa and other areas. In these settings, the Beijing genotype strains are relatively more frequently found in younger patients and are spreading at the expense of other genotypes of M. tuberculosis. In terms of evolution, this reflects a dramatic change in the population structure of this bacterium in a very short time period. Therefore, it is conceivable mankind has forced this selection of more adapted genotypes of M. tuberculosis. Apart from a higher density of worldwide human population and a higher mobility, especially the introduction of two measures; mass BCG vaccination and worldwide treatment of tuberculosis by anti-tuberculosis drugs may contribute to this phenomenon. It is therefore not surprising that in many areas, under which Europe, the Beijing genotype is associated with (multi-drug) resistance. A new EU project (2007–2010) is initiated to investigate the basis of this higher ability of successfully spreading genotypes to gain resistance. There are strong indications that the DNA repair mechanism in the predominant genotypes of M. tuberculosis is changing. Moreover, in Vietnam the emerging lineage of Beijing strains is correlated with BCG vaccination of patients, which is another indication of selective spread of Beijing strains. In Vietnam the targets of the WHO regarding cure rate and case detections are met since 1997, but the rates are not decreasing as anticipated. This may be related to changes in the causative agent of tuberculosis.

CONCLUSION Presumably 20–30% of the worldwide tuberculosis cases are caused by Beijing strains, which are emerging and seem to have selective advantages. Next step should be the investigation of the population structure of M. tuberculosis in Africa.

INV 12
Development of highly active HIV microbicides
R. Shattock1
1Cellular and Molecular Medicine, St George’s, University of London, London, UK

Heterosexual transmission is the leading mode of HIV-1 infection worldwide, with women particularly vulnerable to HIV-1 infection as they often cannot control sexual encounters or insist on condom use. In the absence of an effective vaccine there is an urgent need to develop alternative prevention strategies. The immediate events between exposure to infectious virus and the establishment of infection are still poorly understood. Defining the mechanisms of HIV-1 transmission, the target cells involved and how the virus attaches to and fuses with these cells is revealing new ways to block the sexual spread of the virus. Initial efforts to develop vaginal microbicides focused on killing the virus through membrane disruption using surfactants, and blocking viral entry using polyanionic compounds that interact with the positively charged areas of the viral envelope proteins, many of which are currently in phase II/III trials. However recent advances in HIV pathogenesis and therapeutics are now bringing a wide range of new products into the development pipeline that specifically target different stages in the viral life cycle. This talk will present rigorous pre-clinical evaluation of candidate microbicides prior to selection for clinical trials, providing considerable savings in costs and time, given the expense and length of formal efficacy trials. Selection criteria include: high activity against cell free and cell associated virus in mucosal explant models; low irritation potential based on a range of preclinical irritation assays; high in vitro activity in the presence of semen; and effectiveness in animal models using challenge virus that is relevant to sexual HIV transmission. This presentation will discuss how our increasing knowledge of the ways in which HIV-1 is transmitted has sharpened the development of new, more sophisticated intervention strategies based on the application of vaginal or rectal microbicides.
INV 13
AIDS in Africa and beyond
J. M. A. Lange
1Center for Poverty-related Communicable Diseases, Academic Medical Center, University of Amsterdam, Amsterdam, Netherlands

Sub-Saharan Africa is the hardest hit region by the HIV/AIDS epidemic. Of the 40 million people living with HIV/AIDS globally, almost 26 million (65%) live in sub-Saharan Africa. The seven countries with an adult HIV prevalence of more than 20% are located in southern Africa and especially in this region there is an increasing feminization of the epidemic. Preventive strategies and measures fall short, often simply because they are not available or are largely male-controlled. A preventive HIV vaccine is still far away; thus the drive to develop alternative prevention technologies, such as microbicides and oral pre-exposure prophylaxis, that could be female-controlled. Beside a pressing need to scale up HIV prevention efforts, there is a similar need to scale up access to HIV/AIDS care and antiretroviral drug treatment. Funding to support has increased greatly over the past years through several mechanisms (World Bank Multicountry AIDS Program, Global Fund to Fight AIDS, TB and Malaria, and the US President’s Emergency Plan for AIDS Relief), yet the reality on the ground in sub-Saharan Africa is that only about 20% of those in immediate need receive antiretroviral therapy. There are considerable obstacles to a further scale up and to its sustainability. In the long-term, treatment of HIV/AIDS can only be effectively addressed in the context of strengthening general health care delivery and its financing through introduction of robust insurance schemes.

Cysticercosis

INV 14
Establishing and implementing a global campaign to combat cysticercosis
A. L. Willingham1, Bellagio Conference Groups on Establishing and Implementing a Global Campaign for Combating Cysticercosis
1Department of Veterinary Pathobiology, Faculty of Life Sciences, WHO/FAO Collaborating Center for Parasitic Zoonoses, University of Copenhagen, Frederiksberg C. Denmark

Conferences were held at the Rockefeller Foundation’s International Conference Center in Bellagio, Italy on ‘Establishing a Global Program for Combating Cysticercosis’ and ‘Implementing a Global Program for Combating Cysticercosis’ in September 2004 and September 2006, respectively. The conferences built on outcomes of the International Action Planning Workshop on Cysticercosis/Taeniosis held in Arusha, Tanzania in August 2002 which emphasized the need and instigated the international initiative for establishing a global-level ‘driving force’ for combating cysticercosis.

OBJECTIVES The overall objective of convening the conferences was to improve human health and well-being, smallholder pig production, the domestic food supply and export opportunities for pork in endemic countries by further facilitating organization of a global campaign for combatting the burden of cysticercosis.

METHODS The conferences were organised by the WHO/FAO Collaborating Center for Research and Training on Parasitic Zoonoses and DBL–Institute for Health Research and Development with the Rockefeller Foundation providing the venue for both meetings. Due to Bellagio Conference Center restrictions a maximum of 23 people were invited to participate in each meeting. Participants were selected with regard to equitable representation of different geographical regions, genders and professional backgrounds. The involvement of persons from different sectors (e.g. health, agriculture, industry, etc.) with various areas of expertise and experience promoted an integrated approach to the issue. Emphasis of the meetings was on inclusion of participants involved in conducting research and/or control activities on cysticercosis/taeniosis in endemic countries. As the conferences were not intended as technical meetings emphasis was not placed on specific tools for surveillance, prevention and control of cysticercosis but rather on general needs and utilization of such tools. Several international organizations (e.g. WHO, FAO, ILRI and GALVmed) were represented at the conferences.

RESULTS An international consensus was reached for establishing and implementing a global campaign for combating the burden of cysticercosis and a global action plan (GAP) for implementing and monitoring such a campaign.

CONCLUSIONS The global campaign should serve as a platform for advocacy and networking efforts with high priority on establishing and supporting regional cysticercosis working groups. These regional working groups would then be responsible for planning, implementing, monitoring and evaluating activities regarding research, training, surveillance, prevention and control based on regional needs and priorities. Establishment/strengthening of cysticercosis working groups for the endemic regions (i.e. The Americas, Eastern and Southern Africa, Western and Central Africa, South and Southeast Asia) was deemed essential for accomplishing the campaign’s long-term goals.

Dengue

INV 15
Dengue, an update
M. G. Guzman
1Pedro Kouri Tropical Medicine Institute, Virology Department, Havana, Cuba

According to the World Health Organization (WHO), 2.5–3 billion people live in areas where dengue viruses can be transmitted. An estimated 50–100 million of cases occur annually, with 24 000 deaths and around 500 000 DHF/DSS cases. The disease is endemic in the Americas, South-east Asia, the Western Pacific islands, Africa and the Eastern Mediterranean. A significant economic and health toll is associated with epidemics. Population growth, uncontrolled urbanization, inadequate management of water and waste, migration, climate factors are some of the factors involved in the emergence of this disease. Dengue virus infection can be asymptomatic or lead to an undifferentiated febrile illness, the classical DF or the severe DHF/DSS. Plasma leakage characterized DHF/DSS. In most of cases, DHF/DSS is observed in the course of a secondary infection by a different dengue serotype. An early mechanism (antibody dependent enhancement) was proposed to explain the severe syndrome. Later, a T-cell activation, the role of the virus strain and more recently a possible autoimmune phenomenon could be involved in disease pathogenesis. Host factors and particularly possible genetic host factors are of importance. Taking into account the global dengue situation, several new international initiatives have arisen. The clinical evaluation of the current WHO clinical classification of cases, the validation of commercial diagnostic tests, the evaluation of the usefulness of several vector indices, the integral strategy for dengue control, the role of the community, the vaccine initiatives are some of them. An update of the dengue situation, the challenges of the control and the new initiatives under development are presented here.
INV 16
Management of dengue hemorrhagic fever/dengue shock syndrome

T. H. Nguyen

Dengue is a disease complex which includes two distinct syndromes—dengue fever (DF) and dengue hemorrhagic fever (DHF). Dengue shock syndrome (DSS) is a severe form of DHF. It is caused by dengue viruses which belong to the family Flaviviridae; they can be classified in four serotypes (DEN-1, DEN-2, DEN-3 and DEN-4). In the past 15 years, there has been a dramatic increase in the global incidence of dengue and DHF. More than 2.5 billion people are now at risk in over 100 countries worldwide, and every year approximately 50 million infections occur, including 500,000 cases of DHF and DSS. The main hallmark differentiating DHF from DF is an increase in vascular permeability in the critical leakage phase, usually between the third and the sixth days of illness, resulting in plasma leakage of fluid from the intravascular compartment to the extravascular space. In less severe cases (nonshock DHF grade I, II) plasma leakage is mild to moderate, and patients will recover spontaneously or shortly after intravenous fluid administration. In more severe cases (DHF grade III, IV; DSS), when plasma loss is critical, hypovolemic shock ensues and can progress rapidly to profound shock. The patient in shock may die within 12–24 h if appropriate treatment is not promptly administered. Volume replacement is the mainstay of treatment of DHF/DSS. DSS is a medical emergency, prompt and vigorous volume replacement with extreme care to avoid fluid overload is essential. The intervention measures taken to improve case management of DHF/DSS patients to reduce the fatality rate of the disease are emphasized. Proper organization and good triage in the hospital, supplying enough essential equipment and intravenous fluids for the hospital, and well-trained medical staff were essential factors to contribute to the reduction of fatality rates in DHF/DSS.

Dermatology

INV 17
Geographical dermatology

S. Tahan

Besides the many difficult-to-solve public health problems in most of the states in the Brazilian Amazon region, there are a number of socio-economical challenges to be faced. In spite of the large area of primary and untouched forest and rivers with very important resources, most of the population does not benefit from these potentialities. The native population has been the most affected by the process of colonization of this region in the last years. It is difficult to understand and accept the poverty of these people, living in such a rich region. Gold mining and mercury contamination of the soil and water, opening of new roads, deforestation and large scale soy bean production, extensive cattle raising, always with minimal labor needs are among the many factors that have led to the progressive migration of the population to the urban areas of the Amazonian states. Invasion and destruction of the existing primary forests in the periphery of these cities as a consequence of the migration process creates new slums and foci of malaria, dengue, viral hepatitis, tuberculosis, intestinal parasitosis, skin diseases and other diseases related to poor sanitary conditions. AIDS is an emerging disease in most of the urban areas of the Amazon region. Leprosy, cutaneous leishmaniasis and other cutaneous parasitosis, deep and superficial mycosis, pyoderma, sexually transmitted diseases, and cutaneous manifestations associated with AIDS are among the most important skin diseases. Skin conditions account for 20% of the diseases diagnosed in most of our health centers. In this presentation it will be discussed the main epidemiological and clinical aspects of skin diseases observed in the largest state of the Amazon basin – the state of Amazonas. It has over 1.5 million km² and a population of approximately 3 million inhabitants.

Disease Modelling

INV 18
Stochastic simulation of malaria epidemiology and control

T. Smith

OBJECTIVES Dynamic models of malaria have generally focused on the general principles elimination. However, most intervention programs in endemic areas of Africa aim to achieve only disease control. To decide on the best mix from many different intervention strategies there is an urgent need for models that make robust quantitative predictions of effectiveness in reducing morbidity and mortality, while allowing for transmission dynamics and health system factors. We are using microsimulation to achieve this.

METHODS We use individual-based stochastic simulations with 5 day time steps to model Plasmodium falciparum epidemiology, incorporating (i) variations in host exposure to mosquito bites; (ii) naturally acquired immunity to infection and disease; and (iii) effects of co-infection. We use underlying within-host models based on descriptions of the course of parasitaemia in malaria-therapy patients and apply a genetic algorithm implemented via volunteer computing to fit models for large human populations to a set of 61 field scenarios from sub-Saharan Africa. These comprise field data on seasonality, age-patterns of infection, parasite density, clinical episodes, severe malaria and mortality. We here illustrate modelling of interventions using simulations of intermittent preventive treatment in infants (IPTi) and of malaria vaccines delivered via the Expanded Program on Immunisation (EPI). In both cases parameterising the models of intervention using estimated drug/vaccine effects from recent efficacy trials and using a health system model based on Tanzanian field data.

RESULTS We can reproduce reasonably well the malariological patterns in endemic areas, including non-monotonic relationships between the parasite prevalence and incidence of disease and host age. Preliminary comparisons of the predicted effects of IPTi using sulphadoxine-pyrimethamine with those of ‘leaky’ pre-erythrocytic malaria vaccines found comparable effectiveness in averting deaths, with the latter having greater effect in averting uncomplicated malaria episodes. The approach can be readily extended to simulate a complete range of interventions including vector control and health system strengthening.

CONCLUSION Microsimulation can simultaneously capture the dynamics inherent to malaria epidemiology, those of malaria control interventions and those of human demography. The availability of vast computing power via volunteer computing platforms makes it possible to fit multiple models to a wide range of field datasets, to carry out probabilistic sensitivity analysis, and to analyse ensembles of different models. This leads to plausible quantitative predictions making it realistic to compare effects and cost effectiveness of a comprehensive set of different intervention strategies including integrated control.
### Inv 19

**Tropical pathology – an update**

S. Lucas

Viewed from the industrialised countries—who invented ‘tropical medicine’—the whole pattern of tropical pathology has been transformed by ever-increasing international travel, more rapid communications, and by pandemic HIV infection. In this view, ‘tropical pathology’ is the study of infectious diseases more common in tropical regions and causing more morbidity and mortality there because of poverty and poor health care resources. All known, emerging and re-emerging infectious diseases can be encountered in any country through rapid travel. At the same time, histopathology experience in European industrialised countries of tropical diseases is declining as pathologists work abroad less than hitherto, and the trend of specialisation (based on organ cancers) discourages pathologists and their employers to invest time in infectious disease pathology.

**Specific issues of current concern include**

- Diagnosis of leprosy—relatively few patients in Europe, but the diagnosis is usually made two years after first presentation, and it is highly treatable.
- Leishmaniasis—very common, and a combined parasitological & histopathological approach is optimal.
- Falciparum malaria—fatalities occur in Europe, usually because of late diagnosis and treatment. The role of histopathology is to diagnose unknown cases, and confirm or refute suspected ones.
- Imported viral haemorrhagic fever cases—few but difficult to manage and present problems at death regarding health and safety if an autopsy is required.
- Rarities imported from the tropics that are easily not thought of or missed pathologically—eg free-living amoebic infections, larva migrans syndromes.
- There is progress in pathogenesis—eg understanding of Mycobacterium ulcerans infection (Buruli ulcer).
- HIV disease—the European experience has been transformed by immigration, mainly from Africa, but also eastern Europe and South America. Locally important infections (e.g. Penicillium and Chagas’ disease) and different patterns of infection (e.g. tuberculosis and HCV) present new diagnostic problems.
- Bioterrorism using ‘tropical’ infectious agents—no one knows what will happen, but awareness and contingencies are being raised.

Tropical pathology cannot exist in isolation but depends on close links with tropical and infectious disease clinicians, and with interested microbiologists and parasitologists. Regular combined audit provides continuing education and probably improves patient care.

### Inv 20

**Teaching child health in a conflict zone: experience from the Palestinian occupied territories**

T. Waterston

**OBJECTIVES** To set up a teaching programme in child health for doctors and nurses in the West Bank and Gaza.

**METHODS** Members of the Royal College of Paediatrics and Child Health in the UK assessed the child health needs in the country and also the learning requirements of the doctors and nurses in primary care, and worked with Palestinian paediatricians to establish a year’s course based on self-directed learning and use of the internet to circumvent the difficulties of access owing to the conflict.

**RESULTS** There is a high proportion of children in Palestine (at least 50% of the total population) and at the present time they are suffering increasing poverty and as a result, malnutrition and infectious disease as well as high rates of emotional and behavioural problems. The doctors and nurses have had no postgraduate training in child health and the quality standards in MOH clinics are low. We have successfully delivered six of the 11 modules with 3 monthly visits from UK tutors on subjects from acute paediatric care to child mental health and disabilities. The situation in the country however makes it extremely difficult to practice to the benefit of the population owing to harassment and difficulties with access.

**CONCLUSION** A teaching programme can be carried out in a country driven by conflict using outside assistance as long as there is close partnership with local physicians assisted by web-based learning. Close attention must be paid to the ethical and political dilemmas of working in such a situation.

### Inv 21

**Undergraduate education in International Health in Europe**

J. Yudkin

Medical students are in the vanguard of demands for introducing international health in the medical curriculum. This is in part because of a growing interest in health and health care as part of the issue of development, with a more global perspective among many students than in the traditional faculty of medical schools. The justification for exploiting this interest is in part that health and health care are globally determined and influenced, in part that most graduates will deal increasingly with a multicultural and international population, and in part because many young doctors will intend to travel as part of their career plan. The International Health and Medical Education Centre at University College London has been in existence for 7 years, and initiated a one-year full time Bachelor of Science degree in International Health in 2001. To date around 120 students have completed this course, studying health policy, poverty and development, and conflict and migration as compulsory modules. These students and doctors have developed a deeper understanding of the causes of ill health and inequality, and the possible ways of tackling these higher level determinants. Interest in international health has led to a clamour for career opportunities in clinical international health, but also in international public health, this having possible advantages for the development of the specialty in the student’s countries of origin.
the third in AccessXP. (Van den Ende et al. 1997) For developing countries it is a didactic tool that challenges the student with cases electronically assembled from a randomly generated disease and randomly chosen related presenting symptoms. The student should find the diagnosis with a set of disease characteristics, available in the context of a hospital in developing countries. The logical engine is based upon both pattern recognition and Bayesian logic. For a Western context the programme offers also an expert system for imported fever, based on a prospectively generated database of over 2000 patients, in the former version (Kabisa III), a student could make the correct diagnosis with one or two disease characteristics, if at least he had reached the therapeutic threshold. This does not reflect a real clinical situation: it might be that some elements with a high excluding power would bring the disease again under the threshold. The tutor will suggest the student to work this diagnosis out. However, he will always test if the available disease characteristics have a sufficient sum of excluding power to bring the final probability under the threshold. Otherwise, this request would not make sense. This feature is a modified application of the principle of the test-treatment threshold described by Pauker and Kassirer (1980). Once the proposed diagnosis is worked out correctly, the tutor will examine if other dangerous and treatable diagnostic hypotheses are still active: if so, he will suggest testing them also. This is to avoid that e.g., the diagnosis of the flu is (correctly) made, while meningitis has not been excluded appropriately. These new features bring the Kabisa logic close to the threshold driven panoramic clinical logic (Van Puympbroeck et al. 2003). The expert module is innovative with the suggestion of new tests based on the data already provided by the user. In this suggestion, the same threshold driven panoramic logic is followed: for the highest ranked diagnosis strong excluders are asked for, once this diagnosis is worked out less probable hypotheses are examined also. Ranking of suggested tests takes into account power, feasibility, risk and cost.

**Equity and Health Services**

**INV 23 Health sector reforms: how can policy implementation be strengthened?**

L. Gilson

1University of Witwatersrand/London School of Hygiene and Tropical Medicine, Johannesburg, South Africa

**OBJECTIVES** Objectives are (i) to review the available evidence on the factors influencing the implementation of new, equity-oriented health sector reform policies; (ii) to draw conclusions about how to strengthen future policy implementation.

**METHODS** (see below)

**RESULTS** There is widespread evidence that health system performance in low and middle-income countries is inequitable. Some evidence also indicates that the benefits of new policies and interventions intended preferentially to benefit the poorest are largely captured by more wealthy and powerful groups. However, much less is known about the implementation process underlying these poor policy outcomes. In order to contribute to debates about how to strengthen health systems, this paper will present theoretical ideas and empirical evidence about the key factors influencing the process of implementation. It will draw from a recent review of relevant literature and from a set of empirical case studies that are currently being undertaken in Africa and Asia.

**CONCLUSION** Finally, it will provide some initial ideas about how to support more effective implementation of health sector reforms.

**INV 24 From tropical diseases to poverty related diseases**

P. Mocumbi

1European and Developing Countries Clinical Trials Partnership, Hague, Netherlands

Despite the enormous technology advances during the past 100 years of tropical medicine, diseases prevalent in warm climates have become a global concern and affect seriously the health of people in the developing world. To develop the quality of global health and achieve the Millennium Development Goals what is needed it is not just aid to the developing countries. Nowadays the burden of diseases in DCs is no longer due only to communicable diseases for which we still lack tools for their effective control; it includes also the new epidemic of chronic diseases. Building on my recent experience I will focus on partnerships based on sharing knowledge to address the challenges of increasing equity in health and equity in health outcomes in our ‘common but’ confronted with old communicable diseases, newly emerging diseases and the new epidemic of chronic diseases. To anticipate the changing nature of disease and responses to it, we will need to rethink of the experience gained to ensure that decisions to invest in what is needed have been made in a timely and inclusive manner. The Netherlands Society of Tropical Medicine and International Health is called to reflect on how best to invest more in initiatives and partnerships aimed at building collaborative relations for empowerment through knowledge sharing and transfer of technology and information to make appropriate decisions and use of tools to reduce disease burden and promote sustainable development.

**INV 25 Alternative approaches to reaching the poor**

A. J. Mills

1London School of Hygiene and Tropical Medicine, Public Health and Policy, London, UK

**OBJECTIVES** To explore the policy options facing low income country governments who wish to improve the degree to which health services reach the poor.

**METHODS** A conceptual framework will be established to examine the extent to which health services reach the poor, and to explore the major barriers which hamper access of the poor. Evidence from the literature will be drawn on to evaluate policy options.

**RESULTS** Evidence will be summarised relating to both demand-side and supply-side policy options, including community-based insurance, strengthening public delivery of services, out-sourcing health service provision, and working with the retail sector.

**CONCLUSION** As with many areas of health system research, good quality evidence is scarce making it difficult to draw firm conclusions on policy options. Research is needed not only on the impact of policies on the poor, but also on the explanations for effects found, if the evidence base is to be improved.

**Issues in International Health**

**INV 26 Obligations to research participants and to communities in developing countries**

R. Macklin

1Albert Einstein College of Medicine, Bronx, USA

**OBJECTIVES** Explore viewpoints on what is owed to research participants and communities during and after clinical trials.
METHODS Literature review and analysis.

RESULTS Viewpoints vary considerably.

CONCLUSION Research in developing countries is justified only if benefits accrue to the participants and communities after a successful trial is completed. After many years in which industrialized countries and industry conducted clinical research in low-resource countries without substantial benefits to the latter, a consensus has begun to emerge that research participants, communities from which they are recruited, and the country as a whole should receive some benefits after clinical trials are completed. Controversy continues to exist regarding: (i) who should be the recipients of benefits; (ii) whom does the obligation fall to provide any benefits; (iii) what is the nature of the benefits to be offered; (iv) for how long a period must benefits be provided. Authors of published articles have expressed different views on these questions, and consultations conducted by WHO and UNAIDS have also included different viewpoints. However, although unanimity does not exist, a consensus has been emerging that something is owed to research participants and to the community as a whole when research is completed. This presentation argues for that conclusion based on the aims of public health research and considerations of justice.

INV 27
The best standard for the standard of care
R. van der Graaf
1Julius Centre for Health Sciences and Primary Care, University Medical Centre Utrecht, Utrecht, Netherlands

During the last decennium one of the main issues discussed in research ethics has been the care that should be provided to the control group in a clinical trial. This discussion is also called the ‘standard of care debate’. At this moment, in international ethical guidelines on research ethics a wide variety of standards for the standard of care exists, like the provision of ‘the highest attainable’, ‘the best available’, ‘the best current’, ‘a proven’ and ‘an established effective’ treatment. In my presentation I systematically review the currently used standards. I argue that none of the current standards is adequate to serve as a universal standard for the standard of care. This problem seems to be recognized by guidelines that leave room for double standards. Maintaining double standards is, however, not considered ethically acceptable. On the other hand, merely arguing that double standards should be avoided has become a slogan and needs to be explicated. I argue that we need a universal standard that leaves room for morally relevant differences. In the literature on standard of care Alex London has made a substantial proposal for both a universal and context sensitive standard. However, universally adopting his standard turns out to be problematic. In my presentation I propose a revised version of London’s standard.

Fever, Syndromic Approach

INV 28
Acute undifferentiated fever in South-east Asia
Y. Suputtamongkol
1Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

OBJECTIVE To outline common causes of acute undifferentiated febrile illness among indigenous population and international travelers returned from South-east Asia, and the management of these patients.

METHODS Presentation of three cases; Case A is a young women who presented with unusual presentation of hemorrhagic fever; Case B and C are adult patients who presented with common and rare presentations of murine typhus and scrub typhus respectively at Siriraj Hospital, Bangkok, Thailand. Epidemiological data and management of these infections will be discussed.

DISCUSSION Sudden onset of fever associated with multi-systems illness is a common feature of several infections endemic in South-east Asia, including malaria, dengue, scrub typhus, and leptospirosis. Malaria and dengue infection must be initially excluded in all patients presented with this syndrome. The lack of sensitive and rapid methods for the laboratory confirmation of a tentative diagnosis has been an important problem. Doxycycline would usually be an appropriate initial antimicrobial treatment for individual with suspected either rickettsioses or leptospirosis. Azithromycin could be considered as an alternative treatment when ever doxycycline allergy is suspected.

CONCLUSION Physician in the tropics should aware that malaria, dengue infection, rickettsioses, and leptospirosis are major causes of acute undifferentiated fever. Travelers to endemic areas are also at risk of these infections. Early recognition and appropriate treatment reduce morbidity and mortality.

Haemorrhagic Fever

INV 29
The control of Filovirus infections
R. Colebunders
1Clinical Sciences, Institute Tropical Medicine, Antwerp, Belgium

In order to control Filovirus outbreaks the organization of patient care is an extremely important element. The provision of adequate supportive therapy may increase survival of patients, and proper isolation techniques and education will prevent the transmission of Filovirus infections to health care workers (HCW) and family members. It is important that the population has confidence in the health care system and that patients are stimulated to seek health care. This may improve early case detection and follow-up of patient contacts. An important question remains incompletely answered: how do Filoviruses enter the human body? During the 1995 Kikwit Ebola outbreak, we carried out a case control to determine risk factors for acquiring Ebola Hemorrhagic fever (EHF) by HCW. In a multi-variant analysis the following risk factors were identified: unprotected contact with the blood of an EHF patient, the manipulation of a corpse and the contact with several EHF patients. Hand washing after patient contact was reported in 22 (61.1%) of 36 cases compared with 53 (88.3%) of 60 controls for whom reliable information was available (P = 0.001). One factor explaining the high transmission rate of Filoviruses to HCW could be the high viral load and the fact that Filoviruses are causing an acute and aggressive disease characterized by bleeding, often massive, vomiting and diarrhoea. It is our hypothesis that most Filovirus infections are transmitted through contact of contaminated hands with the mouth mucosa or conjunctiva. We still need to know more about the natural reservoir for Filoviruses. In the Democratic Republic of Congo, in the village of Durba, Marburg outbreaks seem to have occurred over many years (mainly among mine workers) and outbreaks ceased only abruptly with the closure of the Goroumbwa mine. Epidemiologic evidence of multiple introductions of infection into the population was substantiated by the detection of at least nine genetically distinct lineages of virus. The data collected in Durba suggests that the reservoir of Marburg virus inhabits caves and mines. Since long, bats have been considered as the potential reservoir of Filovirus infections. Certain bats, caught between
2001 and 2003 near Ebola affected villages at the Gabon–Congo border, appeared to have been asymptptomatically infected and yielded virus sequences that closely matched those found in the human outbreaks happening about the same time. This knowledge should now be used to develop strategies to prevent future Filovirus outbreaks.

Health Financing

INV 30
Management of mutual health organizations in Ghana
R. Baltussen"1, E. Bruce"4, G. Rhodes"3, S. Nahir-Bana"5 and I. Agyepong"6
1Department of Public Health, Radboud University Nijmegen Medical centre, Nijmegen, Netherlands; 2Dangme West Research Centre, Dodowa, Ghana; 3Eorys Consulting, Rotterdam, Netherlands; 4Dangme-West Research Centre, Dodowa, Ghana; 5Ghana Health Services, Accra, Ghana

OBJECTIVES Mutual health organizations (MHO) emerged in Ghana in the mid-1990s. The organizational structure and financial management of private and public MHO hold important lessons for the development of national health insurance in Ghana, but there is little evidence to date on their features. This paper aims at filling this data gap, and at making recommendations to Ghanaian authorities on how to stimulate the success of MHO.


RESULTS Private MHO had more autonomy in setting premiums and benefit packages, and had higher community participation in meetings than public MHO. MHO in general had few measures in place to control moral hazard and reduce adverse selection, but more measures to control fraud and prevent cost escalation. The vast majority of schemes were managed by formally trained and paid staff. The financial results varied considerably.

CONCLUSIONS Ghanaian authorities regulate the newly established public MHO, but may do good by leaving them a certain level of autonomy in decision-making and secure community participation. The financial management of MHO is suboptimal, which indicates the need for technical assistance.

INV 31
Design of health insurance packages reflecting the priorities of the poor in India
D. Dror"1
1Health Policy and Management, Erasmus University Rotterdam, Rotterdam, Netherlands

Out-of-pocket-spending of households represent the main source of health financing in low-income countries. As households must pool resources to pay for healthcare, such decisions compete with other investments, e.g. agricultural, education, housing etc; and reduced access to healthcare leads to observable low health status. Additionally, unaffordable health events occur unexpectedly. If health insurance installs predictable and affordable costs it can be attractive. But low-cost HII dictates a package compensating only part of costs. We hypothesize that attractive health insurance must represent an optimum match between clients’ needs for and available supply of health care, and demand for health insurance. Analysis of household survey data from rural and urban slum in seven locations in India collected in 2005; and testing of the CHAT simulation exercise. We provide evidence of marked differences across locations in solvent demand for health insurance (proxy: willingness to pay), medical needs (proxy: frequency of illness episodes and the number of days of illness per HH), and supply of healthcare (proxy: type of healthcare provider). We also show that aggregated expenses of consultations and drugs exceed hospitalizations in all locations. Since affiliation to HI is voluntary, the (partial) benefit package must correspond to clients’ perceived priorities, often unknown to insurers. We elaborated a method called choosing healthplans all together (CHAT) to identify priorities of low income clients with a predetermined budget of about US$ 11 per household per year. We field-tested it in India; 302 individuals, organized in 24 groups, participated in the experiment, many of them illiterate, innumerate and without experience with insurance. Judiciousness of the choices was evaluated by three criteria: the ‘reimbursement criterion’ (assuming that insured wish to be reimbursed regardless of the absolute level of expenditure), the ‘fairness criterion’ (postulating that a higher reimbursement rate should apply to higher expenses) and the ‘catastrophic coverage criterion’ (stating that insurance should cover catastrophic exposure). The most frequently chosen packages scored highly on all three criteria. 88.4% of the respondents selected at least three of the following benefits: outpatient, inpatient, drugs and tests, with a clear preference to cover high aggregate costs regardless of their probability. We observed group solidarity in willingness to choose services that are most beneficial to the weaker segments of the community. And respondents were keen to obtain those packages and pay the requisite premium.

Health Systems Research

INV 32
Swellengrebel lecture – the health systems contribution to disease control
A. Haines
1London School of Hygiene and Tropical Medicine, London, UK

Based on current trends many low income countries, particularly in sub-Saharan Africa, are unlikely to achieve the millennium development goal (MDG) health targets by 2015. Despite a growing number of effective and affordable interventions and increasing international development assistance for specific diseases, the goals of reducing child mortality, improving maternal health, combating HIV/AIDS, malaria and other diseases, are still far from being achieved. There is growing awareness that weak health systems compound the devastating effects of high disease burden in many low income countries. Analyses of barriers to improving delivery of interventions for priority health problems suggest many of these are common to a range of priority areas such as maternal and child health, TB, malaria and HIV/AIDS. They include: inadequate availability of human resources, poor quality of care, weak service management capacity, poor coordination between multiple providers in public and private sectors and inequitable availability of services. There has been a tendency to tackle these barriers and constraints independently and in parallel for each priority area but such approaches can lead to inefficiencies, e.g. because of duplication of drug delivery or information systems. They can also lead to distortions in care, e.g. creating a separate cadre of better paid health workers for a specific programme may deplete staff from other key, but less well resourced, functions. System-wide approaches attempt to avoid these unintended adverse consequences by addressing common barriers to delivery of a range of interventions. However a potential disadvantage is that benefits may take longer to result and there may be a loss of focus on key priorities. Whilst there is growing awareness of the problems associated with weak health systems, there is still a relative lack of evidence about effective policies and strategies. Nevertheless there is emerging evidence about a number of important health systems topics, including
financial mechanisms to improve access to healthcare of the poor, approaches to improving the quality of care in low income countries, impact of community participation and community health workers on selected health outcomes, and experiences from the scaling-up of access to antiretroviral therapy. There is now an opportunity to build on this emerging evidence-base by ensuring that approaches to improving access to effective healthcare are rigorously evaluated. Improving health systems performance and strengthening disease control programmes should not be seen as mutually antagonistic objectives. There is potential for synergies between both approaches and in order to attain the MDGs this potential must be exploited.

**Human Resources in Health**

**INV 33**

**The global health professional crisis: national and international responses**

E. Manipe¹

¹Faculty of Health Sciences, Uganda Martyrs University, Kampala, Uganda

In order to achieve most of the millennium development goals (MDGs), adequate numbers of well-trained, multi-skilled, equitably distributed, motivated, well-equipped human resources for health (HRH) are a crucial sine qua non. Yet, the global HRH situation indicates that almost all the above prerequisite conditions are lacking. Though all the factors above are interlinked, their major effect is felt as a shortage in numbers. The numbers are inadequate globally. In developed countries, despite high demand for health workers due to aging populations, few people are attracted to health professions given their loss of lustre due to relatively poor pay compared to other jobs, the availability of other less strenuous and better-paying employment options especially for women, avoiding possibility of costly litigation and the long duration of training required, among others. The numbers are also inadequate because of governments’ decision not to invest in costly and long training but rather to take advantage of globalization and obtain the required services from the global market of health workers, especially from the developing world. In developing countries, the numbers of health workers are few because of market failures like the restricted entry into the health care market (very competitive and high entry requirements into health care training, long duration of training, strict professional codes of conduct etc), negative gender perspectives on healthcare work which is dominated by women, the poor pay and limited chances of earning extra income from health care work, and, of recent, HIV/AIDS, attrition into other activities and international migration, among others. The effects of inadequate staffing, training and equipment have been shown to include demotivation, work overload, staff burnout, attrition and poor quality of care, among others. Responses taken to address the said problems both by individual countries and by international bodies and groups of countries include incentives in place to attract people to health care professions, such as better and separate pay packages for health workers than other civil servants through structured job evaluation and allowing a later retirement age for health workers. Some countries have increased the training capacity through creating more medical and nursing schools, lowering the intake requirements into medical and nurse training and expanding the intake. Other efforts have focused on widening the range of services offered by cadres through the training of, for instance, nurse practitioners, to have multi-skilled staff. Establishment of ethical codes for international recruitment of health workers and official export of skilled labour, have been tried. Extra training to develop multiple skills in health workers, training of internationally unmarketable substitute and support cadres to conduct the duties of marketable cadres and post-training bonding mechanisms have also been tried. Other efforts include agitation and advocacy for compensation for internationally recruited workers as well as signing memoranda of understanding to obtain technological and financial support from the receiving countries. In order to retain staff especially in rural areas, some countries have created incentives targeting hard-to-reach and hard-to-stay areas, such as monetary incentives, easier access to loans, scholarships for post-graduate training etc. The results of all these responses have been mixed in different countries. International and binding efforts to mitigate the negative effects of international migration of health workers are still needed. Country level policies to increase health sector funding from which appropriate incentives may be obtained are also needed. Sharing of lessons between countries will go a long way in exposing best practices that may be adapted to suit individual country circumstances.

**Immunology**

**INV 34**

**Lack of immune responses to Mycobacterium tuberculosis: DosR regulon proteins following BCG vaccination**

T. Ottenhoff¹

¹LUMC, Leiden, Netherlands

BCG is widely used as a vaccine against tuberculosis (TB) despite its variable protective efficacy. Relatively little is known about the immune response profiles following BCG vaccination in relation to protection against TB. Here we tested whether BCG vaccination results in immune responses to DosR (Rv3133c) regulon encoded proteins. These so-called TB latency antigens are targeted by the immune system during persistent *Mycobacterium tuberculosis* infection and have been implicated in protective immunity against latent *M. tuberculosis* infection. In silico analysis of the DosR regulon in BCG and *M. tuberculosis* showed at least 97% homology in amino acid sequence, with 41 out of 48 genes being identical. Transcriptional profiling of 14 different BCG strains, under hypoxia and nitric oxide exposure *in vitro*, revealed a functional DosR regulon similar to that observed in *M. tuberculosis*. Next, we assessed human immune responses to a series of immuno-dominant TB latency antigens and found that BCG vaccination fails to induce significant responses to latency antigens. Similar results were found in BCG vaccinated BALB/c mice. In contrast, responses to latency antigens were observed in individuals with suspected exposure to TB (as indicated by positive IFNγ responses to TB specific antigens ESAT-6 and CFP10), and in mice vaccinated with plasmid DNA encoding selected latency antigens. Since immune responses to TB latency antigens have been associated with control of latent *M. tuberculosis* infection, our findings support the development of vaccination strategies incorporating DosR regulon antigens to complement and improve the current BCG vaccine.

**Approaches of the Social Determinants of Health**

**INV 35**

**Confronting Africa’s health crisis: addressing the challenge of social determinants and weak health systems**

D. Sanders¹

¹School of Public Health, University of the Western Cape, Bellville, South Africa

**OBJECTIVES** To describe Africa’s current health crisis and review the major local and global determinants of this situation. To
Almost thirty years after the policy of Primary Health Care was formally endorsed progress towards Health for All has been uneven. Although the global PCH initiative has been successful in selected programs that have reduced substantially the impact of certain (mostly infectious) diseases, gains already achieved are under threat and manifest in stagnation, and more recently reversal, of Africa’s health status indicators. This presentation will briefly describe Africa’s current health crisis and review the major local and global determinants of this situation. Some key aspects of globalization and health sector reform will be reviewed as well as the crisis of health human resources and the HIV/AIDS epidemic. Achieving the millennium development goals and health equity, especially in Sub-Saharan Africa will require interventions that ameliorate the underlying local and global social and environmental health determinants, ensure greater equity in access to decentralized and sustainable health systems, and assist in the rebuilding of public health capacity in poor countries. Suggested responses from the Public Health community will be illustrated by examples from South Africa. These include research on: health systems with a focus on operational issues and program evaluation, determinants operating at both local and global levels, and case studies of comprehensive responses to key health problems. Such research should integrate both capacity development as well as advocacy action. Public Health training initiatives need to respond to the above key challenges and to the differentiated needs of practitioners. In light of Africa’s needs it is urgent that Public Health leaders reconsider their mission and priority activities in research and training.

**INV 36**

**Health in an unequal world**

*M. Marmot*

1Epidemiology & Public Health, University College London, London, UK

The 20th century has seen impressive gains in health and life expectancy in many parts of the world. But these improvements are unequally distributed. In every country, poor people and those from socially disadvantaged groups get sicker and die sooner than people in more privileged social positions. Not only is there a gap in health between the best off and the worst off in society, there is a gradient in health running between them. People living in extreme poverty have worse health than those who are less poor, who in turn have worse health than those above them in the social hierarchy. Between countries too, there are gross inequalities in population health. In recent decades health inequalities between and within countries have widened. We need to orientate our thinking away from a sole concentration on ill health among the poor to focus on the social gradient in mortality and morbidity that runs from the top to the bottom of society. This social gradient can be linked clearly to social and economic conditions. This is true for both communicable and non-communicable disease. Attention to the causes of health inequalities will produce a society with greater levels of well-being for all. The Commission on Social Determinants of Health was set up by the World Health Organisation to collate global evidence, raise societal debate and recommend policies with the goal of improving health of the world’s most vulnerable people. A major thrust of the Commission is turning public health knowledge into political action.

**Intestinal Helminths**

**INV 37**

**How may the gains in the control of soil-transmitted helminthiasis be sustained?**

D. Crompton

1Institute of Biomedical and Life Sciences, University of Glasgow, Glasgow, UK

OBJECTIVES First, to review progress in control made since soil-transmitted helminthiasis was accepted as a serious public health problem. Secondly, to summarize the diverse interventions that enable the control of morbidity due to STH infections to be achieved. Thirdly, to highlight the challenge of trying to sustain progress in endemic countries where competition for resources for public health programmes is so intense.

METHODS Present and interpret published information from peer-reviewed journals, the reports of meetings and publications from the World Health Organization.

RESULTS Groups accepted as being at high risk of overt morbidity from soil-transmitted helminthiasis include school-age children, adolescent girls, women of reproductive age, unborn and newborn children. There is mounting evidence to indicate that subtle morbidity should not be ignored. The effects of the infections on human iron status will be discussed. Success in controlling morbidity has come from wider access to safe, effective oral drugs and the benefits that accrue from the generosity of donors working in collaboration with governments and other partners. Achieving sustainability, however, will require an increase and improvement in delivery systems, operational research, behaviour change and affordable sanitation. How and when can this need for the provision of sanitation be met?

CONCLUSION Soil-transmitted helminthiasis, now recognized as one of the major ‘neglected tropical diseases’, can be controlled even in communities where poverty dominates everyday life. Unless more resources are made available such good progress will be reversed. Efforts must begin now to prepare for more sustainable approaches to the control of these infections.

**Leishmaniasis**

**INV 38**

**Human leishmaniasis vaccines: prophylactic and therapeutic**

F. Modabber

1DNDi, Geneva, Switzerland, France

Prophylactic: The most effective vaccine against human leishmaniasis is the inoculation of live *Leishmania* – ‘Leishmanization’ (LZ). Practiced in Israel, Uzbekistan and Iran is abandoned due to changes of virulence of the parasite during *in vitro* culture, loss of virulence by repeated passage, difficulty of delivery (Leishmania have not been successfully lyophilized), fear of HIV co-infection or superinfection of lesions. However, attempts have been made to standardize the production in order for LZ to be used as a live challenge for testing candidate vaccines [1]. Having a live challenge system is a huge advantage over field efficacy trials for developing a vaccine. We can protect the most susceptible mouse strain, but the progress toward human vaccines has been very limited. The protective antigens/immunogens identified have ended in publications but not beyond, because of lack of interest in industry for large commitments required for vaccines. Only crude
DNDi. (reports in preparation).

(CpG’s), i.e. dSLIM and the MIDGE technology [6]. I anticipate are however, new hopes with non-toxic synthetic adjuvants for use of immunochemotherapy. Only one defined vaccine (Leish-
post kala-azar dermal leishmaniasis (PKDL) are good indications ALM plus BCG added to the standard chemotherapy for persistent program) [3], Mayrink’s vaccine, killed L. amazonensis, added to low dose antimony treatment in Brazil [4] and Khalil et al’s alum-ALM plus BCG added to the standard chemotherapy for persistent post kala-azar dermal leishmaniasis (PKDL) are good indications for use of immunochemotherapy. Only one defined vaccine (Leish-
111F + MPL-SE) is in clinical trials in Brazil and Peru [5]. There are however, new hopes with non-toxic synthetic adjuvants (CpG’s), i.e. dSLIM and the MIDGE technology [6]. I anticipate that immunochemotherapy would receive more attention soon. This was recommended by experts at two meetings of WHO/TDR and DNDI. (reports in preparation).

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INV 39
Leishmaniasis – where are we
S. Sundar1
1Medicine, Banaras Hindu University, Varanasi, India

There has been a progressive increase in the cases of all forms of leishmaniasis globally. Diagnosis of visceral leishmaniasis is a major challenge, though rk39 rapid tests is a major advance, but low sensitivity in Sudan is an area of concern, these antibody based tests do not indicate active diseases, and there is an immediate need to develop tools, one such latex agglutination test (KAtex), lacks consistency, and efforts are required in this direction. Diagnosis of cutaneous leishmaniasis (CL) is relatively simple. In recent years several new treatment have become available for visceral leishmaniasis including oral miltefosine, paromomycin, lipid formulations of amphotericin B, and few are in the process of development like sitamaquine. Other than that there is no lead for leishmaniasis so we will not have a new drug in the clinic for next 10–15 years. Major therapeutic obstacles in the treatment of visceral leishmaniasis (VL) include the alarming increase in amphotericin unresponnsiveness especially in Bihar, India and HIV-Leishmania co-infected patients. The therapeutic armamentarium for VL is currently plagued with several limitations as the available drugs are toxic, majority are effective only parenterally and need to be administered for an extended period. The first orally effective drug, miltefosine has been approved for treating VL. In antimony refractory zones, pentavalent antimony has been largely replaced by amphotericin B deoxycholate, but prolonged hospitalization, toxic effects, and requirement for monitoring greatly hamper its widespread application in endemic regions. Lipid formulations of amphotericin B, a remarkable advance in amphotericin B therapy, have greatly reduced toxicity enabling large doses to be delivered over a short period. Even a single dose treatment with liposomal amphotericin B cures >90% patients; however, the stumbling block is its prohibitive cost that precludes its widespread acces-
sibility in endemic countries. After completion of successful phase III trial of paromomycin is now approved for use in India. Antimonials (intralresional or systemic) remain the mainstay of treatment of all forms of CL. Miltefosine has been successfully used in some forms of cutaneous leishmaniasis. Azoles, allopurinols etc have been successful in unique forms of CL. Lack of well controlled randomised clinical trials for CL is an important drawback. Efforts to combine various drugs or immunomodulation via vaccines, cytokines or anticytokines, in an attempt to shorten the duration of treatment, improve compliance, decrease cost and prolongation of lives of effective drugs are beginning and is a step in right direction.

INV 40
Epidemiology, diagnostic and treatment of leishmaniasis
J. Alvar1
1WHO, Neglected Tropical Diseases (NTD/DMI), Geneva, Switzerland

Epidemiology: Leishmaniasis is endemic in 88 countries and 350 million people are considered at risk, affecting an estimated 14 million people with roughly 2 million new cases per year, 500 000 of which are visceral (VL) and 1 500 000 cutaneous (CL). Global mortality from visceral leishmaniasis is estimated at 59 000 (35 000 men, 24 000 women), although in some regions the CFR is three times higher in women than in men. The disease burden is 2 357 000 DALYs, a significant rank among communicable dis-
 ease. The real impact of leishmaniasis is unreliable because no prospective and broad study has ever been carried out. CL has a tendency to heal spontaneously leaving scars which, depending on the Leishmania species, may evolve into recidivans, diffuse cutane-
ous, or mucocutaneous leishmaniasis. Post-kala-azar dermal leish-
maniasis is a complication of VL due to L. donovani. Progression of the disease, outbreaks and association with HIV are a matter of concern. The impact that the disease has on propagating poverty is important, since treatment is expensive and either unaffordable or involves loss of wages. Diagnosis and treatment: Improved control reduces both mortality and morbidity. Active case detection in decentralized health centres has proved cheaper than passive detection (US$ 25 vs 145, the later implies unforeseen deaths). Nevertheless, early detection is difficult because either patients are unaware of the initial symptoms or health systems are poorly staffed and lack equipment in remote rural areas, where transmission occurs. Definitive diagnosis relies on identification of the parasite under the microscope. Rapid serological tests are available for VL, although specificity and sensitivity vary upon regions. In addition, there are few drugs available for leishmaniasis which are toxic calling for hospitalization, expensive, require long duration cycles and develop resistance due to poor use and compliance. Patients have to overcome major logistic problems to access treatment such as transport, great a loss of wages, etc. Vector control using indoor spraying of insecticides is always determined by the endo/exophilic and endo/exophagous behaviour of the sand fly species in each area. Whatever the case, periodic spraying of walls is difficult to sustain over time. However, combined campaigns targeting Anopheles mosquitoes and sand flies are cost-effective. A suitable alternative is the use of ITNs. Perspectives: Strategic research has produced encouraging results: (i) rapid and reliable non-invasive diagnostic techniques; (ii) new drugs, such as oral miltefosine –phase IV finished- or IM paromomycin –now at phase IV-, and sitamaquine undergoing phase II/III clinical trials; (iii) immunochemotherapy trials based on a combination of a vaccine and a first- or second-line drug; (iv) studies of drug combinations that reduce the risk of resistance; and (v) the completed mapping of the genome of some Leishmania species is making possible to carry out exhaustive
research into proteomics offering new prospects for diagnosis, treatment and vaccines. The most pressing research tasks in control are the search for alternative and cheap drugs for oral or parenteral administration involving shorter treatment cycles; and the identification of mechanisms to facilitate access to existing control measures, including health sector reform in some developing countries.

Leptospirosis

INV 41
Genetic studies in pathogenic Leptospira strains
M. Picardreu, F. Ristow, P. Bourny, F. McBride, C. Pereira Figueira,
1Institut Pasteur, Paris, France; 2Fundação Oswaldo Cruz, Salvador, Brazil

Pathogenic mechanisms of L. interrogans, the causal agent of leptospirosis, remain largely unknown. This is mainly due to the lack of tools for genetic manipulations of pathogenic species. We recently provided the first evidence of gene transfer in a pathogenic Leptospira strain, involving the transposition of a transposon of eukaryotic origin (Bourny et al. 2005). We characterized several mutants obtained by insertion of the transposon Himar1 into L. interrogans genes. One of the transposon mutants exhibited an insertion in a putative gene encoding an outer membrane protein of 22-kDa. The mutant was attenuated in virulence in the guinea pig and hamster models of leptospirosis, whereas the genetically complemented strain was restored in virulence. Our results therefore indicate that this protein is a virulence determinant, the first identified for this pathogen of major public health importance worldwide. We are currently testing other genes that could be involved in one or several steps of the infectious process. Further progress in our understanding of the virulence of Leptospira should contribute to the development of novel strategies for the treatment and prevention of this neglected emerging disease.

Malaria Treatment

INV 42
Malaria
N. White
1Wellcome Trust Research Units, Southeast Asia, Mahidol University, Bangkok, Thailand

The global mortality from malaria has risen in the past 20 years. This is attributed directly to worsening drug resistance in Plasmodium falciparum. Control of malaria depends on vector control and effective drugs—there is no vaccine, and there will not be a widely deployed vaccine in the near future. Resistance has now emerged in Plasmodium falciparum to all classes of antimalarial drugs with the exception of the artemisinin derivatives. The progressive decline in chloroquine susceptibility made this drug partially or completely ineffective in most malaria affected countries. The usual successor to chloroquine was sulfadoxine-pyrimethamine, but high resistance to this antifol combination usually developed within five years of use. Plasmodium vivax also developed resistance to antifolts, and more recently in Asia and Oceania, to chloroquine. The emergence of drug resistance can be slowed or prevented altogether by the use of combinations of antimalarial drugs with different modes of action. The Chinese plant derived artemisinin derivatives have emerged as the most effective of all antimalarial drugs. Artemisinin based combination treatments (ACTs) have proved highly effective and well-tolerated in extensive trials and operational use. By 1994 mefloquine resistance had reached 30%. Since then the systematic deployment of artemisinin based combinations led to a ninefold reduction in the incidence of falciparum malaria and a reversal of drug resistance. In the management of severe malaria most of the world still relies upon quinine. The artemisinin derivatives are more rapidly acting and they are safer and easier to use. In the largest ever randomised trial in severe malaria conducted in four Asian countries artesunate reduced mortality by 33% compared with quinine. A variety of adjuvant treatments have been evaluated in severe malaria but none has proved beneficial—and several (steroids, dexamethasone, anti-TNF antibody, desferrioxamine and high dose phenobarbitone) proved harmful. In particular the better assessment of severity, the recognition of hypoglycaemia and metabolic acidosis as frequent and dangerous manifestations of severe malaria, the improved management of fluid balance and severe anaemia, and the aggressive early management of acute renal failure in adults have been important developments. In 2006 the World Health Organisation published new treatment guidelines; ACTs should be first-line treatment for falciparum malaria everywhere in the world. Whether artesunate should replace quinine for the treatment of severe malaria in African children will depend on the results of ongoing trials, but elsewhere it should now be the drug of choice.

INV 43
Challenges of artemisinin-based combination therapy roll out in Africa
M. Kanyi
1Department of Medicine, Makerere University, Kampala, Uganda

OBJECTIVES Currently, treatment of uncomplicated malaria in Africa is undergoing dramatic changes. In response to widespread resistance to commonly used monotherapies, particularly chloroquine (CQ) and sulfadoxine-pyrimethamine (SP), many African countries have recently adopted artemisinin-based combination therapy (ACT) as first-line for the treatment of uncomplicated malaria. We review here the potential advantages and challenges of ACT roll out in Africa.

METHODS Review of published and unpublished reports on ACT use in Africa.

RESULTS ACTs are highly efficacious with rapid clearance of parasites, safe and well-tolerated and currently no documented resistance. It is important that all ACTs are not considered equivalent regimens. However, the relative merits of different ACTs have been determined in only few high transmission settings. The success of an ACT regimen is dependent on the ability of the longer acting partner drug to clear residual parasites. In addition, different partner drugs can have different post-treatment prophylactic effects resulting in different levels of risk of recurrent malaria due to new infections when ACTs are compared. To maximize the benefit of artemisinin-based combination therapy in Africa, treatment should be integrated with aggressive strategies to reduce malaria transmission intensity. Combining ACTs with other malaria control interventions will decrease ACT drug pressure. ACTs present implementation challenges of choice of regimen, rational use, cost, availability, methods of delivery, sustainability and assuring a reliable supply to match the demand. In the role out of ACTs, operational studies are needed to optimize case management such as improved drug delivery, pharmacovigilance, reaching those at greatest risk and maximizing impact.

CONCLUSION Artemisinin combination therapy offers an important step forward for the treatment of malaria in Africa but challenges to optimize case management remain significant. Continued research into effective, safe, and affordable antimalarial regimens, and integration of treatment with preventive methods, will be necessary to establish effective and sustainable malaria control policies.
Malaria Vaccines

INV 44

Vaccine development for the 21st century
S. A. Pledger

1University of Pennsylvania, Sanofi Pasteur, Doylestown, USA

The reputation of vaccination rests on a two hundred year old history of success against major infectious diseases. In general, two achievements have been crucial to the success of vaccines: the induction of long-lasting immunological memory in individuals and the stimulation of a herd immunity that enhances control of infectious diseases in populations. However, when one reviews the vaccines now available it is apparent that most successes have been obtained when the microbe has a bacteremic or viremic phase during which it is susceptible to the action of neutralizing antibodies, and before replication in the particular organ to which it is tropic. Both poliovirus and infections by capsulated bacteria are examples where vaccination has worked efficiently. Some success has also been achieved against agents replicating on respiratory or gastrointestinal mucosae. Influenza, pertussis and rotavirus vaccines are examples of such agents, against which it has been possible to induce immune responses acting locally as well as systemically. Control of intracellular pathogens has not been achieved, except partly with the BCG vaccine against tuberculosis, and modern efforts are directed towards pathogens against which cellular immune responses are critical. Practically all of the diseases present in developed countries are also present in tropical countries, often at a higher incidence and severity. However, certain vaccines merit particular discussion, including vaccines for dengue, rotavirus, human papilloma viruses and meningococci; as well as vaccines against major targets such as malaria, tuberculosis, HIV and avian influenza. Newer approaches in vaccine production such as nucleic acid immunization, vectors, reverse genetics and additional routes of administration may circumvent prior difficulties. The target of vaccination will shift towards adolescents, adults, patients in hospital and those with chronic diseases, and possibly will extend to therapy as well as prevention. The biggest problems in the 21st Century will be the increase in anti-vaccination sentiment in the developed world, the financial difficulties in extending vaccination to the poorest countries, insufficient vaccine supplies and the paucity of manufacturers willing to produce vaccines for small markets.

INV 45

Malaria in pregnancy: prospect for a vaccine
T. G. Theander

1Centre for Medical Parasitology, University of Copenhagen, Copenhagen, Denmark

OBJECTIVES To review the current knowledge about the mechanisms leading to sequestration of malaria parasites in the placenta and possibility of preventing this by vaccination.

METHODS Review of recent findings.

RESULTS The phenotype of Plasmodium falciparum parasite sequestered in the placenta are unique because they express a variant antigen (VAR2CSA) on the surface of infected erythrocytes, which not are found on parasites causing disease in children, non-pregnant women or in men. These VSA mediate binding of the infected erythrocytes to the placental receptor chondroitin sulfate A (CSA) and allow the parasites to sequester in the placenta, where they cause disease and death for the mother and her offspring. In endemic areas women develop immunity to placental malaria as a function of parity. Immunity is mediated by antibodies, which block the adhesion of parasites to CSA. Most current evidence indicates that VAR2CSA is the parasite ligand for placental sequestration. Var2csa is transcribed in high levels by CSA selected parasites and parasites isolated from the placenta and the protein is expressed on the on the surface of erythrocytes infected with these parasites. Moreover, anti-VAR2CSA antibodies are acquired as a function of parity, and pregnant women with high levels of these antibodies have more favourable birth outcomes than women with low levels. Finally, parasites which have had the var2csa gene knocked out seem to loose their CSA binding potential. VAR2CSA is a large protein (m.w. 300 kDa) consisting of six DBL domains. Little is known about the tertiary structure but the interaction with CSA probably depends on correct folding. A VAR2CSA based vaccine must probably induce adhesion-blocking antibodies recognizing conformational epitopes. With current (and foreseeable) constraints on genetic engineering and protein production it is not possible to produce entire VAR2CSA proteins and it will be necessary to assemble smaller parts of the molecule with the desired characteristics. Although VAR2CSA is an extremely conserved PfEMP1 molecule, it contains stretches in which amino acid sequences vary between parasites. To induce antibodies targeting a high proportion of placental parasite, we will have to identify the part of the molecule that vary and investigate how sequence variation affects CSA and antibody binding. Thus vaccine strategies will probably require production of sub-unit constructs that accurately mimic in vivo molecular conformations. This can only be designed on the basis of insight into the structure of the native protein.

Military Medicine

INV 46

Military medicine in operational missions
J. E. Touze1, M. Vergos1 and P. Vitard1

1French Joint Military Medical Service, Paris, France

French armed forces were deployed these last years over many operational theatres either national or multinational (European Union, NATO, UN). In 2006, France was involved in 12 operational missions (6 of 12 were under a multinational mandate including more than 450 health practitioners each year). In all these missions, infectious diseases, vectors and environmental risks (technological, industrial, NBC weapons) were a key challenge for armed forces. In this context, French Joint Military Medical Service had to conduct a medical and surgical support as well a medical and humanitarian aid for local populations. For all these reasons, a health policy has been introduced including four objectives: prevention of infectious diseases, hygiene and sanitary policy in operations, enhanced epidemiological surveillance and permanent upgrading of medical and surgical support. Among health priorities, malaria fighting remains a key public health problem for the 40 000 French soldiers deployed each year in malaria transmission areas. Epidemiological data showed that imported malaria is increasing in French forces. This could be explained by a neglected chemophrophylaxis among returning soldiers, repeated short missions and more P. vivax and P. ovale infections. In this context, doxycycline monohydrate remains the first line chemophrophylaxis regimen for French forces regarding its low cost and tolerability compared to mefloquine. However, its short half-life requests a full compliance. Chemophrophylaxis should be associated to vector control measures and personal protection (impregnated bed nets, protective clothing, repellents...
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New Diagnostics

INV 47
Essential diagnostics for HIV, TB and malaria
P. Klaasen1
1Royal Tropical Institute (KIT), KIT Biomedical Research, Amsterdam, Netherlands

HIV, TB and malaria have in common that the evidence-based control strategies for these diseases depend on applying timely diagnostic and monitoring methods. However, the diagnostic capacity cannot presently meet the needs of global health initiatives that focus on infectious disease therapy and control. Case-finding, clinical care, and disease surveillance are often compromised by the lack of effective and appropriate diagnostics, or their improper use or interpretation. Accurate, appropriate diagnostic testing is therefore increasingly recognised as a strategic need to improve global health and reach millennium development goals (MDG). However, it should be clear that for any diagnostic test to be useful, it must deliver information that is used to make a medical decision, including for patient management, surveillance and for epidemiological studies. Unfortunately, for diseases that are predominantly endemic in poor populations, market-driven incentives for diagnostic research rarely exist. Companies with interests in these areas may be small and under-resourced. Larger, better-resourced companies may also be uninterested because of perceived low returns on investments. Furthermore, companies are often unfamiliar with diagnostic product specifications to appropriately address public health needs, cannot access reagents, strains, and specimens to accelerate research and development, and may lack partners to conduct evaluations and regulatory approvals for sustainable introduction. Private companies in the medical arena do however have the knowledge of project management, intellectual property and quality management. Furthermore, they have a marketing and distribution network in place. Available diagnostic techniques for HIV do not yet fulfil criteria of affordability and simplicity, whereas those for TB are relatively simple but lack sensitivity. Rapid and simple tests for use in the periphery are available for the diagnosis of malaria and lessons from their use can benefit development and application of rapid tests for other diseases. Apart from biomedical research needed for test development, community and user need assessments, evaluations, implementation, and impact research are as important. There is a need for coordinated essential diagnostics pipelines which entail these consecutive steps that start with community and user needs assessments and finalize with a diagnostic test sustainably used at the point of care.

Pathology

INV 48
The biology of erythrocyte invasion by the malaria parasite
A. A. Holder
1National Institute for Medical Research, Parasitology, London, UK

The malarial parasite must invade an erythrocyte in order to replicate within the blood stream. The invasive form, the merozoite, is a polarised cell equipped with specialist apical organelles (for example the micronemes and the rhoptries) and a molecular motor to invade the host cell. The current model of invasion is that proteins on the parasite surface mediate the first interaction between merozoite and red cell. This interaction is augmented by proteins derived from the micronemes to form a tight junction between the two cells. The actomyosin motor, which lies under the surface of the merozoite, moves the tight junction towards the rear of the merozoite resulting in the parasite moving into the vacuole that is formed by invagination of the red cell plasma membrane. Components of the rhoptries are transferred to this parasitophorous vacuole and may function in vacuole development or other post-invasion processes. We have studied several parasite components to determine their role in the process of invasion.

Primary Health Care

INV 49
International policies, primary health care, disease control and integration
J.-P. Unger
1Public Health Department, Institute of Tropical Medicine, Antwerp, Belgium

OBJECTIVES To review the evidence base for the health care/ disease control policy promoted by international agencies in developing countries since 1993 and – as an alternative, to update some primary health care concepts.

METHODS A synthesis of recent work publications will be presented.

RESULTS International agencies do have a doctrine on aid and international aid policies: whenever possible, these policies allocate disease control to the public sector and curative health care to the private sector. Since a few years, WHO has also been promoting private sector providers’ involvement in TB control, a component of the new Stop TB Strategy and the global plan to stop TB. Such policies are neoliberal in their promotion of commoditization and privatization. To assess their impact on access to quality health care, we refer to an analysis of the health policies of three countries showing how health care privatization failed in Colombia and Chile, and what an alternative health policy can achieve (in Costa Rica and Chile). We conclude that together with other factors (such as Structural Adjustment Programs and WTO GATS negotiations), orthodox policies are responsible for poor access to care. On disease control, we present epidemiological trends of target diseases (AIDS, tuberculosis and malaria). To understand their control’s failure, we performed simulations to estimate the success likelihood of malaria control in Africa under orthodox aid principles. We also refer to works suggesting an insufficient evidence base for the strong promotion of public-private-mix-DOTS by WHO. We conclude that together with other factors, these policies are responsible for the lack of effectiveness of disease control in low and middle-income countries, and for many avoidable deaths in LIC/MIC.
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CONCLUSION Alternative aid and international health policies are justified. We propose a social and democratic strategy updating several primary health care features. We highlight its health care (quality criteria for medical care in publicly oriented services), integrated disease control, managerial and socio-political features. In particular, we plead for family and community health in publicly oriented services, publicly oriented hospitals with systemic responsibilities, local health systems, reflexive methods to bridge the gap between the medical and public health identities of health professionals, a reorientation of international research and in-service training efforts. To implement these methods, we consider different strategies fit for different health systems categories.

Methods Based on fieldwork in India and drawing on relevant experiences in other countries, the address examines challenges, opportunities and benefits of implementing public-private partnerships and explores how partnerships with the private sector are designed to deliver health care services to the poor as well as the consequences for beneficiaries.

Results Because collaboration with the private sector in health service delivery is influenced by the conceptual and ideological perspectives of stakeholders, the address will review the policy relevance of these perspectives.

Proteomics

INV 50

Functional analysis of a Plasmodium berghei gametocyte translational repressor complex

A. Waters 1

1 Lumc, Leiden, the Netherlands

Meiosis and its attendant generation of genetic diversity in Plasmodium is dependent on the transmission of male and female haploid sexual precursor cells (gametocytes) to the mosquito vector where fertilization takes place; the diploid zygote then transforms into a polarized cell that is motile and known as an ookinete which penetrates the midgut into the surrounding epithelium. This early sexual developmental program depends on the transcription and storage, rather than translation, of certain mRNAs already in blood-stage gametocytes. Assembly into and maintenance of mRNAs in translationally quiescent mRNPs is known as translational repression (TR) and depends on the activity of an evolutionarily conserved DEAD-box RNA helicase, Plasmodium development of zygote inhibited (DOZI). A DOZI::GFP fusion protein localizes to distinct positions in the cytoplasm of female gametocytes that contain transcripts known to be translationally repressed. Analyses of DOZI::GFP immunoprecipitation eluates by mass-spectrometry identified numerous proteins that potentially also reside in this Plasmodium repressor complex, a number of which have now been analysed by gene disruption. The annotated Plasmodium genome contains relatively few obvious transcription factors and our data suggest that TR and mRNA turnover can be key influences on stage-specific gene expression in Plasmodium. This developmental programme reflects a response to a selective need to produce a polarised cell quickly whilst undergoing meiosis which is not thought to support accurate gene transcription. The stored mRNA species effectively form a smoking gun that might be exploited to prevent transmission of the parasite to the mosquito vector thereby interrupting the parasite life cycle.

Public Private Partnership

INV 51

Public-private partnership in health services delivery

J. W. Bjorkman 1

1 Institute of Social Studies, staff group on States, Societies, World Development, Den Haag, Netherlands

Objectives Public-private partnerships are increasingly advocated to alleviate deficiencies in the public health system as well as to reduce economic stress on those who seek services from an expensive, burgeoning and unregulated private health sector.

Reducing Stigma and Discrimination

INV 52

Stigma: formulating concepts and priorities for a public health agenda

M. G. Weiss 1

1 Public Health and Epidemiology, Swiss Tropical Institute, Basel, Switzerland

Objectives Ideas about stigma have changed dramatically over time from a morally acceptable means of social control to an arbitrary and unacceptable imposition of social suffering that complicates illness and efforts to treat and control disease. Stigma as a mark intended to evoke shame and disgrace has become an archaic notion, giving way to its formulation as a feature of social interactions that unfairly affects those who are vulnerable to discrimination and denies them needed support. In this paper we review the concept of stigma as it applies to the interests of health and illness, implications for interventions to serve the interests of public health, and questions for research concerning the priority of stigma in the context of other public health priorities.

Methods Based on essential features of Goffman’s formulation of stigma as ‘the situation of the individual who is disqualified from full social acceptance,’ we examine ways in which the concept has been applied in studies of problematic social responses to health problems. We consider frameworks for study of stigma and experience in a four-country study of gender and tuberculosis in Bangladesh, India, Malawi, and Colombia.

Results According to Scambler’s hidden distress model, stigma may be enacted in experiences of discrimination, or felt as a product of perceived intent but not enacted in social relations. Felt stigma may be further differentiated as internalized or anticipated. Laws may afford protection from discriminatory acts, and social support and counselling may help people who accept and internalize discriminatory views of society. Experience from a multicountry study of gender and tuberculosis indicates an approach to identifying indicators, indices, and narratives of stigma in a cultural epidemiological framework. Gender and cross-site differences indicate the effects of socio-cultural factors and the epidemiology of HIV/AIDS on the stigma of TB. Findings suggest questions about the impact of stigma on delayed help seeking, treatment adherence, and both benefits and problems from linking control activities for HIV/AIDS and TB.

Conclusion Public health concerns about stigma appropriately focus on reducing stigma and increasing social support. Different aspects of stigma suggest different approaches for public health actions to deal with it. New mixed-methods approaches to stigma studies contribute to a clear formulation of stigma that recognizes its distinct features, their effects on risk-related and help-seeking behaviour, and interventions that amplify or mitigate stigma.
Rolling out HAART

INV 53
Scaling up antiretroviral therapy in resource-constrained settings
Y. D. Mukadi
Family Health International, Care and Treatment, Arlington, USA

OBJECTIVES To describe approach used for scaling up ART in resource-constrained settings

METHODS Family Health International has designed and is implementing a scale-up plan that incorporates both the health sector and the community. The scale up process focuses on expanding regional coverage of treatment services through a three-tiered ART decentralization model aimed at rapidly building the capacity of health facilities at all levels of care.

- Health facilities that have in place a minimum infrastructure and that with little additional input can meet the essential criteria for ART services are selected as initial sites. The capacity of health care staff at these sites is developed.
- At initial sites require less direct supervision and support, new health facilities in the same and new districts are identified and prepared to offer ART. Maintenance assistance continues for the initial sites as required, while with the local partners we complete a rapid assessment, upgrade infrastructure and systems and build capacity for ART at the second tier sites. Some of the initial sites can serve as learning or mentorship sites where staff of new sites can have experiential training and coaching on starting up and delivering quality ART services. To effectively reach peri-urban and rural areas, we establish an Outreach Service where ART-experienced doctors from district and referral hospitals travel to distant health centers on scheduled days to manage patients and mentor staff.
- As treatment services are established at sites, we also improve ART literacy and treatment preparedness within communities served by the facility by engaging influential traditional leaders in advocating for ART services. Working with PLHA we implement behavior change interventions that highlight the benefits of HIV testing, generate demand for services and educate the public about the care and treatment services. We also establish formal referral systems that systematize linkages through a local coordination unit, standardized referral and coordination procedures.

RESULTS This process was developed in scaling-up ARV programs in Ghana, Kenya and Rwanda and has since been applied to rapidly expand ART programs in six additional countries. With the incorporation of ART within the framework of HIV care and treatment, sites have experienced increased capacity to respond to the key challenges of expanding access to ART.

CONCLUSION The effective scaling-up of ART in resource-constrained settings requires the commitment of the government and key stakeholders in the community, and the involvement of PLHA in the design.

Safe Motherhood

INV 54
Cervix carcinoma and HPV
J. Louwers
Free University Medical Center, Obstetrics and Gynaecology, Amsterdam, Netherlands

OBJECTIVES Cervical cancer is one of the leading causes of cancer mortality in women in the world. For the year 2002, 493 000 new cases and 274 000 deaths have been reported worldwide. 83% Of all cases of cervical cancer occur in developing countries, where it accounts for 15% of all female cancers.

METHODS A persistent infection with a high-risk human papillomavirus (hrHPV) has been identified as the key causative agent of cervical cancer. At this moment, thirteen high-risk HPV types have been identified by the World Health Organisation (WHO). Worldwide HPV 16 accounts for more than 60% of all cervical cancers, with HPV 18 adding approximately another 10%. HPV is a sexually transmitted virus. Primary infection occurs mostly in young adults, shortly after they become sexually active. The prevalence is so high that the chance of acquiring a HPV infection during lifetime is estimated up to 85%. But, only if a hrHPV infection is persistent, progression of a pre-malignant lesion occurs. Approximately 80% of all hrHPV infections however are transient and asymptomatic. Therefore, a cervical carcinoma can be seen as a rare complication of a frequent infection. Clearance of hrHPV precedes regression of pre-malignant lesions. After a period of 3 years, 50% of all mild and moderate dysplasia will regress, while the regression rate of high-grade lesions in women with hrHPV is much lower. Since hrHPV infection has been established as the primary cause of cervical cancer the development of prophylactic vaccines has been subject to research. At this moment in time, two of such vaccines have been finalized and seem highly effective in the prevention of pre-malignant lesions, related to the hrHPV types present in the vaccines.

RESULTS Research has shown a protection rate of 100% in young, HPV-naive girls in the prevention of high-grade HPV 16 and 18 related pre-malignant lesions (CIN 2/3) for both vaccines.

CONCLUSION At this moment, the efficacy of the vaccines in older (non HPV-naive) women, in HIV positive women and in men is subject to research. Although further research is necessary, the preliminary results seem promising.

INV 55
Maternity care and undocumented female immigrants
H. van den Muijsenbergh
Department of Family Medicine/Womens Studies Medicine, University Medical Center ST Radboud, Nijmegen, Nijmegen, Netherlands

OBJECTIVES Many of the 25 000–50 000 female undocumented immigrants living in Dutch cities have children or get pregnant. Each year 1200–2000 undocumented children are born. Presumably, these women suffer from specific health problems, related to the (domestic) violence they have suffered, as well as problems in the area of reproductive health. As they cannot obtain medical insurance, the access to medical and maternity care is hindered. The aim of our study, that started September 2005, is to obtain insight in their problems and experiences with Dutch medical care.

METHODS Semi structured interviews and a medical examination are conducted in 100 undocumented women in four cities.

RESULTS A total of 44% of the 60 women who were interviewed, have experienced sexual violence, 58% had problems with contraception and 51% had at least one abortion. Besides this, nearly all women suffered from anxiety disorder, sleeplessness and tension; 55% had unexplained loss of weight and 33% complained about urinary incontinence. When pregnant, most of them do find a midwife willing to help them, but antenatal controls start late and are infrequent, maternity nursing is hard to get and access to gynaecologists is hampered. Often hospitals request payment before the undocumented patient is allowed entrance. Midwives often are not able to refer their pregnant patient to the gynaecologist or family doctor. The problems they describe with antenatal care have also been confirmed by international studies.
A study involving 1283 women from 10 European countries revealed that immigrant women, in comparison to women born in their country of residence, were three times more likely to receive inadequate prenatal care; those without medical insurance however, were 19 times more likely (Delvaux 2001). Another study in Belgium indicated that 46% of uninsured pregnant women received no antenatal care and that perinatal deaths were increased 6-fold in this group (Barlow 1994). Illegal residence also appeared to be a risk factor for severe pre-eclampsia, eclampsia and HELLP-syndrome (Haeltterman 2003).

CONCLUSION It seems that the emotional and practical problems of the mothers effect the health of their children as well.

INV 56
Maternal health in Tanzania: the health system and health policy
S. Massawe1
1Muhimbili National Hospital, Obstetrics and Gynaecology, Dar es Salaam, United Republic of Tanzania

OBJECTIVES Improve maternal health and reduce maternal deaths in Tanzania to achieve the Millennium Development Goals. RESULTS After Independence in 1961, Tanzania adopted a policy of free health services for all. The government built primary health care facilities to be as close as possible to the people, and trained paramedical personnel to provide health care at these facilities. Maternal and child health (MCH) is prioritized, and comprehensive maternal health care services including services, including antenatal care (ANC), delivery care and family planning are provided through MCH clinics which are present in all levels of health facilities free of cost. Since the early 90s the health sector is undergoing reform in phases, which focus on decentralized health management, diversification of health financing, and on public/private mix in the provision of health services. Due to this there is cost sharing for services at all levels, but the health policy provides for free services for pregnant women and under-five children. However Tanzania is one of the countries with a very high maternal mortality ratio, estimated at 578 per 10,000 live births. Despite a high attendance for antenatal care at 98%, only 46% deliver in a health facility with skilled provider while the rest deliver at home. Over the years there is a trend towards decreased assess to skilled care at childbirth for the women, despite positive maternal health care policies, and this corresponds to an observed increase in maternal mortality and morbidity including obstetric fistula.

CONCLUSION Despite positive maternal health care policies, maternal mortality and morbidity increases.

INV 57
Severe maternal morbidity in the Netherlands: a nationwide confidential enquiry and audit
J. Zwart1, D. J. Jonkers2, J. M. Richters1, P. Ory3 and J. van Roosmalen1
1Obstetrics and Gynaecology, Leiden University Medical Center, Leiden, Netherlands; 2Department of Obstetrics, Leiden University Medical Center, Leiden, Netherlands; 3Department of Public Health and Primary Care, Leiden University Medical Center, Leiden, Netherlands; 4TNO Prevention and Health Care, Leiden, Netherlands

OBJECTIVES To assess the incidence and characteristics of severe maternal morbidity in the Netherlands and to assess the use and feasibility of auditing cases of severe maternal morbidity.

METHODS In a 2-year nationwide confidential enquiry, all cases of severe maternal morbidity were prospectively collected using five categories: intensive care unit (ICU) admission, uterine rupture, eclampsia, major obstetric haemorrhage (four or more units of blood) and other severe maternal morbidity including to the opinion of the clinician. Incidences and case fatality rates were calculated and substandard care was assessed in subgroups. As immigrant women are disproportionately represented in Dutch maternal morbidity statistics, special attention was paid to the ethnic background of women.

RESULTS All 98 Dutch maternity wards participated in the study. Severe maternal morbidity was reported in 2562 cases, giving an overall incidence of 7.0 per 1000 deliveries. There were 47 maternal deaths during the study period. Major obstetric haemorrhage accounted for 45% of inclusions, only a third of all cases were admitted to ICU. 216 cases of uterine rupture and 234 cases of eclampsia were reported. Twenty-four percent of all cases were immigrant women (RR 1.6; 95% CI 1.5–1.8). In 79% of assessed cases, the majority of the assessors indicated the presence of substandard care. Delay in diagnosis and treatment of major obstetric haemorrhage and suboptimal treatment of hypertensive disease were the most frequently scored substandard care items.

CONCLUSION Severe maternal morbidity complicates at least 0.7% of all pregnancies in the Netherlands, with immigrant women experiencing an elevated risk. Since substandard care was found in the majority of assessed cases, reduction of severe maternal morbidity should be an important goal in countries where maternal mortality is low.

INV 58
Reducing maternal mortality in Kigoma, Tanzania
G. Mbaruku1
1Obstetrics and Gynaecology, Regional Hospital Kigoma, Kigoma, United Republic of Tanzania

OBJECTIVES An intervention programme aiming at a reduction of maternal deaths in the Regional Hospital, Kigoma, Tanzania. METHODS A retrospective study was carried out from 1984–86 to constitute a background for an intervention programme in 1987–91. RESULTS The retrospective study revealed gross under-registration of data and clarified a number of potentially useful issues regarding avoidable maternal mortality. An intervention programme comprising 22 items was launched and the maternal mortality ratio was carefully followed in 1987–91. The intervention programme paid attention to professional responsibilities with regular audit oriented meetings, utilisation of local resources, schedules for regular maintenance of equipment, maintenance of working skills by regular on-the-job training of staff, norms for patient management, supply of essential drugs, the need for a small intravenous fluids production unit, the creation of culture facilities for microbiology findings, and to efforts to stimulate local fund raising. CONCLUSION The results indicate that the maternal mortality ratio fell from 933 to 186 per 100,000 live births over the period 1984–91. Thus it is underscored that the problem of maternal mortality can be successfully approached by a low-cost intervention programme aimed at identifying issues of avoidability and focusing upon locally available solutions.
INV 59
Failure to thrive and maternal mental health
A. Rahman1, Z. Iqbal2, J. Bunn1, H. Love3 and R. Harrington4
1University of Manchester, UK and Human Development Research Foundation, Pakistan, Islamabad, Pakistan; 2Human Development Research Foundation, Islamabad, Pakistan; 3Liverpool School of Tropical Medicine, Liverpool, UK; 4University of Manchester, Manchester, UK

OBJECTIVES Risks for emotional and behavioural problems are known to be high among children of depressed mothers. The objective of this research was to examine the impact of antenatal and postnatal depression on physical development of the infants.

METHODS We carried out case-control and cohort studies in rural Rawalpindi, Pakistan to examine if maternal depression is associated with infant undernutrition.

RESULTS The case-control study showed high odds (OR 3.9, 95% CI 1.9–7.8) of maternal depression in underweight (below 10th centile) infants. In the cohort study, relative risk for being underweight (weight-for-age z-score < -2 SD) was 4.0 (95% CI 2.1–7.7) at 6 months and 2.6 (95% CI 1.7–4.1) at 12 months, while the risks for stunting (length-for-age z-score < -2 SD) was 4.4 (95% CI 1.7–11.4) at 6 months and 2.5 (95% CI 1.6–4.0) at 12 months. Relative risk for ≥ 5 diarrhoeal episodes per year was 2.4 (95% CI 1.7–3.3). Chronic depression carried a greater risk for poor outcome than episodic depression. The associations remained significant after adjustment for confounders by multivariate analyses.

CONCLUSION Early treatment of antenatal and postnatal depression could benefit not only the mother’s mental health but also the infant’s physical health and development. However, psychological management of maternal depression in developing countries poses special challenges. Strategies for development of such an intervention are discussed.

INV 60
Introducing the advanced life support in obstetrics (also) course in Malawi
T. Megid1, K. Keating2 and P. Ameen-Kargiwi3
1Department of Obstetrics and Gynaecology, Kamuzu Central Hospital and Bwaila Hospital, Lilongwe, Malawi; 2ALSO Malawi, Lilongwe, Malawi

OBJECTIVES Malawi is one of the poorest countries in Africa and has the highest Maternal Mortality Ratio (MMR of 984/100 000) of a country not at war, or emerging recently from armed conflict, in the world. Malawi also struggles with severe shortage of staff and poor quality of services as well. The ICM has learnt that it is important to strengthen professional associations to facilitate the development of effective partnerships and collaboration and to advocate for women and newborn care in a manner that will influence the equitable distribution of resources for the benefit of women and children.

Resources used:
• Beyond the Numbers: Reviewing maternal deaths and complications to make pregnancy safer. WHO Geneva 2004.
Schistosomiasis

INV 62
Schistosomiasis: from drug discovery to integrated control
J. Utzinger1, J. Keiser1, P. Yountsou1, S.-H. Xiao2 and M. Tanner1
1Swiss Tropical Institute, Basel, Switzerland; 2National Institute of Parasitic Diseases, Shanghai, China

Although schistosomiasis affects more than 200 million individuals, it remains one of the so-called ‘neglected tropical diseases’ because it primarily affects poor populations in rural areas of the developing world. The current mainstay of control in high-burden areas is praziquantel-based morbidity control. Praziquantel has been developed 30 years ago and to date over 100 million doses have been administered without any severe adverse events and usually resulting in high cure and egg reduction rates. Praziquantel has become inexpensive, and hence there has been little incentive for innovations in other fields, such as the development of vaccines, new drugs and diagnostics. In this talk, we will first emphasise that relying on a single drug for individual treatment and community-based morbidity control of schistosomiasis is a dangerous situation. We will then review recent progress made in discovery and development of novel antischistosomal drugs, placing emphasis on the synthetic trioxolanes and the artemisins. We will present findings from a systematic literature review and meta-analysis regarding the risk of schistosomiasis in relation to close proximity to water resources development and management. Progress made with geographical information system and remote sensing technologies, coupled with Bayesian spatial statistics for risk mapping and prediction, will be highlighted. Finally, challenges and opportunities for integration of schistosomiasis control with other neglected tropical disease control programmes will be discussed and pressing research needs outlined.

Severe Malaria

INV 63
The treatment of severe malaria
A. M. Dondorp1
1Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

Severe malaria carries a high mortality rate of 10%, increasing to as high as 50% when multiple organs are involved. Few clinical studies have been directed at improving the management of severe malaria over the years, but this situation is slowly changing. In the SEAQUAMAT trial parenteral artesunate was shown to be associated with a 35% lower mortality than quinine, and is now the recommended treatment for severe malaria in low transmission areas and in the 2nd and 3rd trimesters of pregnancy. A trial is underway to establish its role in African children. Development of GMP formulations should make parenteral artesunate more widely available in the future. Another important development is the use of artesunate suppositories to treat patients with severe disease in remote rural settings, delaying the evolution into more severe malaria and buying them time to reach a health care facility. No adjunctive therapy has been shown to improve the outcome of severe malaria, but most studies have been underpowered. Future trials of interventions shown to be promising in pilot studies should be large and adequately powered. Many ‘resource poor’ countries are at a stage where basic ICU care in regional hospitals is becoming feasible, a development which has great potential to further reduce the unacceptably high mortality rate of this disease.

Understanding severe malaria

INV 64
M. Wahlgren1
1Karolinska Institutet, MTC, Stockholm, Sweden

OBJECTIVES understand the molecular pathogenesis of severe malaria.

METHODS Multiple different methods were used.

RESULTS Two forms of abnormal adhesive capability, cytoadhesion to the vascular endothelium and rosetting – binding of normal erythrocytes around parasitised ones – are thought to be the principal factors behind the particular virulence of Plasmodium falciparum malaria by promoting the sequestration of erythrocytes in the micro-vasculature. Adhesion to both red blood and endothelial cells has been associated with the development of knobs, i.e. electron-dense surface membrane protrusions, one of many major morphological, functional and antigenic changes of the red cell induced by the intraerythrocytic development of the P. falciparum parasite. After being transported from the internal parasite, adhesins involved in the binding to other cells are concentrated and subsequently exposed to the exterior of the erythrocyte membrane at the knobs. One major parasite derived group of antigens has been suggested to hold a role as adhesin, PiEMPI.

CONCLUSION The molecule piEMPI and PfEMP in the sequestration of infected erythrocytes and the role in the pathogenicity mechanisms of the disease will be discussed.

Sexual and Reproductive Health

INV 65
Reproductive health in Africa: major challenges and opportunities
N. Madise1
1African Population and Health Research Center, Nairobi, Kenya

Women in sub-Saharan Africa face some of the greatest sexual and reproductive challenges in the world. African women have the highest fertility, highest HIV infection rates, highest risk of dying during childbirth and they have the highest unmet need for contraception. Thirteen years after Cairo, there has been progress in reproductive health globally, but variations across countries persist, with the poorest countries in Africa still exhibiting some of the worst reproductive health indicators. In part progress has been hampered by the HIV epidemic, the scale of which makes it the worst epidemic that the human race has ever experienced to date. Programmes for reproductive healthcare and those for HIV prevention and mitigation have adopted vertical approaches although the main causal factors and determinants of poor reproductive health and HIV infection are the same. Efforts to integrate family planning in HIV programmes and vice-versa are woefully inadequate given the scale of the epidemic and the high unmet need for family planning among both HIV positive and negative women. Another recent development is the reduction in funding for family planning, resulting in stagnation or reversal in fertility trends in some African countries. In this paper, I use multiple sources of data to show trends in some reproductive health outcomes (unmet need for family planning, marital mortality, and HIV prevalence rates). There has been progress in some of these indicators and lessons must be learnt from those countries that are making progress. However, for most of the continent, the challenges are many and the continent needs to take advantage of opportunities to ensure that reproductive health care improves. I argue that a synergistic approach to HIV prevention and reproductive health especially family planning will lead to improvements in women’s health. I also argue that moving
Towards gender equality and improving female education are important for healthier women and families.

**TB Treatment**

**INV 66**

**Priorities for the eradication of tuberculosis through shorter treatment durations**

A. Jindani

1 International Consortium for Trials of Chemotherapeutic Agents in Tuberculosis (INTERTB), St George's, University of London, Cellular and Molecular Medicine, London, UK

**OBJECTIVES** During the 1960s and 70s, the introduction of rifampicin and pyrazinamide enabled tuberculosis treatment duration to be reduced to 6 months. At this point, the eradication of tuberculosis seemed an achievable target. However, events have proved otherwise and tuberculosis now seems to be out of control. There is universal agreement that, if tuberculosis is to be eradicated through treatment, effective treatment regimens of 3, 2 and even 1 month will have to be developed.

**METHODS** Such short treatments will have to come through new drug development. Several pharmaceutical companies are exploring promising new candidate drugs which could lead to significant reduction in treatment durations. However, new drug development, from discovery to marketing, is a long, complex and expensive process. The whole process could take as much as 20 years at a cost of 50–100 million dollars. Moreover, the regulations governing clinical trials become more rigorous and complex. There is a possibility that currently used drugs could also lead to reduction of treatment duration. There is evidence that dose increases of the rifamycins could lead to improved sterilisation and, possibly to treatment reduction. There is also compelling evidence that the strategic use of some quinolones could also achieve this objective. Whereas Phase II trials require relatively smaller number of patients, Phase III trials need larger numbers and require the participation of at least five centres in one trial. Thus, there will be competition for patient numbers. Additional capacity will be needed to meet the need for increased numbers of trial participants. Current significant imbalances in the funding of new and existing drugs may compromise the development of shorter treatment regimens.

**RESULTS** Trials of higher doses of the rifamycins together with the quinolones may allow a treatment reduction to 3 months in the short and medium term while new drug development is proceeding. Capacity to participate in clinical trials can be strengthened through training programmes. The best way to build and develop capacity is to carry out a clinical trial.

**CONCLUSION** New drug development could take as long as 20 years to achieve treatments of very short duration. Concurrent clinical trials of rifamycins with quinolones should be carried out to identify regimens of 4 or 3 months. Such trials could also be used to build additional and strengthen existing capacity to carry out trials of new drug combinations. The imbalances in the funding of the two strategies need to be redressed.

**TB Vaccines**

**INV 67**

**Update on TB vaccines**

S. H. E Kaufmann

1 Immunology, Max Planck Institute for Infection Biology, Berlin, Germany

Globally, more than 8 million individuals acquire active tuberculosis and 2 million die of this disease annually. The available vaccine against tuberculosis Bacille-Calmette-Guérin (BCG) protects newborn from miliary tuberculosis, but fails to prevent pulmonary tuberculosis in their parents. This shows that Mycobacterium tuberculosis can be controlled (though not eradicated) by immunity induced by natural infection. Acquired immunity against tuberculosis is primarily T cell-dependent. The T-cell system comprises distinct populations with CD4 T cells undoubtedly being of central importance for protection and CD8 T cells contributing to resistance in addition. Furthermore, unconventional T cells seem to participate in immunity against Mycobacterium tuberculosis. Subunit vaccination strategies are aimed at boosting the immune response evoked by priming with BCG. The identification of protective antigens represents an essential prerequisite for the success of this type of vaccines. Viable attenuated vaccines are aimed at replacing the current vaccine BCG.

Two major strategies are being pursued: Knockout mutants of Mycobacterium tuberculosis and improved recombinant BCG. We have constructed an improved BCG which expresses lipo-olysin and is deficient in urease-C (r-BCG Delta-ureC:Hly). This vaccine induces more potent protection against the laboratory strain M. tuberculosis H37Rv and a clinical isolate of the ‘Beijing/W’ family. Improved protection is probably due to two mechanisms which are not mutually exclusive. First, the vaccine facilitates egression of antigens into the cytosol. Second, the vaccine induces apoptosis in infected host cells which subsequently paves the pathway for crosspriming that ultimately allows superior T cell stimulation. Head-to-head testing of different vaccine candidates in clinical trials could be accelerated by precise knowledge of biomarkers indicative for protection. We have performed transcriptome analyses of peripheral blood leukocytes from individuals with latent and active tuberculosis. Comparative transcriptomics will provide guidelines for clinical trial testing of novel candidate vaccines and anti-infectives.

**TB-HIV**

**INV 68**

**Diagnosis and management of the HIV-infected TB patient, with particular reference to sub-Saharan Africa**

A. Harries

1 Family Health International, HIV Unit, Lilongwe, Malawi

The dual epidemic of HIV/AIDS and tuberculosis (TB) is most heavily felt in sub-Saharan Africa. HIV adversely affects the management of TB in a number of ways. There is an increase in the number of new cases and cases of recurrent TB after TB treatment has been completed; TB diagnosis becomes more difficult as a result of more cases of smear-negative and extrapulmonary TB, which are problematic to diagnose in resource-poor settings; there is an increase in morbidity as a result of HIV-related disease and adverse drug reactions; there is an increase in case fatality rates as a result of serious HIV-related disease; and HIV facilitates transmission of MDR- and XDR-TB. The proper case management of TB in a high HIV-prevalent area involves: (i) attention to improved diagnosis of TB, and particularly a focus on not missing HIV-infected patients who are starting antiretroviral therapy (ART) as a result of weight loss and chronic fever and the HIV wasting syndrome; (ii) ensuring that all TB patients are HIV tested and counselled through a provider-initiated ‘opt-out’ approach; (iii) providing cotrimoxazole preventive therapy to HIV-infected TB patients; and (iv) providing ART to HIV-infected TB patients. There are many issues around the subject of anti-TB treatment and ART that include: the best time to start ART in relation to anti-TB
Adherence levels in Africa have been found to be
T. b. gambiense (West African form) and
T. b. rhodesiense (East African form). The high demand for 2nd line
treatments (currently ten times more expensive than 1st line ART)
remains a major challenge. A high demand for 2nd line
treatments persists in many countries due to the limited availability of 1st line ART.
Adherence is critical for the success of ART, and various strategies are required to achieve high adherence levels.

Tropical Medicine and International Health
VOLUME 12 SUPPL I PP 1–24 MAY 2007

Abstracts of the 5th European Congress on Tropical Medicine and International Health

Treatment Adherence

INV 69
Hunger, waiting time and transport costs: time to confront challenges to ART adherence in Africa
A. Hardon

OBJECTIVES Adherence levels in Africa have been found to be better than those in the US. However, adherence is an ongoing challenge, with many patients expressing difficulty in adhering to treatment. A high demand for second-line treatments (currently ten times more expensive than first-line ART) undermines the sustainability of African ART programs. There is an urgent need to identify context-specific constraints to adherence and implement interventions to address them.

METHODS We used rapid appraisals (involving mainly qualitative methods) to find out why and when people do not adhere to ART in Uganda, Tanzania and Botswana. Multidisciplinary teams of researchers and local health professionals conducted the studies, involving a total of 54 semi-structured interviews with health workers, 73 semi-structured interviews with ART users and other key informants, 34 focus group discussions, and 218 exit interviews with ART users.

RESULTS All the facilities studied in Botswana, Tanzania and Uganda provide ARVs free of charge, but ART users report other related costs (e.g., transport expenditures, registration and user fees at the private health facilities, and lost wages due to long waiting times) as main obstacles to optimal adherence. Side effects and hunger in the initial treatment phase are an added concern. We further found that ART users find it hard to take their drugs when they are among people to whom they have not disclosed their HIV status, such as co-workers and friends. Conclusions and recommendations: The research teams recommend that (i) health care workers inform patients better about adverse effects; (ii) ART programs provide transport and food support to patients who are too poor to pay; (iii) recurrent costs to users be reduced by providing two or three-months, rather than one-month refills once optimal adherence levels have been achieved; and (iv) pharmacists play an important role in this follow-up care.

Trypanosomiasis

INV 70
Drug resistance in human and animal African trypanosomes
S. Geerts and V. Deleersna

Considering that most current trypanocides have been used for many decades, we have been very fortunate that serious problems of drug resistance (DR) have manifested themselves only relatively recently. Resistance against pentamidine remains anecdotal probably due to the fact that P2-type purine transporters are not the only way of uptake of the drug. DFM0 which is active against T. b. gambiense only is frequently used against melarsoprol refractory infections. Concerns arise, however, about the oral administration of DFM0 to patients with late-stage T. b. gambiense sleeping sickness that may not produce adequate therapeutic plasma and CSF levels, which could speed up the development of DR. Yet, resistance to melarsoprol, diminazene aceturate (DA) and isometamidium chloride (as well as quinapyramine) is now undermining the further utility of these compounds. Even the belated introduction of combination therapy will thus not eradicate the existing resistance genotypes in the human-infective and veterinary trypanosome populations. Added selective pressure on these populations must be avoided as much as possible and thus the introduction of DA for the treatment of early stage sleeping sickness is not considered as a good option. The human-infective population already contains a large proportion of melarsoprol resistant parasites – and melarsoprol and diminazene are cross-resistant. Introduction of DA for human use thus risks to further increase melarsoprol treatment failures while no satisfactory alternative treatment for late stage HAT is yet available. Furthermore, DA offers very limited advantages over the existing treatments of stage I sleeping sickness, which are not seriously threatened by drug resistance. A similar judgement may need to be made for DB289, especially if this treatment will need to be taken orally over several days and compliance is not assured. Priority should thus be given to the development and licensing of new treatments without cross-resistance to existing therapies. Nifurtimox combinations, meanwhile, look like the best short-term solutions to deal with melarsoprol-refractory stage II gambiense HAT.

INV 71
Management of human African trypanosomiasis (HAT)
C. Mika Mia Bilenge

Sleeping sickness is caused by the protozoan parasites Trypanosoma brucei gambiense (West African form) and T. rhodesiense (East African form). In the late 1990s WHO had emphasized the recrudescence of the disease and a dramatic lack of awareness about the disease situation. The resulting under-surveillance had led to approximately 25 000 reported new cases per year and estimates reached over 300 000 total cases. Meanwhile, major events have impacted the control of the disease like the interruption of war and civil conflicts in several regions, the commitment of non-governmental organizations to combat HAT under extremely difficult circumstances, the investments of governments in large-scale bilateral projects and the donation of the medication by multinational pharmaceutical companies. Hence during the past 5 years, surveillance activities have increased, raising the total number of people screened through active case-finding, leading to a substantial decline in the number of new cases. The reported number of cases per year decreased to 17 500 and the cumulative rate to 50 000–70 000 cases. In view of this significant progress the ISCTRC at its 26th conference in Addis Ababa in September 2005 recommended that WHO should launch an elimination programme for HAT. Only a very limited number of drugs are available for treatment of the disease and there is no vaccination: For treatment of early stage T. b. gambiense sleeping sickness pentamidine developed 1940 and administered by the i.v. route is the drug of choice, for T. b. rhodesiense, suramin developed in...
Vector Control

INV 72
Malaria: vector control
A. Githeko

OBJECTIVES
Assess the effectiveness of available vector control tools in Western Kenya.

METHODS
Studies were carried out on the spatial and temporal distribution of malaria vector and human infections in the Western Kenya Highlands. Indoor residual spraying was targeted at the foci of transmission which contained 98% of the vectors and covered only 25% of the affected village. The impacts on adult vectors and human malaria infections were assessed. B. sphericus (BS) was applied in breeding habitats in valley bottoms and its effects on malaria vector and human infections determined. A cost analysis was carried out on the use BS for malaria control the distribution of insecticide treated nets in the one of the study areas was assessed over a three year period. Nappier grass was planted along major breeding habitats in reclaimed swamps and the effects on larval breeding assessed.

RESULTS
In the target zone, malaria prevalence was reduced by 69% and by 38.5% in the whole village. The median infection time was delayed by 39 days in the target zone. Mosquito density was reduced by >99% in the target zone and about 70% in the whole village. There was a significant reduction in larval and adult density and malaria prevalence and incidence in the villages where the biocide (BS) was applied compared to the non-intervention villages. An increase in the distribution of insecticide treated bed nets from 15% to 70% in the villages was associated with a >80% reduction in malaria prevalence. Planting of nappier grass along breeding habitats suggests that larval densities of A. gambiae can be reduced by >80%.

CONCLUSION
These results indicate that targeted application of IRS, biociding and the use of ITNs can significantly reduce malaria prevalence and incidence in the epidemic prone highlands of Western Kenya. The absence of malaria epidemics during the 2006–07 El Nino may be proof of this impact. Use of BS has been shown to be cost effective in malaria control. These results now form the bases for integrated vector management strategies for the control of malaria in the highlands.

Venomous and Poisonous Animals

INV 73
Advances in clinical toxinology
D. A. Warrell

Animal-derived antisera or ‘antivenoms’ are the only specific antidotes that effectively neutralise animal and plant toxins. Employed since the end of the 19th century, they have proved effective in humans envenomed by snakes, lizards, fish, scorpions, spiders, lepidoptera, ticks and cnidarians and poisoned by some cardiac-glycoside-containing plants. While the supply of snake bite antivenoms for needy countries, especially in Africa, is under threat, the efficacy, safety and range of activity of some antivenoms has been improved. The relative merits of whole IgG and its fractions, such as Fab and Fab, and methods of reducing the risk of adverse reactions resulting from aggregation, immune complex formation and complement activation are fundamental considerations in antivenom design. Freeze drying prolongs the shelf life of antiserum stored in high ambient temperatures but faulty technique may result in denatured protein that is ineffective and reactogenic. Recently, the use of Fab fragments and whole IgG refined by caprylic acid solution has been revisited. Horses remain the most commonly used animals for raising antivenoms but dogs, rabbits, sheep, camelids such as llamas and even chickens (egg IgY) antibodies are attracting interest. A new WHO initiative is aimed at improving the quality, quantity, distribution and use of antivenom. Manufacturers will be encouraged and supported, through a system of prequalification (as with other essential drugs), to achieve ‘Good Manufacturing Practice’. Medical staff will be trained to deploy antivenoms more appropriately as part of overall treatment strategies enshrined in regional guidelines.

Unfortunately, there remains a dearth of clinical trial evidence on which to base such guidelines. Although envenoming and poisoning by natural toxins can claim to be a neglected disease, the supporting political argument is weakened by a lack of sound epidemiological evidence and a continued reliance on inadequate hospital-based data. However, community surveys and national data based on more reliable ICD death certification are increasingly pointing to unacceptable levels of morbidity and mortality in some parts of the world such as the Western African savanna region, India, Sri Lanka, Nepal, New Guinea and the Amazon basin. At a more specific level, several popular first aid methods have been discredited, some medically important species have been discovered, new pathophysiological mechanisms have been recognised and animal toxins have continued to excite interest as possible drug models.
Oral abstracts

Amoebiasis Genome and Regulation of Gene Expression I

**O24-1**

Reannotation of the *Entamoeba histolytica* genome

E. Caler1, H. Lorenzi1, M. Thiagarajan1, J. Wortman1, O. White1 and N. Hall1

1TIGR, a division of JCVI, Bioinformatics, Rockville, MD, USA

**OBJECTIVES** In order to improve the current *Entamoeba histolytica* assembly to be used as the reference genome for comparative genomics studies, we have reassembled and reannotated the genome.

**METHODS** We have used the Celera assembler to generate an improved assembly. A new and optimized gene training set was created to generate new gene predictions with improved gene structures. Functional annotation was revised based on generation of protein families, database searches to non-redundant protein databases were refreshed, EC numbers and gene ontology terms assigned.

**RESULTS** Comparison to the previous assembly (Loftus et al. Nature. 2005 Feb 24;433(7028):865–8) revealed the existence of a large number of artifactual tandem duplicated regions. The new 20.8 Mb assembly has 1499 scaffolds, ranging from 906 bp to 0.53 Mb. Existing gaps are currently being closed. The gene models from the old scaffolds were remapped onto the new assembly. The new dataset predicts 8268 genes, with a total of 7449 (out of 9988 originally predicted genes) remapped to the new assembly. A set of 1754 genes underwent major structural modification and 383 new genes have been created. A total of 1241 genes are supported by ESTs. We also mapped *Entamoeba histolytica* repetitive elements, and genes previously predicted in these regions were removed from the core proteome. No evidence of functional (uninterrupted) elements was found. In summary, as the result of the new assembly remapping, elimination of redundant contigs and artifactual tandem duplications, identification of repetitive elements, and deletion of small ORFs (under 300 bp with no evidence) we have been able to reduce the core proteome by 20%. Finally, all *vs.* all blastp sequence comparison and clustering of the *Entamoeba histolytica* proteome identified 34 protein families containing novel domains.

**CONCLUSION** This reannotation effort was essential to obtain a high quality reference genome to be used as template for the comparative genomics project between *Entamoeba histolytica*, *Entamoeba dispar* and *Entamoeba invadens*. We have started the annotation these two species, sequenced to 5X coverage and they have been assembled using the same parameters that led to the improved *E. histolytica* assembly. *E. dispar* and *E. invadens* assemblies reveal genomes of 20 and 40 Mb, respectively. Altogether, this project will shed light into the pathogenesis of this important human parasite.

**O24-2**

Pathema-Entamoeba: a clade specific bioinformatics resource center

T. M. Davidsen1, A. Garapathy1, E. Kelsey1, L. Brinkac1, S. Angiuoli1, W. Nelson1 and O. White1

1TIGR, a division of the JCVI, Bioinformatics, Rockville, USA

**OBJECTIVES** Pathema-Entamoeba (http://pathema.tigr.org) is a clade specific NIAID Bioinformatics Resource Center designed to support the *Entamoeba* biodefense and infectious disease research community. Pathema-Entamoeba targets the detailed curation of *E. histolytica* HM1:IMSS, but will also include all other available *Entamoeba* sequenced isolates.

**METHODS** An extensive subjective assessment has been performed to determine the types of research and information the *Entamoeba* community is currently conducting and gathering, as well as the types of tools and utilities those researchers are frequently utilizing. The data collected from this assessment is being used to design and implement a customized suite of sophisticated bioinformatics software, an extensive library of literature and manually curated data, and comparative analysis tools customized to retrieve, display, and compute results in a way best suited for the *Entamoeba* researcher.

**RESULTS** Curated datasets of *Entamoeba* proteins, protein families and metabolic pathways, as well as bioinformatics tools for comparative genomics analysis across various *Entamoeba* species are specifically integrated into Pathema-Entamoeba to assist in the identification of potential targets for vaccine development, therapeutics, and diagnostics. Additional utilities include a community annotation tool and community submissions of *Entamoeba* specific protocols and experimentally characterized genes. There are no license restrictions for user access to this data and all source code for Pathema-Entamoeba is managed under an open-source collaborative development paradigm. In addition, a training course is offered at TIGR to provide instruction on the use of this system and the underlying databases.

**CONCLUSION** Pathema-Entamoeba serves as a focal point for the biodefense research community by disseminating data resulting from *Entamoeba* genome sequencing projects and providing access to the results of multi-genome comparisons.

**O24-3**

Patterns of evolution in the unique tRNA gene arrays of the genus *Entamoeba*

B. Tswari1, I. K. M. Ali1, C. Scot1, M. A. Quail2, M. Berriman2, N. Hall2 and C. G. Clark2

1London School of Hygiene and Tropical Medicine, Infectious and Tropical Diseases, London, UK; 2The Sanger Institute, Cambridge, UK

**OBJECTIVES** Genome sequencing of *Entamoeba histolytica* HM1:IMSS revealed that almost all the tRNA genes are organised into tandem arrays that make up over 10% of the genome. The 25 distinct array units contain up to five tRNA genes each and some also encode the 5S RNA. Between adjacent genes in array units are complex short tandem repeats (STRs). To investigate the origins and evolution of this unique gene organisation, we have investigated the array unit structure in other isolates of *E. histolytica* and have undertaken a genome survey for four other species of *Entamoeba*: *E. dispar*, *E. moshkovskii*, *E. terrapinae* and *E. invadens*.

**METHODS** DNA samples from *E. histolytica* isolates for STR comparison were obtained during the recent development of a genotyping method based on STR variation. A majority of samples were from Bangladesh, with the others coming from 11 different countries. The four species genomes were surveyed by sequencing of plasmid inserts from small insert libraries (ca. 2.5 kb). At least
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O24-4 Evolutionary situation of glucosephosphate isomerase of Entamoeba histolytica in amitochondriate eukaryotes
E. Razigi1, A. Haghighi2, M. Rezaei3 and T. Nezaki4
1Iran University of Medical Sciences and Health Services, Medical Parasitology, Tehran, Iran, Islamic Republic of Iran; 2Shahed Beheshti University of Medical Sciences, Department of Parasitology and Mycology, Tehran, Iran, Islamic Republic of Iran; 3University of Medical Sciences, Department of Medical Parasitology and Mycology, School of Public Health and Institute of Public Health Research, Tehran, Iran, Islamic Republic of Iran; 4Gunma University Graduate School of Medicine, Department of Parasitology, Maebashi, Japan

OBJECTIVES The eukaryotic protozoan parasite Entamoeba histolytica lacks features of aerobic eukaryotic metabolism. Entamoeba histolytica has adapted to its microaerophilic environment, and therefore has to gain metabolic energy mainly by glycolysis, consequently in E. histolytica, an extended glycolysis pathway is present. Sequences of the Glucose-6-phosphate isomerase (One of the key enzymes in the glycolytic pathway) genes have been obtained for four representative strains of E. histolytica. Phylogenetic analyses of glucosephosphate isomerase show some aspects of the evolutionary situation of E. histolytica in amitochondriate eukaryotes.

METHODS Sequence alignments were constructed using the program CLUSTAL W version 1.83 with the BLOSUM matrix. Phylogenetic analysis was performed with the Neighbor-Joining method with Kimura’s correction using CLUSTAL W.

RESULTS Phylogenetic data showed that three E. histolytica GPI proteins found in four isolates formed a single well-separated clade, where they had the highest similarity to mammals (approximately 60% sequence identity) and formed a well separated clade in the subfamily I, including vertebrate and Escherichia coli. They have only 30% sequence identity to GPI from subfamily II and were distantly related with GPI from two Escherichia coli. They have only 30% sequence identity to GPI and have adapted to its microaerophilic environment, and therefore has to gain metabolic energy mainly by glycolysis, consequently in E. histolytica, an extended glycolysis pathway is present. Sequences of the Glucose-6-phosphate isomerase (One of the key enzymes in the glycolytic pathway) genes have been obtained for four representative strains of E. histolytica. Phylogenetic analyses of glucosephosphate isomerase show some aspects of the evolutionary situation of E. histolytica in amitochondriate eukaryotes.

CONCLUSION The origin of this unique gene organisation in the genus Entamoeba clearly predates the common ancestor of the species investigated to date and their function remains unclear.

O24-5 The Entamoeba histolytica genome: primary structure and expression of proteolytic enzymes
I. Bruchhaus1, M. Tillack1 and E. Tannich1
1Bernhard Nocht Institute for Tropical Medicine, Molecular Parasitology, Hamburg, Germany

A number of studies have shown that peptidases and in particular cysteine peptidases constitute major pathogenicity factors in Entamoeba histolytica. Recent studies have shown that a considerable number of genes coding for proteolytic enzymes are present within the E. histolytica genome and questions remain about the mode of expression of the various molecules. By homology search within the recently published amoeba genome, we identified a total of 86 E. histolytica genes coding for putative peptidases. These comprise (i) 50 cysteine peptidases of different families but most of which belong to the C1 papain superfamily, (ii) 22 different metallo peptidases from at least 11 different families, (iii) 10 serine peptidases belonging to three different families, and (iv) four aspartic peptidases of only one family. Using an oligonucleotide microarray, peptidase gene expression patterns of seven different E. histolytica isolates as well as of heat stressed cells were analysed. A total of 20 out of 79 amoeba peptidase genes analysed were found to be significantly expressed under standard axenic culture conditions whereas the remaining are not expressed or at very low levels only. In heat-stressed cells the expression of two and three peptidase genes, respectively, were either decreased or increased. Only minor differences were observed between the various isolates investigated, despite the fact that these isolates were originated from asymptomatic individuals or from patients with various forms of amoebic diseases. This work was supported by the Deutsche Forschungsgemeinschaft (BR1744/7-1).

Amoebiasis Genome and Regulation of Gene Expression

O24-6 Epigenetic transcriptional silencing of multiple genes in Entamoeba histolytica
R. Bracha1, Y. Nuchamowitz1, M. Perskiy2, N. Wender1 and D. Mirelman1
1Weizman Institute of Science, Biological Chemistry, Rehovot, Israel

OBJECTIVES (i) To induce transcriptional silencing to several amoeba virulence genes and to obtain a non-virulent sub-strain with a potential to serve as a live vaccine, (ii) to investigate the mechanism of epigenetic gene silencing in Entamoeba.

METHODS Based on our previous findings (ref 1) we constructed plasmids containing other genes directly ligated at their 5end, to the 473 bp fragment of the 5 upstream region of the amoebapore A (EhAP-A) gene. Plasmid BB-9 included the gene coding for a cysteine protease (EhCP-5) and the light subunit of the Gal-lectin (Ehlg1). The plasmid was transfected into the plasmid-less G3 trophozoites which were previously silenced in the expression of the EhAP-A gene. Other plasmid constructs contained genes that code for the light subunit 5 of the Gal-lectin (Ehlg5), the gene encoding the Arginine-Methyl transferase (EhPRMT1) and a plasmid with a gene coding for a Lim-domain protein (Ehlim). Transfections were done separately using the same principle. For as yet unknown reasons this procedure failed however, to silence a number of additional genes.

RESULTS Following the selection of transfected amoeba with G418, the trophozoites were analysed for the expression of the genes that were cloned in the plasmid construct. No expression...
was detected, both from the plasmid encoded gene copy nor from the genomic copy. Once established, silencing remained stable even after removal of the plasmid. Trophozoites devoid of the three virulence gene products (AP-A, CP-5 and Lgl1) were incapable of causing damage to mammalian cells and did not induce any liver lesions in hamsters. Their potential to serve as a live vaccine will be tested in other animal models. Trophozoites silenced in Ehlim and EhPRMT1 had only slight phenotype changes.

CONCLUSION The results demonstrate that our gene silencing procedure can be used to suppress, in trans, the expression of selected genes of choice in E. histolytica. Unfortunately concomitant suppression can only be done in the G3 silenced trophozoites. In previous work we reported that histone modifications appear to induce the epigenetic transcriptional silencing. Arginine methyl transferase (PRMT1) is one of the enzymes known to be involved in histone modifications in other organisms. Silencing of the EhPRMT1 gene did not result in the reactivation of the transcription of the EhAP-A gene. The effects of EhPRMT1 silencing on the expression of other genes is currently being investigated with the use of microarrays.

O24-7
Silencing of the amoebapore gene in Entamoeba histolytica does not require the T-rich region preceding the SINE element
M. Anbar1, R. Bracha1, Y. Nuchamowitz1 and D. Mirelman1
1Weizmann Institute of Science, Biological Chemistry, Rehovot, Israel

OBJECTIVES To understand the mechanism and the involvement of SINE elements in epigenetic gene silencing in Entamoeba histolytica.

METHODS An epigenetically modified strain of the virulent HM-1:IMSS was created by introducing a plasmid containing a 473 bp fragment of the 5’ flanking sequence of the amoebapore gene.

RESULTS Trophozoites of HM-1:IMSS strain were epigenetically silenced in three genes of the amoebapore family Ehap-a, Ehap-b and the Saposin-like coding gene (SAPLIP1). The plasmid that initiated the silencing contained in addition to the ap-a promoter a truncated SINE element preceded by a thymidine rich (T-rich) region. Silenced amoeba produce a single stranded small RNA of about 100–140 nt which hybridizes with a probe containing the 5′ region of the SINE element. These small ssRNAs accumulate and are retained in the nucleus. Sequencing of these ssRNAs revealed that they are not polyadenylated and are identical and probably derived from the SINE element adjacent to the amoebapore gene. Furthermore, this SINE element is over expressed in the silenced amoeba compared to the parental strain. Plasmids in which the T-rich was replaced or deleted were still able to silence the amoebapore gene but were incapable of promoting SINE transcription. We are currently investigating whether argonaute proteins are involved in this phenomenon.

CONCLUSION We hypothesize a model in which the plasmid containing the 5′ ap-a promoter region penetrates the amoeba nucleus. The presence of this episomal sequence homologous to the genomic region triggers a cascade in which the SINE element adjacent to the ap-a gene is both overexpressed and cleaved to small ssRNAs. These small ssRNAs recruit and guide silencing factors that locally modify the chromatin and cause the shut down, in-trans, of the expression of the ap-a gene.

O24-8
AP-A silencing and reconstitution in Entamoeba histolytica
H. Irmer1 and E. Tanisch1
1Bernhard-Nocht Institut, Hamburg, Germany

Transcriptional silencing by trans-inactivation can contribute to the regulation of gene expression in eukaryotic cells. In Entamoeba histolytica, trans-inactivation of the amoebapore-A gene (AP-A) was recently achieved by episomal transfection with the plasmid psAP1 (Bracha et al. 2003). Although the mechanism of AP-A trans-inactivation is largely unknown, previous studies have suggested that a partial short interspersed transposable element (SINE) present on the plasmid is required and that reconstitution of AP-A expression is not achieved by episomal transfection. By transfection of amoebae with various psAP1-deletion constructs, we have found that sequences of an E. histolytica tRNA array, located on psAP1 in close proximity to the AP-A upstream region and comprising the tRNA genes for glutamic acid and tyrosine were indispensable for AP-A silencing. In contrast to previous reports, SINE was not required for AP-A trans-inactivation. Moreover, AP-A expression was regained in silent cells by episomal transfection of the AP-A coding region under control of a heterologous E. histolytica promoter. This was achieved by introducing an E. histolytica -specific intron with putative enhancer properties between the promoter and the AP-A coding region. The reconstitution was dependent on the presence of the episomal plasmid as AP-A expression was reverted back to silence after the plasmid was lost.

O24-9
Identification of a diverse repertoire of endogenous small RNAs in the deep-branching eukaryote Entamoeba histolytica: potential roles in regulating gene expression
H. Zhang1 and U. Singh1
1Stanford University School of Medicine, Internal Medicine, Stanford, USA

OBJECTIVES Small interfering RNAs and microRNAs regulate gene expression in diverse processes including chromatin remodeling, maintenance of genome architecture and developmental control. Genes in the RNAi pathway have been identified in the Entamoeba genome and dsRNA and siRNA-based silencing have been reported in E. histolytica. However, no small RNAs have been identified in E. histolytica. Our goal is to identify small RNAs in E. histolytica and to dissect their effects in amebic biology.

METHODS We used a small RNA library cloning and sequencing approach to identify small RNAs in E. histolytica HM-1:IMSS trophozoites.

RESULTS We have identified a large repertoire of endogenous small RNAs in the eukaryotic parasite Entamoeba histolytica. Three groups of small RNAs were identified including those that map (i) antisense to the 3′ end of coding regions, (ii) only to non-coding regions, and (iii) to both coding and intergenic regions. Interestingly, we did not identify any small RNAs derived from retrotransposon elements, despite the abundance of retrotransposons in E. histolytica. Microarray expression data revealed that essentially all genes to which antisense small RNAs map were not expressed under trophozoite conditions, the parasite stage from which the small RNAs were cloned. However, a number of these genes were expressed in E. histolytica cysts or in E. histolytica strains with altered virulence potential. Additionally, a substantial number (66%) of small RNAs that map to intergenic regions have predicted stable
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O24-10
Characterization of an unusual epigenetic machinery in the protozoan parasite Entamoeba histolytica
T. Lavi1, E. Isakov1, H. Harony1, R. Siman-Tov1, C. Weber2, N. Guillen2 and S. Ankri1
1Faculty of Medicine, Rappaport Institute, TECHION, Molecular Microbiology, Haifa, Israel; 2Institut Pasteur, Unité de Biologie Cellulaire du Parasitisme, Paris, France

OBJECTIVES In most eukaryotes, cytosines are methylated by DNA methyltransferases belonging to the DNMT1 and DNMT3 families. Schematically, methylated cytosine recruits methylated CpG binding proteins that interact with histone deacetylase to alter the chromatin structure and lead to the silencing of gene expression. In the parasite Entamoeba histolytica, the formation of methylated cytosine is catalysed by an unexpected DNA methyltransferase from the DNMT2 family. Methylated targets include LINE retrotransposon, rDNA and S/MAR element which suggests that methylation plays a role in the control of repetitive elements. We recently identified a protein, EhMLBP, that binds with high affinity to methylated LINE retrotransposon and rDNA. EhMLBP lacks homology with methyl-CpG binding proteins and it shares a weak sequence identity with several prokaryotic histone H1. EhMLBP may serve as a sensor for methylated repetitive DNA. Our objectives are: To characterize proteins that interact with EhMLBP, To downregulate EhMLBP expression. To study the role of histone acetylation in the regulation of E.histolytica genes expression.

METHODS We used the two hybrid analysis to identify proteins that interact with EhMLBP. The downregulation of EhMLBP was performed by antisense technology and by silencing in G3 amoebae (a gift from D.Mirelman, Weizmann Institute, Israel). We examined the effect of Trichostatin A (TSA), a histone deacetylase inhibitor on E. histolytica virulence (cytoplasmic and hemolytic activity) and we applied DNA microarray technology to identify genes regulated by TSA.

RESULTS We identified by two hybrid analysis two hypothetical proteins that interact with EhMLBP. One of them shares a significant homology with a Saccharomyces cerevisiae protein that is involved in the establishment and maintenance of chromatin architecture. EhMLBP expression has been successfully downregulated (~50% inhibition) by antisense technology without apparent phenotype. In contrast, transfection of the G3 trophozoites with a plasmid in which the 473 bp 5' upstream Eh-a fragment was directly ligated to EhMLBP leads to the formation of dwarf trophozoites. Trophozoites grown with TSA for 48 h have higher cytoplasmic and hemolytic activities than untreated trophozoites. DNA microarray analysis shows that some virulence-related genes like the light lectin subunits (lgs) and Jacob that encodes a protein expressed during encystation, have their transcription upregulated by TSA.

CONCLUSION The unusual components of E.histolytica epigenetic machinery highlight this parasite as an informative model to study the evolution of epigenetics in eukaryotic cells.

O24-20
Molecular and functional characterization of EhPAK3, a p21 activated kinase from Entamoeba histolytica
S. Dutta, P. Sen, and S. Raha
Saha Institute of Nuclear Physics, Crystallography & Molecular Biology, Kolkata, India

OBJECTIVES p21-activated kinases (PAKs) are a family of serine/threonine kinases whose activity is regulated by the binding of the small Rho family GTPases as well as by RhoGTPase independent mechanisms. PAKs have wide-ranging functions which include cytoskeletal organisation, cell motility, cell proliferation and survival. We wanted to characterize a MAP4K/PAK in Entamoeba histolytica which may have a role in cell survival/motility.

METHODS We sequenced, cloned, expressed a PAK from the partial genome database of E. histolytica (EhPAK3). Antiserum to the recombinant protein was raised. The antiserum recognized a 53 kDa protein in the parasite cell lysate. Confocal microscopy and western blotting were used to identify the functions of the EhPAK3.

RESULTS EhPAK3 was distributed in the cytoplasm of unstimulated amoebae (a gift from D.Mirelman, Weizmann Institute, Israel). We performed antisense technology and by silencing in G3, the formation of EhPAK3 was downregulated in vivo. Invasion of amoebae was reduced by ~50% and in vitro invasion of G3 amoebae was reduced by ~70%. Invasion of G3 amoebae was reduced by ~50% and in vitro invasion of EhPAK3 was reduced by ~70%. Invasion of G3 amoebae was reduced by ~50% and in vitro invasion of EhPAK3 was reduced by ~70%.

CONCLUSION This is the first comprehensive characterization of a PAK protein from E. histolytica, which has constitutive activity and has demonstrated a strong involvement in receptor capping and motility.

O24-22
Characterization of a modulated putative transcription factor in Entamoeba histolytica
A. Hochreiter1, C. Gilbert1, S. Connell1, C. Evans2, Y. Zhang3, O. Crasta4, B. Sobral2, B. Mann2, and W. Petri Jr3
1University of Virginia, Department of Medicine, Division of Infectious Diseases, Charlottesville, USA; 2Virginia Bioinformatics Institute, Blacksburg, USA; 3University of Virginia, Department of Medicine, Division of Infectious Diseases and Department of Microbiology, Charlottesville, USA; 4University of Virginia, Department of Medicine, Division of Infectious Diseases and Department of Pathology, Charlottesville, USA

OBJECTIVES Entamoeba histolytica is the causative agent of amebiasis, and generally prevails in areas of poor sanitation. Invasion of E. histolytica trophozoites may depend on the expression of key transcriptional factors controlled by environmental cues. Previously, a microarray-mediated transcriptome analysis performed by Gilchrist et al. (2006) revealed that mRNAs from several putative DNA/RNA regulator factors are more abundant in the in vivo mouse colon than in the in vitro culture environment. One such putative factor, termed 3.mn0577, was studied further and is thought to be a high mobility group B (HMGB) protein. Proteins of the high-mobility group superfamily are divided into three families.
including HMGB proteins, which contain one or several copies of the HMG box DNA binding motif. It has been shown that some HMGB proteins regulate transcription by binding and binding DNA so as to assist nuclear proteins in enhancing or repressing transcription. We hypothesize that 3.m00577 regulates transcription in vivo and thus may play a role in virulence.

RESULTS To test our hypothesis we overexpressed 3.m00577 in HM1:IMSS amoeba using a plasmid containing an N-terminal c-myc tagged copy of the gene (3.m strain). Whole-genome microarray analysis was used to compare 3.m strain amoebic RNA to RNA from amoeba transfected with an empty vector. The data was normalized using the gcRMA program and statistical significance was determined by the use of LIMMA (Linear Models for Microarray Data). Overexpression of 3.m00577 resulted in 46 modulated transcripts, 26 of which had also been altered in vivo. Surprisingly, 69% of the genes show a reversed pattern of expression as compared to their pattern in vivo. Potential virulence factors including Lgl subunits, a cysteine protease, and an AIG1 protein were among those with modulated expression in both the 3.m strain and in vivo.

CONCLUSION In conclusion, our data support a role for 3.m00577 in regulation of E. histolytica genes within the intestinal environment because overexpression results in modulated expression of 5% of the genes known to change in vivo. Because 3.m00577 overexpression does not fully recapitulate the pattern of gene expression within the intestine, it is likely that other factors may also play a role in regulation. We are now in the process of testing the 3.m strain amoeba in a mouse model of infection, and we plan to further characterize this strain’s cytotoxic and invasive abilities as well as examine other putative RNA/DNA regulatory factors with modulated expression in vivo.

Amoebiasis Cell Biology and Signaling Pathways I

O24-11 Defining the epimodal ribosomal DNA promoter of Entamoeba histolytica

S. Pal Ghosh, G. Jingiari and S. Bhattacharya

1Jawaharlal Nehru University, School of Environmental Sciences, New Delhi, India

OBJECTIVES 1. To functionally map the core promoters of the E. histolytica rDNA I and II transcription units. 2. To identify the proteins in the Pol I transcription complex.

METHODS Deletions of the putative core promoter were generated and cloned upstream of a reporter sequence. E. histolytica trophozoites were transiently transfected with these constructs and transcription measured by quantitative RT-PCR. Gel shift assay and immuno-affinity purification was done to identify proteins binding to the core promoter.

RESULTS We had earlier identified the transcription start points (tsp) of the two transcription units- rDNA I and rDNA II in the E. histolytica rDNA episme, by primer extension. Although rDNA I and rDNA II differed completely in the sequences of their upstream intergenic spacers, there was remarkable sequence conservation in a 50-nt stretch upstream of the tsp in both units. The requirement of this and adjoining sequences in promoting transcription was measured by reporter transcript (luciferase) assay. Apart from 100 nt upstream of the tsp, sequences downstream of the tsp were also essential for transcription. A fragment from this region could bind to nuclear proteins, as revealed by electrophoretic mobility shift. Deletion analysis showed that protein binding was mediated by a region −32 to −73 of the tsp. Within this region the sequences at −55 to −68 were essential. Identification of the protein(s) binding to this region is being attempted. To identify the protein components of the Pol I transcription complex we have cloned and expressed the genes for some of the Pol I subunits and transcription factors, to raise Pol I-specific antibodies. Stable transfectants of E. histolytica expressing epitope-tagged Pol I subunits are also being generated. Using these reagents the affinity-purification of Pol I transcription complex and identification of the components by mass spectrometry will be achieved.

CONCLUSION A detailed analysis of the Pol I transcription machinery is being performed in a parasitic protozoan. Comparison with known model systems may reveal interesting evolutionary features.

O24-12 The Entamoeba histolytica EhADH protein is a novel member of ALIX family proteins

C. Barjuelos1, G. García-Rivera1, I. López1, M. Leobardo2, A. González-Robles2 and E. Orozco1

1CINVESTAV IPN, Experimental Pathology, Mexico, Mexico; 2Universidad Autónoma de la Ciudad de Méx and Escuela de Medicina IPN, Programa de Ciencias Genómicas, Mexico, Mexico

OBJECTIVES Here we studied the EhADH and the EhADH-Bro1 domain functions and its contribution to endosomal and phagocytic processes.

METHODS This study was performed after cloning of truncated proteins and transfection experiments, we also used confocal and electron microscopy to characterize the trophozoites. Virulence proteins of transfectant trophozoites were also measured. Finally, EhADH was located by cellular fractioning and Western blot assays.

RESULTS EhADH is one of the two proteins that form the Entamoeba histolytica EhCPADH complex involved in the parasite virulence. It is a member of the Alix family, composed by Bro1 domain-containing proteins that participates in a broad spectrum of cellular functions from apoptosis and signaling to multivesicular bodies formation. Here we studied the EhADH and the EhADH-Bro1 domain functions and its contribution to endosomal and phagocytic processes. Trophozoites mutants which overexpress the first 166 EhADH amino acids (ANeoBrO) were dominant negative for phagocytosis in comparison to the wild type trophozoites of ANeo population, but presented wild type adherence efficiency and cytolytic properties. Through confocal microscopy, EhADH was detected in the plasma membrane, phagosomes and cytoplasmic vacuoles of trophozoites, whereas the Bro1 exogenous protein accumulated in vesicles. Ultrastructural studies confirmed the presence of EhADH in plasma membrane and in numerous vesicles of different size forming multivesicular bodies participating in vesicle fusion processes. During phagocytosis, EhADH appeared around and inside RBC and in vesicles surrounded RBC. In contrast, the Bro1 overexpressed protein was not detected in the plasma membrane and it appeared concentrated in huge vesicles. During phagocytosis, Bro1 showed up in the proximity of RBC containing phagosomes, but rarely within them. By subcellular fractioning, endogenous EhADH was mainly found in soluble fractions whereas the overexpressed EhADH-Bro1 domain, also soluble, seems to be associated with different proteins that form complexes maybe involved in the multivesicular bodies pathway.

CONCLUSION Taken together, our findings suggest that EhADH may participates in membrane trafficking and protein sorting during endocytic processes in phagocytic and non-phagocytic trophozoites.
O24-13
Survival and death of *Entamoeba histolytica* under conditions of stress
A. Sarda1, S. Dutta1, D. Ray1 and S. Raha1
1Saha Institute of Nuclear Physics, Crystallography & Molecular Biology, Kolkata, India

OBJECTIVES We studied stress-induced survival and death of *Entamoeba histolytica* in connection with a key signaling protein – the *E. histolytica* MAP kinase (EhMAPK-GenBank accession number AY460178; Gene 346:41–50, 2005).

METHODS Cell viability (Trypan blue exclusion) and DNA fragmentation (TUNEL assay and DNA gel electrophoresis) were measured in *E. histolytica* after subjecting the parasite to different kinds of stresses such as heat, serum/glucose deprivation, and oxidative stress. Antiserum raised against the recombinant EhMAPK was used for the detection and immunoprecipitation of the EhMAPK. Commercially available phosphospecific antibody was used to detect phosphorylation status of EhMAPK.

RESULTS H2O2 (0.75–2.0) mM produced considerable DNA fragmentation detected by TUNEL assay and DNA gel electrophoresis. Heat stress or serum/glucose deprivation for a few hours produced no changes in these parameters. Phosphorylation and activation of EhMAPK upon serum/glucose deprivation, and heat stress were observed. Under these conditions loss of cell viability was not detected. During H2O2 stress loss of cell viability and DNA fragmentation were not accompanied by phosphorylation of EhMAPK.

CONCLUSION In conclusion, certain stress conditions in *E. histolytica* induced enhanced phosphorylation and increased activity of EhMAPK which did not result in loss of cell viability. However, stress condition such as H2O2 stress is accompanied by loss of cell viability but did not result in activation of EhMAPK. Therefore, EhMAPK may be associated with cell survival under stress in *E. histolytica*.

O24-14
Distribution of clathrin during electron dense granule secretion of *Entamoeba histolytica* trophozoites
M. d. L. Muñoz1 and R. Tovar1
1Centro de Investigacion y de Estudios Avanzados del IPN, Genetics and Molecular Biology, Mexico D. F., Mexico

It is well known that *in vitro* interaction of *Entamoeba histolytica* with collagen induces intracellular formation and release of electron-dense granules (EDG) and stimulation of collagenolytic activity. Moreover purified EDG contain collagenase activity, consequently we have postulated that EDG participates in tissue destruction during invasive amebiasis. Which make very important the study of this cellular process. Clathrin mediates cargo selection and vesicle fusion at the TGN, in the endosomal, lysosomal, and regulated secretory pathways as well as endocytosis at the plasma membrane of eukaryote cells. More recently it has been also demonstrated that reassembly of the Golgy apparatus required the presence of clathrin heavy chain. Because the importance of this cellular process and the role of clathrin in EDG secretion are unknown the main aim of our study was to determine the role of this protein in this cellular process by using specific antibodies and confocal microscope. Our results showed that clathrin participates in *E. histolytica* EDG secretion.

O24-15
Regulation of secretion of cysteine proteases by Rab11B small GTPase and proteinous inhibitors in *Entamoeba histolytica*
T. Nozaki1
1Gunma University Graduate School of Medicine, Department of Parasitology, Gunma, Japan

OBJECTIVES To understand the molecular basis of secretion of the major virulence factor cysteine proteases (CPs), we examined a role of vesicular trafficking mediated by Rab11B and also of protozoa-specific proteinous inhibitors, inhibitors of CP (ICPs), in the secretion and activation of CPs in *E. histolytica*.

METHODS *E. histolytica* transformants that overexpressed Rab11B, or one of two ICP isotypes (ICP1 or 2) were created. We examined changes in the secretion of CPs and *in vitro* destruction of CHO monolayers, caused by overexpression of these proteins.

RESULTS Overexpression of Rab11B caused 15-fold increase in the secreted cysteine protease activity concomitant with augmentation of CHO destruction. The oversecretion was not specific to CP species and insensitive to brefeldin A. Overexpression of Rab11B also enhanced exocytosis of the incorporated fluid-phase marker, and inhibited endocytosis, phagocytosis, and growth.

OVEREXPRESSION OF ICP1 OR ICP2, WHICH HAS OR DOES NOT HAVE THE AMINO-TERMINAL SIGNAL PEPTIDE, RESPECTIVELY, RESULTED IN THE SIGNIFICANT DECREASE IN BOTH INTRACELLULAR AND SCRETED CP ACTIVITY.

CONCLUSION These data indicate that both vesicular trafficking and the intrinsic inhibitors play pivotal roles in the regulation of CP secretion and therefore expression of virulence in this parasite.

O24-16
Endo-reduplication and irregular division lead to heterogeneity of genome content in *Entamoeba histolytica*
C. Mukherjee1, P. Ghosh Dastidar1, S. Majumder1 and A. Lohia1
1 Bose Institute, Biochemistry, Kolkata, India

OBJECTIVES To study the regulation of cell cycle progression in *Entamoeba histolytica* trophozoites.

METHODS Flow cytometry, scanning cytometry, confocal microscopy, bioinformatic analysis, gene expression, functional genomics, dsRNA knock-down in stable transformants, kinase activity.

RESULTS Fidelity and stability of the genome are crucial for the propagation of any species and therefore must be maintained during proliferation of the organism. The eukaryotic cell cycle follows strict control mechanisms that ensure faithful duplication and segregation of the genome. The progression of the *Entamoeba histolytica* cell division cycle shows important differences with this paradigm. Heterogeneity of genome content is commonly observed in axenic cultures of *E. histolytica*. Cells with multiple nuclei and nucleoli with heterogeneous genome contents suggest that regulatory mechanisms that ensure alternation of DNA synthesis and mitosis in typical eukaryotes are absent in this organism. Thus, several endo-reduplicative cycles of DNA synthesis occur without mitosis in *E. histolytica*. Our data also shows that, unlike other organisms that switch to a fixed number of endo-reduplicative cycles under special circumstances, *E. histolytica* does not execute a precise number of endo-reduplicative cycles. We show that irregularity in endo-reduplication and genome-partitioning events lead to heterogeneity in the genome content of *E. histolytica* trophozoites in their proliferative phase. Analysis of the genome sequence shows absence of sequence homologs of several eukaryotic cell cycle regulatory proteins. Additionally, functional analysis of sequence
homologs of CDKs and cyclins show important differences in their temporal activity during the amoeba cell cycle compared to the eukaryotic cell cycle. These findings suggest changes in the molecular mechanisms that regulate the cell cycle of *E. histolytica* compared to other eukaryotes.

CONCLUSION Proliferating cells, in general, ensure the constancy of their genome by various mechanisms during each cycle. In this context, *E. histolytica* is an exceptional case because it can tolerate variations in its genome content. Our studies form the basis for understanding if variations in genome content affect the pathogenicity of *E. histolytica*.

O24-17

**Insights in DNA repair and homologous recombination in Entamoeba histolytica: molecular characterization of the EhRAD51 recombinase**


*Universidad Autónoma de la Ciudad de México, Posgrado en Ciencias Genómicas, México, D.F., México; CINVESTAV-IPN, Departamento de Patología Experimental, México, D.F., México; Escuela Nacional de Medicina y Homeopatía-IPN, Programa Institucional de Biomedicina Molecular, México, D.F., México*

In *E. histolytica* molecular mechanisms engaged on homologous recombination and DNA repair remain still unexplored. To initiate the study of recombinational DNA repair, we surveyed the parasite genome and identified a core set of highly conserved predicted proteins involved in DNA double-strand breaks (DSBs) repair by homologous recombination. These proteins include homologous members of yeast RAD52 epistasis group encoded-genes (MRE1, RAD50, NBS1, RAD51, RAD51-C, RAD52, RAD54, RAD54B, and RAD59). The presence of these putative proteins suggests that *E. histolytica* is skilled to perform homologous recombination, in a similar way as described in other organisms. As a first experimental approach, we induced DSBs in *E. histolytica* by UV-C irradiation. DNA damage was evaluated by TUNEL assay. In yeast and human cells, histone H2AX becomes rapidly phosphorylated when DSBs are introduced into chromatin. We evaluated if the *E. histolytica* H2AX was phosphorylated after UV-C irradiation, using a human H2AX antibody. WB assays showed that EhH2AX becomes phosphorylated 10 min after UV treatment. These findings indicate that DSBs have been generated and early EhH2AX histone modification is occurring when cells trophozoites are exposed to UV-C, as it has been described in other systems. RT-PCR assays revealed that *E. histolytica* homologous RAD52 epistasis genes were differentially expressed at different times after UV irradiation. Then, we focused in the characterization of the putative recombinase EhRAD51 of *E. histolytica*. EhRAD51 has a similar architecture to the RECA/RAD51 family members and exhibits close phylogenetic relationships to eukaryotic RAD51 enzymes. Interestingly, EhRAD51 mRNA was expressed only after UV-C treatment. In addition, EhRAD51 transcript levels were highest during S phase of cell cycle, suggesting a role in the repair of replication forks generated during DNA synthesis. In WB assays, anti EhRAD51 antibodies did not detected the protein in basal conditions. In contrast, 30 min after UV irradiation anti-EhRAD51 antibodies detected a 41 kDa protein in cytoplasmic fraction, and a 46 kDa polypeptide in both nuclear and cytoplasmic fractions, that may possibly result from post-translational modifications of EhRAD51. By means of laser confocal microscopy EhRAD51 protein was detected in nuclear foci-like structures in trophozoites submitted to UV-C exposition. Finally, biochemical studies showed that purified EhRAD51 exhibits single and double stranded DNA binding, as well as DNA pairing and exchanging between homologous strands in vitro.

These findings allow us to conclude that EhRAD51 is a bona fide recombinase protein.

O24-21

**Entamoeba histolytica chemotaxis requires parasite adherence through the galactose/N-acetylgalactosamine lectin activity**

S. Blazquez, C. Weber, E. Labruyere and N. Guillen

*Institut Pasteur, Unité Biologie Cellulaire du Parasitisme and INSERM U786, Paris, France*

During invasive amoebiasis, there is an early production of pro-inflammatory compounds. Although parasite migration is an essential process in amoebiasis, how cells reach their final destination is not well understood. Secreted inflammatory molecules are known to have a migratory effect, but it remains unclear whether such molecules act as directional guidance cues or as motility regulators. However, in our precedent work, the critical role of cytoskeleton and adhesion though the Gal/GalNAc lectin in parasite motility has been demonstrated using animal models of experimental amoebiasis combined with living imaging [1]. The data will focus on the analysis of parasite cytoskeleton changes and signalling leading to directional motility, based on our recent studies showing that *E. histolytica* is attracted up a tumour necrosis factor (TNF) concentration gradient [2]. Chemotaxis-induced signalling was P3K-dependent and could lead to modifications in the polarisation of certain cytoskeleton-related proteins. To analyse the effect of TNF signalling on gene expression, we used the technique of microarray transcripts screening [3]. Interestingly, we found that the heavy subunit and the light subunit of the Gal/GalNAc lectin were upregulated during chemotaxis and a functional test indeed demonstrated the role of this protein complex in chemotaxis. Several genes coding proteins involved in cytoskeleton dynamics were also modulated during chemotaxis. Among them, an alpha-actinin-like protein appeared as an important candidate to link the Gal/GalNAc lectin to the cytoskeleton during chemotaxis signalling. These results have given us an insight on how *E. histolytica* changes its cytoskeleton dynamics during chemotaxis and discovery of a new role for the Gal/GalNAc lectin.

REFERENCES


O24-18

**A class of novel multiple EF-hand calcium binding proteins of Entamoeba histolytica**

N. Padhan, R. Jain, N. Sahoo, P. Chakraborty, N. Guillen, K. V. R. Chary, S. Gourish, S. Bhattacharya and A. Bhattacharya

*Jawaharlal Nehru University, School of Life Sciences, New Delhi, India; Jawaharlal Nehru University, School of Environmental Sciences, New Delhi, India; Institut Pasteur, Unité de Biologie Cellulaire du Parasitisme, Paris, France; Tata Institute of Fundamental Research, Department of Chemical Sciences, Mumbai, India*

Calcium plays a pivotal role in a large number of fundamental processes of eukaryotic systems. It is also reported to be involved
in the pathogenesis of amoebiasis by modulating the cytopathic properties of the parasite, *Entamoeba histolytica*. However, the mechanistic role of Ca²⁺ and various signaling molecules remains poorly understood. Since calcium signaling is perceived and transduced through calcium binding proteins (CaBP) it is important to characterize these proteins in order to understand mechanistic details of calcium signaling. Our genome wide in silico analysis revealed the presence of 27 CaBPs with multiple EF-hand calcium-binding domains. Majority of these proteins are likely to be calcium sensors with no apparent enzymatic activity or other functions. Since a large fraction of these genes are expressed in the trophozoites it is likely that these are not pseudogenes but likely to have some function. Among these proteins three (EhCaBP1-3) are currently being characterized at both structural and functional level. Structural analysis of the three CaBPs showed these proteins to be quite distinct from calmodulin, a four EF hand calcium sensing protein in spite of overall organizational similarity. The variation is with respect to both calcium binding domains as well as central linker region. The three CaBPs also differed in their structures, central linker region showing maximum variation. Functionally EhCaBP1 has been characterized in detail. It is involved in dynamic processes like movement, erythropagocytosis via direct interaction with cytoskeletal elements. Using multidimensional time-lapse microscopy the dynamics of EhCaBP1 in these processes has been studied in cell lines expressing GFP fused EhCaBP1. Our data suggest that the appearance and disappearance of EhCaBP1 occurs in less than a minute after the attachment of RBC. In actively motile cells EhCaBP1 has been shown to concentrate at the pseudopods during protrusion as compared to the retraction of the pseudopods. Though EhCaBP2 is very similar to EhCaBP1 in amino acid sequence (78% identity) our results suggest that these two genes are functionally different and are unlikely to be allelic copies. On the other hand EhCaBP3 was found to be present in the nucleus as well as cytoplasm unlike other two proteins. Though this protein showed high level of sequence similarity with calmodulin it was found to be functionally different. Our studies show that *E. histolytica* has a large intricate calcium signaling system different from many other organisms.

**O24-19**

**GFP expressed in Entamoeba histolytica is an adequate tool to monitor protein localization and cytoplasmic streaming in living amoebae**

J. Díaz, N. Villegas and I. Meza

1Centro de Investigación y de Estudios Avanzados-IPN, Biomedicina Molecular, México Distrito Federal, Mexico

OBJECTIVES To monitor localization and fate of GFP-labeled proteins during cell motility and erythropagocytosis in living amoebae. To register protein localization and cytoplasmic motility during erythropagocytosis.

METHODS A plasmid expressing GFP/EhRhoA1 fusion protein in trophozoites of *E. histolytica* HM-LIMSS, was generated. The expression plasmid, pKT3M-GFP (kindly provided by Dr. T. Nozaki), which contains the cysteine synthase promoter, the gene encoding GFP, and SmaI and XhoI restriction sites was used. The EhRhoA1 protein coding region without the stop codon was ligated in frame into SmaI-XhoI sites of pKT3M-GFP in order to produce pKT3M-GFP/EhRhoA1. Trophozoites were transfected by electroporation with pKT3M-GFP or pKT3M-GFP/EhRhoA1. Transfected cells were selected in the presence of 10 μg ml⁻¹ G418 and G418 concentration was gradually increased to 20 μg ml⁻¹ in cells that were subjected to analyses. Transfected amoebas expressing GFP or GFP/EhRhoA1 were plated onto 35 mm plastic culture dishes, for 30 min at 37°C, then, human red blood cells labeled in red with PKH were added with a ratio of 10 RBCs for 1 amoeba. A 2% agarose slice of 1 mm thickness prepared in PBS was carefully layered over amoebae. Time-lapse microscopy was performed with an Olympus inverted microscope equipped with fluorescence and images captured at 3 s intervals. Recorded by Image Pro software.

RESULTS Neither expression of GFP nor GFP/EhRhoA1 affected cell growth or morphology. We examined the behavior and subcellular localization of EhRhoA1 during cell motility. EhRhoA1 was localized to small vesicles corroborating previous reports using fixed cells (Franco Barraza et al., 2006) and with time these vesicles fused into larger compartments. Cytoplasmic streaming was analyzed in amoebae that were expressing GFP that remained restricted to the cytoplasm. Upon, interaction with erythrocytes, cytoplasmic streaming was induced, and the cytoplasmic content moved toward the nascent pseudopods surrounding the erythrocytes. Pinocytic cups were also generated and cytoplasmic protrusions were rich in GFP. Some erythrocytes were digested after 60 min while others were released by amoebae.

CONCLUSION Although EhRhoA1 subcellular localization was already reported, this is the first time that amoebic GTPase recruitment into the membrane of vesicles has been visualized as well as the fusion of these vesicles. The dynamic behavior of EhRhoA1-containing vesicles suggests its participation in cell contractility-dependent functions or in the reorganization of actin cytoskeleton. During erythropagocytosis, the use of fluorescent amoebae allowed tracing the cytoplasm movements without perturbing its normal functions following the fate of erythrocytes engulfed.

**TB Control and Epidemiology**

**O25-1**

**Improving access to prompt and effective malaria treatment: better drugs are not enough**

M. W. Hetzel, N. Itoba, C. Lengeler, B. Obrist, A. Dillip, S. Alba, A. Makeomba, C. Mshana, A. Schulze and H. Mshinda

1Swiss Tropical Institute, Public Health & Epidemiology, Basel, Switzerland; 2Ifakara Health Research and Development Centre, Ifakara, Tanzania, United Republic Of; 3Novartis Foundation for Sustainable Development, Basel, Switzerland

OBJECTIVES Appropriate treatment of malaria episodes, especially in young children, is a mainstay of the malaria control strategy in endemic countries. The Abuja target of reaching 60% of those suffering from malaria with effective treatment is still far from being reached in many sub-Saharan settings. Access to appropriate and timely treatment is hampered by inter-linked factors at different levels (household, health system, policy). We assessed the relative importance of a range of potential obstacles to effective malaria treatment within a comprehensive programme to improve access to malaria treatment in rural Tanzania (ACCESS Programme), with the aim to develop effective interventions.

METHODS Our studies were conducted in the area of a Demographic Surveillance Site (DSS) in south-western Tanzania. We used semi-quantitative cross-sectional community surveys to investigate disease perception and treatment seeking behaviour, complemented by quantitative and qualitative studies on drug availability and quality of care.

RESULTS We found that between October 2004 and May 2006, antimalarial stock-outs had occurred in 60% of all health
facilities surveyed and availability in the private retail sector had decreased following the introduction of sulphadoxine-pyrimethamine (SP) in 2001. Children attended health facilities more frequently than adults (78% vs. 53%) while still 30% of the antimalarials given to children and 41% taken by adults were bought from shops. Of 80 fever cases in children <5 years, 88% received a recommended antimalarial (SP, amodiaquine or quinine in 2004). A large proportion of treatments were wrongfully dosed. Taking into account the symptoms reported by the caretakers, only 7 (9%) children received the ‘correct treatment’. Descriptive and logistic regression analyses were used to identify factors significantly correlated with a positive treatment outcome (administration of correct dose of recommended first-line antimalarial within 24 h of onset of symptoms). Dependant variables comprised among others: demographic information, recognition of symptoms, perceived severity of the illness, distance, availability and quality of nearest care or treatment providers, and socio-economic status.

CONCLUSION A large number of factors can positively or negatively influence access to treatment and their importance may vary considerably between settings. To design effective interventions to improve access to malaria treatment it is crucial to know the relative importance of these factors in a given setting so that limited resources can be invested most effectively.

O25-2
Randomised controlled trial of intermittent preventive treatment in schoolchildren: impact on malaria, anaemia and school performance
S. E. Clarke1, M. Jukes2, B. Estambale3, K. Njag4, L. Khassakala5, C. Crudder6, J. Otiso7, B. McGione1, P. Magnusson1, B. Greenwood1 and S. Brooker1
1London School of Hygiene and Tropical Medicine, London, UK; 2Graduate School of Education, Harvard University, Cambridge, USA; 3University of Nairobi Institute for Tropical & Infectious Diseases, Nairobi, Kenya; 4Division of Malaria Control, Ministry of Health, Nairobi, Kenya; 5African Mental Health Foundation, Nairobi, Kenya; 6Institute for Health Research and Development, Copenhagen, Denmark

INTRODUCTION Although malaria risk is greatest in early childhood, significant numbers of school-aged children remain at risk from malaria morbidity and mortality. Asymptomatic infection contributes to anaemia and may reduce concentration and learning in the classroom. An effective intervention in infants and pregnant women, intermittent preventive treatment (IPT) could be a valuable addition to school health programmes and contribute towards meeting the millennium development goals in health and education.

OBJECTIVES A cluster-randomised placebo-controlled trial was undertaken in primary schools in Western Kenya to examine whether IPT can reduce parasitaemia and anaemia amongst schoolchildren and improve school performance.

METHODS Thirty primary schools in Bondo District, Western Kenya, an area of intense perennial transmission, were randomly selected to take part in a trial in 2005–2006. Study schools were randomly allocated to intervention or control arms. Pupils with individual informed parental consent were eligible for treatment in schoolage range 4–16 years). IPT was administered three times per year, given once per term, in intervention schools. Mass treatment with anthelmintics was given in all schools. Pre- and post-intervention surveys were carried out to establish haemoglobin level, prevalence and intensity of P. falciparum and intestinal helminth infections, and nutritional status. Class-based attention tests were conducted amongst children aged 10–14 years on the day prior to clinical assessment. During the intervention period, children in stds 6 and 7 were taught a common curriculum in social studies in all study schools and later tested to compare learning in the intervention and control arms.

RESULTS The prevalence of P. falciparum infection was markedly lower in schoolchildren receiving three rounds of IPT per year than those receiving placebo [per protocol analysis]: protective efficacy = 90% (95% CI 82–95%), P < 0.0001, whilst the prevalence of anaemia was halved: protective efficacy = 55% (95% CI 20–74%), P < 0.01. Similar findings were obtained in intention-to-treat analyses. Analysis of the results on attention in class and learning is yet to be completed and will also be reported.

CONCLUSION Intermittent preventive treatment can substantially reduce malaria parasitaemia and anaemia among older semi-immune children and holds promise as a new school-based strategy to reduce the impact of anaemia in school age children.

O25-3
Intermittent preventive treatment in infancy: a randomized, double-blind, and placebo-controlled trial in northern Ghana
1Charité - University Medicine Berlin, Institute of Tropical Medicine Berlin, Berlin, Germany; 2Northern Region Malaria Project (NORMAP), Tamale, Ghana; 3Ministry of Health, Regional Health Administration Bolgatanga, Bolgatanga, Ghana; 4School of Medicine and Health Sciences, Tamale, Ghana; 5University Medical Center Hamburg-Eppendorf, Department of Internal Medicine, Section for Tropical Medicine, Hamburg, Germany; 6Ministry of Health, Regional Health Administration Takoradi, Takoradi, Ghana; 7Charité - University Medicine Berlin, Institute of Biostatistics and Clinical Epidemiology, Berlin, Germany

OBJECTIVES Morbidity and mortality of malaria remain unacceptably high among young children in sub-Saharan Africa. Control of malaria is hampered by limited access to early diagnosis and effective treatment, currently the mainstay ofcontrol. In this context, intermittent preventive treatment in infancy (IPTi) alongside the established Expanded Programme on Immunization (EPI) might be a promising option.

METHODS A randomised, double-blind and placebo-controlled trial of IPTi with sulphadoxine-pyrimethamine (SP) was performed among 1200 children in the hyperendemic area of Tamale, northern Ghana. SP or placebo were given alongside routine EPI vaccinations at approximately 3, 9, and 15 months of age. Children were followed-up until 24 months of age, and malaria and anaemia were recorded by active and passive case detection.

RESULTS During the first year of life, IPTi reduced the incidence and risk of malaria as well as the risk of severe anaemia (haemoglobin < 7 g/dl) by approximately one third. The malaria-protective effect was pronounced for a period of one month after each treatment, and strongly reduced afterwards. For the second year of life, no substantial protective effect of IPTi could be observed, consequently halving the overall protective efficacy until the second birthday in reducing the incidences of malaria and severe anaemia. No effect of IPTi on mortality and no rebound of malaria after stopping the intervention was observed. Although generally well tolerated, one case of severe skin reaction followed SP application.

CONCLUSION IPTi reduces malaria morbidity and anaemia in infants in northern Ghana. Although this effect is substantial only in the first year of life, this simple intervention needs to be considered as one of the few available preventive measures against malaria in endemic regions.
O25-4
High dosages of chloroquine are used for the treatment of children with presumptive malaria in Guinea Bissau – can this explain the moderate and unchanged resistance in the country?

J. Ursing1, P.-E. Kofod2, P. Gil3, B. Schmidt4, M. Lebbad5 and L. Rombo2
1Karolinska Institutet, Department of Infectious Diseases, Stockholm, Sweden; 2Research Initiative of Health Services, Department of Paediatrics, Kolding, Denmark; 3Karolinska Institutet, Malaria Research Unit, Stockholm, Sweden; 4Smittskyddsinstitutet, Department of Parasitology, Mycology and Water, Stockholm, Sweden; 5Malarisjukhuset, Division of Thoracic Medicine and Infectious Diseases, Stockholm, Sweden

BACKGROUND Chloroquine resistant falciparum malaria was first detected in Guinea-Bissau in 1990. According to our repeated in vivo and in vitro tests (Ursing et al., Infect. Genet. Evol. in press) as well as our genetic data (Ursing et al., Am. J. Trop. Med. Hyg. in press), resistance is surprisingly moderate and unchanged. We have previously shown that the double dose of chloroquine has a 92% efficacy. We have also noted that high doses were commonly prescribed in Bissau.

OBJECTIVES To evaluate treatment recommendations, adherence to these, chloroquine concentrations and adverse events before, during and after therapy.

METHODS Children recommended chloroquine treatment for presumptive malaria were visited once daily whilst taking chloroquine and 1, 4 and 14 days after the end of therapy. Guardians were asked for concomitant medications and for possible adverse effects at each visit. Solicited questions were asked for fever, nausea, pruritus, vomiting, diarrhoea, cough, rapid breathing, convulsions, pallor and numbness. In addition, unsolicited questions were asked. Capillary blood drug concentrations were measured by HPLC.

RESULTS A total of 102 children with a mean weight of 9 kg and mean age of 16 months were included from the suburb of Bandim, population 90 000. The mean chloroquine dose prescribed was 7.4 mg/kg, 2.4 times a day for 4.8 days corresponding to a total of 80 mg/kg. Chloroquine intake as reported by guardians was 7.4 mg/kg per dose, 2.1 times a day for 4.7 days corresponding to a total of 78 mg/kg. The median (inter quartile range) concentration before therapy and at day 1, 4 and 14 after the end of treatment were 0 (0-205), 894 (383–1845), 626 (290–1630) and 204 (104–365) μmol/L. Adverse events were only detected during the first days of treatment; they were mild and not associated with high chloroquine concentrations. 39% of the children had concentrations that were equal to or higher than those found by us when the double dose was taken in a previous study.

CONCLUSION The used dosages were in line with statements given by other health workers in Bissau. High doses of chloroquine are prescribed and taken. We did not find any serious adverse events probably explained by the small amount of chloroquine taken at each single dose. Ginsburg (Acta Tropica 2005) suggests that chloroquine resistance comes at a cost of fitness and might be overcome with higher/repeated dosages. The treatment tradition in Bissau might explain the low prevalence of P. falciparum resistance.

Dihydroartemisinin-piperaquine rescue treatment of multidrug-resistant Plasmodium falciparum malaria in pregnancy: a preliminary report

M. Rijken1, M. Boel2, M. Barends1, N. Lindegardh3, R. McGready4 and F. Nosten1
1Shoklo Malaria Research Unit, Mae Sot, Thailand; 2Maidhol University, Faculty of Tropical Medicine, Bangkok, Thailand

Dihydroartemisinin-piperaquine is one of the most promising artemisinin-containing antimalarial combination therapies that has been developed. It is a co-formulation, effective against multidrug resistant falciparum malaria and a 3 day treatment course is relatively low-cost - approximately 1USD per adult treatment. Recent randomised clinical trials in e.g. Vietnam and Thailand indicate excellent tolerability and high cure rates. The drug is being used increasingly in South East Asia and is already part of national treatment recommendations in Cambodia and Vietnam. There is a paucity of published data on the use of the drug in pregnancy.

OBJECTIVES To assess the safety and efficacy of Dihydroartemisinin – piperaquine (DHA-PPQ) rescue treatment in pregnant women with multiple recrudescence falciparum malaria infections.

METHODS Between June 2006 and January 2007, we treated and prospectively followed 45 Karen pregnant women with multiple recrudescence P. falciparum infections, who were resistant to all other antimalarials, with dihydroartemisin – piperaquine (total dose: 6.4 mg DHA/kg, 51.2 PPQ/kg). All drug administrations were supervised and adverse experiences were recorded during admission, as routinely done in our clinics. Weekly malaria smear and day 7 druglevels were taken during follow up until delivery. Women were encouraged to deliver in the unit and babies were examined after birth and at 1 month of age.

RESULTS The treatment was well tolerated and we found no evidence of toxicity for the mothers and the fetus. We found clinical (day 63) cure rates of 76% (34/45), PCR genotyping data and druglevels will be presented during the congress.

CONCLUSION The combination of dihydroartemisinin-piperaquine may provide a much needed 3-day treatment for pregnant women exposed to multidrug-resistant P. falciparum malaria, although cure rates are low with the current treatment dose. DHA-PPQ blood drug levels might be suboptimal for pregnant women, as we showed modified pharmacokinetics of antimalarials in pregnancy before (McGready et al., Eur J Cln Pharm 2003;59(7):545–552, and McGready et al. Eur J Cln Pharm 2006 May;62(5):367–71). These preliminary observations strongly urge to proceed to pharmacokinetic studies of dihydroartemisinin – piperaquine in pregnancy before it is widely introduced as malaria treatment for pregnant women.

O25-6
Border malaria in Vietnam: a regional problem calling for a regional solution

H. Le1, Q. T. Nguyen1, A. Erhart2, K. T. Le1, U. D’Alessandro3 and M. Coosemans4
1National Institute of Malariology, Parasitology and Entomology (NIMPE), Epidemiology, Tu Liem District, Vietnam; 2Institute of Tropical Medicine (ITM), Antwerp, Parasitology, Antwerp, Belgium

Border malaria is one of the most difficult challenges faced by the Vietnamese Malaria Control Program. Indeed, malaria remains difficult to control in the eight central provinces bordering Laos and Cambodia (from Quang Binh to Binh Phuoc) and two Northern provinces bordering Laos (Lai Chau and Dien Bien). Annual incidence rates in these 10 provinces ranged from 3 to 18/1000 people in the last 2 years, the highest in a country having a mean incidence rate of about 1/1000/year. Border malaria is a complex problem due to multiple and interacting human, parasitological and entomological factors. Malaria control is difficult at international borders as these artificially divide an area where different approaches are implemented, despite the relative
homogenous environment on both sides of the border. The main characteristics of border areas between Vietnam, Laos and Cambodia, are their remoteness, the presence of ethnic minorities with poor education and socio-economic status and the difficult access to local health facilities. More importantly, these ethnic groups extend across the border and have strong family linkages on both sides, determining a substantial amount of unofficial population movements that maintain the parasite reservoir. The solution to the problem of border malaria is at regional level, since the problem has regional roots. Therefore, control interventions should be implemented and coordinated at regional level. In the framework of the Bilateral Cooperation project between ITM, Antwerp and NIMPE, Hanoi, the main human factors influencing malaria transmission will be identified with a socio-anthropological approach. Subsequently, control strategies will be defined and coordinated among the different countries. In a third stage, the cost-effectiveness of a cross-bordering control strategy will be evaluated and lessons learned communicated to countries with a similar problem.

Q25-7
Controlling malaria in pregnant women living in Boromo health district, Burkina Faso, through intermittent preventive treatment with sulfadoxine-pyrimethamine

S. Ges1, S. O. Coulibaly2 and U. D’Alessandro1
1Prince Leopold Institute of Tropical Medicine, Parasitology, Antwerp, Belgium; 2UFR Sciences de la Santé, Université de Ouagadougou, Ouaga- dougou, Burkina Faso

OBJECTIVES To evaluate the impact of intermittent preventive treatment with sulfadoxine-pyrimethamine (IPT/SP) on peripheral and placental parasitaemia, anaemia and birth weight when supported by a promotional campaign.

METHODS The impact of an educational campaign specifically targeted to pregnant women was tested in Boromo health district. Twelve health centres were randomly assigned to one of three interventions: IPT/SP with the community-based educational campaign, IPT/SP alone or weekly chloroquine (CQ).

Prim- and secundigravidae were identified and followed up until delivery (blood sample for parasitemia and PCV around 32 weeks of gestation and at delivery; and a placental smear). Newborns were weighed at birth or within the first week when home delivery. RESULTS Between March 2004 and February 2006, 6339 pregnant women were identified, among them 2766 primi- and secundigravidae. As IPT/SP started in April 2004, we present data of 2288 women who delivered after August 2004. Peripheral parasitaemia around 32 weeks was significantly higher in the CQ arm (29.9%) than in the IPT/SP arm without (19.6%) and with (20.1%) the promotion arm (P < 0.001). Similarly, peripheral and placental parasitaemia at delivery were also significantly higher in the CQ arm than in the other two groups (P < 0.001). Differences between IPT/SP arms with or without promotion were more pronounced for deliveries during the rainy season. Anaemia (PCV < 33%) was significantly more frequent in the CQ group compared to the IPT/SP groups both, before and at delivery. Mean birth weight did not differ significantly between study arms but the proportion of low birth weight babies (<2500 grams) was higher in the CQ arm than in any of the IPT/SP arms (22.4%, 18.6% and 16.2% respectively, P = 0.02); this was particularly pronounced during the dry season (22.2%, 14.7% and 14.5%, P = 0.01). CONCLUSION IPT/SP can efficiently reduce the burden of malaria in pregnant women if antenatal clinic attendance is good.

Schistosomiasis I: Clinical Aspects and Treatment

Q25-8
Evidence on metrifonate as useful drug for treating urinary schistosomiasis due to S. haematobium: a meta-analysis
A. Danso-Appiah1
1Liverpool School of Tropical Medicine, International Health Group, Liverpool, UK

OBJECTIVES To evaluate efficacy and safety of drugs for treating urinary schistosomiasis.

METHODS We searched all related databases, conference proceedings and reference lists of articles. We also contacted experts in schistosomiasis research for unpublished and ongoing trials. Dichotomous outcomes were combined using relative risk (RR) and weighted mean difference (WMD) for continuous data, both with 95% confidence intervals (CI).

RESULTS There is utter lack of standardization in schistosomiasis research. Four trials assessed metrifonate, one measuring failure at 1–3 months of follow up showed marked effect against placebo (RR 0.42), as were three trials measuring failure at 3–12 months (RR 0.45; n = 680). Egg reduction rate was over 90% and no serious side effects were recorded. Clearly a single 10 mg/kg dose of metrifonate was inferior to three doses of 10 mg/kg given fortnightly. Praziquantel given at the standard dose of 40 mg/kg clearly was effective in four trials at follow-up of 6–13 and 3–12 months (RR 0.34; n = 534 and RR 0.22; n = 433, respectively), and egg reduction rate of over 98% in six trials reporting this. No serious adverse events were recorded and mild events were few in two trials. Metrifonate (10 mg/kg × 3, given once every 4 months for one year) showed no obvious benefit with artesunate (RR 0.91 95% CI 0.73 to 1.14).

CONCLUSION Praziquantel and metrifonate are both effective and safe for the treatment of urinary schistosomiasis. The evidence is unequivocal and we suggest metrifonate be reinstated, perhaps as second-line treatment in urinary schistosomiasis endemic areas given the mounting pressure on praziquantel and the potential for resistance developing against this drug.

Q25-9
Effects of paeoniflorin on hepatic fibrosis of schistosomiasis japonica in vitro
J. Shen1, D. Chu1, Q. Luo1 and Q. Wu2
1Anhui Medical University, Key Laboratory of Gene Resource Utilization for Severe Diseases, Hefei, China; 2Anhui Medical University, Department of Pathology, Hefei, China

OBJECTIVES To find a drug of anti-fibrosis with high efficiency to prevent or reverse the hepatic fibrosis caused by schistosomiasis by testing paeoniflorin (C23H28O11, PAE), one of predominant fragments of paeony (Paeonia radix) root, a traditional medical herb in Asian countries, elicits anti-hepatic fibrosis in S. japonica.

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METHODS The peritoneal macrophages (PMs) and HSCs of mice were cultured and induction of fibrogenic cytokines from PMs driven by SEA(soluble eggs antigen) of S. japonicum was tested followed by measurement of peritoneal macrophages conditioned medium (PMCM)-stimulated HSCs proliferation and collagens secreted by HSCs.

RESULTS It was found that the SEA could stimulate TGFβ1 from PMs at transcription and protein levels, and PMCM driven by SEA could promote the proliferation of HSCs and secretion of Col I and III. PAE could inhibit the production of TGFβ1 from PMs in a concentration-dependent manner.

CONCLUSION PAE could be a potential and effective therapeutic medicine to hepatic fibrosis of schistosomiasis by down-regulates Smad3 protein expression and phosphorylation through TGFβ1 signaling.

O25-11
Antischistosomal efficacy of artesunate plus sulfamethoxypyrazine-pyrimethamine and artemether-lumefantrine administered as treatment for uncomplicated falciparum malaria

I. Adam1, O. Elhardello2, M. Elshadi3, D. K. Elmardi4 and H. Jansen5
1University of Khartoum, Obstetrics & Gynecology, Khartoum, Sudan; 2New Halfa Hospital, Surgery, New Halfa, Sudan; 3National Malaria Control Programme, Ministry of Health, Khartoum, Sudan; 4Dafra, Drugs, Belgium; 5Tropical Medicine and International Health

OBJECTIVES investigated whether treatment with artesunate plus sulfamethoxypyrazine-pyrimethamine (AS+SMP) and artemether-lumefantrine (AT-LU) for uncomplicated falciparum malaria in eastern Sudan have an impact on infections with Schistosoma mansoni.

METHODS Fourteen (their age range between 6–40 with the mean of 13.7 years) out of 306 patients who were entered into a clinical trial of antimalarial treatment were excreting S. mansoni eggs in their stool at presentation. Eleven of these patients received AS+SMP orally as a fixed combination either as one single tablet every 12 h (six patients) or one single tablet every 24 h (five patients) and the three received six doses of AT-LU.

RESULTS For all regimes, the overall cure rate was 100% at 28 days post treatment.

CONCLUSION Our findings indicate that AS+SMP and AT-LU, in addition to being very effective treatment for uncomplicated falciparum malaria, can also treat the S. mansoni effectively.
stool sample in 10 (59%). All patients were treated with praziquantel at standard dosage, in association with corticosteroids in 15/17 cases.

CONCLUSION The triad of high fever, cough and eosinophilia, with a history of exposure to freshwater in endemic areas, is classically considered sufficient to diagnose Katayama syndrome. In our series cough was present in 76% of cases, and a chronic cough in 59%. In particular, this was the only symptom in 24%. Katayama syndrome should be considered in the differential diagnosis of chronic cough in patients coming from endemic areas. Eosinophilia, the notion of a recent fever or ‘malaria’ and that of exposure are the clues to diagnosis. Once clinical suspicion is raised, the laboratory confirmation (both direct and indirect) can be obtained in virtually all patients if it is adequately performed.

O25-13
Uro-genital schistosomiasis in rural Madagascar: ultrasonographical findings
C. E. Ramaroko1, P. Leutscher2, B. S. Randrianasolo1, V. Ramaniraka1, R. Mligan1, N. O. Christensen1 and V. E. Ravaoalimalala1
1Institut Pasteur de Madagascar, Epidemiology Unit, Antananarivo, Madagascar; 2Institut Pasteur de Madagascar, Danish Bilharziasis Laboratory, Epidemiology Unit, Antananarivo, Madagascar; 3Danish Bilharziasis Laboratory, Charlottenlund, Denmark; 4Ministère de la santé, Institut Pasteur de Madagascar, Laboratoire Central de la Bilharziose, Antananarivo, Madagascar

BACKGROUND Ultrasonography is a useful tool to assess morbidity due to S. haematobium on upper and lower urinary tract. The Niamey protocol 1996 issued in 2000 is helpful to classify morbidity on only the urinary tract but lesions on genital organs (male and female) were not in taking account.

OBJECTIVES The study aims to identify ultrasonographical detectable pathology on the genital area and its correlation with others biological parameters. Design: Inhabitants male and female aged 15 to 49 years old from study village named SIRAMA and control village named MATAIPAKO were enrolled for this survey. Apart clinical questionnaire regarding S. haematobium infection and STI co-infection, biological and ultrasonographical parameters were obtained. Sonographical examination use Fukuda® machine connected with two probes: 3.5 Mhz convex probe for the urinary tract and 5 Mhz sectorial transducer for vaginal or perirectal examination (genital organ). Specific treatment of STI were given prior to praziquantel 40 mg/kg body weight. Follow-up were conducted 6 weeks later.

RESULTS A total of 330 inhabitants from SIRAMA (166 females and 164 males) and 297 inhabitants from MATAIPAKO (164 female and 133 males) took part to the study. Prevalence of S. haematobium infection is significantly high in SIRAMA vs. MATAIPAKO and was respectively 68.9% and 23.9% (P < 0.0001). Classification of lesion on upper and lower urinary tract detected by ultrasonography is clear. Urinary tract lesion was significantly high in SIRAMA vs. in MATAIPAKO (P < 10–6). Indirect parameters ultrasonographically detectable do exists such as hyperechogenic foci, calcification of the uterus, hydrosalpinx and cyste in female and hyperechogenic foci or calcification of the prostate and seminal vesicle, cyste of epididym and hydrocele in male. Male uro-genital pathology regress significantly at 6 weeks follow up figures being in urinary tract (P < 10–6) in prostate (P < 10–7) and seminal vesicle (10–3). Changes in vagina, cervix, salpinx or ovarian ecostructure were not significant with regards of urinary tract (P < 10–3).

CONCLUSION Classification of urogenital schistosomiasis is clear by ultrasound using Niamey protocol. Parameters in genitals tract need to be assessed by ultrasound and taking in account. Post therapeutical change were observed in male an female genital tract as observed in the urine bladder.

Immigrant Health in Europe
O25-15
Illegal women have many untreated health problems
M. Schoevers1, M. Muijsenbergh vd1 and T. Lagro-Jansen2
1Radboud University Nijmegen Medical Centre, General Practice/Women’s Studies Medical Sciences, Nijmegen, Netherlands

OBJECTIVES Physicians in the developed world are increasingly confronted with care seeking illegal immigrants. In most cases their access to health facilities is difficult because of financial and other barriers. Female illegal immigrants are even more vulnerable. Little is known about their health status and problems to access medical care. In this study our aim is to gain insight in the health problems and problems with access to health care of female illegal immigrants.

METHODS Semi-structured in depth interviews and a medical examination were conducted with 100 illegal immigrant women in five cities in the Netherlands. After the examination they received a medical record. For this qualitative study we aimed to achieve as much diversity amongst these women as possible.

RESULTS Preliminary results after 49 interviews: 47% of all women judged their own health as poor, 29% as moderate, 21% as good, 2% as very good and 2% as excellent. Most commonly mentioned health problems were headache (74%), anxiety (88%) sleeping disorders (84%), fatigue (82%) and dental problems (59%). Psychological complaints were rarely treated; 47% were victims of sexual violence; only 12% had been tested for sexually transmitted diseases. Female illegal immigrants face many problems in access to health facilities. Many women were afraid to visit a doctor or hospital or were unaware of their right to health care. Most reported problems concerned secondary care.

CONCLUSION Undocumented women have many health problems that may require treatment. This may be influenced by their limited access to health facilities. Policy makers should include this in their health strategies. Many problems, such as untreated psychiatric and gynaecological problems (e.g. STDs) can be very harmful to these women. However, this may have financial implications and consequences for public health policy as well.

O25-16
Patient-held records for female illegal immigrants
M. Schoevers1, M. Muijsenbergh vd1 and T. Lagro-Jansen2
1Radboud University Nijmegen Medical Centre, General Practice/Women’s Studies Medical Sciences, Nijmegen, Netherlands

OBJECTIVES General practitioners (GPs) consider the care for illegal immigrant women as burdensome, partly because of lack of medical record information. Availability of medical record information might improve the care for illegal women. Therefore, we decided to investigate the potential benefit of a patient-held record (PHR) for illegal women. We were interested if undocumented women keep and use their PHR and in their experiences with the PHR and GPs.

METHODS Semi-structured interviews and questionnaires were conducted with 100 illegal immigrant women in five cities in the Netherlands to obtain insight in their problems and experiences with Dutch medical care. All women received a PHR based upon medical examination. For this qualitative study we aimed to achieve as much diversity amongst these women as possible. After
3–6 months semi-structured interviews were held to evaluate the use of the PHR. Because these results were disappointing we will evaluate the experiences of the women through focus group discussions as well. Three groups of 6–8 women, led by an independent interviewer, will participate in these discussions.

RESULTS (Preliminary results) Surprisingly most women did not use the PHR. However, reasons why they did not use the PHR were hardly given in the individual interviews. In the first focus group discussion most women were more explicit in their views and opinions than in the individual interviews. Most common reasons for not using the PHR were ‘forgotten’ and ‘do not want to bother the doctor’. Surprisingly most women in the first focus group preferred a male GP, even for gynaecological problems.

CONCLUSION PHRs are not widely used by undocumented women. Reasons for not using the PHR are not clearly given in individual interviews. Focus group discussions might be a more efficient way to explore opinions and views of this patient group.

Sexual and Reproductive Health

O25-17
Sexuality and vaginal practice in Thai women
C. Wacharasin1 and W. Imam1
1Burapha University, Faculty of Nursing, Muang, Thailand; 2Mahidol University, The Institute for Population and Social Research, Bangkok, Thailand

OBJECTIVES This qualitative study is aimed to explore various forms of vaginal practices related to sexual health and to understand the motivations, intent, perceptions, experiences, and impacts of vaginal practices in Thai women.

METHODS Information was obtained from in-depth interviews and focus group discussions with men and women from various backgrounds in urban areas at Bangkok and rural areas at Chonburi province. Snow ball technique and theoretical sample were used to select studied participants. Twenty-three key informant interviews, 78 individual interviews and 11 focus group discussions were conducted. Content analysis was used to analyze data.

RESULTS The findings revealed that there were two purposes of vaginal practices in these participants: (1) Sexual health: cleaning externally with water or lukewarm water, soap, feminine hygiene solution and toothpaste; douching inside vagina with gel and alum solution; decorating genital hair; tightening vagina by practicing Kegel exercises, traditional medicine. (2) Sexuality: sex stimulants by friction condom, penile rings, small peas/rounded stones/substances inside the condoms; surgical operation. In addition, the most common form of vaginal practices, particularly among those with high socio-economic status, is the use of feminine hygiene solutions for hygienic cleansing. Women in rural areas and poorer city women also use a variety of traditional preparations to please their sexual partner and to treat internal genitalia infections. No severe consequences of using vaginal practices were found.

CONCLUSION Participants used vaginal practices as the important methods to keep marital relationship. Cleanliness, dryness and tightening of the vagina help women feel confident, and to negotiate and sexually seduce male partners. This study suggests that vaginal practices are a key problematic element of Thai women’s reproductive and sexual health. Knowledge of these practices ranges from products and practices passed on through generations to innovations developed and distributed through a modern market economy. Further study needs to concentrate on how health personnel, policy makers and women’s health advocates perceive vaginal practices and interpret the place of such behavior in the context of risk and health.

O25-18
Sexuality counselling: findings of a systematic review
A. van der Kwaak1, R. Ploem1, K. de Koning1, R. Dickson2 and A. Martin-Hibber3
1KIT, Amsterdam, Netherlands; 2Liverpool University, Liverpool, UK; 3WHO, Geneva, Switzerland

BACKGROUND A systematic review into sexuality counselling was carried out by KIT/WHO in 2005–2006. The results of the review informed the development of a conceptual framework that is being used to assess quality of counselling and factors influencing quality in sexuality counselling.

OBJECTIVES To present the findings of a systematic review on sexuality counselling and discuss implications for health interventions.

METHOD From 534 reviewed articles and abstracts 27 studies, presenting original findings in developing countries were included in the systematic review.

RESULTS The study shows that there is little evidence base for determining the effectiveness of sexuality counselling. Outcomes of the studies that investigated the effects of sexual health counselling (although the description of what exactly was meant by this was lacking) show health benefits and change of behaviour in clients and providers. Training that includes value transformation, supervision, support to prevent burn out were identified as conditions for the provision of sexuality counselling. Non-judgmental attitudes and client centered language, age and sex of providers, confidentiality and privacy, duration and referral options influence the perceived quality of sexuality counselling. Some evidence is emerging that couple counseling is more effective than counselling of women only, and different needs and expectations of the counselling by men and women and differences in behaviour of providers towards women and men.

CONCLUSIONS This systematic literature review has identified that the integration of sexuality into SRH and HIV/AIDS counselling is an important health care issue that currently is limited by a lack of consistent definition of terms and good-quality research. There is a need for: (1) the creation of a more unified understanding as to what the integration of sexuality into SRH and HIV/AIDS counselling interventions entails; (2) good-quality empirical research on the integration of sexuality into SRH and HIV/AIDS counselling; and (3) continued support for evaluating the implementation of sexuality counselling into SRH and HIV/AIDS counselling interventions into existing services.

O25-19
Successful safe motherhood practices in India: a study
N. Sultana1 and V. R. Kalikin2
1Society for Social Development, Non-Governmental Organisation, Tirupati, India; 2Sri Venkateswara University, Anthropology, Tirupati, India

BACKGROUND The focus of this paper is on successful provision of maternal health services to women in a rural community in Andhra Pradesh, India. Before the commencement of the safe motherhood programme, most of the deliveries (80%) used to take place at home. Only a few (25%) make use of hospital facilities during pregnancy and delivery. Severe malnutrition was found among pregnant and lactating mothers. The incidence of STIs was very high. Adoption of Family Planning was very low. Hence, to bring down maternal mortality and morbidity and improve their overall health status, this programme was designed and implemented in this community in 2003.

OBJECTIVES 1. To bring down maternal mortality and associated morbidity; 2. To improve the overall health status of women.
METHODS AND MATERIALS A cluster of 136 villages with a population of about 325,000 was selected for the programme. The programme was carried out with the help of trained social workers and paramedics at the village level. At the clinic/hospital, paramedics, social workers and doctors provided different health and supportive services to the rural people.

PROGRAMME. INTERVENTIONS Community education and mobilization; information, education and communication programmes; newborn and infant child health services; enactment of dramas; folk media; distribution of literature on STIs/HIV/AIDS, maternal health, nutrition, family planning/condoms; group discussions; meetings; one-to-one meetings; involvement of fathers in maternal health programmes; pre-natal, natal and post-natal care at the doorstep and at the hospital; family planning services; applied nutrition programme for pregnant and lactating mothers; immunization programme for pregnant women; voluntary counseling and testing of HIV; HIV-pre- and post-test counselling; treatment for STIs and common ailments; condom promotion and free condom distribution; medical termination of pregnancy (in certain cases).

RESULTS The number of people using maternal health services has been on the increase year after year. Adoption of family planning, the number of persons taking treatment for STIs, number of persons seeking abortion, number of persons attended for voluntary counseling and testing of HIV have been rising annually. The incidence of HIV and STI and the maternal mortality rate are declining fast. The couple protection rate and institutional deliveries are also increasing rapidly. Many more achievements of the programme have been described with figures from 2003 to 2006 in comparison with national and state figures in the full-length paper. It seems certain that the Millennium Development Goals pertaining to maternal health can be achieved by 2015.

CONCLUSIONS The programme interventions are worth replicating in all developing countries of the world where maternal morbidity and mortality are high; they would help to achieve the Millennium Development Goals by 2015.

TB Control and Epidemiology

O25-20 Comparison of symptoms and treatment outcomes between actively and passively-detected tuberculosis cases

S. Den Boon, S. Verve, C. Lombard, E. Bateman, E. Irusen, D. Enarson, M. Borgdorff and N. Beyers

1KNCV Tuberculosis Foundation, The Hague, Netherlands; 2Medical Research Council, Biostatistics Unit, Cape Town, South Africa; 3University of Cape Town, Department of Medicine, Cape Town, South Africa; 4Stellenbosch University, Department of Internal Medicine, Cape Town, South Africa; 5International Union Against Tuberculosis and Lung Disease, Paris, France; 6Academic Medical Centre, CINIMA, Amsterdam, Netherlands; 7Stellenbosch University, Desmond Tutu TB Centre, Cape Town, South Africa

OBJECTIVES To compare symptoms and treatment outcome in tuberculosis (TB) cases who were actively detected during a community survey with cases who were passively detected in the routine TB program.

METHODS In a community survey in Cape Town, South Africa, we detected 27 bacteriologically positive TB cases who had not started anti-tuberculosis treatment. They all completed a questionnaire about their symptoms. In 2004/2005 the National Tuberculosis Program (NTP) passively detected 473 TB cases for whom we obtained information on treatment outcome from the clinical register. Of those passively-detected TB cases completed the questionnaire. Actively and passively detected cases were compared with logistic regression analysis.

RESULTS Seven of 27 (26%) actively detected TB cases did not start treatment within 2 months and were considered initial defaulters. For those actively detected cases who did start treatment, the treatment success rates were not different from passively-detected TB cases (both 80%) (OR: 1.01, 95% CI: 0.33–3.09). Passively detected cases reported the presence of the symptoms cough (OR: 3.72, 95% CI: 1.47–9.39), haemoptysis (OR: 3.20, 95% CI: 1.03–9.93), night sweats (OR: 3.35, 95% CI: 1.40–7.99), fever (OR: 4.28, 95% CI: 1.21–15.14), and weight loss (OR: 11.14, 95% CI: 4.17–29.74) more often than those detected actively. In the multiple logistic regression analysis only weight loss remained significant.

CONCLUSION This study shows that a community survey is able to detect additional TB cases although these cases are less symptomatic and probably have less severe disease. Although the TB cases detected by the community survey had similar treatment outcomes as TB cases detected in the TB program, they experienced a high initial default rate.

O25-21 Improving the national TB control program in Indonesia: explorations with a health systems model

R. A. Ahmad, Y. Mahendra Kanta and S. J. de Vlas

1Erasmus MC, University Medical Center, Public Health, Jogyakarta, Indonesia; 2Institute of Tropical Medicine, Antwerp, Public Health, Jogyakarta, Indonesia; 3Erasmus MC, University Medical Center, Public Health, Rotterdam, Netherlands

OBJECTIVES Indonesian TB control is mainly based on passive case-finding, which relies on TB patient’s care seeking behavior and their decision to use DOTS facilities. Different options for increasing use of DOTS facilities have been suggested. However, selecting the appropriate strategy requires effectiveness justification. Through explorations with a mathematical model describing the movement through the TB care system, we aim to compare the impact of three intervention strategies: health education, involving hospitals in DOTS strategy, and involving private practitioners to refer TB suspect patients to DOTS facilities.

METHODS We have developed a model of TB patient care seeking behavior. The model consists of compartments that represent logical steps of movement through the health system, including patient, and health system delays. We take the model of TB natural history into account. Output of the model are TB-related death, spontaneous recovery, and treatment outcome (i.e. full or partial cured) We estimated the quantification of TB care seeking practices using a two rounds Delphi survey, with five Indonesian TB experts. The quantification represents TB patients and health system situation in Jogyakarta province in Java, Indonesia, which consists of urban and rural districts. Effectiveness of each intervention was assumed on the basis of existing studies or published articles.

RESULTS The expert panel suggested that 10% of TB patients would never do anything, 50% of those who seek care will go to the public sector (DOTS), 30% to the private sector (non-DOTS), and the remaining 20% will visit the alternative sector. The public sector was assumed to have better diagnostic quality, faster diagnostic process, better treatment outcome, and less partial cure, compared to the private sector. The experts suggested that delay between onset of symptom to treatment initiation is around 4–5 weeks, while national surveys found 11 weeks. Thus, the experts’ opinion needs to be adjusted for underestimation. To this end, we have selected three scenarios,
Abstracts of the 5th European Congress on Tropical Medicine and International Health

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METHODS Prospective study of confirmed cases of pulmonary tuberculosis and their contact persons as identified through the public health authorities in BW from 01.01.2003 to 31.12.2005. Data were obtained from routine data collected within the framework of the revised law for protection from infectious diseases (IfSG), through structured questionnaires addressing social interactions between the indigenous population and migrants, and from molecular typing (DNA fingerprints).

RESULTS A total of 742 cases of pulmonary tuberculosis were enrolled in the study, representing 57.8% of all cases diagnosed in BW over the study period. Epidemiological contact tracing information was collected for 671 contacts. The majority of cases (55.5%) had German nationality whilst only 40.4% were actually born in Germany. Of the study participants, 132 (17%) belonged to 48 genetic clusters, with cluster sizes ranging from 2–8 persons. Conventional epidemiological methods only helped finding/confirming 25% of the clustered cases. For the probability of cases among mixed clusters to be caused by foreign-born cases we obtained preliminary estimates of 19.2%, which are similar to the findings from studies carried out in The Netherlands and Spain. We observed a trend to mixed clusters with increasing time spent by migrants with the receiving low-prevalence population. Detailed analysis of clusters, their spatial distribution and the social interactions within clusters will be presented.

CONCLUSION Combining epidemiological, molecular and social interaction data prospectively over time gives important insights into the transmission dynamics of tuberculosis between high and low prevalence populations. This will help to improve tuberculosis control with a more targeted approach.

O25-25
Tuberculosis in immigrants: a case control study in a university general hospital in Spain
R. M. Góñi1, D. Torruella1, S. Eznol1, C. López-Rodriguez1 and J. Portilla1
1University General Hospital of Alicante, Internal Medicine and Infectious Diseases Department, Alicante, Spain

OBJECTIVES To describe epidemiologic and clinical characteristics of tuberculosis in immigrants in a reference hospital. Determine if there are differences between the immigrants and local population in clinical management and treatment of tuberculosis.

METHODS Observational and retrospective study. Case-control design. Subjects: patients diagnosed of tuberculosis between January 2002 and December 2006 at the University General Hospital in Alicante (Spain). Data source: clinical documentation (CMBD), microbiologic and epidemiologic surveillance database and patients clinical charts. Descriptive and bivariate analysis were performed. Epidemiological and clinical variables were compared between immigrants (cases) and local population (controls). The Chi square test or Fisher test was used to compare qualitative variables and the T Student test or U Mann-Whitney for quantitative variables.

RESULTS We analysed 120 tuberculosis cases in this period, 67 were immigrants (56%); 80% were men; participants’s age was 35.4 ± 12.9 years (mean ± SD). 17% showed HIV coinfection; of these, 70% had a CD4 count <200/mm³. 71% had pulmonary tuberculosis and a microbiological or histopathologic diagnosis was obtained in 93% of cases. Cure rate: 76%; adherence rate: 85%. Immigrants’ origin: 42% Latin America, 24% northern Africa, 18% sub-Saharan Africa, 15% eastern Europe. Mean time of stay in Spain: 47.7 ± 51.6 months. Immigrants were more younger than local patients (mean age: 31.9 vs. 39.7 years, P = 0.001). Time from initial symptoms to diagnosis was 32 days in immigrants and 18 days in local patients (P = 0.02) and time from diagnosis to treatment start was 32 days in immigrants and 25 days in local patients (P = 0.06). Frequency of treatment with more than three tuberculostatic drugs was 52.2% in immigrants vs. 32.1% in natives (P = 0.027; RR: 2.32, 95% CI 1.09–4.90). No differences were obtained in sex, HIV coinfected, tuberculosis location, cure rate and adherence.

CONCLUSION Immigrant patients with tuberculosis were younger than local patients. There is a delay in the diagnosis and treatment of tuberculosis in immigrants, which may have repercussions for public health.

Health Systems Research

O25-26
Lessons for health care reform from the less developed world: the case of the Philippines
K. Obermann1, M. Jowett2, M. Mercado3 and J. Taleon1
1University of Applied Sciences of the German Red Cross, Economics and Ethics in Health, Goettingen, Germany; 2GTZ Philippines, Manila, Philippines; 3PhilHealth, Manila, Philippines; 4Department of Health, Manila, Philippines

International technical and financial cooperation for health sector reform is usually a one-way street: concepts, tools and experiences are transferred from more to less developed countries. Seldom, if ever, are experiences from less developed countries used to inform discussions on reforms in the developed world. There is, however, a case to be made for considering experiences in less developed countries. We report from the Philippines, a country with high population growth, slow economic development, a still immature democracy and alleged large-scale corruption, which has embarked on a long-term path of health care and health financing reforms. Based on our experience between 2002 and 2005, we have identified five crucial factors for achieving progress on reforms in a challenging political environment: (i) strive for local solutions, (ii) work towards pragmatic and practical solutions, (iii) make use of available technology, (iv) form a ‘coalition of the willing’ and (v) work on the margins with your ethical goals and principles in mind. We present case studies and possible application in more advanced health care systems. Some reflection on these crucial factors could stimulate and inform the debate on how health care reforms are implemented in developed countries.

O25-27
Evaluation of the health sector-wide approach (SWAp) at district level, pilot case study: Kwimba district, Tanzania
V. Zinzen1, D. Pongricon2, C. Paul2 and A. Robert1
1Université Catholique de Louvain, Ecole de Santé Publique, Bruxelles, Belgium; 2Université de Liège, Santé Publique, Liège, Belgium

OBJECTIVES To develop and test an evaluation framework for assessing whether the health SWAp in Tanzania has improved health service delivery at district level in terms of quality, equity, efficiency and effectiveness.

METHODS Information was collected from literature review, local health reports, observation, focus group discussions, semi-structured and in-depth interviews. The pilot study was conducted in June 2006 in Kwimba district. It covered 10 villages, eight dispensaries, two health centres, the district hospital, district management team members (11), health workers (64), patients (117) and community representatives (189). The sampling approach was based on targeted variables, interviewed people and required information. Elements to evaluate were extracted from the Tanzanian Health Strategic Plan. Quantitative methods (Prevalence Ratio with 95% CI, χ², Fisher Exact, Mann-Whitney or
Kruskal-Wallis tests) to ensure statistical significance and qualitative methods to investigate for possible causal effects were used.

**RESULTS**

Improved quality of service delivery was perceived in all interviewed groups. As compared to a few years ago, people reported improvements in drugs and supplies availability, in attitude of staff and in infrastructures. Financial accessibility was no longer a problem in that district but community participation, referral system and working conditions demonstrated slow improvements. Major health indicators did not significantly change. The reasons mentioned to explain the results were mainly a mix of the new policies such as decentralisation of planning and decision-making, community sensitisation, increasing of funds, staff trainings and recruitment of new health workers.

**CONCLUSION**

This pilot study allowed establishing, testing and correcting tools. The improved framework will be used in four other districts to evaluate more widely the results of a SWAp at district level for the health sector.

**O25-28**

Health sector policy and health systems development in Kenya — a review of its evolution

T. Gakuru, L. Bijlmaerkers, A. Abebe Abadachew and J. Chaboe

**OBJECTIVES**

To analyse the achievements, success factors and constraints in health sector development in Kenya.

**METHODS**

Key informant interviews, desk review of available policy documents and programme evaluations.

**RESULTS**

A common intervention framework for all actors that have a stake in the Kenyan health sector has been agreed upon for a five-year period (2005–2010) with a set of agreed goals and targets. From a rather top-down approach through which health districts used to derive their annual plans and budgets from this national framework, the sector is now moving fast towards a more bottom-up way of planning, whereby districts set their own targets and elaborate comprehensive annual plans that take into account all resources, irrespective of who provides them. The key factors that have enabled the MOH to assume its stewardship role are: (1) the emphasis on performance and accountability, (2) the innovative definition of the Kenya Essential Package for Health (KEPH), based on a lifecycle approach, and (3) the elaboration of a set of health sector support systems that were being strengthened at the national level so as to improve service delivery and respond to clients’ expectations. As a result, six of the main donor agencies are in the process of aligning their support to the jointly agreed priorities and targets for the sector. This should greatly reduce the transaction costs of external aid. Annual performance reviews have been instituted as a mechanism to assess progress in implementing operational plans at all levels and the outcomes of these reviews will determine whether in the future more health can be achieved for the money that is available.

**CONCLUSION**

The main constraints that affect performance at all levels of the health system is the persistence of centralised decision making (especially with regard to staff deployment, human resource management) and the late arrival of funds at the district level. A great challenge that remains is the reorganisation of the way national programmes tend to do their business, so as to better align their resources (technical and financial) with the capacity and requirements of health districts. Another challenge lies in promoting civil society and NGOs, including faith-based organisations, to take their part in strengthening health systems and providing health services. This will require that they enter into formal agreements with the Government/MOH that stipulate what performance is expected from them in return for a certain share of the national resource envelope.

**O25-29**

Operations research on HIV/AIDS, tuberculosis and malaria control in global fund-supported programs

E. L. Korenromp, R. Komatsu, S. Xuereb, B.-A. Plowman, D. Low-Beer and B. S. Schwartzlander

**OBJECTIVES**

To promote the inclusion of Operations Research (OR) in Global Fund grants, to improve implementation and tackle obstacles in the scale-up of control services for HIV/AIDS, tuberculosis and malaria.

**METHODS**

A desk review was done of approved grant proposals from Rounds 1–6, to identify intentions to carry out OR. The actual research implementation and use of findings for improvement of service delivery remain to be evaluated. In the 7th call-for-proposals launched in March 2007, a checklist was added to the tools package accompanying the submission form, to facilitate applicants’ consideration of OR. The Global Fund is collaborating with technical partners to develop guidance documents, generic research methods and example costed plans, that applicants could use when designing OR.

**RESULTS**

Of 358 approved proposals from Rounds 1–5, 54 (15%) included an OR component. The median budget for OR in 17 grants that specified this was US$ 500 000, over a median duration of 5 years. Of 85 approved Round 6 proposals, half had an OR component (34% of HIV proposals, 56% of TB proposals and 74% of malaria proposals). The median 5-year budget for OR and information systems’ was US$ 434 000 or 4.4% of overall grant budget. For all three diseases, proposed topics are generally in line with research priorities suggested by WHO technical programs. Certain topics that have emerged during the ongoing scale-up of key interventions (such as, the reproductive safety of artemisinin-based antimalaria therapy, DDT for malaria vector control and antiretroviral treatment) are not addressed in existing grants.

**CONCLUSION**

Global Fund resources enable countries to conduct OR, but opportunities are not yet fully utilized to ensure that recipient programs are optimally learning during ongoing implementation and scale-up. This presentation aims to solicit feedback on research topics relevant to future recipients, lessons learnt from research conducted in the context of early Global Fund grants, and strategies to promote quality OR in grants.

**O25-30**

The 7th European Framework Programme for Research - opportunities for international cooperation in health systems research

J. Paehler

**OBJECTIVES**

The international scientific cooperation of the European Union aims to generate, share and use knowledge through equitable research partnerships taking into account the country, regional and socio-economic context and knowledge base of partner countries. The strategic approach is to enhance European competitiveness and global sustainable development through such partnerships between the European Union and third countries at bilateral, regional and global levels based on mutual interest and benefit. Since 1984 the European Union supports international
research collaboration on the basis of multi-annual framework programmes. In contrast to previous programmes the Seventh Framework Programme for Research (FP7, 2007–2013) integrates the support to international cooperation in each thematic area of its cooperation programme through: The opening of all activities to researchers from all International Cooperation Partner Countries and industrialised countries. In addition, third country participation is encouraged in identified areas of mutual interest, such as anti-microbial resistance, HIV/AIDS, malaria, tuberculosis, emerging pandemics, public health and health systems. Specific cooperation actions dedicated to third countries in the case of mutual interest in cooperation on particular priorities such as health systems and policy, maternal and child care, reproductive health, and neglected communicable diseases. These actions serve as privileged tools for implementing the cooperation between the European Union and these countries and are aimed at reinforcing the research capacities and cooperative capacities of candidate, neighbourhood, and developing and emerging countries. Particular attention will be paid to facilitating access of the relevant third countries, notably developing countries, to these actions. The first work programme of FP7 for health that includes calls for proposals in the new area of ‘optimising the delivery of health care’ with a deadline of 18 September 2007 has been published on http://cordis.europa.eu. It lists topics on translating the outcome of clinical research into clinical practice, health systems, health promotion and disease prevention. Two topics encourage the participation of third countries: mobility of health professionals to, from, and within the European Union and longitudinal and cross-sectional trends of population health. Specific cooperation actions target specific regions and include: • Epidemiologic investigations into long-term trends of population health • Universal and equitable access to health care and health financing • Optimising hospital care • Improving pre-natal and maternal care. Proposals have to address a specific topic and will be reviewed by at least three external evaluators. Interest to serve as evaluator can be registered at https://cordis.europa.eu/emnfp7/

Buruli Ulcer


B. L. Woolven1, C. Steffen2 and M. Smith2
1 Cairns Base Hospital, Department of Surgery, Cairns, Australia;
2 Mossman Hospital, Mossman, Australia

‘Daintree Ulcer’ is the local name for Mycobacterium ulcerans infection (Buruli ulcer) occurring in the sparsely populated catchment of the Daintree River in far North Queensland, Australia.

OBJECTIVES To examine the burden of Buruli Ulcer in Far North Queensland and compare the management and outcomes to other populations.

METHODS All cases managed at the Cairns Base Hospital and its affiliates in Far North Queensland, Australia from 1986 to June 2006 were studied. Demographic information on the patients, the type and site of the lesion, the surgical procedure performed and the outcome of the treatment were recorded.

RESULTS Sixty-four patients were treated in the study period. The patients ranged in age from 2 to 88 years with a mean age of 42 years. There were 12 paediatric cases (19%). The commonest site was the lower limb (52 cases). Sixty-two of the patients presented with localised disease (97%). Only two had diffuse oedematous disease. Sixty patients were managed surgically (94%), of these 36 required only simple excision, 23 required excision and skin grafting and one patient required below knee amputation for extensive ulceration in the context of AIDS. There were four recurrences (6%) which were successfully managed with re-excision and grafting. Four patients had no surgery.

CONCLUSION Local research and education campaigns in this limited geographical area have raised community awareness hence late presentation is rare. Case series of Buruli Ulcer managed by surgery have reported cure rates of up to 84% with wide local excision and recurrence rates after surgery of 6–17%. In our first world setting with localised disease and a population informed about Buruli, in most cases cure can be effected with relatively minor surgery.

O25-32 Factors associated with functional limitations in Buruli ulcer disease treated patients

C. Rapp1, C. Ficko2, E. Caumes1 and T. Debord1
1 Begin Military Hospital, Infectious and Tropical Diseases, Saint-Mandé, France;
2 Hôpital de la Pitié Salpêtrière, Infectious and Tropical Diseases, Paris, France

OBJECTIVES To assess factors associated with functional limitations in Buruli ulcer disease (BUD) treated patients.

METHODS A case-control study was carried out from August 2005 to January 2006, in three care centers dedicated to the management of BU in Ivory Coast. A case was defined as: patient affected by BUD, over 5 years old, who had finished their treatment more than 3 months earlier by one of the following treatment (excision, excision-graft, dressings under anesthesia) and presenting with functional sequelae. Functional limitations were quantified by a simplified score inspired from the Buruli functional limitation score (BUFLS) validated in Ghana in 2004. We compared characteristics of cases patients with those of care-center controls subjects (1 case/2 controls) using conditional multiple logistic regression analysis.

RESULTS A total of 102 cases and 204 controls with a median time of 5 months (3–12) passed since the end of the treatment were included. The sex ratio M/F was 0.82. The cases’ median age was 12 (56% were below 15 years old). 12 patients were amputated. 73 patients ceased their activities due to BUD. In multivariate analysis independent risk factors for sequelae were time to management, articular topography, distal feature of the lesions, superinfection and delay of cicatrisation. Host-related factors, as well as available therapeutic means, were not significantly associated with sequelae.

CONCLUSION Prevention of BU sequelae relies on the application of the WHO’s strategy: early diagnosis and minor surgery. Rehabilitation and reconstructive surgery programmes are urgently needed.

Amoebiasis Pathogenesis

O24-23 Natural immune response and vaccine-induced protective immunity in amebic colitis models

X. Guo1, E. Houpt1, and V. Petri1
1 University of Virginia, Charlottesville, VA, USA;
2 University of Virginia, Internal Medicine, Charlottesville, VA, USA;
3 University of Virginia, Internal Medicine/Microbiology, Charlottesville, VA, USA

OBJECTIVES To characterize the natural host immune response and vaccine-mediated protective immunity in a murine amebic colitis model.
METHODS A total of 129 or CBA/J mice were inoculated with 2 x 10^6 E. histolytica trophozoites intracecally and infection defined upon sacrifice by cecal antigen detection, omega culture and cecal histopathology. Mesenteric lymph node (MLN) cells were in vitro stimulated with amebic antigens and cecal cytokine profiles were assessed by qRT-PCR. Vaccine regimens utilized intranasally and intraperitoneally administered immunofluinity purified E. dispar. In vivo infection

RESULTS Our previous work on this mouse model has utilized C3H mice. Here we show that intracecal injection of trophozoites into 129/Sv mice led to persistent cecal infection in 46% of mice as determined by cecal antigen and histopathology. The pathologic changes include crypt hyperplasia, epithelial ulceration, and submucosal infiltration. The cecal cytokine profile of infected mice revealed upregulated IL-4 (P < 0.01) and mast cell protease-2 (P < 0.01) expression. Interestingly, 129/Sv Rag2KO mice were more susceptible to amebic infection, and this phenotype was observable as early as 5 days, suggesting it may not reflect a defect in omega-specific acquired immunity. Vaccination of CBA/J mice with lectin elicited a potent antigen-specific serum IgG and fecal IgA response compared to PBS controls (P < 0.001). Lymphocytes from vaccinated mice secreted significantly higher Th1 (IL-2, IFN-γ, IL-12, TNF-) and Th17 cytokines (IL-17A, IL-17F), but not Th2 cytokine (IL-4) in response to lectin restimulation. This lectin immunization regimen provided 71% efficacy, with 13 out of 15 PBS-treated mice successfully infected (86.7%) versus 4 out of 16 lectin-treated mice (25%; P < 0.001).

CONCLUSION Our data suggests a Th2 response may predominate in immunity during chronic stage of amebic infection, which might contribute to the immunopathogenesis of amebiasis. In contrast, lectin immunization induced high levels of antigen-specific humoral response and cellular response mediated by Th1 and Th17 cells, and this response correlates with protection. Investigations for the mechanisms underlying protective and deleterious immunity are ongoing.

O25-34
Ultrastructural and inflammatory responses at invasion of the human colon explants by E. histolytica
D. Bansal1, P. Roux2, A. Danchar1, P. Ave1, S. Kerneis1, N. Guillen1 and E. Labruyère1
1Institut Pasteur, Biologie Cellulaire du Parasitisme, INSERM U 786, Paris, France; 2Institut Pasteur, Plate-Forme d’Imagerie Dynamique, Paris, France.

Amebiasis, a human intestinal infection developed by 50 million persons every year, is caused by the protozoan parasite, Entamoeba histolytica. The molecular dialogues between E. histolytica and human colonic mucosa are not well understood, in particular are unknown the signal inducing the switch from commensal to virulent trophozoites, the human molecules influencing the parasite penetration and the amoebic molecules inducing the early inflammatory response of the tissue. To investigate the molecular mechanisms governing the invasion of the human tissue by E. histolytica, an ex-vivo human colonic model has been developed in the laboratory. The early stages of the intestinal invasive process in regard to parasite motility and tissue responses were studied using these human colon explants. Surgical gut pieces were collected from the patients undergoing colectomy (in collaboration with surgeons from Parisian Hospital). After surgical rules of histopathological analyses, healthy tissue fragments were processed according to French biomedical research law. The sections of colon biected longitudinally were micro dissected to keep the mucus, the mucosa and the submucosa. Then tissues were incubated during different period of time with pathogenic E. histolytica and non-pathogenic E. dispar as a control. We have determined the behaviour of the trophozoites and/or invasion process by scanning electron microscopy and histological analysis and to see the response of the tissue, cytokine production and LDH release were assessed. By the scanning microscopy and histology analysis it has been shown that during the first two hours of incubation, E. histolytica degrades the mucus, and then adheres to the epithelium and detaches the enterocytes and penetrates into the lamina propria. As expected, E. dispar was enable to invade the colonic mucosa. The LDH was released as soon as E. histolytica reach the epithelium, which corresponds to the histology analysis. The level of the pro-inflammatory cytokines like IL-1 beta, IL-8, IFN gamma, and TNF was significantly higher in the supernatant of E. histolytica, suggested Th1 type of immune response. In addition, we have also estimated the kinetics of E. histolytica and E. dispar trophozoites by confocal microscopy live imaging and quantitative image analysis, during invasion. In conclusion, human colonic explant is a good model to mimic the early steps of invasion and further study are in development to see the impact of trophozoites or human environmental elements on the colonic tissue invasion. This work is supported by a grant from the Transversal Research Program of the Pasteur Institute.

O25-35
Entamoeba histolytica and Entamoeba dispar interactions with enteropathogenic bacteria synergize damage to epithelial cells, amending the inflammatory response
I. Meza1, M. Galván-Moroyoqui1, M. C. Domínguez-Robles1 and E. Franco1
1Centro de Investigación y de Estudios Avanzados-IPN, Molecular Biomedicine, Mexico DF, Mexico

OBJECTIVES E. histolytica virulence seems to be increased after ingestion of certain bacteria. We analyzed the effects produced by E. histolytica and the non-pathogenic E. dispar on epithelial monolayers, after ingestion of enteropathogenic bacteria, as in endemic areas for amoebiasis mixed bacteria Entamoeba infections are common.

METHODS A non-pathogenic E. coli strain and the pathogenic ETEC, EPEC, Salmonella enterica, serovar Typhimurium, and Shigella dysenteriae were co-cultured with amoeba. After bacteria ingestion, amoebae were cultured for virulence, adhesion to epithelial cells, effects on cellular permeability, induction of proteolytic activities and migration to pro-inflammatory cytokines and media from epithelial cells co-cultured with the bacteria strains. Survival of bacteria inside amoeba was assessed by CFU and confocal fluorescence microscopy.

RESULTS Ameoba internalized bacteria at different rates, but only E. histolytica digested bacteria, with the exception of S. dysenteriae, which survived and was released from amoeba. Bacteria also survived in E. dispar. E. histolytica virulence and adhesion to epithelial cells were increased as well as cysteine proteinase activities, in particular after ingestion of S. serovar Typhimurium and S. dysenteriae. E. dispar avirulence was not modified. Pre-culture of epithelial cells with pathogenic bacteria increased further cell damage by E. histolytica, after priming an inflammatory response which enhanced amoebae and neutrophil migration toward lesioned sites.

CONCLUSION We propose a model where presence of enteropathogenic bacteria and their survival in and release from amoeba would synergize the inflammatory response of epithelial cells to E. histolytica infection, facilitating tissue invasion. Survival of
bacteria inside amoebae would further contribute to recurrent and/or chronic colon inflammation.

**O25-36**

**TLR9-dependent macrophage activation by Entamoeba histolytica DNA**

C. Ivory and K. Clade

1University of Calgary, Microbiology and Infectious Diseases, Calgary, Canada

**OBJECTIVES** Activation of the innate immune system by bacterial DNA and other invertebrate DNA represents a pathogen recognition mechanism. The aim of this study was to determine if DNA from the intestinal protozoan parasite Entamoeba histolytica could activate macrophages.

**METHODS** E. histolytica genomic DNA (E.h DNA) was purified from log phase trophozoites and treated with RNase A before use in experiments. The mouse macrophage cell line, RAW 264.7, was used in all experiments. Cells were treated with E.h DNA or with positive controls: LPS, Salmonella typhimurium DNA or CpG ODN or with negative controls: calf thymus DNA and GpC-ODN. Macrophage activation was determined by MAPK activation, NF-kB activation and Real-time PCR was used to measure TNF-alpha mRNA. TLR9 signaling was determined by a luciferase reporter assay in HEK cells and pre-treatment of cells with chloroquine or monensin.

**RESULTS** RAW cells treated with E.h DNA demonstrated an increase TNF-alpha mRNA and protein production. This TNF-alpha production was blocked by pre-treatment with chloroquine or monensin, which block endosomal acidification. In fact, an NF-kB luciferase reporter assay in HEK cells transfected with human TLR9 demonstrated that E.h DNA signaled through TLR9 similar to CpG-ODN. This signaling was abolished by DNase treatment and was not blocked by polymyxin B, indicating an E.h DNA specific cellular activation. Immunofluorescence confirmed NF-kB activation in RAW cells, as seen by nuclear translocation of the p65 sub-unit. Western blot analysis of cellular extracts of treated RAW cells demonstrated MAPK activation (p-p38, p-JNK and p-ERK) by E.h DNA.

**CONCLUSION** Recognition of E.h DNA by TLR9 activates macrophages and may provide an innate defense mechanism, characterized by the induction of the inflammatory mediator TNF-alpha.

**O25-37**

**Amebic liver abscess: why females do better than males**

H. Lotter1, T. Jacobs2 and E. Tannich1

1Bernhard Nocht Institute for Tropical Medicine, Molecular Parasitology, Hamburg, Germany; 2Bernhard Nocht Institute for Tropical Medicine, Immunology, Hamburg, Germany

Amebic liver abscess (ALA) is the most common extraintestinal manifestation of invasive amoebiasis as more than 99% of E. histolytica -induced abscesses are located within the liver. The disease is characterized by rapidly evolving, massive tissue destruction due to apoptotic and necrotic disintegration of hepatocytes. In contrast to intestinal amoebiasis, the occurrence of ALA greatly predominates in males (>85%) but is rare in females. We recently established an ALA model in immunocompetent mice, which revealed a similar sexual dimorphism as found in humans. When intrahepatically challenged with E. histolytica trophozoites, female mice were able to rapidly control the infection whereas male mice harboured the parasite within the liver for at least 14 days and developed significant abscesses. Analysis of the immune response revealed that male and female mice differ in their early cytokine production. The results suggest that females are able to rapidly activate macrophages in response to amebic infection of the liver via the IFN-gamma-pathway, whereas development of ALA in males is due to inadequate activation of accumulated immune cells within the liver tissue. Preliminary studies indicate that the differences in the immune response are mediated by testosteron.

**Malaria Control by Treatment and Prophylaxis I**

**O25-38**

**Comparison of all-cause and malaria-specific mortality from two West African countries with different malaria transmission patterns**

R. Ndugwa1, H. Ramroth1, O. Mueller1, J. Momodou2, B. Kouyate3

1University of Heidelberg, Department of Tropical Hygiene and Public Health, Heidelberg, Germany; 2MRC Laboratories, Farafenni, Gambia; 3Centre National de Recherche et de la Formation sur le Paludisme, Ouagadougou, Burkina Faso; 4London School of Hygiene and Tropical Medicine, London, UK

**OBJECTIVES** Malaria is one of the leading causes of death in children under-5 years in sub-Saharan Africa. We systematically compared patterns of all-cause and malaria-specific mortality from children under-5 in a mesoendemic malaria area (The Gambia) with those from a hyper/hoendoemic area (Burkina Faso). We searched for studies on overall and malaria-specific mortality from Burkina Faso and The Gambia. The online search was done in Medline, Embase and Popline, using key words: ‘Africa, The Gambia, Burkina Faso, Malaria, Plasmodium falciparum, mortality, child survival and morbidity’. Subsequent literature was obtained by reviewing reference lists in each paper. Information on observed person-years (PY), deaths and cause of death was extracted. Missing person-years were estimated and all-cause and malaria-specific mortality was calculated as rates per 1000 person-years (PY). Studies were classified as longitudinal/clinical studies or surveys/censuses. Linear regression was used to investigate mortality trends over calendar periods.

**RESULTS** Overall, 39 and 18 longitudinal/clinical studies plus seven and 11 surveys and censuses were identified from The Gambia and Burkina Faso respectively, covering the period 1960 to 2004. All-cause mortality rates declined in both countries, but significantly more stronger in The Gambia. The weighted-average malaria-specific mortality rate per 1000 Person-years for Burkina Faso (13.4, 95% CI: 13.0–13.8) was higher than that observed in The Gambia (9.5, 95% CI: 9.1–10.1). Malaria mortality rates did not decline significantly over time in both countries.

**CONCLUSION** Child mortality in both countries declined significantly in the period 1950 to 2004 due to socio-economic development, improved health services and specific intervention projects. The period after 1990, this decline in mortality experienced a slow-down. This period also coincides with the emergence of malaria parasite resistance to chloroquine, a malaria first-line drug. The difference in malaria mortality rates across countries points to differences in national disease control policies and disease transmission patterns. Because all-cause mortality rates declined significantly without a significant decline in malaria mortality rates, the decline in overall mortality was less likely due to malarial disease control programs.
Abstracts of the 5th European Congress on Tropical Medicine and International Health

O25-39

Rapid assessment of the burden of malaria in pregnancy in Madhya Pradesh, India

R. Ahmed1, N. S. Singh1, F. O. ter Kuile1, V. Udnyayakumar2, M. R. Desai1, A. P. Dash1 and D. J. Terlouw2

1National Institute of Malaria Research, Malaria Research Centre Field Station, Jabalpur, India; 2Liverpool School of Tropical Medicine, Child and Reproductive Health Group, Liverpool, UK; 3Malaria Branch, Division of Parasitic Diseases, Centers for Disease Control and Prevention, Atlanta, USA; 4National Institute of Malaria Research, Delhi, India

OBJECTIVES There is sparse data on the burden of malaria in pregnancy (MiP) in areas in Asia with predominantly low and seasonal transmission of *P. falciparum* and *P. vivax* malaria, limiting the development of evidence-based control policies. We determined the burden of MiP and the relative contribution by *P. falciparum* and *P. vivax* in Madhya Pradesh, central India, using a rapid assessment methodology.

METHODS In 2006, two 6-week cross-sectional surveys were conducted in antenatal clinics (ANC) and delivery units (DU) in three districts in Madhya Pradesh during the dry (April–May) and post-rainy (October–November) season, corresponding to the anticipated peak prevalence of *P. vivax* and *P. falciparum*, respectively.

RESULTS A total of 2837 pregnant women (ANC n = 1812, DU n = 1025) were enrolled in the dry season (n = 1229) and post-rainy season (n = 1608) surveys. The corresponding prevalence of maternal parasitaemia in the two seasons was 1.9% and 6.4% in the ANC and 0.8% and 2.9% in the DU. Placental malaria (microscopy) was found in 0.3% and 2.6% of cases. About two-thirds of the infections were due to *P. vivax* in the dry season, whereas this was only 11% in the post-rainy season (*P* = 0.0003). This shift was related to an increased *P. falciparum* prevalence (5.7%) in the post-rainy season, as the prevalence of *P. vivax* remained similar between the dry and post-rainy season (1.1% and 0.7%, respectively). Overall, 53% of the women with *P. vivax* and 65.8% of those with *P. falciparum* infections were asymptomatic (axillary temperature 37.5°C or a history of fever in the previous week). Gravidity was not associated with the risk of malaria infection. There was a marked variation in the peak prevalence of malaria between the three study sites in the post-rainy season, ranging from 0.3% (maternal parasitaemia at ANC) and 0.5% (placenta malaria) in Jabalpur (urban) to 20.4% and 3.7%, respectively, in Maihar (rural plains). An analysis of the association between malaria infection and maternal anaemia and adverse birth outcomes is ongoing and will be presented.

CONCLUSION The overall prevalence of malaria infection during pregnancy in Madhya Pradesh was low, with marked differences between the three districts reflecting local transmission patterns. These rapid assessments proved a useful tool to provide a snap shot assessment of the burden of MiP in the region, but year round surveys may be required to capture the seasonal variation in species and the corresponding effect on maternal and newborn health.

O25-40

Pilot study of the implementation of seasonal intermittent preventive treatment in children (IPTc) with community participation in Senegal

B. Cisse1, S. Faye2, Y. Dial1, O. Faye1, O. Gaye1 and P. Milligan2

1Université Cheikh Anta Diop de Dakar, Dept Parasitologie - Mycologie, Dakar, Senegal; 2London School of Hygiene and Tropical Medicine, Epidemiology and Population Health, London, UK

OBJECTIVES In the Sahel most malaria deaths occur among children 1–4 years old during a short transmission season. Seasonal intermittent preventive treatment (IPTc) can substantially reduce the incidence of malaria in these areas. In trials of this intervention drugs have been administered by research teams, it was therefore important to investigate the feasibility of delivering the intervention to children in rural areas through the routine health service, and the acceptability of the intervention to communities. The aim of this study was therefore to identify an effective method of delivery and to pilot delivery during one transmission season to assess coverage, compliance, the incidence of adverse events, and the acceptability of IPTc by the community and health care providers.

METHODS We piloted implementation of IPTc with SP plus AQ in three health post areas in Senegal, organised by the district health services with drugs delivered by community health volunteers (relais communitaires). Acceptability by the community was investigated using direct observation, in-depth interviews, and focus group discussions. Carers were visited after each treatment round to ask about adverse events and compliance. For comparison, carers of children living in nearby villages outside the study area, who did not receive IPT, were asked the same questions about adverse events. IPT coverage was measured by a cluster sample survey of the children in the project area. Incidence of malaria was recorded by passive case detection using rapid diagnostic tests.

RESULTS A total of 5292 children received at least one dose. 81% of eligible children received all three scheduled doses. 88% received at least one dose. The most common reason for not receiving IPT doses was being away from the village at the time of the treatment round. Incidence of solicited adverse events recorded on day 4 after the IPT treatment was similar among children who received IPT and children who did not receive IPT treatments, for all symptoms (including vomiting), except for fever, which was more common in the children who did not receive IPT. Good adherence despite complaints about the bitterness of AQ, was associated with recognition by parents of the risks of malaria in children under 5 years, and commitment of the health workers who administered IPT at home. Effective community sensitisation is important for good uptake.

CONCLUSIONS High coverage of IPTc with SP+AQ can be achieved when delivered by community health volunteers in Senegal, treatment was acceptable and was not associated with common adverse reactions.

O25-41

Cost effective malaria control strategy for Madhya Pradesh, India: a GIS based approach

A. Srivastava1, B. N. Nagpal2, P. L. Joshi2 and A. P. Dash1

1National Institute of Malaria Research, Delhi, India; 2National Vector Borne Disease Control Programme, Delhi, India

In India, annually, about 2 million malaria cases are being reported by National Vector Borne Disease Control Programme. Of these 40% constitute *Plasmodium falciparum*, Madhya Pradesh (M.P.) situated at the midst of the Country had 46 tribal groups living in undulating forested area and was 2nd highly malarious state in the country. The state contributes about 16% of total malaria cases of the country. GIS provides a new dimension and unparalleled flexibility to effectively target the problem was used to formulate control strategy. In M.P. there are 48 districts consisting of 313 blocks and a population of nearly 68 million. For GIS study blockwise/districtwise georeferenced digital maps were prepared. Census data such as population, Schedule
Caste/Schedule tribe population etc. was attached to the map. Besides this data on malaria incidence, blood slide collected, radical treatment etc for six years i.e. from 2000 to 2005 was attached to the map and was used for analysis for formulation of control strategies in MP. Spatio temporal evolution of malaria reveals high incidence during the years 2000 and 2001 and mostly from the blocks which are situated on southeast of MP. Schedule Tribe populations showed a good correlation with malaria incidence both at the district as well as block level. Disease incidence, specifically PlF%, showed a good correlation with forest cover and GIS based distribution of the vector species An. fluviatilis. There are two efficient vectors, An. culicifacies and An. fluviatilis. In general malaria has shown a declining trend but PlF% has increased over the years. Only six districts showed consistently >30% Pf in 2001–2005, but overall 44 blocks in 20 district consistently showed >30 PlF%. A buffer zone was created around these hot pockets and intense control recommended. The overall incidence of malaria in MP, is declining due to the routine interventions but PlF proportions are increasing, perhaps due to drug resistance, socio-cultural behavior, transmission window, forest base economy and vector bio ecology. A pilot study in seven districts of MP revealed a transmission window in Oct and March. Thus the malaria spray schedule will be revised accordingly. Malaria control activities would be strengthened in areas with Tribal populations and areas with >30 Pf%.

**O25-42**

**Plasmodium** antibodies as surrogate markers of malaria exposure


1Walter Reed Army Institute of Research, Silver Spring, MD, USA; 2Naval Medical Research Center, Silver Spring, MD, USA; 3US Army Medical Materiel Development Activity, Frederick, MD, USA

**BACKGROUND** Malaria prophylaxis trials are challenging to conduct in non-immune subjects. A surrogate marker of malaria exposure in subjects taking malaria prophylaxis would be an ideal solution, allowing large field trials to be conducted without a placebo arm.

**METHODS** Critical reagents were identified from serum samples banked from prior clinical trials. These included a baseline and then at least one additional sample at a later time point. These reagents consisted of the following: PF exposed with patent parasitemia, PV exposed with patent parasitemia, exposed subjects taking one of four malaria prophylaxis drugs, and non-exposed subjects taking malaria prophylaxis or placebo. Promising antigens were selected for each species. Three assays were conducted to near Good Laboratory Practice standards, while the other assays were newly developed for this effort. All antigens were assessed with an ELISA assay and a multiantigen assay (Luminex™). Samples were anonymised and assessed blindly to exposure status.

**RESULTS** In total, 910 serially collected samples from 301 subjects from nine studies were evaluated in 23 assays. The 301 subjects included 67 subjects developing PF parasitemia, 64 subjects developing PV parasitemia, 111 subjects taking malaria prophylaxis who were exposed to malaria, and 54 subjects not exposed to malaria. PF MSP was most sensitive for detecting PF infection (70–81%), followed by PF AMA (50–55%), and PF LSA (6–18%). PV MSP was most sensitive for detecting PV infection (31–84%), followed by PV AMA (31–84%), and PV CSP (33–55%). Specificity was <100% for the majority of the assays for CSP, and for those assessed by Luminex™. Antibody responses were essentially undetected in subjects taking causal (liver stage) malaria prophylaxis, but better in those taking mefloquine (blood stage suppressive) prophylaxis. Adjusted for malaria exposure, PF MSP detected 43–64% of subjects exposed to PF, while PV MSP detected ~45% of PV exposures in subjects exposed to malaria while taking mefloquine. The approximate combined sensitivity of these to detect PF or PV exposure is 58% with 100% specificity. Adding more antigens to the combination did not further increase accuracy for either species. The onset of PF MSP responses began at 20–30 days following exposure.

**CONCLUSIONS** Sufficiently sensitive and highly specific antibody responses appear to developing in subjects taking suppressive malaria prophylaxis. This finding should allow a mefloquine arm to replace placebo arms to estimate exposure in malaria prophylaxis trials and might provide insight as to the types of drugs to use for intermittent preventative treatment.

**O25-43**

**War affected children in northern Uganda confronting malaria themselves: its implications to policy and priority healthcare setting**

G. Akello, A. Richters and R. Reis

University of Amsterdam, Amsterdam School for Social Science Research, Amsterdam, Uganda

**OBJECTIVES** This study’s objective was to assess how children living in a conflict-stricken northern Uganda confront common illnesses themselves.

**METHODS** Qualitative ethnographic techniques triangulated with a survey were methods employed in an investigation into how children aged 9–15 years identify, self-diagnose, and manage common diseases themselves.

**RESULTS** Children ranked malaria as highly prevalent. Statistical data was analyzed through obtaining a summary from multiple responses in Statistical Package for Social Scientists (SPSS). Data suggests a high prevalence of malaria with (10.1%) of boys and (8.9%) of girls indicating that they had malaria in a one-month recall. Children used pharmaceuticals in self-medication for malaria episodes. They accessed antimarialarials over-the-counter without prior prescription by professional healthcare workers.

**CONCLUSION** Findings have implications into policy and priority healthcare setting for interventions to alleviate suffering of people in conflict zones. Malaria is a healthcare priority in northern Uganda’s conflict zone. Mis-use and over-use of pharmaceuticals in self-medication by displaced children could contribute to emergency of drug-resistant strains of Plasmodium falciparum which are malaria causing pathogens. Over-use of antimarialarials could point to medicalisation of more complex socio-economic problems including psychological and suffering of socio-cultural natures.

**Haemorrhagic Fever**

**O25-44**

**Yellow fever resurgence in Africa – assessment of the risk of YF outbreak**

S. Brand, T. Nguyen and C. Kambe

1World Health Organization, CDS/EPE/ERI, Geneva, Switzerland; 2World Health Organisation, WHO/AFRO/DDC, Ouagadougou, Burkina Faso

**OBJECTIVES** The objective of this risk analysis is to identify the districts at higest risk of YF outbreak in 12 endemic countries in Africa.
order to carry out preventive vaccination campaigns before reaching crisis level. The Yellow Fever Initiative supported by the GAVI Alliance aims at vaccinating 48 million people before 2010. In the past 10 years the number of YF reported cases and the number of affected areas has increased. Successful attempts to control the disease took place at the beginning of the 20th century. Unfortunately the interruption of those control programs has played a major role in the resurgence of yellow fever in the 1980–90s. Between 1994 and 2004 the number of countries reporting YF cases increased by 3.6 fold. The large proportion of susceptible population is of great concern given the increased urbanization in endemic countries. The risk of urban outbreak is very high.

**METHODS** The vulnerability of the population to YF outbreak is measured by five variables for ‘Exposure’ and one variable for ‘Susceptibility’. A multiple correspondence analysis allows to convert the five exposure variables into a single exposure risk indicator. Districts are then projected on a 2-dimension plan with ‘exposure’ on horizontal axis and ‘susceptibility’ on vertical axis.

**RESULTS** First results in Burkina Faso are very convincing. High risk districts can be easily identified according to their situation on the plan. The mapping of high risk districts helps to plan for preventive campaigns.

**CONCLUSION** The tool proposed to assess Yellow Fever risk is simple, easy to use and is useful for the decision making process to identify priority population to vaccinate quickly.

**O25-45**


P. Roddy

1Médecins Sans Frontières - Spain, Barcelona, Spain

**BACKGROUND** In March 2005, Médecins Sans Frontières (MSF) and others responded to the Marburg haemorrhagic fever (MHF) outbreak in Uige, Angola to contain the epidemic and care for those infected. Community outbreak control is crucial to filovirus haemorrhagic fever (FHF) containment and its components include: epidemiological surveillance, safe burials and disinfection, psychological support, home-based risk reduction (HBRR), peripheral health facility support, and information and education campaigns (IEC). Initially the intervention, focusing only on biomedical aspects, caused community resistance. In response, MSF re-evaluated its approach and made substantial changes to its intervention.

**METHODS** We describe the learning process of MSF-Spain pertaining to community activities. For each outbreak control component, we discuss the initial intervention, protocol modifications, and lessons learnt.

**RESULTS** Initial burial and disinfection procedures upset the community. Protocol modifications ensured transparency and respect for psychological and spiritual needs of families, allowed modified traditional mourning practices while maintaining bio-safety, and resulted in improved community cooperation. HBRR was successfully used as a provisional solution while the patient and family were continuously encouraged to accept hospitalization. Soliciting local authorities to mediate between MSF and the community facilitated case finding, follow-up, and contact tracing. The continuation of properly supported health services during an FHF outbreak was possible. The usefulness of monitoring burial sites remained unclear, particularly in the absence of reliable pre-epidemic mortality figures. The use of local staff in the psychological support programme was instrumental in facilitating the community’s understanding of the disease and acceptance of the intervention. IEC messages should be accurate and realistic as opposed to pessimistic or overly-optimistic.

**CONCLUSION** FHF containment depends upon collaboration of the affected community. The MSF team in Uige made errors, corrected them and underwent a learning process that improved intervention effectiveness. Sharing these experiences with other FHF outbreak response actors will hopefully strengthen future FHF interventions.

**O25-47**

**Viral haemorrhagic fever in Serbia and Montenegro**

R. Cekarac and N. Stajkovic

1Military Medical Academy, Belgrade, Epidemiology, Belgrade, Serbia and Montenegro

**OBJECTIVES** The goal of this work is to present the incidence, lethality and regional distribution of viral haemorrhagic fevers (VHF): haemorrhagic fever with renal syndrome (HFRS) and...

**METHODS**

A retrospective study.

**RESULTS**

During the analyzed period, 586 persons got infected by VHF, from which 491 (83.8%) by HFRS and 95 (16.2%) by CCHF. Mean annual incidence of VHF was 0.69, of HFRS 0.59, and of CCHF 0.10 on 100 000 persons, while CCHF clinically manifested only in territory of Kosovo and Metohija. In the same period VHF lethality was 10.6%, and lethality of CCHF (21.1%) was significantly higher than HFRS lethality (6.8%). The highest incidence of HFRS was recorded in Montenegro (1.2/100 000), while in Vojvodina there were no recorded cases of HFRS lethalities. During the analyzed period, the highest number of infections was recorded in the years with epidemics (199 infected in 1995, and 84 infected in 2002). Although HFRS infections appear year-round, the highest number of infections is recorded from June to October (79.7% of all infections).

**CONCLUSION**

Our results show that the infections by VHF on the territories of Serbia and Montenegro are continuously registered, confirms that active foci of HFRS are mosaically distributed over the territory, while infections of CCHF were registered only in endemic foci in Kosovo and Metohija.

### Approaches of the Social Determinants of Health

**O25-48**

**Social laboratory for healthy urbanization**

K. Havemann,1 P. Pridmore,2 M. Sami,3 and S. Mercado2

1World Health Organization, Kobe Centre, Kobe, Japan; 2School of Lifelong Education and International Development, Institute of Education, London, UK

**OBJECTIVES**

To outline the emerging health and social outcome framework and pathways in the urban setting using a governance equity lens as the entry point which is being developed by the WHO Centre for Health Development in Kobe, Japan.

**METHODS**

Literature review and case studies.

**RESULTS**

Experience has shown that the way we organize our society, the extent to which we encourage interaction among the citizens, and the degree to which we trust, care and associate with each other in communities are important determinants of health.

**CONCLUSION**

The need to address the social dimension in the urban setting moves health into the broader arena of governance, power structures and political agendas that impact society.

**O25-49**

**Physical, social and urban environmental aspects of housing related to the incidence of transmissible diseases of rural migrants in low-income urban areas - a case study of Bellavista, district La Esperanza, city of Trujillo, Peru**

A. Ruiz Rosado

1Universidad Privada Antenor Orrego, Trujillo, Peru; Delft University of Technology; ALßAN Program, Urban Planning and Water Management, Gouda, Netherlands.

**OBJECTIVES**

To show how indoor (physical and social) and outdoor (urbanization and environment) conditions of the dwellings relate to the incidence of transmissible diseases of migrant people of the location of Bellavista, a non-consolidated urban settlement in the periphery of the Metropolitan City Trujillo.

**METHODS**

1 A preliminary participative diagnosis and definition of a theoretical framework. 2 Selection of indicators and the corresponding categories of the following aspects: a. Physical: state of the building, sanitary facilities and indoor climate comfort. b. Social: socio-cultural behaviour of migrants related to indoor conditions. c. Urban environmental: outdoor climate conditions, state of urbanization. d. Selected most frequently transmissible diseases: Respiratory Tract Infections and lung diseases (RI diseases, TB) and Dengue fevers (vector borne diseases). 3) Data collection and 4) Quantitative and qualitative data analysis. The data base came from different sources, interviews, surveys and one socio-economic and housing participative census of Bellavista (1828 families and 1540 dwellings). Observation techniques were applied to diminishing missing data, and to collect data of indoor and outdoor socio-environmental conditions. Linear statistical and Multiple Correspondence Analysis Models (SPSS/MCA) were applied to correlate multiple categorical variables.

**RESULTS**

The results of a multivariable analysis of quantitative and qualitative categorical data were listed showing the relations of main urban environmental, social and physical aspects of the dwellings and the health conditions of the occupants. These results were represented as maps and cadastres, using Computer-Aided Design (CAD) and Geographical Information Systems (GIS), focusing critical areas of health to be prioritized for an efficient local attention. Local stakeholders were involved to participate on this research, not only to pick up verifiable information, but to create synergies towards a participative process of change to improve the quality of health in this area.

**CONCLUSION**

Relevant indicators that encouraged the incidence of transmissible RI, TB and dengue diseases were, among others, in order of importance: lack of permanent current drinking water (houses without a clean domestic elevated freshwater tank); no good domestic hygienic practices of users and houses badly isolated from traffic, wind, humidity and polluted streets.

**OTHER RELATED CONCLUSIONS:** ‘Good houses’ in terms of health are well-constructed ‘adobe-houses’. These are better isolated against cold weather, outdoor air pollution from streets and wind, than houses built with bricks and concrete.- RI diseases, TB and vector borne diseases (Dengue fevers) are strongly related to each other.

**O25-50**

**The Kisumu city integrated approach – Lake Victoria poverty alleviation consortium (LAVIPAC)**

J. A. Kere1

1WUFIP Education and Development, LAVIPAC, Kisumu, Kenya

**OBJECTIVES**

1) To raise access to safe water and environmental sanitation for 20 000 residents of Manyatta A, Obunga (Slums) and (Osiri peri-urban). 2) To improve the income of 600 female-headed households engaged in fishing industry and urban agriculture. 3) To reduce the negative impact and the spread of HIV/AIDS through mobilization for behaviour change and support socio-economic mitigative interventions. 4) To facilitate women’s empowerment through enhanced entrepreneurial skills and better knowledge on human rights and HIV/AIDS. 5) Support Kisumu City Council capacity building for improved urban governance.

**METHODS**

Acknowledging the strength of synergy and integration in poverty alleviation, SANA, CMEDA and WIFIP formed a consortium to address the issues identified in Obunga and other informal settlements in Kisumu City. The integrated programme had the following strategic thrusts: 1) Improvement of health status of the slums by providing safe water and proper sanitation (SANA); 2) HIV and AIDS mitigation focusing education, BCC, VCT, WUFIP; 3) Socio-economic support and Maternal Child Health (WUFIP); 4) OVC and Home Based Care (CMEDA); and Urban...
Agriculture for nutritional support (CMEDA)• Capacity Building for good governance (SANA).

RESULTS • Improved access to safe drinking water and proper sanitation• Individual farmers and orphans are keeping poultry, rearing goats and growing vegetables• VCT services are provided in collaboration with service providers within the community• Positive living practices are in place and community members attest to their activities• Access to information and knowledge on health, diseases and available services is provided through education, group learning and weekly radio programmes• Access to basic health services has been planned to cater for the poor women and their families. Immunization programmes are in line for children and mothers. • Solid waste management has been improved through systematic and hygienic collection. The local authority has never been able to provide this service to the slum dwellers.

CONCLUSION Resourcing public health seeks the enhancement of all people’s well being in a sustainable system that ensures equitable access to essential public health knowledge and services. It emphasizes the importance of enabling currently poor and excluded people to claim their fair share of resources, services and information but also addresses more basic concerns – power, participation, respect and dignity in society. Supportive professional caregivers, and people’s access to knowledge add key elements in the drive to reduce disparities in ill-health and well-being.

O25-51

Network of healthy communities in Brazil – empowering for equity and social change in urban settings

D. Becker1, K. Edmundo2, D. Bonatto2, N. Nunes3 and A. Baptista3
1Federal University of Rio de Janeiro and Center for Health Promotion (CEDAPS), IESC - Institute for Collective Health Studies, Rio de Janeiro, Brazil; 2Center for Health Promotion (CEDAPS), Rio de Janeiro, Brazil

BACKGROUND Poor communities (‘favelas’) in Rio suffer from serious poverty-related problems, aggravated by violence and lack of basic services. Yet, they feature many untapped resources and social networks. Many organized groups are fighting to improve life conditions and promote health. The NGO Center for Health Promotion (Cedaps) started working on HIV/Aids prevention in 1996, using participatory approaches, incorporating local knowledge, culture and perceived priorities. Soon community leaders became mobilized and started to broaden their scope of work into different health promotion activities. The Network of Healthy Communities of Rio de Janeiro was created in 2005, as a civil society initiative for health promotion and development.

OBJECTIVES
- empower each community organization through capacity building, planning and exchange of experiences;
- improve collective power to negotiate resources, programs and public policies;
- decrease the segregation and prejudice against ‘favelas’.

METHODS The methodology uses integrated approaches and is based on ‘Shared Construction of Solutions’, a social technology developed by Cedaps. Using participatory techniques, it enables individuals and groups to plan strategically and develop systematic health promotion interventions, acting upon social determinants and solving local priority problems. Capacity building and networking activities are used to increase political strength and build groups’ autonomy and ability for participation. Building partnerships with public agencies and private organizations is also an important component.

RESULTS There are currently 106 participating community organizations in the metropolitan area of Rio, with more than 1.4 million residents. Most of the groups are led by African-Brazilian women. The results are the mobilization of communities and their members; and diverse social interventions that generate direct benefits to more than 200 000 people, promoting ownership and sustainability. Concrete effects on community and youth empowerment, disease prevention, health promotion and local development will be presented. The Network has grown rapidly and is gaining national and international visibility and recognition as an important stakeholder for public policies.

CONCLUSION While infectious diseases such as HIV/Aids or TB pose serious threats to the health and well-being of the urban poor, when addressed with appropriate frameworks, they can become rallying points for community mobilization and empowerment. In contexts of poverty and limited opportunities, it is crucial to use structured methodologies to develop skills and potentials of community-based groups and to interconnect them in networks. Efforts made to increase their participation and interaction with civil society and State will result in better and more sustainable public policies, fostering equity and social development.

O25-52

Abstract withdrawn.

O25-53

Integrated, multi-level approaches to address the social determinants of health inequalities in urban settings? – implications for global health research

F. Barten1, D. Mitlin2, C. Mulholland2, A. Hardoy3 and R. Stern4
1Radboud University Nijmegen, Faculty of Medicine, Institute for International Health, Nijmegen, Netherlands; 2University of Manchester and 3HED, Manchester, UK; 4WHO HQ, Geneva, Switzerland; 5IIED, Buenos Aires, Argentina; 4University of the Western Cape, School of Public Health, Cape Town, South Africa

This paper draws on an earlier review paper on the effectiveness of WHO Healthy Settings approaches for the WHO Kobe Centre and a background paper on Integrated approaches to address the social determinants of health for reducing health inequity written for the Knowledge Network on Urban Settings. (The original publication is available at www.springerlink.com). The world is becoming rapidly urbanized and poverty is a growing function of the urbanisation process. The problems of the urban social and physical environment posed by these current trends are immense e.g. in many Sub-Saharan cities the people living in informal settlements lacking basic infrastructure already accounts for over 30% of the population. While there are important regional differences, poverty is growing and living conditions are deteriorating in all cities. People in urban settings are exposed to a variety of interconnected health hazards. Improvements in health and health equity demand both changes in the physical and social environment of cities and integrated approaches which take into
account the wider socio-economic and contextual factors and address not only the immediate, but also the underlying and structural causes of poverty, poor health and urban health inequalities. In order for comprehensive approaches such as healthly settings, to address the social determinants of health effectively and at multiple levels, they need to explicitly tackle issues of participation, governance and the politics of power, decision-making and empowerment. Information and access to information can influence the balance of power and contribute to multisectoral and participatory planning and improved health outcomes. This paper argues that there is an urgent need for global urban health research and for addressing these social determinants of health in urban settings through interdisciplinary and participatory approaches.

Health of Nomadic Pastoralists

**O25-54**

**New approaches in health and social services provision for nomadic people in the Sahel**

B. Bonfoh¹, J. Zinsstag², A. Munch³, G. Fokou¹, M. Ould Taleb⁴, M. Bechir⁵ and M. Tannér⁶

¹Institut du Sahel, Bamako, Mali; ²Swiss Tropical Institute, Basel, Switzerland; ³University of Bern, Institute for Islamic and Middle Eastern Studies, Bern, Switzerland; ⁴Institut National de Recherche en Sante Publique, Nouakchott, Mauritania; ⁵Centre de Support en Sante Internationale, N’Djamena, Chad

The continuum of arid and semi-arid regions from Mauritania to Chad in Africa, contains remote or hard to reach zones far away from the decision and planning centers. In those areas, livelihoods of populations are based on extensive production systems ranging from pastoralism to integrated production system. Considering their vulnerability and their economic, institutional and political marginalization, innovations are needed to secure their livelihoods and well-being.

**OBJECTIVES** The aim of this communication is to assess the progress of knowledge on health status and the provision of health and social services to nomadic pastoralists in the Sahel.

**METHODS** We review over ten years of transdisciplinary research in the Sahel, which was continuously validated through a series of stakeholder workshops bringing together decision-makers and communities to define intervention strategies and policy options for equity effectiveness.

**RESULTS** Resilience patterns were identified through a strong social network, alliances and information system. In the total absence of social services, wealthier external relatives either contribute with remittances or with hired private services to offer health care and education facilities. Support to resilience and the set-up allowed to better organize social services delivery. In Chad, joint human-animal health intervention together with intersectoral approach combining health and education was proven to be cost-effective and more adapted than single sector services. In Mali, besides joint health intervention, the Kel Tamashq communities considered that an integrated peaceful environment, infrastructure ‘pumped water’ as well as access to the market are the base for their social development. In Mauritania, cultural-epidemiological studies on tuberculosis provide the basis for current development of an adaptation of DOTS (Directly Observed Treatment, Short-course) to mobile people.

**CONCLUSION** Health and social services developed in close interaction with the concerned population and the authorities have the power to contribute to sustain livelihoods of population and provide them with incentives to better manage their environment in the context of global change.

Access to Drugs and Treatment Adherence

**O25-33**

**Snakebite in rural KwaZulu Natal: incidence, healthcare-seeking behaviour and use of traditional healers**

D. J. Sloan¹, M. J. Dedicoat² and D. G. Laloo³

¹Royal Liverpool University Hospital, Tropical and Infectious Diseases Unit, Liverpool, UK; ²Ngunzane Hospital, Dept of Medicine, Empangeni, South Africa; ³Liverpool School of Tropical Medicine, Liverpool, UK

**OBJECTIVES** Hlabisa sub-district in rural KwaZulu Natal has a population of 220 000 and is served by a 300 bed hospital and 15 Primary Health Care (PHC) clinics. Snakebite is a well reported health problem but data on treatment choices is scarce. Victims visit a mixture of Traditional Health Practitioners (THPs) and allopathic facilities. The aim of this study was to quantify snakebite incidence in Hlabisa and examine healthcare seeking behaviour, focussing on use of traditional medicine, THP consultation and delays in admission to hospital.

**METHODS** Snakebite incidence was calculated by retrospective register review at Hlabisa Hospital (2000–2005) and associated PHC clinics (2005 only). 50 consecutive in-patient snakebite victims were interviewed between April and December 2003 using a standard questionnaire. Bite-to-admission times were calculated for each case. Age, sex, ease of hospital access and use of traditional therapy were recorded for every patient. Factors associated with delayed admission and THP consultation were identified.

**RESULTS** Annual hospital snakebite incidence was 53 bites per 100 000 persons. In 2005, combined hospital and community incidence was 58 per 100 000. 80% of admitted snakebite victims used traditional medicine. 62.5% of these consulted a THP. Median time until admission was 7 h 15 min (interquartile range 4–14.25 h). Median time until THP consultation was 15 min (5–50 min). Patients travelling to hospital via multi-step pathways took longer to arrive. THP consultation was associated with bite-to-hospital admission delays of over 6 hours (Relative Risk: 1.82, 95% CI: 1.09–3.03, P = 0.0016). Non-statistically significant trends towards THP use were observed if hospital access was poor or patients were over 9 years old.

**CONCLUSIONS** Snakebite is a significant health problem in Hlabisa. Use of combined hospital and community data reduces the number of missed cases. Traditional medicine is widely used. THP consultation is associated with delayed admission. Engagement with traditional healers may improve this.

Policy options to assure availability and to control prices of essential medicines

**O25-56**

P. Lang⁴

⁴World Health Organization, Geneva, Switzerland

**BACKGROUND** The World Health Organization and Health Action International have developed a robust methodology to measure the availability and price of selected essential medicines in developing and transitional countries. Over 50 surveys in all WHO regions have been undertaken, examining medicine price, availability, affordability and price components of between 30 and 50 medicines. These surveys have examined both public and private sectors as well as innovator and generic medicines.

**RESULTS** In the public sector, procurement prices have generally been very competitive internationally. However despite...
these low prices, availability in public sector facilities has frequently been very poor. Medicines are often provided free in the public sector but when they are not, prices to patients are frequently three to five times higher than the procurement prices. In the private sector, availability has generally been better, particularly for innovator brand products. However, the price of these medicines may range from five to a hundred times the international reference price. Considerable variation exists between countries and regions in these findings. Price component analysis has tended to show that additional costs such as duties, taxes, wholesaler and retailer markups may more than double the manufacturers selling price.

CONCLUSION Depending on the national situation, governments have many policy options open to address these challenges. Removing duties and taxes is a relatively easy first step. Assessing the levels of markups added by wholesalers and retailers may lead to controls on these additional costs. Promoting generic medicine use, may depend on ensuring the quality of available generics. Where public sector procurement prices are dramatically different to private sector prices of essential chronic medicines, the public sector may need to provide such low-priced medicines for these patients through the private sector. Which ever policy options are implemented, careful monitoring for unintended impacts is likely to be necessary.

O25-57 How product development partnerships could deliver innovation to patients
B. Pecoul
1DNDi, Geneva, Switzerland

OBJECTIVES The objectives of DNDi – a collaborative, patient’s needs-driven, virtual, non-profit drug R&D organisation established in 2003 – is to deliver 6 to 8 new treatments by 2014 against some of the most neglected communicable diseases (malaria, sleeping sickness, leishmaniasis, and Chagas disease) and to establish a strong R&D portfolio that addresses patient needs for treatment.

METHODS A portfolio of 22 projects, which already contains strong projects for two of the target diseases and taps networks of expertise in many different fields, has been built. In 2007, DNDi’s first two products are being delivered: the fixed-dose artesinin-based combination therapies (ACTs), artemether-lumefantrine (ASAM) and artesunet-mefloquine (ASMQ).

RESULTS The partnerships forged by DNDi and its many collaborators provide a first concrete step towards evolving the competitive, market-driven model into a collaborative one that delivers innovation to all. In the case of ASAQ, DNDi has partnered with sanofi-aventis since 2004 on industrial, preclinical and clinical product development to optimise the quality of the drug and to expedite its availability. The DNDi partnership with Sanofi-Aventis has several innovative traits. The development of ASAQ has been in response to the needs of patients for something that is adapted to the field and simple to use. There is a commitment to make the drug available to all patients, right from the start. No patent protection has been sought, to the advantage of an affordable price (US $1 for adults, US $0.50 for children under 5). By partnering with a large pharmaceutical manufacturer, complementary competencies are synergized. Sanofi-Aventis has the capacity to manufacture the product and to register the dossier in many countries. DNDi plays an active role to engage new partners (pharmaceuticals, international organisations, national disease control programmes, NGOs, and governments) to facilitate ASAQ implementation, availability and adoption by endemic countries. DNDi continues to construct its network with those who can implement manufacturing and distribution (at affordable prices), ensure proper drug utilisation and pharmacovigilance, and ensure access to treatments.

CONCLUSION Building effective partnerships at the different stages of the R&D pipeline is critical for a PDP as it must proactively identify research opportunities with the greatest delivery potential to translate into improved treatment options, source such projects, build the full development plan, identify appropriate partners for each step, and ensure access to knowledge from private and public partners. DNDi’s innovative and successful partnership with sanofi-aventis could serve as a model for others.
Access to Drugs and Treatment Adherence II

O25-60
India’s medicine pricing anomalies
S. Srinivasan

1 LOCCOST (Low Cost Standard Therapeutics), Corporate Management, Vadodara, Gujarat, India

OBJECTIVES To present an analysis of the political economy of the pricing anomalies in India’s medicine scenario, efforts of activists and others and possible solutions as seen by those concerned with public health.

METHODS Delineation of pricing abnormalities, narration of advocacy efforts by public health activists, response of the State and examination of some of the reasons behind pricing anomalies. Market failure, severe asymmetry of information, lack of convergence between various health policy, pharma and industry policy of the government of India are identified. Analysis of data available of top-selling medicines and public health requirements reveal considerable dissonance. Some new emerging threats - like IP issues, antimicrobial resistance - are identified. Author’s own data about actual cost of manufacture of medicines will be used inter alia as benchmark. Author works for an NGO that manufactures essential medicines.

RESULTS Medicine availability scenario is a looming tragedy in India – a case of poverty and inadequacy amidst plenty.

CONCLUSION Policy options require considerable political will especially in the context of pressures of the national and international political economy. Paper examines the likely way that government needs to go and the probability of it doing so.

O25-61
Factors that facilitate and constrain adherence to HAART drugs among adults at four public health facilities in Botswana: a qualitative analysis
T. M. Moroka1, R. Ogenyi2, C. Ekzezi3, J. Kgaolweane4, S. Moyo5 and H. Madaki6

1 University of Botswana, Social Work Department, Gaborone, Botswana;
2 Ministry of Health, Clinical Services, Mahalapye Hospital, Mahalapye, Botswana;
3 Botswana Harvard Partnership Program, Gaborone, Botswana;
4 Ministry Of Health, Clinical Services, Gaborone, Botswana;
5 Botswana-Harvard School of Public Health, AIDS Initiative Partnership, Gaborone, Botswana;
6 Ministry of Health, Clinical Services, Molopololo, Botswana

OBJECTIVES To identify factors that facilitate and constrain adherence to antiretroviral therapy and identify possible interventions to improve adherence.

METHODS This is a qualitative, cross-sectional study conducted in four district hospitals (Serowe, Mahalapye, Maun and Molepolole) across Botswana providing ARV treatment (above 18 years). Focus group discussions were held with men and women groups of ARV users and the community members at the selected sites in order to identify key themes. Semi structured interviews with health workers and key informants were also conducted. Analysis revealed that the themes appeared to be linked, and these were then analyzed together.

RESULTS The study identified interrelated themes of constraints to adherence. Key constraints to nonadherence were non-acceptance of positive HIV status and non-disclosure; perceived lack of social support; stigma; transportation costs; and lifestyle-related issues. Key motivators of adherence were also identified as acceptance of one’s status and disclosure; belief in the efficacy of pills in treatment/pre-treatment health state; the desire to live longer and care for others, especially children and the elderly; availability of social support and self-regulatory self-efficacy in the ability to take and adhere to HAART.

CONCLUSION There are differences in the factors associated with adherence among men and women. The results of this study suggest how several factors are interlinked to influence adherence. These factors if explored further, could offer rewarding intervention inroads into promoting optimal adherence among patients on HAART in Botswana.

Equity and Health

O25-55
Is access to essential medicines part of the fulfillment of the right to health enforceable through the courts?
H. Hogerziel1, M. Samson1, J. Vidal Casanovas1 and L. Rahman-Ocora1

1 WHO, Medicines Policy and Standards, Geneva, Switzerland

OBJECTIVE To determine whether access to essential medicines as part of the fulfillment of the right to health is enforceable through the courts.

METHODS Systematic search to identify completed court cases in low and middle-income countries in which individuals or groups had claimed access to essential medicines with reference to the right to health in general, or to specific human rights treaties ratified by the government.

RESULTS We identified and analysed 71 such court cases from 12 countries. In 59 cases, access to essential medicines as part of the fulfillment of the right to health could indeed be enforced through the courts, with most coming from Central and Latin America. Success was mainly linked to constitutional provisions on the right to health, supported by the human rights treaties. Other success factors were a link between the right to health and the right to life, and support by public-interest non-governmental organizations. Individual cases have generated entitlements across a population group, the right to health was not restricted by limitations in social security coverage, and government policies have successfully been challenged in court.

CONCLUSION Skilful litigation can help to promote that governments fulfill their constitutional and international treaty obligations. Some cases are legal landmarks which have changed government policies with great impact on many patients. The main conclusion of this study is therefore that such court cases can indeed make a difference. This is especially valuable in countries in which social security systems are still being developed. The fact that most successful cases so far have taken place in Central and Latin America may now encourage individuals and patient groups in other continents. Redress mechanisms through the courts are an essential function in society, but should preferably be used as a last resort. Rather, policy-makers should ensure that human rights standards guide their health policies and programmes from the outset.

O25-59
Neglected patients in 30 villages of Luang Namtha province, February to June 2006
H. Barennes1, P. Manivongsy1, H. T. Nguyen1, P. Rene1 and M. Strobel1

1 Institut Francophone Medecine Tropicale, Vientiane, Lao People’s Democratic Republic

BACKGROUND Neglected diseases is a well known concept. The concept of neglected patients is less known.

OBJECTIVE Our study had 3 objectives: to seek neglected patients (it means out of the health system circuits), to study the factors...
involve[s] this negligence, and to investigate the health of the people in their village by measuring morbidity and mortality, hygiene conditions, health access.

METHODS We conducted a cross sectional survey in 30 randomised villages in 5 of Luang-Namtha districts. 10 randomised household per village were visited in their house. We performed active tracking of neglected patients. 300 Heads of household, 30 Chiefs of villages and 105 neglected patients were questioned using a standard questionnaire after written consent.

RESULTS Neglected patients were men around 40 years, of ethnic group Lao theung, farmers without schooling, and married. Goitre was the first pathology (23%), with female prevalence (sex ratio H/F = 1/2.5). 13% of the neglected subjects had transmissible diseases (tuberculosis, scabies, urethritsis), dangerous for the community and the family. We found few serious illnesses with lethal prognosis: 5 cases: 1 liver cirrhosis, 1 Pott disease, and 1 severe goitre. All patients but 19% had sought prior health care. Lack of money, absence of severity, need for work, absence of disease knowledge, chronic disease were the major factors for giving up the treatment or seeking care. From January to March there was 282 disease episodes among the 300 families.

CONCLUSION Overall there was a great disparity between villages. The situation seemed less serious than expected but proximity of health centre or unexplored access to drugs or traditional treatment could explain the situation. Mobile patients team could help to improve accessibility to treatment and reduced the number of neglected patients.

O25-62
Improving access to and use of psychotropic medicines
H. Haak1
1CHD- Consultants for Health and Development, Leiden, Netherlands

OBJECTIVES To survey and document ‘best practices’ in improving access to psychotropics in low-income countries.

METHODS Review of published and unpublished literature, calls in internet discussion forums, and interviews with key informants.

RESULTS Mental and behavioural disorders account for a large proportion of the global burden of disease, but only a minority of those suffering from these disorders receive basic treatment. Health systems in developing countries are often unable to provide even the most essential mental care. Possibly more than other diseases, mental disorders can have a crippling effect on surroundings of people suffering from these chronic conditions. In 2001 the World Health Organization called attention for mental health through a focused issue of the World Health Report. Recommendations were made on how to improve care for these conditions. As with other essential medicines, access of populations to essential psychotropics is determined by: (i) a rational selection; (ii) making prices affordable; (iii) ensuring sustainable financing; and (iv) availability of reliable health and social systems. In addition, there are four other determinants of key importance. These relate to (l) presence of strong mental health policies, which define a strategy to achieve improved access; (ii) mental health legislation that enhances, rather than obstructs, access; (iii) appropriate use of psychotropics; and (iv) systematic assessment and monitoring for continuous maintenance and improvement of access to care. However, whereas psychotropics have many aspects in common with other essential medicines, several other aspects need special consideration. Survey findings showed that documented efforts to improve the supply and use of psychotropics are still few, and that there are opportunities in all components of the medicines management cycle. Experiences in improving access to general essential medicines appear little applied in supply and use of psychotropics. Part of the psychotropics access problem may be addressed by improving the availability of independent treatment information and guidelines, based on the essential medicines concept and by an authoritative source such as WHO.

CONCLUSION The paper will deal with strategies to improve access to essential psychotropics and the specific challenges involved.

Non-Communicable Diseases

O25-63
An ‘essential’ method of risk stratification for hypertensives performs in a low-income setting: A prospective field test in Ecuador
F. Avanzini1, M. Anselmi2, P. Prandi2, G. Montalvo2, C. Roncaglioni1, J. Moreira1, S. Ibarra1, M. Márquez1, D. Arman1, C. Caicedo3, F. Colombo4, P. Camisasca5, G. Tognoni5
1Istituto di Ricerche Farmacologiche Mario Negri, Milano, Italy; 2Ospedale Sacro Cuore, Centro Malattie Tropicale, Negrar (VR), Italy; 3Centro de Epidemiología Comunitaria y Medicina Tropical, Esmeraldas, Ecuador; 4Consorzio Mario Negri Sud, Santa Maria Imbaro, Italy

OBJECTIVES Recommended strategies to assess the cardiovascular risk profile in hypertensives are hardly transferable to low-income settings. We wanted to assess the predictive power of an ‘essential’ package of handy data routinely available in field conditions.

METHODS In a remote rural region of Ecuador, a cohort of 1643 hypertensive patients was followed for up to 11 years documenting blood pressure control and the incidence of cardiovascular events according to their baseline cardiovascular risk profile. In a sub-sample of 504 subjects the predictive power of the risk profile produced with ‘essential’ data routinely available in community, which do not include laboratory investigation, was compared with the standard method recommended by the World Health Organization-International Society of Hypertension (WHO-ISH) guidelines.

RESULTS With both the essential and the standard methods a highly significant association was observed between the level of predicted risk and the incidence of cardiovascular events (P < 0.001). Up to 3/4 of all cardiovascular events were reported among subjects classified as at high or very high risk with either method. The two methods did not differ in terms of sensitivity (77% and 78%), specificity (66% and 63%), or predictive accuracy (67% and 65%).

CONCLUSION The risk stratification of hypertensive patients with an essential (i.e. available and handy) package of predictors performs at least as well as the more comprehensive method proposed by WHO-ISH.

O25-64
Differential diagnosis of hemoptysis in developing countries: an experience from a university teaching hospital in Nepal
N. Bhatta1, B.P. Koirala1, D. Ghopa, Dharan, Nepal; B. P. Koirala Institute of Health Sciences, Internal Medicine, Dharan, Nepal; B. B. B. P. Koirala Institute of Health Sciences, Internal Medicine, Ghipa, Dharan, Nepal; 2Department of Pulmonology, LUMC Leiden, Netherlands; 3IBM/OMTA, Erasmus University, Health Policy and Management, Rotterdam, Netherlands

OBJECTIVES Hemoptysis remains a significant clinical symptom in patients attending the health care facilities of developing countries.
countries. But evidence-based studies providing information regarding the clinico epidemiology and the risk stratification of the patients presenting with this important symptom is lacking. We aimed to evaluate the characteristics of patients presenting with different degrees of hemoptysis in a tertiary care hospital in Nepal and to identify the etiology of hemoptysis on the basis of various sociodemographic features and combination of certain clinico-radiological variables easily available to the treating physicians.

METHODS A retrospective observational study conducted at the department of internal medicine at the B.P. Koirala Institute of Health Sciences (BPKIHS), which is a large, 650 bedded tertiary care, university teaching hospital situated in eastern Nepal. The hospital medical records of all the consecutive patients admitted with the complaints of hemoptysis at our study center from January 2003 to December 2005 (3 years) were reviewed retrospectively. Microsoft windows based statistical Package for social sciences (SPSS, version.13) was employed for data analysis. After analyzing the descriptive statistics, patients were compared based on their primary diagnosis and severity of hemoptysis and other variables.

RESULTS During the study period, 360 patients were admitted with hemoptysis at our study center. 63.9% were male; the average age was 48.32 years (age range of 16–80 years). 285 (79.2%) were smokers, 48% of the patients had significant exposure to indoor air pollution due to use of biomass fuels. Active pulmonary tuberculosis (28.9%), post tubercular bronchectasis (27.2%) and lung cancer (26.7%) were the three most common causes of hemoptysis. Other respiratory and non respiratory causes accounted for nearly 15% of cases. The exact etiology could not be elicited in 2% of the patients. Smokers with exposure to indoor air pollution had more severe hemoptysis irrespective of its etiology.

CONCLUSION This study shows that the clinical spectrum of patients presenting with hemoptysis in tropical countries seems to be changing over the past few years and lung cancer appears to be an emerging cause. Recent epidemiologic and sociodemographic transition as well as exposure to other risk factors for respiratory diseases should be considered while formulating the differential diagnosis of hemoptysis and its severity in developing countries.

O25-65
Prevalence of under nutrition among adolescent girls and its impact on their health: a study of semi urban area of Kathmandu

U. Koirala

Tribhuvan University, Central Department of Home Science, Kathmandu, Nepal

OBJECTIVES To assess the nutritional status of adolescent girls and their awareness/practices about health concerns in semi urban area of Capital city Kathmandu

METHODS
- Representative adolescent girls of age 12–19 were randomly selected and anthropometric data (including BMI) were taken then analyzed comparing with NCHS standard references,
- Health awareness data were taken with the help of structured questionnaire,
- Tried to observe biomedical signs (including HB) and symptoms of malnutrition of the respondents,
- Case study.

RESULTS Menstruation is a turning point of adolescent life. Late menstruation is the sign of malnutrition. 38% cases reported menarche at the age of 14 and 32.4% reported menarche at the age of 13. Early marriage is still practiced in this society. The overall percentage of married respondents was 22.4; of these, 17.3% already had one or more children. Discrimination on food distribution prevails to this day, and 56% of respondents said that their brothers were given more food; while 44% said that their brothers get nice food (ghee, curd, milk etc.). The prevalence of thinness among adolescent girls is very high in the study village. Only 48.4% had a normal BMI (>18.5); 18.9% had a BMI of 17–18.49 and 20.5% had a BMI <16. Energy consumption by the respondents was low; only 68% consumed animal protein very occasionally. Despite this, the girls performed many physically demanding tasks, such as washing clothes (94%), cooking (97%), carrying water (86.2%), house cleaning (53%) and collecting fodder from the nearby forest. Only 54.3% saw a doctor for their illnesses; 28.9% used dhamijhakri, pokhuke (traditional faith healer) and puja (worship of god) to cure their health problems.

CONCLUSION The prevalence of malnutrition among female adolescents in semi-urban Kathmandu is very high and can have a negative impact on their health and productivity and that of their children as well.

O25-66
An outbreak of infant beriberi in Mayotte in 2004

C. Puca, A. Tajahmady, D. Sissoko, A. Abaines and I. Quatresous

1Institut de veille Sanitaire, Saint-Maurice, France; 2CIRE Réunion-Mayotte, Saint-Denis de la Réunion, France; 3DASS de Mayotte, Mammoudzou, France

Between April and July 2004, an outbreak of infant beriberi (B1 vitamin deprivation) occurred in Mayotte (population 180,000), a French territory in the Indian Ocean. We report the investigation of this outbreak.

OBJECTIVES To confirm the aetiology of the outbreak, describe its epidemiological patterns and guide implementation of control and preventive measures.

METHODS Definitions of suspect and probable cases were based on clinical symptoms and therapeutic response. Prospective surveillance was organised in health services and all infant deaths that occurred after April 1st was investigated. A case-control study exploring socio-economic as well as nutritional factors associated with the disease was carried out.

RESULTS Between April 4th and July 13th, 32 cases of beriberi were reported in Mayotte, of whom 20 died (case fatality ratio: 62.5%). Age ranged between 1 and 4 months (median 2 months), sex-ratio M/F was 2.6. Two of the cases were biologically confirmed. The majority (n = 17) of cases occurred in the capital city Mamoudzou. All beriberi cases included in the case-control study (n = 21) were breastfed compared to 24 out of 40 controls (OR 29.0, [11.2–81.5]). During postpartum, the mothers of cases consumed the traditional ‘Oubou’ (polished rice washed and boiled) more frequently than control mothers (OR 5.3, [2.0–15.4]). Case mothers also consumed less frequently meat (OR 11.6, [1.2–115.3]) and vegetables (OR 3.9, [1.1–14.5]).

CONCLUSION Public health measures based on vitamin supplementation to both pregnant women and newborns were implemented mid-June and the outbreak ended soon after. This, together with the findings of the case-control study confirmed the aetiology and the nutritional origin of the outbreak. The nutritional behaviour of Mayotte’s population is determined by a combination of both traditional beliefs and access to modern, sometimes over-refined, food. Further investigations are being carried out in order to assess potential vitamin and micronutrient deficiencies and to drive long term preventive measures based on health and nutrition education.
O25-67
Heavy metals in edible green vegetables grown along the sites of the Zanjanrood river in Zanjan, Iran: implications for human health

A. Eslami1, M. Mehrasbi1, M. Peyda1, M. Noorani2 and A. Maleki3
1Zanjan University of Medical Sciences, Department of Environmental Health Engineering, Faculty of Health, Zanjan, Iran, Islamic Republic of Iran; 2Zanjan University of Medical Sciences, Department of Public Health, Faculty of Public Health, Zanjan, Iran, Islamic Republic of Iran; 3Kurdistan University of Medical Sciences, Department of Environmental Health Engineering, Faculty of Health, Sanandaj, Iran, Islamic Republic of Iran

Vegetables constitute essential components of the diet, by contributing protein, vitamins, iron, calcium and other nutrients which are usually in short supply. Vegetables grown at environmentally contaminated sites in Zanjan could absorb and accumulate heavy metals at concentrations that are toxic to human health. The environmental exposure to heavy metals is a well-known risk factor for cancer. The major source of these heavy metals is industrial effluents and indiscriminate disposal of domestic or sewage drainage to the river untreated. We investigated levels of five heavy metals (Cd, Pb, Zn, Cr and As) in various vegetables (roots and leaves of radish (Raphanus sativus L.), leek (Allium ampeloprasum L.), sweet basil (Ocimum basilicum L.), and Italian parsley (Petroselinum crispum) cultivated along the bank of a river passing through the city. They are basis of human nutrition in this region a great relevance to human health. The contributions of the vegetable to the daily intake of the heavy metals from the vegetables were determined. Atomic absorption spectrometry was used to estimate and evaluate the levels of these metals in the vegetables. The results of this survey showed the following ranges (mg/kg): 3.89–32.94, 3.15–27.68, 43.61–223.10, non-detectable, non-detectable for Lead, Cadmium, Zinc, Chromium and Arsenic. Some vegetables contained high levels beyond the safe levels given by FAO and WHO for human consumption. When the mean levels of Lead and Cadmium (10.65 and 9.22 mg/kg) were taken into account the daily intake contribution of the metals was 2.32 and 2 mg for Lead and Cadmium. Increase in vegetable consumption by community the situation could worse in the future. Treatment of industrial effluents and phyto-extraction of metals from polluted environments could reduce health risk.

O25-69
Successful sustainable action towards the achievement of child health

U. Mohammed1
1Sri Venkateswara University, Population Studies and Social Work, Tirupati, India

BACKGROUND The focus of this paper is on successful provision of integrated child health services to the children of Lambadas, a tribal community living in the rural areas of Andhra Pradesh, India. Most of the deliveries (80%) used to take place at home, 60% of the babies born to them were low birth weight babies (<2.5 kg). Only a few (25%) were using hospital facilities during pregnancy and delivery. Infant mortality rate (102) and under-5 mortality rate were very high (123). Peri-natal transmission of HIV was 4%. About 75% of the children were anaemic and under nourished. Many children used to die due to diarrhea and acute respiratory infections. Against this backdrop, to bring down infant and child mortality and morbidity and improve the health status of children, an integrated child health services programme was designed and implemented in this community in the year 2003.

OBJECTIVES 1. To bring down infant and child mortality and morbidity in it2. To improve the overall health status of children.

METHODS AND MATERIALS A cluster of 120 villages with a population of about 220 000 was selected for the programme. The programme was carried-out with the help of trained social workers, paramedics and doctors.

PROGRAMME INTERVENTIONS Community education and mobilization information, education and communication programmes on new born and child health services, such as Enactment of dramas, Folk media, Distribution of literature on newborn and child health services, Group discussions, Meetings, One-to-one meetings, Involvement of fathers in new born and child health
programmes, Pre-natal, natal and post-natal care at the doorstep and at the hospital, Prevention of peri-natal transmission of HIV Applied nutrition programme for infants and children, Immunization programme for infants and children, Treatment for common ailments Counselling

RESULTS As many as 11 475 persons utilized child health services between 2003 and 2006. The number of persons utilizing child health services has been on the increase year after year. Now, all the children are immunized as per the immunization schedule. Many more achievement of the programmes are given in the full length paper. Peri-natal transmission of HIV, infant and under-5 mortality rates, number of low birth babies, and deaths due to diarrhea and respiratory infection are declining fastly.

CONCLUSIONS The programme interventions are worth replicating in all the developing countries of the world, where infant and child morbidity and mortality are high. The programme interventions would certainly help to achieve the millennium development goal No. 4 by 2015.

O25-70
Prevalence of group B streptococcus in pregnant women in Maputo, Mozambique

F. de Steenwinkel1, H. Tak1, A. Muller2, J. Nouwen2, P. Oostvogel2 and S. Mocumbi1
1Erasmus University Hospital, Medical Microbiology and Infectious Diseases, Rotterdam, Netherlands; 2MCHaaglanden, Obstetrics and Gynaecology, The Hague, Netherlands; 3Erasmus University Hospital, Department of Medical Microbiology and Infectious Diseases and Department of Internal Medicine, Rotterdam, Netherlands; 4MCHaaglanden, Clinical Microbiology, The Hague, Netherlands; 5Central Hospital Maputo, Obstetrics and Gynaecology, Maputo, Mozambique

OBJECTIVES Group B streptococcus (GBS) is an important cause of neonatal infectious disease acquired after transmission from mother to neonate. Prevalence of maternal carriage of GBS varies according to the geographical area and in time (1–31%). Despite that only 1–2% of neonates born from colonised mothers develop invasive disease, GBS is a major cause of infectious neonatal morbidity and mortality in the industrialized world. Ten years ago a low prevalence of 1% was found in Mozambique. We performed a study to determine the present prevalence of GBS carriage in pregnant women in Maputo, Mozambique.

METHODS After obtaining informed consent, a rectovaginal swab was taken from women between 35 and 37 weeks of pregnancy visiting the antenatal clinic. The swab was inoculated at 37 °C into a selective broth medium. The broth was subcultured onto blood-agar. GBS suspected colonies were Gram-stained and catalase reaction was performed on Gram-positive cocci in chains. Identification of GBS was performed by a streptococcus grouping method. The broth was subcultured onto blood-agar. GBS suspected colonies were Gram-stained and catalase reaction was performed on Gram-positive cocci in chains. Identification of GBS was performed by a streptococcus grouping method. A baseline study was needed to assess the results of any preventive measures as recommended by the Centers for Disease Control and Prevention (CDC). Since GBS carriage fluctuates in time, future periodic monitoring of GBS carriage in Maputo is indicated to justify deviation of generally accepted and costly preventive measures.

RESULTS Of 113 pregnant women participating in this study only 2 were found to be carriers of GBS. The prevalence of GBS carriage was 1.8% (95%-confidence interval 0.0–4.0).

CONCLUSION The low GBS carriage rate in Maputo as confirmed in our study supports the current practice in Mozambique not to implant preventive measures as recommended by the Centers for Disease Control and Prevention (CDC). Since GBS carriage fluctuates in time, future periodic monitoring of GBS carriage in Maputo is indicated to justify deviation of generally accepted and costly preventive measures.

O25-71
Retrospective study on nephroblastoma in Malawi

W. Lameris1, J. C. H. Wilde2, E. van Hasselt2, E. S. Borgstein3 and H. A. Heij1
1Academic Medical Center, Paediatric Surgical Center of Amsterdam, Amsterdam, Netherlands; 2Academic Medical Center, VU Medical Center, Paediatric Surgical Center of Amsterdam, Amsterdam, Netherlands; 3University of Malaus, Queen Elizabeth Central Hospital, Department of Surgery, Blantyre, Malawi

OBJECTIVES A baseline study was needed to assess the results of the present management of Wilms tumours for future comparison with standardized protocols, in a developing country.

METHODS The case records of 40 patients with a WT (median age 4.2 years; 19 males, 21 females) admitted to QECH from January 1998 to May 2004 were reviewed in a descriptive, retrospective study. General condition at admission, investigations, management and outcome were assessed.

RESULTS 1-year post-operative survival of WT patients lies between 20% and 50%. More than half of the patients presented in poor general condition as defined by clinical examination with a symptomatic mass. 72.5% of all patients could be diagnosed as having a WT by history taking, physical examination and US. Amount and type of chemotherapy varied greatly between patients. 32 patients underwent a total nephrectomy, 1 patient partial nephrectomy. 42% of operated cases had a recurrence (16% local, 22% local + distant, 9% distant).

CONCLUSION At QECH patients with WT are generally in a poor condition and have a bad prognosis. Organizational problems and insufficient follow-up are expected to give problems during a prospective, randomized and multi-centered trial.

O25-72
Predictors of performance of village level workers trained in home based management of young infants

A. Sinha1, R. Rasaily2, S. Kumar3, M. Roy1 and N. C. Saxena3
1Indian Council of Medical Research, Division of Reproductive Health and Nutrition, New Delhi, India; 2Indian Council of Medical Research, Reproductive Health and Nutrition, New Delhi, India; 3Indian Council of Medical Research, RHN, New Delhi, India

OBJECTIVES Newborn health challenge faced by India is bigger than that experienced by any other country. Each year 20% of the world’s infants ~ 26 million are born in India of which 1.2 million die before completing the first 4 weeks of life. This amounts to 30% of the 3.9 million neonatal deaths worldwide. In India about 60% of births occur at homes. To address the issue of high neonatal mortality we are conducting a cluster randomized intervention study which tests the effectiveness of delivering home based management of young infants by village level worker, carried out at 5 districts in rural India. Here we report the findings of training of the village level workers.

METHODS This is a three-arm study with village health worker called the ‘Shishu Rakshak’ (SR) in one arm, the existing Anagawanadi Worker (AWW) in the other arm and control area with existing government health system. The package of intervention is being delivered by these workers after successful completion of a rigorous training conducted in a step ladder fashion by master trainers over a one year period. Interim evaluations at the end of each of the seven workshops and a final evaluation at the end were conducted to assess knowledge and skills of the workers.

RESULTS A total of 210 SRs and 204 AWWs were trained and evaluated at 4 centers. Overall, a higher proportion of SRs (71.4%
Prevalence of enteropathogen bacteria in children under five years old with acute diarrhea in Tehran, Iran

O25-73

P. Jahani1, M. M. Azad2, M. Taghakhoo3, M. Noch2, L. Shokrzadeh2, H. Dadrin1, P. Torabi1, P. Yekta1, M. A. Porooshaneghahi1 and M. R. Zali2

1Research Center for Gastroenterology and Liver Diseases, Shahed Beheshti University of Medical Sciences, National Research Department of Foodborne Diseases and Acute Diarrhea, Tehran, Iran; 2Islamic Republic of Iran; 3Pasteur Institute, Department of Microbiology, Tehran, Iran, Islamic Republic of Iran

OBJECTIVES Diarrhea is one of the most debilitating and fatal disease especially in developing countries such as Iran. This study was investigated the prevalence of different bacterial pathogens in children less than 5 years old with acute diarrhea in Tehran, Iran.

METHODS A total of 1087 fecal samples from children under 5 years of age during April 2003–September 2005 from 4 hospitals and 13 clinical centers in Tehran province were including in this study. All specimens were tested for Campylobacter spp., Shigella spp., Yersinia spp. and Salmonella spp by standard methods. Molecular diagnostic tests were done for Enteropathogenic E. coli (EPEC), Enterotoxigenic E. coli (ETEC), Enteraggregative E. coli (EAEC) and Entoeohemorhagic E. coli (EHEC). Amplification of ipaH and inv genes was used for identify Shigella spp and Salmonella spp by PCR.

RESULTS A total of 1137 children the male: Female ratio was 1.2:1 and 66.5% (n = 364) of samples were obtained from children <1 year of age. In this investigation (n = 555) 51% diarrhea specimens related to pathogenic bacterial and in the other of patients whose specimens did not yield a pathogens (n = 532). Shigella spp was the most prevalent rate and was found in 148 (26.7%) samples. EHEC, EPEC, Campylobacter, Salmonella and ETEC were 92, 70, 60, 42, and 38 respectively. In this study Yersinia was not found in any cases. Campylobacter spp were most frequently associated with watery stools (55%) and blood was observed in stools of 20.3% patients infected with Shigella spp and in 16.25% STEC positive cases.

CONCLUSION Diarrhea is a major public health problem for children in developing countries. Knowledge of the enteropathogenic bacteria responsible for diarrheal illnesses is essential for implementation of appropriate public health measures to control these diseases. The large number of Shigella and EHEC infections was found in this study suggests these organisms are important causes of diarrhea among infants and children in Iran.

Amoebiasis Diagnosis, Epidemiology and Interventions

O25-74

Amebic liver abscess: E. histolytica strains with a non- previously described genotype in Mexican patients

F. Ramos1, G. Garcia1, A. Valdez1, P. Moran1, E. Gonzalez2, O. Valenzuela3, P. Gaytan2, J. Yañez4, E. Melendro and C. Ximenes2

1Faculty of Medicine, Autonomous University of Mexico, Experimental Medicine, Mexico, D.F., Mexico; 2University of Sonora, Hermosillo, Sonora, Mexico; 3Institute of Biotechnology, Autonomous University of Mexico, Cuernavaca, Morelos, Mexico

OBJECTIVES To determine the genotype of Entamoeba histolytica responsible of amoebic liver abscess through the analysis of the polymorphic region of the chitinase gene.

METHODS Three males and one female patients who had amoebic liver abscess (ALA) were studied. The ALA was drainage through a sonography guide hepatic procedure. The material was treated for the DNA extraction using the QIA amp DNA mini kit (Qiagen). PCR of the polymorphic region of chitinase gene was performed with specific oligonucleotides. Amplification products were sequenced using the Big Dye system (Applied Biosystem, CA) and the terminator cycle sequencing fluorescence method (ABI PRISM 3700, Applied Biosystem, CA).

RESULTS The sequences obtained were equal between each other, but the alignment of the sequence with the already CHI reported sequences in Gen Bank data base shown none identity. This new sequence was registered in the Gen Bank with the reference number EF 445962.1.

CONCLUSION This finding support the previous observations related with particular geographic distribution of E. histolytica or E. dispar strains and their particular high genetic variability.

Variations in associated bacterial flora during amoebiasis

O25-98

J. Paul1, R. Rani1 and S. Bhattacharya2

1Jawaharlal Nehru University, School of Life Sciences, New Delhi, India; 2Jawaharlal Nehru University, School of Environmental Sciences, New Delhi, India

OBJECTIVES Trophozoites of Entamoeba histolytica live in the colon of the human intestine together with resident microflora. Little is known about the changes in flora that may occur during AME bic infection or during amebic liver abscess. We attempted to establish whether the change in gut flora is either due to parasitic infection or metronidazole treatment.

METHODS Fecal samples from amebic liver abscess patients; healthy E. histolytica negative individuals and E. histolytica positive asymptomatic individuals and pus samples from amebic liver abscess patients were tested for the presence of various anaerobic and aerobic bacterial genera using genus/species specific primers derived from 16S rRNA gene. PCR products were cloned and sequenced. Stool samples from volunteers were tested during pre- and post-metronidazole treatment. RFLP techniques were employed for characterising the family of nif genes.

RESULTS Statistically significant reduction due to metronidazole treatment in the population of beneficial bacteria like, Bacteroides, Bifidobacterium, Clostridium was observed in stool samples of amebic liver abscess patients and metronidazole treated volunteers. Statistically significant drop in Lactobacillius population in asymptomatic E. histolytica positive individuals and amebic liver abscess patients, was due to E. histolytica infection as no change in
Abstracts of the 5th European Congress on Tropical Medicine and International Health

VOLUME 12 SUPPL 1 PP 25-146 MAY 2007

this genus was observed in metronidazole treated volunteers. Significantly, the presence of two gut resident anaerobic bacteria viz.; Bacteroides and Peptostreptococcus in amebic liver abscess pus samples was recorded. In addition, PCR amplification showed the presence of metronidazole resistance genes in fecal and pus samples of amebic liver abscess patients and in fecal samples of metronidazole treated healthy volunteers. PCR-RFLP studies carried out with the above samples confirmed the presence of nim E genes predominantly when compared to other families of nim genes reported earlier. Few samples showed the presence of nim B genes as well. Presence of IS element ISB6 in the samples positive for nim E gene further confirmed the association of this element with the nim E gene. Association of nim E gene with the Peptostreptococcus-positive samples was quite striking. CONCLUSION This study points to the need to reconsider the ameba-bacterium relationship in the intestine and extraintestinal tissues, and the role of bacteria in amebic pathogenesis.

O25-75
Prevalence of Entamoeba histolytica within a population of food handlers in an urban and rural setting and the impact of hygiene training on positivity trends

E. Njagi1, and L. A. Mambo2
1Kenyatta University, Biochemistry and Biotechnology, Nairobi, Kenya; 2Homegrown (K) Limited, Microbiology, Nairobi, Kenya

Amebiasis is endemic in many developing countries and the 10% global prevalence estimate made though still widely quoted, was based on data collected before the formal redescription of the species and so does not distinguish between infections with E. histolytica and E. dispar. It is now known that even in areas where invasive amebiasis is common E. dispers is by far the more prevalent species. In response to the current public health concerns pertaining to over diagnosis and treatment of E. histolytica, the study objective was to determine the prevalence of E. histolytica in the study population and the effect of hygiene training on positivity trends. Investigations were done using two study groups, one in an urban setting, with access the treated piped water and operatives exposed to hygiene training every 6 months. The other group was based in a rural setting, with minimal access to treated water and given hygiene training every 6 months. Study subjects were further subdivided into clinical and routine cases. Stool specimens positive for E. histolytica IE. dispers using microscopy were subjected to the molecular-based enzyme-linked immunosorbent assay (ELISA) to identify amebic antigens in stool and hence differentiate E. histolytica from E. dispers. Of the 403 clinical cases positive for E. histolytica IE. dispers only 1.2% (5/403) were positive for E. histolytica. Of the 6112 routine cases, 21 were positive for E. histolytica IE. dispers but only 7 of these for E. histolytica. These results indicate that E. histolytica is greatly over diagnosed and that the prevalence in these areas is about 0.11% (7/6112). Also, with continuous hygiene training from 2001 to date, cases of E. histolytica IE. dispers have continuously decreased to almost 0% in the urban population and about 1% in the rural population. These results will have a medical impact because as until now both infections are usually treated because most medical institutions in Kenya have not adopted differential diagnosis. Also, hygiene education will greatly reduce the number of treated cases despite that fact that differential diagnosis may not be adopted due to financial constraints.

O25-76
Use of real-time PCR assay for detection of E. histolytica in diarrheal and non-diarrheal stool specimens in Bangladesh

R. Haque1, D. Mondal1, M. Kabir1 and W. A. Petri Jr.2
1ICDDR, B, Laboratory Sciences Division, Dhaka, Bangladesh; 2University of Virginia Health System, Division of Infectious Diseases and International Health, Charlottesville, USA

OBJECTIVES New approaches to the detection of E. histolytica are based on the detection of an E. histolytica-specific antigen and DNA. Several groups have reported the detection of amebic antigen in stool samples, serum, liver abscess pus samples, and saliva using enzyme-linked immunosorbent assay methods. Several PCR-based tests that detect E. histolytica-specific DNA in stool samples and liver abscess pus specimens are more sensitive than traditional PCR assays and antigen detection test. However, clinical evaluations of these real-time PCR assays have not been performed extensively. The objective of this study was to use real-time PCR assay for detection of E. histolytica-specific DNA in E.histolytica-positive stool samples collected from different sources in Bangladesh.

METHODS Real-time PCR assay and antigen detection tests for specific detection of E. histolytica have been used. The diarrheal stool samples were collected from ICDDR, B’s Dhaka Hospital and from a cohort study in Mirpur, Dhaka. Non-diarrheal stool samples were collected from another hospital in Dhaka.

RESULTS We report here the use of real-time 80% (53/66) of the antigen detection test positive stool samples of ICDDR, B’s Dhaka Hospital stool samples were positive by real-time PCR. But 97% (28/29) of non-diarrheal stool samples that were antigen detection test positive were also positive by real-time PCR assay. Similarly, 99% (76/77) of diarrheal stool samples from the cohort study were also positive by the real-time PCR assay.

CONCLUSION We concluded that real-time PCR assay detected significantly less E.histolytica antigen detection test positive diarrheal stool samples from ICDDR, B’s Dhaka hospital compared to non-diarrheal stool samples as well as diarrheal stool samples from the cohort study.

Syndromic Approach of Fever

O25-77
Evaluation of the performance of the KABISA expert system in diagnosing febrile illnesses occurring after a stay in the tropics

J. Van den Ende1, R. Demeester1, E. Bottejeu1, Y. Van Laethem2 and R. Van Hauwe2
1Institute of Tropical Medicine, Clinical Sciences, Antwerp, Belgium; 2Saint-Pierre University Hospital, Infectious Diseases, Brussels, Belgium

OBJECTIVES The few existing expert systems for imported diseases provide a ranking of possible diagnoses based on the data introduced by the clinician or suggest clinical management. The Institute of Tropical Medicine, Antwerp, upgraded recently its teaching software, KABISA, into an interactive expert system, in which a tutor suggests step-by-step further testing, with reassessment of the case each time a new finding is entered by the user. Since it aims at helping clinical decision at the point-of-care, the list of findings is limited to those usually available on the first day in a travel clinic. This study intends to validate the KABISA expert system with a series of patients from another hospital.

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METHODS From October 2005 to September 2006, all patients presenting with fever after a stay in the tropics at the emergency ward of the Saint Pierre University Hospital, Brussels, Belgium, were prospectively evaluated by the main investigator. The data of all cases found with a definite etiologic diagnosis (n = 54/81) were entered in the KABISA expert system, and the hypotheses generated by the software were compared with the true diagnosis.

RESULTS The cohort (n = 81) was mainly composed by male (59%) adults (mean age = 36 years). Many travelers were native of tropical countries (64%), and the vast majority (81%) was returning or arriving from sub-Saharan Africa. The 54 challenged cases had the following definite diagnoses: Plasmodium falciparum malaria (48%), cosmopolitan respiratory tract infection (24%), non-falciparum malaria (6%), bacterial enteritis (4%), other tropical condition (4%) and other cosmopolitan infection (15%). The correct diagnoses were ranked first in 50 cases (93%). First-ranking reached 100% (26/26) for P. falciparum malaria, 100% (5/5) for the other tropical conditions and 83% (19/23) for the non-tropical infections. Two severe conditions were missed: a pyogenic liver abscess (first-ranked KABISA hypothesis: amebic liver abscess) and a non-typhi salmonella bacteraemia in a HIV-positive patient (first hypothesis: enteric fever).

DISCUSSION AND CONCLUSION The KABISA expert system performed well in this study population, which was characterized by a large proportion of malaria cases (54%), a rather straightforward diagnosis. It might become an effective tool in helping first-line non-expert clinicians confronted with the challenging diagnosis of imported fever. In addition, its long-experienced pedagogical component, which challenges users with software-created cases, might offer a qualitative added-value. Further prospective evaluation with a larger sample size and in other situations is still required.

O25-78 Systemic febrile illness in patients coming from the tropics: analysis of the cases attended in the University General Hospital of Alicante, Spain

C. López-Rodríguez1, D. Torrón1, J. M. Goni1 and J. Portilla1

1University General Hospital of Alicante, Internal Medicine and Infectious Diseases Department, Alicante, Spain

OBJECTIVES To describe the epidemiological characteristics and the etiology of the systemic febrile illness in patients coming from the tropical or subtropical regions.

METHODS Descriptive and retrospective study. We reviewed the clinical histories of patients with imported febrile syndrome attended at the University General Hospital of Alicante (Spain) between 1st of July 2000 and 28th of February 2006. The information was introduced in a protocol. Descriptive and bivariate analysis were performed.

RESULTS We attended 92 patients with systemic febrile illness. The average age was 37 years (23–51). Sex: 47 men (51%) and 45 women (49%). Travellers: 39 (42%), immigrants 53 (58%). Sixty-four cases were from Africa (70%), mainly Guinea Equatorial (39%); 22 patients from Central and South America (24%), most of all, Ecuador (6.5%) and three cases from India. The patients were referred from: Urgency Services (59%), International Vaccination Centres (14%) and Health Centres (17%). 70% of our patients were hospitalized. The first diagnosis was malaria (41%), followed by respiratory infections (14.2%), unspecified viral infections or influenza like syndrome (5%), dengue (5%), travel diarrhea (4%), tuberculosis (4%), urinary infections (3.3%), acute amigdalitis (2.2%), visceral leishmaniasis (2.2%), rickettsial infections (2.2%) and miscellaneous cases (9.9%). Forty malaria cases were diagnosed, 35 (88%) coming from Africa (RR 14.13; 95% IC: 5.4–36.8%; P < 0.001). Malaria cases etiology: Plasmodium falciparum (68.6%), Plasmodium vivax (11.4%), Plasmodium malariae (5.7%) and Plasmodium spp. (14.3%). We diagnosed 38 cases of Paludism (41.3%), 31 in Africa (86%), opposed to only 5 cases in America (14%). Of the total number of 92 patients who presented fever, 63 (68.5%) came from Sub-Saharan Africa (RR 4.95; 95% IC: 3.04–8.06; P < 0.001). All cases of dengue coming from Central and South America.

CONCLUSION 1. Malaria is the most frequent diagnosis in our patients with systemic febrile syndrome coming from the tropic. 2. The risk of suffering malaria is higher in Africa. 3. The probability of dengue diagnosis is higher in patients coming from America.

O25-79 Viral respiratory tract infections among patients with acute undifferentiated fever in Vietnam

L. P. Hoang1, T. T. N. Tran2, G. Vandoornum1, J. Groen1, Q. B. Tran3, T. G. Phan1, Q. H. Le1, V. N. Nguyen1, P. A. Kager4 and P. J. de Vries4

1Cho Ray Hospital, Dept. of Tropical Diseases, Ho Chi Minh city, Vietnam; 2Cho Ray hospital, Dept. of Microbiology, Ho Chi Minh city, Vietnam; 3Academic Medical Center, Dept. of Virology, Rotterdam, Netherlands; 4Focus Diagnostics, Department of Microbiology and Virology, Cypress CA, United States of America; 1Malaria Control Center of Binh Thuan province, Phan Thiet city, Vietnam; 3Academic Medical Center, Dept. of Infectious Diseases, Amsterdam, Netherlands

OBJECTIVES The contribution of viral respiratory tract infections to the total of acute fever, presented to the primary health services, and their clinical presentation were investigated in Binh Thuan province, Vietnam.

METHODS Patients with undifferentiated fever seeking help at thirteen primary health facilities in Binh Thuan were enrolled. Signs, symptoms, patterns of health seeking, presumptive diagnosis, treatment, referral and final outcome were recorded. Serum samples were collected at first presentation (t0) and after 3 weeks (t3) for serological diagnosis. Patients were selected at random from the data and serum archive of 2001 through 2005 after excluding dengue as the cause of their fever. 610 were tested with ELISA for Parainfluenza, Influenza A and B and RSV.

RESULTS In 2005, acute viral respiratory tract infections were confirmed in 32/322 patients (9.9%): 15 (4.7%) parainfluenza, 7 (2.2%) influenza B, 6 (1.9%) influenza A, and 2 (0.6%) RSV. There was no association with age, sex or seasonality. Seroprevalence, indicative of past infections, was also relatively low: Parainfluenza 56.8%, influenza B 12.1%; influenza A 5.9% and RSV 6.8%.

CONCLUSION Acute respiratory tract infections are relatively infrequent causes of acute undifferentiated fever in Southern Vietnam. Parainfluenza viruses are more common than influenza A and B and than RSV.

O25-80 Rickettsiosis in children, an imported infectious disease of increasing importance

R. Roelants1, F. Ruksen1, A. van Meurs1 and G. T. Heikens2

1Juliana Childrens Hospital, Pediatrics, Den Haag, Netherlands; 2Universitair Medisch Centrum Nijmegen, afdeling Huisartsgeneeskunde, Nijmegen, Netherlands; 1College of Medicine - University of Malawi, Department of Paediatrics and Child Health, Blantyre, Malawi

OBJECTIVES To demonstrate the importance of rickettsiosis as a travel related disease in children. - To highlight the difference in clinical features between Mediterranean Spotted Fever and
African Tick Bite Fever, both contracted in the same area, of South Africa.

**CASE PRESENTATION**

Cases A and B are teenagers who have a history and clinical signs suggestive of African tick bite fever (ATBF): both attended a game-drive/ walking safari in a South African nature reserve. One of them observed being bitten by a tick. Case C is a 15 months old child who presented with high fever, myalgia and maculopapular exanthema caused by Mediterranean spotted fever (MSF) contracted in South Africa.

**DISCUSSION:** The genus Rickettsia contains 21 validated species classified in three groups: the typhus group, the ancestral group and the spotted fever group. The latter contains *Rickettsiae aegypti* causing ATBF and *Rickettsiae conorii*, the causative agent of MSF. Both are transmitted by ticks, respectively *Amblyomma variegatum* (the tropical bont tick) and *Amblyomma hebraeum* (the southern African bont tick) and the brown dog tick *Rhipicephalus sanguineus*. The first two are mostly found in rural areas with cattle as reservoir whereas MSF is mostly found in urban areas with dogs as reservoirs. MSF is an acute febrile illness with extensive exanthema characteristically also covering soles and palms, and also myalgia. Complications are seen in approximately 2% of cases. While ATBF often presents with fever, enlarged lymph nodes and (multiple) eschars, without complications and without the exanthema. In diagnostic serology, extensive cross reactivity within the spotted fever group of rickettsiae is present. In clinical practice, this has little impact, as both ATBF and MSF will react promptly to the same antibiotic treatment, i.e. doxycycline.

**CONCLUSION**

Awareness of the risk of contracting rickettsioses should be brought about among physicians, since the disease can occur in all age groups and can have serious consequences which can easily be averted by early recognition and treatment. Travellers to endemic areas should be informed and encouraged to protect themselves and their children against tick bites.

**Human Resources in Health II**

**O25-81**

Towards a community-based general medicine in Africa

D. Desplats1, S. Coulibaly2, K. Nimaga3, C. Razakariason4, P. Brunet1, V. Lafay3 and G. Farnarier5

1Sante Sud, Marseille, France; 2Sante Sud, Bamako, Mali; 3Association des Medecins de Campagne du Mali, Bamako, Mali; 4Sante Sud, Antananarivo, Madagascar

**OBJECTIVES**

African countries have struggled to create medical schools and train their physician workforce. Meanwhile, civil-service staff has been cut back. Therefore, the increasing rate of unemployed doctors is leading to: illegal and competitive practices; job changes; brain drain towards richer countries. Moreover, doctors usually remain in the cities, while over 60% of the population lives in rural areas. Settling general practitioners in remote areas is a key challenge for health policy-makers. The solutions lie in preparing communities and young doctors for each other. Sante Sud, a French NGO that for 20 years has empowered communities in Africa to keep their health workers, describes its experiences.

**METHODS**

Sante Sud has conducted development programmes to establish medical general practitioners (GPs) in rural areas, at the first level of the health care system. - Young graduate doctors are willing to invest in a common community medicine, even in remote areas, providing that their integration is properly prepared and followed, through: previous training; adequate equipment; satisfactory professional environment. - Rural populations can afford to pay for health care, providing previous negotiation with each community to ensure sustainable commitment. - Community-based GPs are a great incentive as regards: cooperative health insurance funds; settling other development actors; social consulting towards civil authorities.

**RESULTS**

In Mali, 100 GPs are settled, in agreement with the National Health Planning. Each one is responsible for more than 10,000 people. In Madagascar, 40 ‘Community General Practitioners’ were settled, through signing contracts with the National Health Service. Each private doctor is responsible for providing health care, prevention and promotion within his area (7000 to 12,000 inhabitants).

**CONCLUSION**

General practitioners are the ‘missing links’ between universities and front-line health care. Since there is a replicable model, new challenges lie in meeting demands in other African countries.

**O25-82**

Quality improvement of hospital care: a tool against brain drain in developing countries

T. W. J. Schulpen1 and S. Kinoti2

1Paediatric Association of The Netherlands, Bilthoven, Netherlands; University Research Co, Quality Assurance Project, Bethesda, USA

Developing countries are facing a critical shortage of health workers. Migration of locally trained doctors and nurses to the Western world is common. In many developing countries over half of them have moved away, in Zambia only 60 of the 500 doctors locally trained since independence are still there. Most professionals however prefer to stay in their home country where living conditions are pleasant within a social and family network, with good housing, low cost of living, household personnel available and an attractive climate. If the income is reasonable with possibilities for good education for their children few will migrate.

Several solutions have been suggested such as legal restrictions, salary top-ups, fees for medical education with local pay off in public service or a compulsory overseas remittance scheme. These solutions address mainly economic aspects and the low remuneration in the country of origin. One of the major causes of the brain drain however is hardly mentioned: poor working conditions and low job satisfaction. During the ‘Global meeting to review hospital improvement for children in developing countries’ from 15-19 January 2007 in Bali, over 60 paediatricians and policy makers from 29 different developing countries drafted a framework and a manual for quality improvement. It was geared towards children, but we believe that good quality of care for this most vulnerable group is an indication for the standards of the hospital as a whole. During the meeting several examples of quality improvement projects in developing countries were presented and compared to initiatives in the Western world. As example served the quality improvement programme of hospital care in the Netherlands with four pillars: site visits by peers, continuous medical and professional education, development of clinical (evidence based) guidelines and patient safety with complication registration. The pros and cons of such an advanced approach were intensively discussed and the universal principle of the Plan-Do-Check-Act cycle was generally accepted.

Several items appeared well applicable and were sometimes already realised like the ‘Pocket book of hospital care for children’ with hundreds of clinical guidelines (WHO 2005), assessment tools (short and long); self assessment tools; sets of indicators; data collection and training of health personnel in quality improvement. During the presentation the possibilities and limitations of the Dutch approach will be addressed. Care for quality will improve working conditions and job satisfaction and if governments and NGO’s support this idea, brain drain might diminish.
O25-83
Training needs analysis for 1st level hospital managers in Zambia
B. Gerretsen1 and A. Mbewe2
1Royal Tropical Institute, Development, Policy and Practice, Amsterdam, Netherlands; 2National Institute of Public Administration, Lusaka, Zambia

BACKGROUND Hospitals have an important function in Zambian districts. However, hospital managers are often appointed without prior experience of training in management tasks. A need for strengthening management capacity in 1st level hospitals is recognized by the Ministry of Health in Zambia and a training needs analysis (TNA) was conducted prior to development of a tailor-made curriculum. A TNA is the first phase in a planning process to come to designing a curriculum and implementation of training.

OBJECTIVES To discuss a systematic approach to identify management training needs of 1st level hospital manager.

METHOD Field test of a step by step TNA tool.

RESULTS The TNA started with identifying tasks for hospital managers. Documents provided by the Ministry of Health (MoH) were used for this purpose. Based on a list of tasks, tools for interviewing, observations and document review were developed in a workshop with a team from the MoH and the National Institute of Public Administration. The tools were used to confirm the tasks in the field and identify training needs in management among the hospital management teams of four first level hospitals. Each team consisted of a director, a hospital administrator and a head of department. The three members indicated to have major problems in fulfilling their management tasks. Gaps in knowledge and skills were identified in areas such as Human Resources, Financial and Supplies management. The document review and observations showed that key documents necessary to perform management tasks were missing in all hospitals visited. Furthermore, the available documents as produced by the Health Management Information System and the Financial and Administrative System were not used as knowledge on existence and use of these systems was missing. The TNA included a stakeholders meeting after the field visit. This meeting confirmed the identified needs for training. It also created support for the development of a curriculum for hospital managers. Furthermore, the stakeholders realized an enabling environment for hospital managers is a prerequisite to manage a hospital.

CONCLUSION A systematic approach facilitates the identification of training needs as is described in the example of Zambia’s first level hospital managers. This TNA made clear that hospital managers need to strengthen their knowledge and skills in management. Besides, it made clear that a manager needs an enabling environment.

O25-84
No significant braindrain among graduates of the College of Medicine, Malawi
E. Zitsera1 and R. Broadhead1
1College of Medicine, Department of Medicine, Blantyre, Malawi

OBJECTIVES To assess where the graduates of the College of Medicine are working and in what capacity.

METHODS Simple audit by obtaining information from graduates, class-mates and College staff.

RESULTS Between 1992 and 2006, 232 students graduated (78% male) with a mean of 17 graduates per year. Of these eight died and 18 are still completing their internship. The remaining 206 are working as follows: specialist [22 (11%)], post-graduate student [60 (29%)], PhD student [five (2%)], medical officer [94 (46%)], administrator [14 (7%)]; not practising are four (2%) and for seven it is unknown (3%). Currently in Malawi are 123 (60%) of total; of these 48 work for the Government (MOH 45, NAC 3), 27 in the COM, 20 in mission hospitals and 11 in private practice. Currently abroad are 83 (40%); 55 are in post-graduate training, 40 (19% of total) are in the UK, 22 (11%) in the RSA and eight (4%) in the USA; 24 are unlikely to return to Malawi.

CONCLUSION The majority of COM graduates are in Malawi and practising. Of those abroad most are in postgraduate training and expected to return.
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O25-86
Health management information systems as a tool for human resource development (HRD) – the case of Uganda
C. Fenenga, P. Mommers and A. de Jager
1Cordaid, East and Southern Africa, The Hague, Netherlands; 2International Institute for Communication and Development (IICD), The Hague, Netherlands

OBJECTIVES To describe how a Health Management Information System (HMIS) can be used for Human resource and organizational development in East-Africa.

METHODS From 2005–2007 the umbrella organization for catholic health facilities in Uganda, UCMB, supported by Cordaid and IICD, implemented a pilot programme introducing ICT in 27 up-country hospitals in order to improve data and information management. The programme involved the introduction of an information management system (using low-level ICT tools) and capacity development for hospital managers and administrative staff in gathering and processing of data. Data processing is centralised at UCMB and sent back in ‘usable’ form (e.g. drug supply, bed occupancy rate, numbers of treatment in OPD/IPD, staffing) to the hospitals for decision-making.[Information flow]

RATIONALE In most developing countries funds for the health sector are decreasing and human resources are scarce. More effective and efficient ways of working are the only solution to keep health services at an acceptable level. This requires strengthening of management systems and human resources at both individual and organizational level.

RESULTS The results of this pilot provided positive developments on:
• Human Resources capacity
• Management capacity
• Access and utilization of HMIS
• Informed decision making

CONCLUSION 1. ICT enhances HRD (# of hospital managers/administrative staff trained on continuous basis). Results on retention of staff are difficult to quantify. 2. Through improved ICT and knowledge development, hospitals have better/easier access to the HMIS and use it more efficient/effective. Time involved in filling out forms, sending information, elaborating feed back reduced enormously which contribute to improved hospital management. 3. The potential use of a sound HMIS is much more powerful than just keeping track of outputs produced in the health sector. When outputs and inputs are analysed on a regular basis, the HMIS can guide the management in decision making processes, including HRD. 4. The HMIS pilot contributed to organizational development as seen in enhanced lobby capacity of most health facilities. HMIS: Health Management Information System. Cordaid: Catholic Organization for Relief and Development Aid. IICD: International Institute for Communication and Development. ICT: Information and Communication Technology.

Vector Control

O25-87
Prevention of malaria epidemics by vector control in Burundi highlands
N. Protopopoff, U. D’Alessandro and M. Coosemans
1Institute of Tropicale Medicine, Antwerp, Belgium

OBJECTIVES A dramatic malaria outbreak occurred in 2000 in Karuzi, a highland province in Burundi. In order to prevent a new epidemic a 4-year vector control programme [indoor residual spraying (IRS) and insecticide-treated nets (ITNs)] was implemented. Yearly IRS targeted houses located near the valleys’ bottom (25% of the population) with the objective of reducing malaria transmission and possibly have a protective effect on the hills top.

METHODS Every year, most houses (92%) were covered by IRS and two ITNs were provided to each household in 2002. Nine cross-sectional surveys were done both before and after the spraying activities in the intervention and control areas. A negative binomial regression was used to compare the anopheles density between areas. The risk (odds ratio) to have parasitemia was assessed with a logistic regression.

RESULTS In the valleys, anopheles density was reduced by 2.5–26 in the intervention compared to control areas. In the control areas the risk of capturing malaria infected mosquitoes was 2.5 (95% CI: 1.3–4.8, P = 0.008) higher than in the intervention areas. The risk of human infection was significantly lower (0.4–0.7) in intervention than in control areas. Despite lower vector density, malaria transmission and prevalence in the intervention valley, no significant impact was observed in the hills.

CONCLUSION Anopheles density and malaria transmission was considerably reduced in the intervention valleys. However, the impact on malaria prevalence was lower than expected. No ‘screen’ effect was observed on the hills, i.e. the observed impact in the valleys did not protect the hills from malaria. Nevertheless, no increase of malaria cases above the emergency threshold was notified during this period whereas the neighbouring highland provinces suffered malaria epidemics.

O25-88
Meteorological determinants in the growth, development and survival of An. gambiae immature in Western Kenya
K. P. Paaijmans1, A. K. Githeko2, A. F. G. Jacobs2 and W. Takken1
1Wageningen University, Laboratory of Entomology, Wageningen, Netherlands; 2Kenya Medical Research Institute, Climate and Human Health Research Unit, Kisumu, Kenya; 3Wageningen University, Meteorology and Air Quality, Wageningen, Netherlands

OBJECTIVES The immature stages of malarial Anopheles gambiae mosquitoes are poikilothermic and therefore unable to internally regulate their body temperature. Their growth, development rate and survivorship are to a large extent determined by the temperature of their surrounding aquatic environment. Mosquito larvae experience a daily variation in thermal distribution within water bodies, caused by solar radiation and processes of turbulent heat exchange. Furthermore, they are confined to their habitat, exposing them often directly to meteorological variables such as precipitation and solar radiation. We studied the effects of meteorological variables on the daily temperature variations in clear and shallow water bodies. Also the direct effects of precipitation on An. gambiae immatures were studied.

METHODS The temperature fluctuations in semi-natural water bodies of different dimensions were examined in Western Kenya by measuring water temperatures at various depths. Local weather conditions were monitored and biological experiments were carried out to study the effects of precipitation on survival, flushing and launching of An. gambiae larvae.

RESULTS Small water bodies had a larger difference between daily minimum and maximum water temperature and the time of day that these temperatures were reached was earlier. Moreover, the small water bodies were more susceptible to changes in weather, such as incoming clouds and precipitation. Besides, it was demonstrated that precipitation resulted in flushing of the mosquito larvae and increased their mortality.

CONCLUSION It is important to monitor or estimate the daily temperature fluctuations in larval anopheline habitats, since these will determine the growth, development rate and survival of the immatures. Larvae can experience a wide range of temperatures during each diurnal cycle, especially in the smaller puddles. Natural conditions such as direct sunlight, daily temperature
variations and/or rain will have an important influence on the life history traits of mosquitoes that will be easily overlooked in laboratory studies and cannot be easily simulated. This interdisciplinary study, combining meteorology and biology, gives us the opportunity to predict the influence of local climate on the existing larval populations and hence, the epidemiology of malaria through change in mosquito densities.

O25-89
Anopheles gambiae, the main African vector of malaria is under incipient speciation process
1Laboratoire de Biométrie et Biologie Évolutive, UMR 5558, CNRS, Université Claude Bernard Lyon 1, Villeurbanne, France; 2Centre de Recherche Médicale et Sanitaire (CERMES), Réseau International de l’Institut Pasteur, Namèy, Niger; 3Laboratoire de Biopharmacie et Technologies Pharmaceutiques, UFR des Sciences Pharmaceutiques d’Abidjan, Abidjan, Côte d’Ivoire; 4Unité de Recherche 016, Institut de Recherche pour le Développement (IRD), CREC, Cotonou, Benin; 5Institut de Recherche en Sciences de la Santé, Bobo-Dioulasso, Burkina Faso; 6Institut Pasteur, Antananarivo, Madagascar; 7Laboratoire de Recherche sur le Paludisme, Organisation de Coordination pour la lutte Contre les Étendues en Afrique Centrale, Yavoué, Cameroun; 8Unité de Recherche 016, Institut de Recherche pour le Développement, Montpellier, France

OBJECTIVES Malaria kills around one million people each year. Various methods have been developed to control its main vector, An. gambiae, which is widely distributed throughout sub-Saharan Africa. The failure of traditional measures together with the spread of drug- and insecticide-resistance in natural vector populations, primarily in sub-Saharan Africa, have spurred attempts to find alternative, unconventional approaches. One of the most innovative strategies sets out to replace the entire wild populations of An. gambiae by genetically modified, Plasmodium-resistant individuals. For this to be successful, we need to know exactly how the populations of this species are structured in nature. Especially, we need an accurate picture of the differentiation throughout their distribution range of the two rDNA haplotypes, known as M and S, which define molecular forms of An. gambiae. These forms are suspected of undergoing speciation, but their differentiation in the entire distribution area of the mosquito remains unclear.

METHODS Insertion patterns of three transposable elements, determined in natural populations from Benin, Burkina Faso, Cameroon, Ivory Coast, Madagascar, and Niger, were analysed by Transposon Display to evaluate genetic distance between molecular forms.

RESULTS Data reveal a clear genetic differentiation between the M and S forms, whatever their geographical origin.

CONCLUSION This indicate an incipient speciation process. Any attempt to control An. gambiae will therefore have to take this differentiation into account.

O25-90
Role of knockdown resistance in conferring pyrethroid and DDT resistance in the Southeast Asian Anoph eles species
K. Verhaeghen1, W. Van Bortel1, H. D. Trung2, T. Sochantha3, T. Backeljau4 and C. Costantini5
1Institute of Tropical Medicine, Parasitology, unit Entomology, Antwerp, Belgium; 2National Institute of Malariaology, Parasitology and Entomology, Hanoi, Viet Nam; 3National Center for Malaria Control, Parasitology and Entomology, Phnom Penh, Cambodia; 4Royal Belgian Institute of Natural Sciences, Brussels, Belgium

OBJECTIVES Insecticide resistance may jeopardize the successful malaria control programmes in Southeast Asia. Therefore, a large investigation was conducted in Vietnam, Cambodia and Laos to assess the susceptibility of different Anopheles species against pyrethroids and DDT. Amongst the main vectors, Anopheles epiroticus is highly resistant to pyrethroid in the Mekong delta of Vietnam. An. minimus lato was pyrethroid resistant at the Vietnamese border with China, whereas low pyrethroid resistance was found in An. dirus sensu stricto from central Vietnam. Potential vectors An. vagus, An. sinensis, An. para liae and An. petidiaeatus, were found to be resistant to DDT and pyrethroid in Vietnam and Cambodia. Knowledge on the different resistance mechanisms is necessary to guide the insecticide use in the vector control. An important resistance mechanism against DDT and pyrethroids, known as knockdown resistance (kdr), is caused by a mutation in a sodium channel gene. This study assessed the role of kdr in the Southeast Asian Anopheles species.

METHODS Molecular techniques based on real-time PCR, allele specific PCR and PCR-RFLP were developed to detect possible kdr mutations in the Southeast Asian Anopheles species.

RESULTS In the main vectors, no kdr mutation was observed. Biochemical assays suggest metabolic resistance mechanisms. In An. vagus, An. sinensis, An. para liae and An. petidiaeatus kdr was present in southern Vietnam and in Cambodia near the Vietnamese border. At population level, the kdr frequencies correlate to the permethrin survival rate. However, at individual level the different kdr genotypes were equally distributed among resistant and susceptible mosquitoes.

CONCLUSION The lack of correlation between the individual kdr genotypes and the resistance status suggests that (I) other metabolic resistance mechanism can be involved, (II) posttranscriptional regulation mediates a correlation at individual level and/or (III) additional subsequent mutations in the sodium channel gene are necessary to survive the bioassay. The complex resistance patterns and involved mechanisms, varying between species and regions, can hamper an uniform vector control strategy in Southeast Asia.

O25-91
A mixture of organophosphates and repellents is more effective than pyrethroids on mosquito nets in an area of insecticide resistance in Burkina Faso, West Africa
C. Penneti e1, S. Liccardi1, C. Costantini2, R. K. Dabire1, F. Chandre1, V. Corbet4, B. Lapede4 and J.-M. Hougard1
1Institut de Recherche pour le Développement (IRD) and Centre de Recherche Entomologique de Cotonou (CERC), Cotonou, Benin; 2Institut de Recherche pour le Développement (IRD) and Institut de Recherche en Sciences de la Santé (IRSS), Centre Muraz, Bobo-Dioulasso, Burkina Faso; 3Institut de Recherche en Sciences de la Santé (IRSS), Centre Muraz, Bobo-Dioulasso, Burkina Faso; 4Laboratoire de lutte contre les insectes Nuisibles (LIN), Institut de Recherche pour le Développement (IRD), Montpellier, France; 5Laboratoire RCIM, Université d’Angers, Angers, France

OBJECTIVES With the spread of pyrethroid resistance in most mosquito vector species and the lack of alternative compounds for public health, the search for new strategies that provide better control of resistant populations has become a priority. A new concept was developed in the laboratory by mixing repellents and non-pyrethroid insecticides. Two field trials investigated the efficacy of insecticide-repellent treated nets (IRTNs) against susceptible and insecticide resistant wild Anopheles gambiae populations.

METHODS Deterrency, induced exophily, blood-feeding inhibition and induced mortality were measured in experimental huts.
Huts are situated in a rice-growing area, near Bobo-Dioulasso, Burkina Faso, where, depending on the season, *Anopheles gambiae* populations are alternatively susceptible and resistant to pyrethroids, organophosphates and carbamates.

**RESULTS** Results showed evidence of synergism between repellents (DEET or KBR) and pyrimiphos-methyl (PM) on nets in field conditions. For the first 3 weeks, PM + DEET and PM + KBR treated nets were as effective as a standard pyrethroid (deltamethrin 25 mg/m²) against susceptible mosquitoes and more effective against resistant mosquitoes. Results also demonstrated that mixtures did not select neither Kdr allele nor AcE1R allele.

**CONCLUSION** These field trials showed that mixing repellents and organophosphates on a bed net has the potential to be a good alternative strategy to manage the spread of resistance. However, significant improvements remain to be done to improve residual effect of Insecticide-Repellent Treated Nets.

**O25-92**

**How do insecticide treated mosquito nets really work?**

O. Skovmand¹, J. Miller², E. Walker³ and J. Gimnic⁴

¹Intelligent Insect Control, Castelnau le Lez, France; ²Michigan State University, Entomology, Lansing, USA; ³Michigan State University, Department of Microbiology and Molecular Genetics, Lansing, USA; ⁴Center of Disease Control and Prevention, Division of Parasitic Diseases, Atlanta, USA

**OBJECTIVES** To demonstrate if insecticide impregnated mosquito nets work by keeping mosquitoes out of a room or by killing mosquitoes in contact with the net, and the implication of this on personal protection, mass effects and the effect of used, holled nets.

**METHODS** Compare literature data, our laboratory data on mosquito behaviour in tunnel tests and experiments carried out in a modified test hut in Kisumu, Kenya.

**RESULTS** Most house studies from East Africa show no reduced entrance rate of mosquitoes into a house with an insecticide treated net whereas hut studies from West Africa show that this mechanism is the most important for personal protection. Our hut studies in Kenya show no reduced entrance rate into rooms with treated nets compared to that into rooms with untreated nets when entrance traps of untreated net is used to create entrance opening. By using net and not solid walls for determining size of entrance openings, we avoided to concentrate the airstream as done with traps constructed out of concrete or wood. Further, our behavioural studies showed that mosquitoes are not repelled from insecticide treated surfaces as long as they have no contacts to them. When contact is allowed, non-directional escape flight and resting on any surface resulted in an apparent repellent effect. This is because any new contact to a treated surface result in new flight, whereas rest on untreated surfaces do not.

**CONCLUSION** Field and laboratory data are reviewed and a hypothesis is created that says that the reduced entrance rate is probably an artefact. It is linked to the special design of test huts used in West Africa with 1 cm narrow entrance traps that concentrate insecticide vapour or dust with the attractent odours and CO². This is different from normal house with eves, doors and windows. In a more realistic test scenario, this effect is not found and mosquitoes are only repelled when in contact with the net. This implies that impregnated holed, used net loose their personal protection effect in proportion to hole size and residual insecticide dosage since there is no effect on distance. Further studies are planned to test this hypothesis.

**Technology Assessment and Priority Setting**

**O25-93**

**Coordinating European action to achieve the Millennium Development Goals (MDGs)**

E. Ireland

International HIV/AIDS Alliance, Brighton, UK

**OBJECTIVES** Despite the progress of some of the Millennium Development Goals (MDGs) the three health-related MDGs (MDG4: Reduce child mortality, MDG5: Improve maternal health and MDG6: Combat HIV/AIDS, malaria and other diseases) remain those least likely to be achieved by 2015. To galvanise greater progress towards meeting the health-related MDGs, 14 NGOs from across Europe have joined together to call on their governments and the EU to fulfil promises made on health in developing countries.

**METHODS** By focusing on the interdependency between child mortality, maternal health and infectious diseases, the European Network for Global Health represents an innovative approach to addressing global health to support the fulfilment of the MDGs. It also brings together, for one of the first times, a partnership of 14 NGOs from across Europe to conduct coordinated actions in Brussels, France, Germany, Italy, Spain and the UK, to push governments, NGOs and the private sector to increase their action to improve healthcare in the world’s poorest countries. Major activities include:

- Policy Analysis
- Dialogue with decision makers
- Networking among NGOs in support of the Health Millennium Development Goals
- Influencing Stakeholders
- Public Campaigning

**RESULTS** The overarching goal of the Network is increased support from Europe to enable developing countries to make substantial progress towards the Health Millennium Development Goals (MDGs) by 2015. Results include:

- Increased commitment and action from European governments – primarily the European Commission, France, Germany, Italy, Spain and United Kingdom – to support the achievement of the Health MDGs in low and middle-income countries, including higher and better-focused financial contributions to health and health-system strengthening.
- Increased capacity, engagement and effectiveness of European NGOs’ advocacy in support of the Health MDGs; with improved policy analysis and networking with the NGO and development policy community, (recognising the role of health as a key lever of development).
- Increased support from European civil society and the private sector for the achievement of the Health MDGs in low and middle-income countries, including a higher profile for global health in European media.

**CONCLUSION** By collaborating with NGOs across Europe, greater coordination of donor efforts and increased commitment to fund health in developing countries can be achieved. This is a result of increased leverage to influence policies and consistent messages reaching the EU and other key donor agencies across Europe.
Abstracts of the 5th European Congress on Tropical Medicine and International Health

O25-94
Participatory priority setting for social science research on HIV/AIDS – experiences from a multi country programme
R. van Poelje
Royal Tropical Institute, DPP/SED, Amsterdam, Netherlands

OBJECTIVES The objective of this study is to assess experiences with participatory priority setting regarding the national agenda for social science research in the field of HIV/AIDS.

METHODS Literature study; development of a tool for participatory priority setting; use of the tool in a multi stakeholder setting in five countries in sub-Saharan Africa; monitoring the progress of the research management process; participatory evaluation of the priority setting process.

RESULTS The priority setting tool was effectively used in five countries. The process of using the tool (together developing and weighing criteria for priority setting) proved an important element for developing a shared vision on SSR & HIV/AIDS. The outcome of the tool, a priority issue list, was acceptable to all involved stakeholders. The priority lists proved a living tool that allowed for the inclusion of other priorities over time. The existence of the priority list provided an important pillar for various multi stakeholder processes and facilitated the selection of research proposals.

CONCLUSION Participatory priority setting in itself does not lead to fixed priority lists, but the process is essential for creating mutual understanding among the stakeholders in social science research on HIV/AIDS.

O25-95
Balancing equity and efficiency in health priorities in Ghana
C. Jehu-Appia1, R. Baltussen2, J. Lauer3, X. Koolman4 and Ghana Health Services Priority Setting Study Group
1Ghana Health Services, Accra, Ghana; 2Radboud University Nijmegen Medical Center, Department of Public Health, Nijmegen, Netherlands; 3World Health Organization, Geneva, Switzerland; 4ErasmusMC, Rotterdam, Netherlands

OBJECTIVES To guide the Ministry of Health in Ghana in the priority setting of interventions by quantifying the trade-off between equity, efficiency and other societal concerns in health.

METHODS Multi-criteria decision analysis was used to identify the relevant criteria for priority setting and weigh their relative importance. Subsequently, a set of health interventions were ranked ordered on the basis of these criteria and associated weights.

RESULTS Policy makers in Ghana consider targeting of vulnerable populations and cost-effectiveness as the most important criteria for priority setting of interventions, followed by severity of disease, number of beneficiaries and diseases of the poor. This translates into a general preference for interventions in child health, reproductive health and communicable diseases.

CONCLUSION Study results correspond with the overall vision of the Ministry of Health in Ghana, and are instrumental in the assessment of present and future investments in health. Multi-criteria decision analysis contributes to transparency and accountability in policy making.

O25-96
Assessing equity of resource allocation in decentralized provinces of Guatemala
W. Flores
CEDIM-Guatemala, Guatemala, Guatemala

OBJECTIVES To measure equity in resource allocation among districts of decentralized provinces.

METHODS Formative evaluation research design in which ultimate users of data (health authorities and technical staff) were involved throughout the research process. Quantitative and qualitative techniques were used to address the research objectives following principles of ‘process evaluation research.

RESULTS The study found inequity of resource allocation in two of the three study provinces. The main source of the observed inequity was the use of historical budgets that favours better-off districts with no consideration of districts’ needs. Recent policies aimed to improve equity, such as extra-budgetary allocations, were not adequately targeted and exacerbated inequity in one province.

CONCLUSION Although equity in resource allocation is a central justification for the implementation of decentralisation, this study demonstrated that in two of the study provinces, equity in resource allocation had not been achieved.

Amoebiasis II: Diagnosis, Epidemiology and Interventions I

O25-97
Targets of nitroimidazole action in E. histolytica – a central role for thioredoxin reductase
D. Leitsch1, D. Kolarich2, I. B. Wilson3, F. Altmann4 and M. Duchene4
1Center for Physiology and Pathophysiology/Medical University of Vienna, Specific Prophylaxis and Tropical Medicine, Vienna, Austria; 2University of Natural Resources and Applied Life Sciences, Department of Chemistry, Vienna, Austria

OBJECTIVES Nitroimidazoles are a class of compounds that find multiple applications in medicine and which require reduction of the nitro group for activity. Although the S-nitroimidazole drug metronidazole has been the gold standard in the treatment of infections with Entamoeba histolytica for more than thirty years by now, its exact mode of action has remained poorly understood. Especially with regard to metronidazole targets in the E. histolytica cell, many questions have remained unanswered.

RESULTS Metronidazole is a nitroimidazole drug that is converted to its reduced form in the cell, which leads to depletion of essential reductants such as cysteine. Accordingly, addition of cysteine rescued E. histolytica cells from otherwise lethal metronidazole concentrations and partially prevented protein adduct formation with proteins. In addition, metronidazole-bound thioredoxin reductase, recombinantly expressed in E. coli, displayed reduced enzymatic activity.

CONCLUSION In our search for protein targets of metronidazole chemotherapy in E. histolytica, we applied two-dimensional gel electrophoresis, mass-spectrometric methods, and enzymatic assays.

RESULTS We discovered a small and discrete number of essential proteins which form adducts with metronidazole and other nitroimidazoles: thioredoxin, thioredoxin reductase, superoxide dismutase and purine nucleoside phosphorylase. This is in contrast to previous findings, which suggested that nitroimidazoles indiscriminately form adducts with proteins. In addition, metronidazole-bound thioredoxin reductase, recombinantly expressed in E. coli, displayed reduced enzymatic activity.

CONCLUSION Non-protein thiol levels were drastically reduced in treated cells, suggesting that metronidazole also forms adducts with non-protein thiols in the cell, which leads to depletion of essential reductants such as cysteine. Accordingly, addition of cysteine rescued E. histolytica cells from otherwise lethal metronidazole concentrations and partially prevented protein adduct formation with proteins. Finally, we propose a new model of metronidazole-activation in E. histolytica, as thioredoxin reductase reduced metronidazole and other nitro compounds in vitro.
CONCLUSION Our data suggest a central role for thioredoxin reductase in nitroimidazole activation in E. histolytica, as nitroimidazole reduction renders thioredoxin reductase itself and associated proteins vulnerable to adduct formation. These findings also have implications for nitroimidazole-activation in other organisms, because thioredoxin reductase is a ubiquitous enzyme. To our knowledge, this is the first study to describe specific protein targets of metronidazole and nitroimidazoles in general, and to suggest a detailed model of metronidazole-action in a microaerophilic parasite. This study was supported by grant P15960 of the Austrian Science Fund.

O25-99
Medical implication of oral amoebiasis
M. Bonner
International Institute of Periodontology, Trois Rivières, QC, Canada

OBJECTIVES Entamoeba gingivalis is present in almost all periodontal diseased patients. Oral amoebiasis then affects 65% of all adult population. Its presence is easy to confirm using a microscope and simple, definite procedures. Tissue destruction caused by proteolytic enzymes in part released from host PMN leucocytes which are lysed by amoebas seem to be the most accurate hypothesis. Local consequence is destruction of the maxillary bone surrounding teeth or periodontitis. The elimination of E. gingivalis ensures rapid healing of chronic and aggressive form of the infection.

METHODS Periodontitis in known to adversely affect glycemic control in diabetes. It may also be associated with an increased risk of cardiovascular complication associated with diabetes. Woman with periodontitis have a seven times increase risk for pre-term low birth weight delivery. Individuals with periodontal disease may have significantly increased risk of coronary heart disease and related events such as angina pectoris and myocardial infarction. Subjects with severe periodontal disease had 3.2 times the risk of cardio renal mortality. Periodontitis is a strong predictor of mortality from ischismic heart disease and diabetic nephropathy with type two diabetes and chronic respiratory disease. The periodontium may serve as a reservoir for ameba, bacteria, inflammatory and immune mediators which can interact with other organ systems remote from the oral cavity.

RESULTS E. gingivalis indirectly has important medical and epidemiological consequences. Our dense urban lifestyles make the transmission of this organism easily accomplished through direct social contact, air born particles and through contaminated cooking utensils. It may also play a key role in serious, debilitating and incapacitating disturbances of the general health.

CONCLUSION The full extent of its adverse impact on the human race will remain unappreciated unless it is fully researched, not just as a specific agent of oral disease, but as a general agent of systemic disease.

Anaemia in Early Childhood

O26-1
Aetiology of severe anaemia in Malawian children
J. Cais1, K. Phiri2, B. Brabin3, M. Holyoake2 and M. Boele van Hensbroek1 on behalf of the Severe Anaemia Study Group
1University of Amsterdam, Amsterdam, Netherlands; 2College of Medicine, Malawi, Wellcome Trust Research Laboratories, Blantyre, Malawi; 3University of Amsterdam / Liverpool School of Tropical Medicine, Emma Children's Hospital, Amsterdam, Amsterdam, Netherlands

BACKGROUND Severe anaemia is a major cause of morbidity and mortality in African children. WHO-advocated preventive and curative strategies focus on treatment of malaria and hookworm (if over 2 years of age) and supplementation with iron and folic acid. Yet the aetiology of severe anaemia has been inadequately studied.

OBJECTIVES To identify possible aetiological factors for severe anaemia in children.

METHODS We conducted a case-control study, enrolling 381 preschool children with severe anaemia (haemoglobin concentration <5 g/dl) and 737 controls without severe anaemia, in an urban and rural setting in Malawi. All important etiological factors that have been associated with severe anaemia in the past were studied. The data were examined using multivariate analysis and structural equation modelling.

RESULTS Bacteremia (Adjusted Odds Ratio, AOR:5.3, P < 0.001), malaria (AOR:2.3, P < 0.001), hookworm (AOR:4.8, P < 0.001), HIV (AOR:2.0, P = 0.04), and deficiency of G6PD (AOR:4.2, P < 0.01), vitamin A (AOR:2.8, P < 0.01) and B12 (AOR:2.2, P < 0.001) were associated with severe anaemia. Iron deficiency was less prevalent in case-patients (AOR:0.4, P < 0.001) and was negatively associated with bacteremia. Malaria was associated with severe anaemia in the urban (seasonal transmission), but not in the rural (holoendemic) setting. Seventy-six percent of hookworm infections were found in children aged under 2 years. Folate deficiency, sickle cell disease and an abnormal inflammatory response were uncommon.

CONCLUSION In severely anaemic children, even in the presence of malaria parasites, additional or alternative diagnoses should be considered. Current recommendations with respect to bacteremia, hookworm, iron and folic acid treatment appear not to be applicable. Our findings may contribute to the assessment of new therapeutic and preventive strategies for Africa.

O26-2
Delayed cord clamping and haemoglobin levels in infancy: a randomized controlled trial in term babies
P. van Rheenen1, L. de Moor2, S. Eschbach3, H. de Grooth4 and B. Brabin4
1University Medical Centre Groningen, Paediatrics, Groningen, Netherlands; 2University of Amsterdam, Amsterdam, Netherlands; 3Mpongwe Mission Hospital, Mpongwe, Zambia; 4Emma Children’s Hospital – AMC, Paediatrics, Amsterdam, Netherlands

OBJECTIVES This study was done to assess whether delaying umbilical cord clamping is effective in improving the haematological status of term infants living in a malaria-endemic area, and whether this is associated with complications in infants and mothers.

METHODS We randomly assigned women delivering term babies in Mpongwe Mission Hospital, Zambia, to delayed cord clamping (DCC, n = 46) or immediate cord clamping (controls, n = 45) and followed their infants on a two monthly basis until the age of 6 months. We compared the haemoglobin change from cord values and the proportion of anaemic infants. Secondary outcomes related to infant and maternal safety.

RESULTS Throughout the observation period infant haemoglobin levels in both groups declined, but more rapidly in controls than in the DCC group [difference in Hb change from baseline at 4 months 1.1 g/dl, 95% confidence interval (CI) 0.2; 2.1]. By 6 months, this difference had disappeared (0.0 g/dl, 95% CI (0.9; 0.8). The odds ratio for iron deficiency anaemia in the DCC group at 4 months was 0.3 (95% CI 0.1; 1.0), but no differences were found between the groups at 6 months. No adverse events were seen in infants and mothers.
CONCLUSION Our findings indicate that DCC could help improve the haematological status of term infants living in a malaria-endemic region at 4 months of age. However, the beneficial haematological effect disappeared by 6 months. This simple, cost-free and safe delivery procedure might offer a strategy to reduce early infant anaemia risk, when other interventions are not yet feasible. (This paper will appear in the May 2007 issue of Tropical Medicine and International Health)

O26-3
Successful reduction of anaemia deaths in children in a rural hospital in Ghana

L. E. Visser1, M. T. Retgo1, S. Kye-Faried1, D. W. Geelhoed2, J. Schagen van Leeuwen3 and J. Van Roosmalen4
1Holy Family Hospital, Berekum, Ghana; 2Regional Health Directorate, Tamale, Ghana; 3Health Alliance International, Sofala and Manica Provinces, Manica, Mozambique; 4St Anthony’s Hospital, Nieuwegein, Netherlands; 5Leiden Universitair Medisch Centrum, Leiden, Netherlands

INTRODUCTION Anaemia is a major cause of childhood mortality in sub-Saharan Africa. Although anaemia is associated with several causes it is a common complication of malaria. In all the hospitals in the Brong Ahafo Region in Ghana, anaemia was for several years the second cause of death. Most deaths of anaemia occurred in children.

OBJECTIVES To develop an intervention to decrease deaths due to anaemia in children.

METHODS As previous transfusions in children followed the pattern of malaria admissions with clear yearly peaks during the rainy season, a multifaceted intervention programme was developed. It included prevention of malaria (promotion of bed-net use) appropriate treatment of malaria when the child was sick, nutritional education including the importance of locally available fresh fruits and vegetables especially for sick children, admission for children who needed transfusion, investigations for contributing factors and follow up at the anaemia clinic of all children with moderate or severe anaemia.

RESULTS In 2 years of careful supervised intervention the transfusions in children in our hospital decreased by 60% (883–374), deaths through anaemia in children decreased by 50% (30–12), overall deaths in children decreased by 40% (155–75) and anaemia became number nine in the cause of deaths list in the hospital.

CONCLUSION The programme of interventions is simple, does not need many high qualified personnel, can be easily implemented in any highly endemic malaria area and is very effective. Childhood mortality from anaemia can be influenced by persistently implementing existing knowledge.

O26-4
Study of the prevalence of anaemia and certain comorbidity factors in Mali

R. Williams1, J. Loslier2, K. Barry3, F. Couturier1, P. M. Roy1 and C. Valois1
1Université de Sherbrooke, Médecine Familiale, St Lambert, Canada; 2Université de Sherbrooke, Community Health, St Lambert, Canada; 3ASACOSE, Segue, Mali

Anaemia is a major health problem in Sub-Saharan Africa. There are multiple consequences, including, among others, loss of workdays, learning difficulties and growth retardation. An assessment of the prevalence of anaemia in nine villages in the area served by the Segue CESCOM (Community Health Center) in Mali was carried out in the fall of 2006. The study population consisted of all children in the area between 0 and 5 years old. Seven-hundred and twenty-six children (out of an estimated total of 800) donated the blood samples needed for the study. The results, which will be presented at the Congress on Tropical Medicine in Amsterdam, will allow for assessment of the prevalence and severity of anaemia and associated comorbidity factors. More specifically, the study measures the rate and severity of anaemia, the rate of malaria and the rate of intestinal parasitic disease, and reveals potential correlations between the weight/height index of this population and the aforementioned indices. The various rates will be compared on the basis of access to health care services in each Segue village. The full results of the study will be available during the congress in May. These results will serve as the basis for the planning of specific measures aimed at reducing anaemia and malaria, to be carried out in the Sagabala commune of Mali.

Treatment of Malaria: ACT I

O26-5
Innovative new approaches to reduce economic access barriers to artemisinin-based combination therapy

N. Grove1, D. Bowles2, J. C. Craft3 and T. Brewer4
1Institute for OneWorld Health, San Francisco, USA; 2CNAP, University of York, York, UK; 3Medicines for Malaria Venture, Geneva, Switzerland; 4Bill & Melinda Gates Foundation, Seattle, USA

OBJECTIVES Artemisinin-based combination therapies (ACTs) are essential components of the World Health Organization global strategy to reverse the significant morbidity and mortality caused by drug resistant P. falciparum. To meet the projected global demand for ACTs and to help reduce economic barriers to their access, three international organizations, each identifying new innovative solutions for producing artemisinin or artemisinin-like compounds, have come together to form a consortium. Artemisinin is extracted from the Chinese wormwood plant, Artemisia annua. And is a drug intermediate used to synthesize artemisinin derivatives (such as artesunate, artemether, and dihydroartemisinin), which are Active Pharmaceutical Ingredients (APIs) used to make ACTs. Even with current efforts to increase cultivation of Artemisia annua, and improve extraction yields all three new technological approaches being developed by the consortium members may be required to meet economic targets and satisfy projected global demand for the artemisinin needed for ACTs to address the serious global health burden of malaria. All three members of the consortium aim to introduce products to the market beginning in 2010.

METHODS The three uniquely structured non-profit organizations run individual programmes via distinctive product development partnerships (PDPs) as well as work collaboratively to achieve common goals. These organizations are the Institute for OneWorld Health (OWH), which is developing microbially derived Artemisinin using the tools of synthetic biology, fermentation, and chemistry; the Centre for Novel Agricultural Products (CNAP) at the University of York, which is developing high-yield varieties of Artemisia annua; and the
Medicines for Malaria Venture (MMV), which is developing synthetic endoperoxides (artemisinin-like molecules) and new ACTs.

RESULTS In this symposium, representatives of the three organizations will present individual strategies, technical progress, their ongoing collaboration, and will describe how these approaches can contribute to lowering the cost of ACTs.

CONCLUSIONS Together, these three novel technological strategies will stabilize the supply of artemisinin, lower the cost of artemisinin production, provide options for potential new combinations, and make ACTs accessible to far more of the people who need them. All three programmes show technical promise to achieve low cost goals and sustain agricultural and pharmaceutical production of ACTs. The collaboration between these groups is an effective and efficient bridge between novel bench science and its conversion to applications for neglected diseases for the developing world.

Q26-6
The effects of sub-curative drug treatment on the outcome of competition for drug resistant parasites in mixed-clone malaria infections
S. Huijben, A. Wargo, D. Drew, D. Sim and A. Read
University of Edinburgh, School of Biological Sciences, Edinburgh, UK

OBJECTIVES Drug resistance in malaria parasites contributes to a large extent to the increasing malaria burden of the recent years. A better understanding of the development and spread of drug resistance is therefore essential to reduce malaria morbidity and mortality. In areas with a high intensity of malaria transmission, multiple-clone infections are the rule rather than the exception. Previous research has shown that within-host interactions between co-circulating parasite strains play an important role in the spread of drug resistance. The timing of drug treatment and the level of clearance of the more virulent sensitive parasite strain will determine whether a resistant strain will benefit from the competition. The objective of this study is to determine the effect of a sub-curative drug treatment on the life history traits of a drug resistant strain co-infecting a host with a drug sensitive strain.

METHODS We used the rodent model Plasmodium chabaudi with drug resistant clone ASpyr-1B and drug sensitive clone AJ in C57 mice. Mice were inoculated with either a single infection or a mixed infection of both clones and treated at day 6 post-infection with either 8 mg pyrimethamine/kg bodyweight (full dose), 3 mg/kg body weight (sub-curative dose), or no drugs (negative control) for 1 day instead of the prescribed 4-day drug course.

RESULTS In the mixed clone infection without drug treatment, the more virulent non-resistant parasites will competitively suppress the resistant parasites. As previous research has shown, a 1-day course of a full drug dose will result in competitive release of the resistant parasite, due to the partial clearance of the drug sensitive parasite. We expect to find that the sub-curative drug dose will result in competitive suppression of the resistant strain, as a consequence of a greater density of the more virulent drug sensitive parasites compared to a full dose treatment. However, the half drug dose should be high enough to decrease malaria morbidity in terms of reduced weight loss and reduced anaemia.

Q26-7
Artemisinin resistance in Cambodia?
H. Noedl1, L. Chanthap2, Y. Se3, D. Socheat2, S. Peou2, K. Schaeche2, S. Srivicha3, P. Teja-Izadovarm2, B. Smith1, K. Jongnakul1, S. Surasri3 and M. Fukuda3
1Medical University of Vienna, Vienna, Austria; 2CNM, Phnom Penh, Cambodia; 3USAMC-AFRIMS, Bangkok, Thailand

Since 2001, more than 56 countries have officially adopted ACTs for the treatment of falciparum malaria. Once it develops and spreads, resistance to artemisinin derivatives will have a major impact on malaria control worldwide. Surveillance reports of higher ACT failure rates along the Thai-Cambodia border compared to non-border areas suggest the need to monitor the efficacy of the artemisinin component independently of its partner drug to determine the extent of potential artemisinin resistance.

OBJECTIVES The principal goal of this project was to investigate reports of developing artemisinin resistance in Cambodia using an integrated in vivo – in vitro approach.

METHODS We conducted a 28-day inpatient randomized, controlled open label clinical trial designed to investigate potential clinical artemisinin resistance in Battambang Province, Cambodia along the Thai border. Sixty patients received supervised artesunate monotherapy (4 mg/kg/day) over 7 days, the remaining 30 received quinine-tetracycline (30 and 25 mg/kg/day). Treatment response (PCT, FCT) and safety parameters were closely monitored throughout the study. In vitro drug sensitivity was assessed by HRP2 assay on admission and in cases with re-emergence of parasitemia. Genetic markers of drug resistance and pharmacokinetic studies are being performed to determine whether patients had adequate drug levels.

RESULTS The 28-day cure rate in the artesunate arm was 93.3 % (95% CE: 83.8–98.2) vs. 100% (89.7–100%) in the control arm. Mean PCT in patients who failed artesunate monotherapy was almost twice that of cures (101.2 vs. 57.5 hrs; P = 0.002) with a maximum PCT of 133 h. Preliminary in vitro results indicate significantly higher IC50s for artemisinins as compared to western Thailand and Bangladesh. Patients who failed therapy had IC50 values up to five times higher than the overall mean. Pharmacologic studies to assess drug exposure are in progress.

CONCLUSION The proportion of artesunate-treated patients with re-emerging parasitemia appears to be low indicating that presently artemisinin resistance is not a widespread problem. However, our data suggest that there may be individual P. falciparum isolates resistant to artemisinins in western Cambodia. Further studies are needed to determine the rate of increase and geographical extent of this problem.
O26-8
A multinational, randomized comparative study to assess the efficacy and tolerability of Coarsucam™ (fixed dose combination of artesunate plus amodiaquine) once or twice daily vs. Coartem® (fixed dose combination of arteether plus lumefantrine) for uncomplicated Plasmodium falciparum malaria

M. Randrianarivelosoa1, L. Randrianarisoa2, A. Ratsimbasoa1, A. Albert Same Eko2, V. Ana Moao1, T. Kuenz1, P. Brasseur2, P. Agnaye3, J. L. Ndaye4, B. Fay4, O. Gaye3, I. Sagra3, A. Traoré3 and Y. Dicko3

1Institut Pasteur de Madagascar, Unité de Recherche sur le Paludisme, Antananarivo, Madagascar; 2Institut Pasteur de Madagascar, Unité d’Épidémiologie, Antananarivo, Madagascar; 3EMSBCHU, Service de Parasitologie, Yaoundé, Cameroon; 4IRD, UR 077, Dakar, Senegal; 5CHU Amiens, Service de Parasitologie-Mycologie, Amiens, France; 6Université Cheikh Anta Diop, Service de Parasitologie, Faculté de Médecine, Dakar, Senegal; 7Conseil de l’Ordre de Médecine, Pluridisciplinaire et Santé du Continent, Université de Bamako, Malaria Research and Training Centre, Department of Epidemiology of Parasitic Diseases, Bamako, Mali

Coarsucam™ is a fixed dose combination of artesunate and amodiaquine developed through a public-private partnership between Sanofi Aventis and DNDi. A multinational, randomized, single blind comparative Phase III trial was carried out in Cameroon, Madagascar, Mali, and Senegal, in order to assess the non-inferiority of the new coformulation vs. Coartem®, and to precise the optimal dosing regimen (one or two daily doses). The primary objective was to demonstrate the non-inferiority of Coarsucam™ one daily dose vs. Coartem®, according to WHO 2003 D28 protocol. The secondary Objectives were to compare the three treatment groups in terms of efficacy as per WHO 2003 D28 day protocol, and in term of clinical and biological tolerability in 66% confidence. The difference of the will be calculated on ITT and PP population (primary analysis will be performed on the ITT one), the acceptance limit for non-inferiority was defined as 5%. Safety will be assessed by incidence of adverse events, and biological tolerability. Any subject with malaria attack confirmed by parasitemia was randomly allocated in one of the three regimens, with dosage according to bodyweight range, after informed consent. A 3-day treatment period and 28-day follow-up period was performed. All treatments were administered by an authorized person, without the knowledge of both investigating physician and biologist. In each bodyweight range the total number of tablets was the same, according to the Coartem reference group, with placebo tablets if necessary. A total of 941 patients, including 437 children under 5 years of age, weighing more than 10 kg, were included in the study between March and December 2006. Analysis is currently ongoing. Primary efficacy results showed a global level of efficacy after PCR correction close to 100%. Detailed results will be presented at the meeting.

O26-9
Twelve year surveillance of Plasmodium falciparum in vitro drug susceptibility on the Thai–Burmese border

M. Barondes1, A. Jadedee1, A. Broscom1, K. Sriprawat1, T. Anderson1, P. Singhasivanon1 and F. Nosten1

1Shoklo Malaria Research Unit, Mae Sot, Thailand; 2Southeast Foundation for Biomedical Research, San Antonio (TX), USA; 3Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

OBJECTIVE Multi-drug resistance in Plasmodium falciparum has emerged at an alarming rate in Southeast Asia, and nowhere is the situation more serious than in the Thai border areas. Surveillance of antimalarial drug resistance is essential for early changes in drug policies. We therefore continuously monitored the antimalarial susceptibility of P. falciparum since the introduction of Mefloquine-Artesunate combination therapy in 1995. This study describes the in vitro antimalarial susceptibility patterns of P. falciparum isolates collected in Northwestern Thailand during a 12-year period.

METHODS A total of 1121 parasite isolates were obtained from non-pregnant patients with primary P. falciparum malaria attending the clinics of SMRU. In vitro cultures of these isolates were set up in the SMRU-laboratory on pre-dosed drug plates, and cultured for 42 h. Parasite growth was assessed by the radioisotope microdilution assay and dose response curves were analysed using WinNonLin software.

RESULTS The geometric mean IC50 values for 2006 only, were: atovaquone 0.69 ng/ml (n = 55), artesunate 2.59 ng/ml (n = 73), chloroquine 158.31 ng/ml (n = 60), dihydroartemisinin 0.16 ng/ml (n = 59), doxycycline 2442.31 ng/ml (n = 70), lumefantrine 2.91 ng/ml (n = 72), mefloquine 17.89 ng/ml (n = 72), and quinine 107.62 ng/ml (n = 70). A significant trend for increased susceptibility (lower IC50 values) during the study period was detected for atovaquone, dihydroartemisinin, doxycycline, lumefantrine and quinine, while mefloquine (despite its extensive use) has remained stable. There was a significant increase in in vitro susceptibility for artesunate until 2002, but this trend reverted in 2003 and IC50 levels have returned to values described in 1995. In vitro sensitivities to chloroquine have shown two peaks of decline, one between 1997 and 1999 and the other between 2002 and 2003.

CONCLUSION Only small changes in responses to antimalarial drugs were observed between 1995 and 2006, suggesting that the situation of drug resistance for these drugs is stabilizing. A possible explanation for the temporal trend in antimalarial resistance may be the spatial distribution of sample location, coming mainly from a refugee camp during the first period of sample collection and mainly from migrant sites during the second half. The artemisinin derivatives remain an important part of the treatment of multidrug-resistant falciparum malaria. Although there is no evidence that resistance to the artemisinin derivatives is emerging, caution is warranted and the continuing monitoring, both in vivo and in vitro, is essential.

O26-10
Pyronaridine artesunate (Pyramax®) in the treatment of children with acute uncomplicated Plasmodium falciparum malaria

M. Ramharter and P. G. Kremarner

Albert Schweitzer Hospital, Medical Research Unit, Lambarene, Gabon

OBJECTIVES The fixed combination of pyronaridine artesunate (Pyramax®) is being developed for the treatment of Plasmodium falciparum and Plasmodium vivax malaria and has been shown to be effective in a large phase II trial in adults. In order to develop pyronaridine artesunate for paediatric patients, an open label, dose escalation study was performed in Gabon to assess efficacy, tolerability and safety of three dose levels of pyronaridine artesunate (6:2 mg/kg, 9:3 mg/kg, 12:4 mg/kg) tablets and a paediatric granule drug formulation (9:3 mg/kg), with 15 patients per group.

METHODS Patients aged between 2 and 14 years with a body weight between 10 and 40 kg suffering from uncomplicated falciparum malaria (1000–200 000 asexual parasites per microliter blood) were included in this study. Treatment was administered once daily for 3 days and patients were followed weekly for 6 weeks for efficacy and safety assessment.

RESULTS The overall PCR corrected day 28 cure rate was 100% in per protocol analysis at all dose levels. Median PCT was 16.4 h at 6:2 mg/kg, 16.1 h at 9:3 mg/kg, 8.1 h at 12:4 mg/kg for tablets and 8.3 h for the 9:3 mg/kg paediatric granule formulation (per-protocol population). Rapid onset of parasite and fever clearance were further indicators for good efficacy. Overall tolerability of the combination of the study drugs was acceptable and no dose
limiting treatment related side-effects were encountered. Adverse events were mild or moderate, transient and mostly associated with malarial disease; two of which led to patient withdrawal. Two non-drug related serious adverse events were observed.

CONCLUSION Pyronaridine artesunate is a promising drug combination for the treatment of uncomplicated falciparum malaria in paediatric patients.

Trypanosomiasis

O26-11
Cardiac autonomic evaluation in the co-infection T. cruzi and HIV
D. Correa1, R. Molina1, L. A. Resende1, C. J. D. Barbosa1, A. Prata1 and V. J. D. Silva2
1Federal University of the Triângulo Mineiro, Infectious Disease, Uberaba, Brazil; 2Federal University of the Triângulo Mineiro, Fisiology, Uberaba, Brazil

INTRODUCTION HIV infection and Chagas’ disease are common causes of cardiomypathy in Latin America. Cardiac autonomic impairment has been well characterized in chronic chagasic cardiomypathy as well as in HIV/AIDS related heart involvement.

OBJECTIVES Evaluate the cardiac autonomic function by using the computerized analysis of heart rate variability in patients with the co-infection HIV/Chagat disease.

METHODS With the ethical approval, we studied 57 patients, gender- and age-matched, 19 (T.cruzi-HIV group), 19 (HIV group) and 19 (control group). A continuous ECG recording in DII lead was performed in supine rest, cold face and passive tilt tests and R–R intervals were acquired. The overall variability of R–R series was assessed in the time and frequency domains using autoregressive power spectral analyses.

RESULTS The groups were similar regarding gender and age. The electrocardiographic analyse of mean values of R–R intervals did not differ in the three studied groups (P = 0.814). In baseline, the HIV group showed a statistically significant increase of the low frequency area, compared with the co-infected group (P = 0.01), a decrease of normalized low frequency area, compared with co-infection group (P = 0.03), an increase of the high frequency area compared with co-infected (P = 0.03). The variance was significantly higher in the co-infected group compared with the HIV-group (P = 0.03).

CONCLUSION Patients with the co-infection presented, in baseline a shift of cardiac sympathovagal balance suggestive of an impairment of sympathetic modulation.

O26-12
Abstract withdrawn.

O26-13
Another possibility to detect and identify by PCR Trypanosoma spp. in tsetse flies
F. Ferreira1, J. Cano2, A. Furtado2, N. Ndong-Mahale3, P. Ndong-Assuma3, A. Benito2, J. Pinto2, M. O. Alonso1, J. Seixas1, J. Asougua1 and S. Centeno-Lima1
1Instituto de Higiene e Medicina Tropical, Unidade de Clínica das Doenças Tropicais/Centro de Malária e Outras Doenças Tropicais, Lisbon, Portugal; 2Instituto de Saúde Carlos III, Centro Nacional de Medicina Tropical, Madrid, Spain; 3Instituto de Higiene e Medicina Tropical, Centro de Malária e Outras Doenças Tropicais, Lisbon, Portugal; 4Sleeping sickness National Control Programme Equatorial Guinea, Bata, Equatorial Guinea; 5Instituto de Higiene e Medicina Tropical, Unidade de Entomologia Médica/UPMM, Lisbon, Portugal

OBJECTIVES To test a new approach to detect Trypanosoma spp. in tsetse flies that uses the entire insect vector for DNA extraction and PCR analysis, thus avoiding fly dissection.

METHODS Glossina palpalis palpalis from Sleeping Sickness foci in Angola (72 flies, Soyo, Zaire province) and Equatorial Guinea (62 flies, Rio Campo) were used for DNA extraction, performed according with a protocol for tick DNA extraction (d’Oliveira et al. 1997). Glossina tubulin PCR was performed (Hao et al. 2003) as a control of DNA extraction efficiency. Trypanosome detection with species-specific primers was conducted for T. congolense savannah (Majiwa et al. 1994) T. congolense Kilifi, T. congolense forest (Masiga et al. 1992) and T. brucei (Moser et al. 1989) with modified conditions. T. vivax amplification was performed with a forward primer, ILO1265, (Masake et al. 1997) and reverse, TVM R primer (Masake et al. 1994), using the PCR conditions described by (Morlais et al. 2001). Samples were organized in pools of four for trypanosome detection, followed by individual analysis every time a pool yielded a positive amplification signal.

RESULTS DNA extracted from all tsetse flies from Equatorial Guinea was successfully amplified with the Glossina spp. tubulin primers, thus confirming the DNA extraction efficiency. One fly was positive for T. vivax and another fly was positive for T. brucei s.l. An overall infection rate of 3.23% (2/62) was obtained. Only five out of the 77 tsetse from Angola displayed an amplified product for Glossina tubulin. No species-specific primers reactions were performed due to the low quality of the DNA obtained.

CONCLUSION The original approach we describe allows the molecular detection of parasites without the need for laborious tsetse dissection, and although not giving direct information on the infectivity, supplies knowledge on trypanosome species infecting the vector population in the studied foci, allows an effective processing of a large number of samples in a central laboratory and averts the need for entomologically skilled on-site personnel, thus being potentially important for application in HAT and animal trypanosomiasis control activities in all endemic African countries.

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O26-14
Imported Chagas disease in Spain
J. Muñoz1, B. Trevisiol2, M. Vergés2, I. Clavería3, P. Lopez Chejade4, E. Salvador5, M. Porrás1, E. Posada1, E. Avila5, J. Gómez i Prat1, S. Sanz1, M. Gallego5 and J. Gascon1
1Hospital Clinic Barcelona, Centre de Salut Internacional, Barcelona, Spain; 2Unitat de Medicina Tropical i Salut Internacional Drassanes, Barcelona, Spain; 3Facultat de Farmacia, Universitat de Barcelona, Laboratoris de Parasitologia, Barcelona, Spain

OBJECTIVES Chagas disease is an endemic zoonosis in Latin America. Migratory movements have increased the prevalence of this imported disease in European countries and particularly in Spain. This work analyses clinical and epidemiological features of
Latin American patients coming to two different travel clinics in

METHODS This is a descriptive study of patients from *T. cruzi*
endemic areas attending two travel clinics in Barcelona. Two
serological tests were used to diagnose *T. cruzi* infection (two
ELISA with different antigens). Nested-PCR and/or real time PCR
was performed on samples with positive serology. Epidemiological
and clinical data were recorded, and patients were classified into
the classical clinical forms of Chagas disease through clinical
history, physical examination, electrocardiogram and thorax
X-ray. Haematology, biochemistry, and HIV serology were also
performed on all seropositive patients. Other exams were per-
formed according to different clinical symptoms reported by
patients.

RESULTS Four hundred and fifty-eight people were screened for
*T. cruzi* infection of whom 171 (37%) were positive for serologies. PCR was
positive for 19.3% of the 154 seropositive samples tested. Eighty-
one per cent of *T. cruzi*-infected patients were women, and the
mean age was 36 years. The predominant country of origin was
Bolivia for 86% of the patients followed by Argentina. Seventy-
eight percent of patients had lived in rural areas, 5.5 % had
received transfusions in an endemic country and 4.6% had been
blood donors in Spain. Most patients were classified in the
indeterminate form of the disease. Twenty-three per cent of
patients presented electrocardiographic alterations suggesting
chronic chagasic myocardopathy, and one of them suffered a
sudden death caused by a myocarditis. Three patients were
HIV-infected, and two patients presented immunosuppression
associated with antineoplastic agents. None of these immunosu-
pressed patients showed reactivation of Chagas disease.

CONCLUSIONS Latin American patients who visited our travel
clinics had an elevated rate of *T. cruzi* infection. Most patients
were women from Bolivia and almost a quarter of the infected
patients had electrocardiographic disorders suggesting chagasic
cardiopathy.

Human Resources in Health I

**O26-16**

The pharmacy workforce crisis – stepping up global and
national action

T. Wuliji

*International Pharmaceutical Federation (FIP), The Hague, Netherlands*

OBJECTIVES To explore key human resource issues affecting the
pharmacist workforce worldwide and the roles of global and
national stakeholders. To generate greater awareness, knowledge
and understanding of the roles of pharmacists and human resource
issues in pharmacy. To build a global evidence base on the human
resource issues in pharmacy and mechanisms through pharmacy
workforce capacity can be developed.

METHODS In 2004, the International Pharmaceutical Federation
(FIP), as the global federation of national organisations of
pharmacists and pharmaceutical scientists, undertook a global
survey study to gather data from professional and regulatory
bodies, training institutions and governments to describe the
pharmacist workforce and identify key issues affecting the phar-
macist workforce. Following the report of the findings, FIP has
commenced several projects focusing on the scaling up on
pharmacy education and training, definition of the role of the
pharmacist, migration of pharmacists and pharmacist workforce
policy and development.

RESULTS Key issues surrounding workforce regulation and
description, shortages, distribution imbalances and Continuing
Professional Development and practice role development were
identified and reported in the 2006 FIP Global Pharmacy Work-
force and Migration Report. Results from an international pilot
study on pharmacy student migratory intentions have demonstrate
the interplay between classic ‘push/pull’ factors and the influence
of students’ attitudes towards the professional practice environ-
ment and political and social environment on the intention to
migrate. There is a considerable gap in knowledge on pharmacy
workforce issues and a demand for greater research and attention
to this neglected area.

CONCLUSION Given the scarcity of international knowledge on
human resources for pharmacy, the exploratory research under-
taken by FIP is needed to generate greater understanding of the
workforce issues affecting the pharmacist profession. This research
coupled with action at country level will seek to build a baseline
level of international knowledge and examine the key policy issues
in this relatively new field.

**O26-17**

Nurses’ experiences of recruitment and migration from
developing countries: a phenomenological approach

P. Troy and E. Mc Auliffe

1Beaumont Hospital, Dublin, Ireland; 2Centre for Global Health, Trinity
College, Dublin, Ireland

OBJECTIVES This study aims to establish the perceptions and
opinions of those involved in the recruitment process on their role
in the recruitment and the effects recruitment has on both source
and destination countries.

METHODS In-depth interviews were conducted with Irish and
Overseas Directors of Nursing and overseas nurses working in
Ireland. A phenomenological approach was used to analyse the data.

RESULTS There were pronounced differences in opinions between
the Irish and the Overseas Directors on recruitment and its effects
on the health systems of the source countries. Difficulties in the
retention of staff were highlighted by both groups of Directors.
Other findings included the language and cultural differences
experienced by the overseas nurses.

CONCLUSION The recruitment of overseas nurses should not be
left to the individual employer even in the presence of government
guidelines. An international effort from all the involved parties is
required to formulate a solution to this complex issue in order to
protect both the health systems of individual countries and the
nurse’s right to migrate.

**O26-18**

Engaging with health professionals in the diaspora for the
transfer of knowledge and skills to strengthen human
resource capacity

A. Davies

*International Organization for Migration, Migration Health, Geneva,
Switzerland*

OBJECTIVES The overall objective of this project is to address
brain drain and facilitate brain circulation of health professionals.

THE SPECIFIC OBJECTIVES ARE TO:

- Utilize the available skills, expertise and experience of Ghanaian
migrant health professionals living in the Netherlands and other
European countries.
- Contribute to health system capacity building in Ghana in line
with the national human resources development strategy.
Abstracts of the 5th European Congress on Tropical Medicine and International Health

O26-19  
Attraction and retention of health workers to remote rural areas: case studies from Malawi and South Africa  
T. Martineau1, U. Lehmann2, P. Matwa3, J. Kadyola2 and K. Storey4  
1Liverpool School of Tropical Medicine, International Health Group, Liverpool, UK; 2University of Western Cape, School of Public Health, Cape Town, South Africa; 3Commonwealth Secretariat, London, UK; 4Malawi Institute of Management, Lilongwe, Malawi

OBJECTIVES A key factor in equitable access to health care is availability of sufficient competent health workers, in particular in remote rural areas of poorer countries. The factors contributing to inequitable distribution of staff are quite well known, but the objective of this study was to explore the differences in retention rates and related factors of PHC staff by levels of training, including untrained staff.

METHODS The case study approach was used in the sub-Saharan African countries of Malawi and South Africa combining staff surveys, in-depth interviews and reviews of institutional data. The study was conducted in three remote districts in Malawi (75 trained and 46 untrained staff were surveyed) and in three remote Local Service Areas in Eastern Cape Province, South Africa (64 trained and 30 untrained staff were surveyed).

RESULTS Surprisingly, retention rates by levels of training differed little and overall were relatively good. Contributing factors were older women being able to get postings near their families (South Africa) and similarly in Malawi some staff saw the benefit of rural postings. Others, however, felt ‘dumped’ and unable to move. The relatively promising statistics on retention belie the fragility of the staffing situation. In South Africa, many Professional Nurses stated an intention to leave if they could and 89% were within 15 years of retirement age and little new recruitment to these remote areas was taking place, signalling a serious impending staffing crisis. Similarly in Malawi, there was little new recruitment to the three study districts and the combined effects of resentment of those who felt trapped and the expansion of alternative jobs opportunities suggests that attrition levels will probably increase.

CONCLUSION These studies confirm the importance of addressing retention issues. However, perhaps action rather than more research on retention is needed now. Local level managers need to monitor attrition rates and the causes and identify appropriate and affordable initiatives to encourage staff to stay. What does need further research, however, is how individual preferences and organisational deployment policies and practices are resulting failure to attract new staff to the study locations. Both strategies would improve staffing and, in turn, equitable access to health care in remote rural areas.

O26-20  
Explaining the global crisis in human resources for health: political economy of migration and market and government failure  
S. Nayak  
Kit, Royal Tropical Institute, Amsterdam, Netherlands

Over the past few years, the human resources situation in the public sector has reached a point of severe crisis and inability to provide basic health services (WHR & GHW 2006). One of the major factors contributing to this crisis is emigration of skilled health professionals (medical brain drain). Research also shows that international migration leads to internal migration: from rural to urban, public to private and from primary to specialist care. Inequitable distribution of human resources leads to inequity in access, utilisation and quality of health care services. This Results in unequal impact on health outcomes and health status of the poor and marginalized. Unfortunately, international migration is so far absent from global health equity research agenda and hence no in-depth theoretical and analytical work is available. The present paper discusses theories of (i) market failure, externalities, asymmetric information; (ii) global public goods and (iii) global political economy of migration and inequitable resource use as the consequences of emigration of health professionals. Estimates of the extent and scale of skilled health professionals immigration from developing countries confirm that it is a major phenomenon, e.g., from Ghana, 50% and 75% of each batch of graduates emigrate in 4.5 and 9.5 years respectively. More than 60% of doctors produced between 1985 and 1994 had already left the country, mainly to the UK and USA. UN-ILO calculated that two thirds of Sudan’s professionals had left the country and more than half of Zimbabwe, Zambia and Uganda’s high level manpower did the same. In India, it is estimated that 40% of the doctors who work in the private sector migrate outside the country. Medical expertise like any other professional skill has become an internationally marketable commodity. The persistence of the problem reflects the ineffectiveness of the policies so far implemented to reduce it. Remittances do not help health development because cost of training from public purse goes to private households or investments, or conspicuous consumption. Relevant international membership organisations provide a forum for the potentially equitable and optimal information, negotiation and determination of global
public goods (GPGs) for health that potentially affect the entire constituency of member states. The paper discusses the interface with GPGs through international ‘institutional architecture’ for international collective action to formulate new policies and institutions to restrict migration including international financing of GPGs for health and the effect of recent GATS negotiations on further migration of health professionals.

**TB Treatment and Drug Resistance**

**O26-21 Multidrug-resistant tuberculosis treatment outcomes in Karakalpakstam, Uzbekistan: treatment complexity and the risk of XDR-TB**

K. Braker¹, H. S. Cox², V. Szaire³, C. Mills⁴ and Z. Davletmuratova⁵

¹Medecins Sans Frontieres, Berlin, Germany; ²International Health Research Group, Burnet Institute for Medical Research and Public Health, Melbourne, Australia; ³Medecins Sans Frontieres, London, UK; ⁴Medecins Sans Frontieres, Amsterdam, Netherlands; ⁵Ministry of Health, Republic of Karakalpakstam, Nukus, Uzbekistan

**OBJECTIVES** A pilot programme to treat multidrug-resistant TB (MDR-TB) was implemented in Karakalpakstam, Uzbekistan in 2003. This region has particularly high levels of MDR-TB, 13% and 40% among new and previously treated cases respectively. This study describes the treatment process and outcomes for the first cohort of patients enrolled in the programme, between October 2003 and January 2005.

**METHODS** All patients had been treated with a DOTS category 2 regimen previously. Confirmed MDR-TB cases were treated with an individualized second-line drug regimen based on drug susceptibility test results, while suspected MDR-TB cases were treated with a standardized regimen pending susceptibility results. Regimens aimed to contain at least five effective drugs and treatment was continued for 18 months after sputum culture conversion.

**RESULTS** Of 108 MDR-TB patients, 87 were started on treatment during the study period. Of these, 57 (66%) were infected with strains resistant to at least one second-line drug at baseline, but none had initial ofloxacin resistance. Treatment was successful for 54 (62%) patients, with 13 (15%) dying during treatment, 12 (14%) defaulting and 8 (8%) failing treatment. Poor clinical condition and baseline second-line resistance contributed to treatment failure or death. Treatment regimens were changed in 71 (82%) patients due to severe adverse events or drug resistance. Ofloxacin resistance was seen in strains from 14 (16%) patients during treatment and four of six patients who failed treatment and were still alive at the time of follow-up were infected with extensively drug resistant TB (XDR-TB) at the time of treatment failure.

**CONCLUSION** While acceptable treatment success was achieved, the complexity of treatment and the creation of XDR-TB among treatment failures are important issues to be addressed when considering scaling up MDR-TB treatment.

**O26-22 Does an intermittent regimen increase the risk of MDR-TB?**

A. Maug¹, M. a. h. Salim¹, E. Declercq², A. Van Deun³ and L. Blok⁴

¹Damien Foundation Bangladesh, Dhaka, Bangladesh; ²Damien Foundation Belgium, Brussels, Belgium; ³Institute of Tropical Medicine, Mycobacteriology Unit, Antwerp, Belgium; ⁴Royal Tropical Institute (KIT), Amsterdam, Netherlands

**OBJECTIVES** The aim of the study is to compare the risk of resistance development to anti-TB drugs under intermittent regimen (2 months daily treatment with Rifampicin, Isoniazid, Ethambutol & Pyrazinamide followed by 4 months Rifampicin & Isoniazid three times weekly), with earlier treatment regimen (2 months daily with the four main drugs as above followed by 6 months daily with Isoniazid & Thioacetazone/Ethambutol).

**METHODS** Culture and drug susceptibility testing is performed as a standard measure on sputum samples found positive after treatment for all smear positive TB patients in 13 districts of Bangladesh where Damien Foundation is active since 1991. The results of cultures done on new cases in 2004/2005 (2HREZ/ 4HR3) were analysed and compared with those of 2001/2002 (2HREZ/6HT).

**RESULTS** Out of 309 smear failure cases amongst 20 786 patients treated with the 6-month regimen, 288 were sent for culture of which 74 had positive tuberculosis cultures (true failure). Amongst these 41 (54%) turned out to be Multidrug-Resistant-TB (MDR-TB), defined as resistant to H+R. In the 8-month regimen group 254 out of 18 572 patients failed to clear sputum. 107 of 241 samples sent for culture showed growth of Mycobacterium Tuberculosis, of which 23 (21%) was MDR.

**CONCLUSION** While the study found a higher treatment failure rate in the 6-month treatment group as compared to the 8-month group, this was not confirmed by culture, possibly to be explained by continued excretion of dead bacilli. To the contrary the study showed that also in Bangladesh true failure to Rifampicin-based regimen is lower than to HT-based regimens (0.4% vs. 0.6%). However, not surprisingly, once failure occurs the chances are much more prominent that this is due to MDR-TB, which has consequences for management of failure cases. 13% of percentage of MDR related failures among the two treatment groups seemed to have increased (from 0.1–0.2%), however as no culture is done at start of treatment it is not possible to distinguish primary resistance from acquired resistance. An important question remains whether replacement of the intermittent regimen by a daily regimen of RH can further reduce failure rates and chances of MDR-TB.

**O26-23 Pharmacokinetics and tolerability of high vs. standard dose of rifampicin in pulmonary tuberculosis patients**

H. Nijland¹, R. Ruslami², B. Alisjahbana³, I. Parwati¹, R. Crevel van⁴ and R. Aarnoutse¹

¹Radboud University Nijmegen Medical Centre, Department of Clinical Pharmacy, Nijmegen, Netherlands; ²University of Padjadjaran, Department of Pharmacology, Bandung, Indonesia; ³Hasan Sadikin Hospital, Department of Internal Medicine, Bandung, Indonesia; ⁴University of Padjadjaran, Department of Clinical Pathology, Bandung, Indonesia; ⁵Radboud University Nijmegen Medical Centre, Department of Internal Medicine, Nijmegen, Netherlands

**OBJECTIVES** A long-term goal for tuberculosis (TB) control has been to shorten the duration of treatment. The currently applied 10-mg/kg dose of rifampicin may be too low and available data suggest that increasing the dose of this pivotal TB drug may allow a reduction of treatment duration.

**METHODS** A double-blind randomized clinical trial was performed to investigate the effect of a higher dose of rifampicin in terms of pharmacokinetics and tolerability. Fifty newly diagnosed adult Indonesian TB patients were randomized to receive a standard (450 mg; corresponding to 10 mg/kg in Indonesian patients) or high (600 mg) dose of rifampicin besides other antituberculosis drugs. A full pharmacokinetic curve for rifampicin, pyrazinamide and ethambutol was recorded after 6 weeks of daily TB treatment and safety and tolerability were assessed during the 6-month treatment period.
RESULTS Geometric means (95% CI) of exposure to rifampicin (AUC-24 h) were 79.7 mg·h/l [69.6–91.4] in the high-dose group vs. 48.5 mg·h/l [43.2–54.3] in the standard dose group (65% increase, P < 0.001). Maximum rifampicin concentrations (Cmax) were 15.6 mg/l [13.3–18.4] vs. 10.5 mg/l [9.3–11.9] (49% increase, P < 0.001). The percentage of patients with rifampicin Cmax >8 mg/l was 96% vs. 79%, P = 0.094. The pharmacokinetics of pyrazinamide and ethambutol were similar in the two study arms. No relevant differences in tolerability were observed.

CONCLUSION Increasing the dose of rifampicin is associated with a more than dose-proportional increase in the mean AUCO-24 h and Cmax of rifampicin without affecting the incidence of serious adverse effects. Follow-up studies are warranted to assess whether tuberculosis treatment can be shortened with a higher dose of rifampicin.

O26-24 Isoniazid and its toxic metabolite hydrazine induce pyrazinamide toxicity in vitro

A. Tostmann1, H. J. Boeree1, W. H. M. Peters2, H. M. J. Roelofse2, R. E. Aarnoutse1, A. J. A. M. Van der Ven1, P. N. R. Dekhuijzen1

1Department of Pulmonary Diseases and University Lung Centre Dekkerswald, Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands; 2Department of Gastroenterology, Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands; 3Department of Clinical Pharmacy, Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands; 4Department of Internal Medicine, Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands

OBJECTIVES Anti-tuberculosis drug-induced hepatotoxicity (ATDH) complicates treatment of 5–10% of the patients treated for active tuberculosis. Knowledge on the mechanism of toxicity is still incomplete. Toxic metabolites of anti-tuberculosis drugs may play an important role in the development of ATDH, also because drug interactions can cause induction of biotransformation enzymes. We studied toxicity and interactions between standard antituberculosis drugs in an in vitro model.

METHODS Interactions between isoniazid, its toxic metabolite hydrazine, rifampin and pyrazinamide were studied in human hepatoma cells (HepG2). Cells were pre-treated with non-toxic concentrations of one of these four compounds for 24 h, washed and exposed to increasing concentrations of isoniazid, hydrazine, rifampin or pyrazinamide. To determine whether pre-treatment increased toxicity, changes in the concentration at which 50% of cell growth was inhibited (IC50) were quantified by using the WST-1 cytotoxicity assay.

RESULTS Pre-treatment with isoniazid, hydrazine or rifampin increased isoniazid toxicity by 24%, 26% and 15%, respectively. Pyrazinamide toxicity was increased by isoniazid or hydrazine pre-treatment by 30% and 38%, respectively. Hydrazine or rifampin toxicity was not affected by pre-treatment.

CONCLUSION The present study is the first to demonstrate that pre-treatment with isoniazid or its toxic metabolite hydrazine increases in vitro toxicity of pyrazinamide. In addition, pre-treatment with isoniazid, hydrazine or rifampin increases the in vitro toxicity of isoniazid.[Effect of pre-treatment on isoniazid toxicity.][Effect of pre-treatment on pyrazinamide toxicity.][The bars indicate mean isoniazid (first graph) and pyrazinamide (second graph) IC50 (±standard error) after 24 h pre-treatment with 5 mM INH, 5 mM Hz, 50 µM RIF or 5 mM PZA. Values are expressed as percentage of the control IC50 value (i.e. isoniazid or pyrazinamide without pre-treatment).] *P-value < 0.05 INH = isoniazid; Hz = hydrazine; RIF = rifampin; PZA = pyrazinamide.

Intestinal Helminths

O26-25 Control of human oesophagostomiasis in Northern Ghana

J. B. Ziem1, P. Magnusson1, J. Horton2, E. A. T. Brienen1 and T. Polderman1

1Department of Parasitology, LUMC, Leiden, Netherlands

OBJECTIVES Oesophagostomum bifurcum is known to be locally common in northern Ghana and Togo. Infection rates vary geographically but may be as high as 50–90% at the village level. Although limited in its geographical distribution, the infection causes significant pathology in the endemic region. The objective of the research project was to assess whether control of infection and elimination of oesophagostomiasis as a public health problem can be achieved with albendazole mass treatment.

METHODS Control efforts consisted of three rounds of albendazole mass treatment given by the project staff and a fourth by the Lymphatic Filariasis Elimination Program, in a well demarcated population of some 13,000 inhabitants of an isolated rural District in Northern Ghana. Infection was measured with stool cultures as Oesophagostomum eggs cannot be distinguished microscopically from those of hookworms. The impact of treatment on pathology was monitored with the use of ultrasound examination of the large bowel. The overall potential of control was evaluated by comparing the impact of intervention on Oesophagostomum with that on hookworm.

RESULTS The Oesophagostomum prevalence went down from 53% before intervention to 0.8% 2 years after. In the same period the hookworm prevalence went down from 86.9% to 23.4%. Ultrasound recognisable lesions of the intestinal wall were seen in 38.2% before intervention to 6.2% a year later. After 24 months intervention was stopped for a year: Oesophagostomum infection rates continued to go down while those of hookworm started to increase again.

CONCLUSIONS The results suggest that transmission of Oesophagostomum stopped as a result of repeated albendazole treatment while that of hookworm is only temporarily reduced. Elimination of human oesophagostomiasis would therefore seem possible. This favourable conclusion is likely caused by the vulnerability of the Oesophagostomum life cycle in man, as compared to that of hookworm, by the efficacy of albendazole for O. bifurcum treatment, by the limited size of the endemic area, enabling coverage of the entire endemic area, and by the lack of success of the commonly present simian O. bifurcum to infect man.

O26-25 Simultaneous detection, species differentiation and quantification of human hookworm-like infections in faecal samples using multiplex real-time PCR

J. J. Verweij1, E. A. T. Brienen1, J. Ziem2, L. Yelifari3, A. M. Polderman1 and L. van Lieshout1

1Parasitology, Leiden University Medical Center, Netherlands; 2School of Medicine and Health Sciences, University for Development Studies, Tamale, Ghana; 3Ministry of Health, Upper East Region, Bolgatanga, Ghana

OBJECTIVES Anclylostrongylus duodenale and Necator americanus are one of the most common geohelminthic infections and a major cause of anaemia within endemic areas. Traditionally transmission patterns of hookworm species are determined by microscopic stool examination, with intensity of infection, i.e. the counted number of eggs in a Kato-Katz smear, being the most important epidemiological index. However, microscopy is labour-intensive and the outcome highly reader dependent. Moreover, microscopy does not allow hookworm species differentiation. Therefore we developed a
multiplex real-time PCR assay for simultaneous species specific detection and quantification of human hookworm infections, applicable for stool samples collected under field conditions. METHODS Specific primers and Taqman detection probes were designed on the Internal Transcribed Spacer 2 (ITS2) sequences of *A. duodenale* and *N. americanus*, as well as on the ITS2 sequence of the hookworm related *Oesophagostomum bifurcum*. All were optimized as a multiplex real-time PCR, together with primers and probe for the detection of an internal control. The PCR was evaluated with a panel of well described positive stool samples (*n* = 50) and a wide range of parasitic, bacterial and negative controls (*n* = 150). DNA isolated from stool samples (*n* = 339) collected in northern Ghana was used to compare the performance of the real-time PCR with microscopy based techniques, namely direct smear, Kato-Katz and coproculture examination.

RESULTS The multiplex real-time PCR for the detection of *A. duodenale*, *N. americanus*, and *O. bifurcum*-specific DNA in human faecal samples showed excellent specificity and sensitivity for each of the three nematode species. A highly significant correlation was demonstrated between microscopically determined intensity of infection and the Ct-values of the species-specific PCRs.

CONCLUSION The simple faecal sample collection procedure and the high throughput potential of the described PCR approach provides a powerful diagnostic tool, either to study species-specific transmission patterns or to monitor intervention programs of human hookworm-like infections.

**O26-27**

*Diphyllobothrium latum*: an outbreak in Switzerland

Y. Jackson¹, R. Pastore², P. Sudre², L. Loutan² and F. Chappuis³

¹Travel and Migration Unit, University Hospital Geneva, Geneva, Switzerland; ²Department of Health, Geneva, Switzerland

OBJECTIVES *Diphyllobothrium latum* is endemic in Switzerland. In Geneva, the number of infections increased by about 2-fold from 2003 to 2006. Twenty-six healthy individuals consumed raw marinated perch (*Pesca fluviatilis*) during a wedding dinner party in Geneva in June 2006. Several guests were diagnosed with *D. latum* infection during the following 6 weeks. Therefore, we conducted an epidemiological investigation of this outbreak.

METHODS All individuals who attended the wedding dinner (*n* = 32) were contacted by phone approximately 3 months after the party. All were asked about raw fish consumption at the wedding or during the previous 5 years and about symptoms. All guests who consumed raw fish had a single stool sample examined. A confirmed case was defined as a person having a positive stool exam; a probable case was defined as a person reporting rectal elimination of worm segments without stool examination.

RESULTS Of 26 guests who reported consumption of raw perch, six developed symptoms (23%) and eight were infected (attack rate: 31%) with seven confirmed and one probable cases. Cases were mostly females (63%). None of the cases reported other raw fish consumption in the five previous years, nor did the uninfected persons. All cases were parasitologically and clinically cured, seven with a single dose of praziquantel (10 mg/kg) and one with albendazole (400 mg/day for 3 days).

CONCLUSION This is the first reported outbreak of *D. latum* human infections in Western Europe. We found a high attack rate of *D. latum* infection after consumption of a single dish of raw perch. Most patients were asymptomatic and treatment with praziquantel or albendazole was successful in 100% of cases. Eating raw freshwater fishes as sushi, sashimi or carpaccio exposes individuals to *D. latum* infection in areas where fish is not routinely frozen before consumption. Food regulations and information to restaurant owners and fishmeat handlers must be adapted to new food habits.

**O26-28**

Serologic diagnosis of Strongyloides stercoralis in La Merced, a Peruvian Rainforest City

M. A. Canales¹, K. Polman², J. Pekelharing³, A. van Hoogdalen³, A. Terashima³, E. Gotuzzo³ and J. J. Verweij³

¹Universidad Peruana Cayetano Heredia, Institute of Tropical Medicine Alexander von Humboldt, Lima, Peru; ²Parasitology, Institute of Tropical Medicine, Antwerp, Antwerp, Belgium; ³Parasitology, Leiden University Medical Center, Leiden, Netherlands

OBJECTIVES Strongyloides stercoralis is a nematode frequently found in Peru, and a causative agent of life-threatening hyperinfection among immuno-compromised patients. At the Instituto de Medicina Tropical Alexander von Humboldt (IMTAVH) in Lima, Peru, patients with Strongyloides hyperinfection are seen regularly in combination with the human T-cell lymphotropic virus type-1 (HTLV-1), which is endemic in Peru. An accurate and sensitive diagnosis of *S. stercoralis* infections is therefore essential. A descriptive study using microscopy and serology for the detection of *S. stercoralis* infections was performed in La Merced, Peru.

METHODS In the summer of 2005 and 2006, one to three faecal samples and one serum sample were collected from 290 *S. stercoralis* cases living in different districts in La Merced, Peru. Stool-samples were examined by direct microscopy and Baermann method for the presence of *S. stercoralis* larvae. Antibodies directed against *S. stercoralis* were detected using ELISA. Sensitivity, specificity, positive and negative predictive values (PPV and PTN) were calculated. Data were analysed with SPSS 12.0.1.

RESULTS The total prevalence of *S. stercoralis* found with microscopy in La Merced was 26% with higher percentages found in the districts situated along the rivers. Detection rates were increased if multiple stool samples were available. The ELISA for the detection of antibodies directed against *S. stercoralis* showed a high negative predictive value (>95%) but a low positive predictive value (60%) using the presence of *S. stercoralis* larvae in one or more stool samples as gold standard. In this study *S. stercoralis* could not be correlated with the presence of antibodies against HTLV-1 due to the low numbers of HTLV-1 positive cases.

CONCLUSION A high prevalence of *S. stercoralis* infection was found in La Merced on the basis of 1–3 stool specimens; true prevalences will thus probably be even higher. The ELISA shows promise as a test for epidemiologic screenings of *S. stercoralis*. A newly developed PCR for a more sensitive detection of *S. stercoralis* DNA in stool samples will be tested in the near future.

**O26-29**

Imaging diagnosis of clonorchiasis

S.-T. Hong¹ and D. Cho²

¹Parasitology and Tropical Medicine, Seoul National University, Seoul, Republic of Korea; ²Radiology, Samsung Medical Center, Seoul, Republic of Korea

OBJECTIVES Among several diagnostic tools for clonorchiasis (*Clonorchis sinensis* infection), radiologic examinations are commonly used in clinical practices. During the past two decades, many reports regarding imaging findings of clonorchiasis were introduced.
METHODS The present study is to summarize radiological findings of clonorchiasis. Sonograms, cholangiograms, CT scans, and MRI images of clonorchiasis patients were reviewed and categorized. Their images of clonorchiasis patients were compared with those of controls.

RESULTS The basic imaging finding of clonorchiasis is diffuse dilatation of the peripheral intrahepatic bile ducts, without dilatation of the large intrahepatic or extrahepatic bile ducts. By this finding, however, active clonorchiasis cannot be differentiated from cured infection. Some recent radiologic studies suggested specific findings of active clonorchiasis. Besides direct demonstration of worms, increased periductal echogenicity on sonography and periductal enhancement on dynamic contrast-enhanced CT or MR imaging possibly represent active clonorchiasis. Those images of the liver clonorchiasis are known to be correlated with worm burdens (EPG counts) in their frequency and also severity. The images of cholangiocarcinoma associated with clonorchiasis showed both of the tumor with obstruction images and diffuse dilatation of the peripheral intrahepatic bile ducts.

CONCLUSION Radiological images can be a good practical alternative diagnostic method of clonorchiasis.

Molecular Epidemiology of \textit{P. vivax} and \textit{P. falciparum}

O26-30 Genotyping of \textit{Plasmodium vivax} infections using microsatellite markers and MSP1

P. Van den Eede\textsuperscript{1}, V. Van den Auwer\textsuperscript{a}, C. Van Overmeir\textsuperscript{b}, T. Ngo Duc\textsuperscript{c}, A. Erhart\textsuperscript{d}, L. X. Hung\textsuperscript{e}, J. Anne\textsuperscript{f} and U. D’Alessandro\textsuperscript{a}

\textsuperscript{1}Institute of Tropical Medicine Prince Leopold, Antwerp, Belgium; \textsuperscript{2}Parasitology and Entomology, National Institute for Malariaology, Hanoi, Vietnam; \textsuperscript{3}Catholic University of Leuven, Leuven, Belgium

\textit{Plasmodium vivax} is the most widely spread of the four malaria species and the main cause of malaria outside the African continent. The difficulty of its control is mainly due to the relapsing liver forms. In order to understand the dynamics of \textit{P. vivax} transmission and its epidemiology it is necessary to have reliable genotyping techniques. Our objective is to develop genotyping methods using new microsatellite markers for \textit{P. vivax}.

METHODS Microsatellites are commonly used for genotyping several organisms and appear to be useful markers for a wide variety of studies. Tandem repeats were identified in silico by analyzing the \textit{P. vivax} genome on plasmodb. Microsatellite repeats with more than 20 times a unit of 2–6 bp were selected. Oligonucleotide primers were developed against the flanking region of the microsatellite region.

RESULTS Six microsatellites of 20 were selected. Two of them were discarded due to mispriming of one of the primers. Therefore, four microsatellites were used to analyze blood samples from Vietnamese patients infected with \textit{P. vivax} and results were compared with those obtained with merozoite surface protein 1 (MSP1). Parasite DNA amplification was obtained up to the concentration of 0.01–0.001 fg DNA/µl with cloned PCR product and at a density of 1–5 parasites added to the reaction mix. No misamplification was detected using DNA from other human plasmodial species (\textit{P. falciparum}, \textit{P. malarial}, \textit{P. ovale}, and \textit{P. vivax}), Anopheles mosquitoes, and human pathogens like \textit{Leishmania donovani}, \textit{Trypanosoma cruzi}, \textit{Schistosoma mansoni}, HIV, \textit{Mycobacterium ulcerans} and \textit{Mycobacterium tuberculosis}. Preliminary results show that the selected microsatellites tend to display a higher degree of polymorphism than MSP1. In conclusion microsatellites could be more useful for genotyping \textit{P. vivax} and help to understand its epidemiology, particularly in endemic areas of South East Asia and South America, where \textit{P. vivax} control remains a challenge.

O26-31 Recent independent evolution of \textit{msp1} polymorphism in \textit{Plasmodium vivax} and \textit{Plasmodium cynomolgi}

K. Tanabe\textsuperscript{1}, A. Escalante\textsuperscript{2}, N. Sakihama\textsuperscript{3}, N. Arius\textsuperscript{4}, J. Horii\textsuperscript{1}, R. Culleton\textsuperscript{1}, T. Hayakawa\textsuperscript{1}, T. Hashimoto\textsuperscript{5}, S. Pathiran\textsuperscript{6} and S. Hamburoh\textsuperscript{7}

\textsuperscript{1}Research Institute for Microbial Diseases, Osaka University, Osaka, Japan; \textsuperscript{2}School of Life Sciences, Arizona State University, Tempe, USA; \textsuperscript{3}Institute of Biological Sciences, University of Tsukuba, Tsukuba, Japan; \textsuperscript{4}Faculty of Medicine, University of Colombo, Colombo, Sri Lanka

OBJECTIVE The \textit{Plasmodium} merozoite surface protein 1 (MSP-1) is a strong malaria vaccine candidate. However, the highly polymorphic nature of the MSP-1 gene (msp1) presents a potential obstacle for effective vaccine development. To assess how rapidly parasites are able to generate novel \textit{msp1} diversity, investigations of the evolutionary history of \textit{msp1} polymorphism are crucial. Here, we conduct comparative molecular phylogenetic and evolutionary analyses of \textit{msp1} sequences from \textit{P. vivax} and seven \textit{P. vivax}-related monkey malaria parasite species.

METHODS We obtained \textit{msp1} sequences from \textit{P. cynomolgi} (11 isolates), \textit{P. knowlesi} (11 isolates), \textit{P. coatneyi}, \textit{P. fragile}, \textit{P. inui}, \textit{P. bolybati}, \textit{P. simiovale}, and compared those sequences with \textit{P. vivax} \textit{msp1} alleles (31 isolates) we obtained previously. We used the maximum likelihood method to construct phylogenetic trees and performed population genetic tests to detect positive selection in \textit{msp1} sequences.

RESULTS The ML tree shows that all \textit{P. vivax} \textit{msp1} alleles cluster in the \textit{P. vivax} lineage and are not distributed among other species. Similarly, all \textit{P. cynomolgi} \textit{msp1} alleles cluster in the \textit{P. cynomolgi} lineage. Such clustering in each lineage is also seen when \textit{msp1} sequence is divided into the \textit{S}, central and \textit{S}′-regions. This suggests that, in contrast to presumed ancient origin of \textit{msp1} polymorphism of \textit{P. falciparum}, the origin of \textit{P. vivax} \textit{msp1} polymorphism is relatively recent, with estimated time of 594 000 ± 76 000 years ago, assuming the \textit{P. vivax}\textsuperscript{1}/\textit{P. knowlesi} divergence occurred 6 million years ago. Population genetic tests of neutrality, \textit{dN}/\textit{dS} ratio test, the McDonald-Kreitman test and Tajima’s D test, revealed strong positive selection in the \textit{P. vivax} lineage but not in \textit{P. cynomolgi}. Also, positive selection acts on different regions of \textit{msp1} in \textit{P. vivax} and \textit{P. falciparum}. Discussion: These data present evidence showing that the evolutionary history of \textit{msp1} differs greatly among parasite lineages, highlighting the importance of understanding protective immunity to MSP-1 in a species-specific context.

O26-32 Molecular epidemiology of \textit{Plasmodium vivax} malaria in endemic areas of the newly independents states (NIS) countries

C. Severini\textsuperscript{1}, M. Menegon\textsuperscript{1} and G. Majori\textsuperscript{1}

\textsuperscript{1}Department of Infectious, Parasitic and Immunomediated Diseases, Istituto Superiore di Sanità, Rome, Italy

OBJECTIVES Outside of tropical Africa, \textit{Plasmodium vivax} is the most prevalent parasite with an estimated burden of 70–80 million cases annually and accounting for about 50% of all malaria cases in endemic countries of Middle East, Asia, Western Pacific and Latin America. A research project on
P. vivax malaria resurgence in Newly Independent States of the former USSR was launched at the end of year 2000, with the aim to exploit recent parasitology tools for analysing different malaria epidemiological patterns in this area. The project, funded by the European Commission (INCO COPERNICUS2 project contract ICA2-CT-2000-10046) and coordinated by the Istituto Superiore di Sanità in Rome, included a network of six participants: Armenia, Azerbaijan and Uzbekistan, CNRS in Montpellier, University of Montpellier, and WHO-EURO in Copenhagen.

METHODS During project activities, both passive and active detection of malaria cases were performed in several endemic region of study areas. Patients who were positive by microscopy examination of blood film were informed about the study and were considered for the survey. Blood samples, spotted onto filter papers, were taken for the molecular analysis of vivax isolates before drug treatment was given and kept dry at room temperature, pending analysis. For all blood samples, identifying information were removed and each sample processed was made anonymous. Plasmodial DNAs extracted from human blood samples were genotyped using pvmsp1, pvcs, pvdhfr and pvdhps as genetic markers. Mutations were detected by direct sequencing of PCR-amplons.

RESULTS The main results achieved within 5 years of project activities have been the assessment of genetic variability of P. vivax isolates circulating in the study areas by polymorphism analysis of pvmsp1 and pvcs genes, and the analysis of the extent of polymorphism of pvdhfr and pvdhps genes, two molecular markers for drug resistance in P. vivax. In particular, the analysis of the selected gene markers identified 19 vivax sub-type in 36 isolates from Azerbaijan and 17 vivax sub-types in 24 isolates from Uzbekistan, showed the high prevalence of the wild type profile in the codons linked to the pyrimethamine resistance for pvdhfr and pvdhps genes and allowed the identification of size polymorphism in the pvdhps tandem repeats region.

CONCLUSION In conclusion, the results obtained in the frame of the project provide the scientific community with new genetic features of P. vivax in Central Asia, highlighting the importance of studies entirely devoted to this major human parasite.

O26-33 Distribution of erythrocyte binding antigen (EBA-175) forms of Plasmodium falciparum and clinical status in Iran

A. Heidari1, H. Keshavarz2, S. Dittrich3 and T. Jelinek4
1Department of Medical Sciences, Ministry of Sciences, Tehran, Islamic Republic of Iran; 2Medical Parasitology, Tehran University of Medical Sciences, Tehran, Islamic Republic of Iran; 3Institute of Tropical Medicine, Berlin, Germany; 4Berlin Center for Travel and Tropical Medicine, Berlin, Germany

OBJECTIVES The erythrocytic stage of Plasmodium falciparum causes the most severe form of malaria and several million deaths yearly. The erythrocyte binding antigen 175 kDa (EBA-175) of Plasmodium falciparum is protein that binds its receptor glyco- phorin A on human erythrocytes during invasion. It is considered a prime target for an invasion blocking vaccine. EBA-175 has been sequenced from the FCR3 and CAMP strains of P. falciparum and it has dimorphic nature. The main propose of this study was to determine the distribution of EBA-175 genotypes according to clinical status in Iran.

METHODS The southeast of Iran is the endemic area of falciparum malaria and bordered by Pakistan and Afghanistan. The nested polymerase chain reaction method and specific primers which improves EBA-175 genotyping were used. Sixty-eight microscopically positive blood samples derived from asymptomatic and symptomatic falciparum malaria individuals in southeast of Iran.

RESULTS In the present study that performed first time in Iran, CAMP strains (714 bp) and FCR-3 strains (795 bp) were found in 11/31 (35.5%) and 20/31 (64.5%) symptomatic patients respectively and in 15/39 (38.5%) and 24/39 (61.5%) asymptomatic individuals respectively. The prevalence of mixed C/F infection was 2 (2.9%) cases.

CONCLUSION These results showed that the two dimorphic EBA-175 were present in Iran. Our data illustrated that the FCR-3 genotype is more prevalent in main endemic region of Iran. There wasn’t any significant association between dimorphism of EBA-175 antigen and clinical status in southeast of Iran.

O26-34 Genetic characterisation of Plasmodium falciparum populations in São Tomé and Principe Islands, West Africa

J. L. Vicente1, P. Salgueiro2, A. P. Aroz1, P. V. L. Cravo1, C. Ferreira3, V. E. Rosário1 and J. Pinto1
1Instituto de Higiene e Medicina Tropical, Centro de Malária e outras Doenças Tropicais, Lisbon, Portugal; 2Ministério da Saúde da RD STP, Centro Nacional de Endemias, São Tomé, São Tome and Principe

OBJECTIVES We have characterised the genetic diversity of Plasmodium falciparum populations in São Tomé and Principe islands (STP), West Africa, in order to assess patterns of population substructure and to relate these with epidemiological and control aspects of malaria.

METHODS Blood samples were collected from 3 locations of São Tomé and from Principe in 2000 (rainy season). Plasmodium falciparum isolates identified by nested-PCR were genotyped for the surface antigen genes msp1 and msp2 and for genes associated with chloroquine-CQ (pfcrt) and pyrimethamine/sulfadoxine-SP (pfdhps, pfdhfr) resistance.

RESULTS A total of 121 P. falciparum isolates were identified in 267 blood samples. Prevalence of infection was 44% in São Tomé and 49% in Principe. The 6-15 years-old group presented the highest prevalence. Sixteen and 19 different alleles were obtained for msp-1 and msp-2, respectively. Genetic diversity was higher in the southern sample of São Tomé followed by Principe island sample. MOI values were comparable between islands (1.3-1.6) and highest in 6-15 year-olds. The pfcrt K76T mutation related with CQ resistance was found in 97% of the isolates. All pfdhps and pfdhfr codons examined were polymorphic. The most frequent mutations at pfdhfr were: S108N (89%), N51I (85%) and C59R (60%). The triple mutation (51I/59R/108N) occurred in 45% of the samples. For pfdhps, the A437G mutation was found in 71% of isolates and the K540E in 3%. Four isolates (3%) carried the quintuple mutation (S11I/S9R/108N/437G/540E).

CONCLUSION Both prevalence and MOI were higher in 6-15 year-olds, which may reflect lower immune status and/or higher infection exposure in this group. Genetic diversity at msp1 and msp2 was comparable similar to with continental populations. Genetic differences within São Tomé suggest restrictions to gene flow coupled with different selective pressures between north and south of this island. The high frequency of mutations found in drug resistance genes agrees with high levels of resistance to CQ and SP observed in STP.
Echinococcosis

O26-35
M. Stojkovic1, M. Zwihr2, W. Hosch3, A. Kapaun4, J. Werner5, H. Fries1 and T. Junghanss1
1Section of Clinical Tropical Medicine, Tropical Hygiene and Public Health University Hospital Heidelberg, Heidelberg, Germany; 2Department of Social and Preventive Medicine, University Berne, Berne, Switzerland; 3Radiology, Heidelberg University Hospital Hospital, Heidelberg, Germany; 4Surgery, University Hospital Heidelberg, Heidelberg, Germany

OBJECTIVES Evaluation of treatment in patients with cystic echinococcosis.

METHODS We present a prospective patient cohort study of 111 patients with CE mainly of the liver and lung. All patients attending our CE clinic were monitored in a standardised way at every follow-up visit. Depending on localisation, size and number of cysts patients were treated (i) by surgery; (ii) medically; (iii) by PAIR or (iv) watch and wait approach. At each visit a set of patient, laboratory and cyst data was extracted from the patient records and entered into a database. Cyst staging was performed by the same radiologist (US, CT, MRI) over the whole period.

RESULTS After 10 years of experience these data were analysed. Results of 111 patients are presented with regard to (i) cure/recurrence with different treatments; (ii) cyst stage specific response; and (iii) cyst and drug related complications.

O26-36
‘Watch and Wait’ for active and transitional echinococcal cysts
E. Brunetti1, F. Castelli1, A. Grisolia1, G. Mariani1 and C. Filice1
1Division of Infectious and Tropical Diseases, University of Pavia, IRCCS S. Matteo Foundation, Pavia, Italy

INTRODUCTION The ‘watch and wait’ (WW) approach for echinococcal cysts is an increasingly recognised fourth management option after surgery, albendazole and percutaneous treatments. WW can be adopted when the other options have either failed or are not cost-effective. We report our experience with a cohort of patients followed with WW, either because of previous failure of medical/surgical treatment or contraindications to percutaneous treatment.

PATIENTS AND METHODS From 1998 to 2006, 40 patients with 52 cysts (19 CE2 and 33 CE3b), i.e. prevalently solid with daughter cysts) were followed with WW, including ultrasound (US) and serological monitoring -IHA and ELISA- every 6–12 months. The mean WW time was 39 months (range:9–105). We monitored for cyst-associated complications, including anaphylactic shock, intrabiliary rupture and bacterial infection. We graded the changes in US appearance as follows: (i) no change; (ii) involution; and (iii) reactivation. Involution was defined as the change from CE2 to CE3b and from CE3b to CE4. Reactivation was defined as the change from CE3b to CE2 and CE4 to CE3b.

RESULTS Observed cyst changes were as follows: 36 cysts (61%) showed no changes, 11 (29%) showed persistent involution, 5 (10%) reactivated. We interrupted WW in seven patients. In five of them, this was simply a cautionary measure: 4 cysts showed a reactivation, while 1 cyst increased in size, with unchanged stage. One patient reported nicturia, possibly related with a retrovescical unchanged cyst. In one patient, a CE2 cyst ruptured into the biliary tree. The complication was managed with ERCP at first and then surgically because of persistent pain.

CONCLUSION WW is a safe option in patients that cannot undergo ‘active’ treatments for EC. In over 90% of cases cysts either spontaneously underwent a process of involution or remain unchanged. No adverse consequences occurred, except for nicturia possibly related to retrovescical cyst, and an episode of intrabiliary rupture that was treated first endoscopically and then surgically. Evaluation of WW in larger cohorts is needed to confirm these findings and to identify factors that lead to spontaneous involution of the cysts.

O26-37
Clinical management of cystic echinococcosis: 20-year experience in a single center
E. Brunetti1, C. Gasparetto1, A. Grisolia1, G. Mariani1 and C. Filice1
1Division of Infectious and Tropical Diseases, University of Pavia, IRCCS S. Matteo Foundation, Pavia, Italy

BACKGROUND Cystic echinococcosis (CE) is a complex disease that requires a multidisciplinary, integrated approach and long-term follow-up. There is no consensus as to what is the best treatment, since well controlled clinical trials comparing outcomes of different treatment options are lacking. Until this information is available, clinical decision-making will depend largely on expert opinion and on data from large referral centers. With this in mind, we contribute the long-standing experience of our center to the debate on treatment decisions.

METHODS We searched the clinical files of patients evaluated for CE in our center from 1987–2006, to assess clinical manifestations, clinical evolution, previous therapy, indications for therapy, type of treatment, follow-up and relapse rates.

RESULTS Of 550 patients referred to our center for CE, 474 (86.2%) had actually CE, while 76 (13.8%) had non-parasitic cysts. Of the CE patients, 255 were males, 219 females; (mean age 45, range 4–90), 383 (80.8%) were Italian born, 91 (19.2%) were from other countries, mostly in East Europe and North Africa. The mean size of the cysts was 74 mm (range: 10–180 mm). There were 255 (53.7%) cysts in the liver, 13 in the lung, 15 in liver and lung, 17 in the liver and other organs, 13 in the lung and other organs, 2 in the brain, 2 in the heart.

Seventy-six (16%) of the referred patients had already had surgery, 27 (5.7%) of whom with multiple interventions. There where 124 (26.2%) active cysts, 52 (11%) transitional cysts, 164 (34.6%) inactive cysts, and 30 (6.3%) post-surgical cavities. We treated 110 patients with Albendazole (ABZ) and performed PAIR on 73 cysts in 64 patients. Complete solidification was obtained in 84.5% of the cysts treated with PAIR and combined PAIR/ABZ treatment.

DISCUSSION Despite alternatives such as ABZ and PAIR, many of the referred patients had been previously treated with surgery. Our experience with ABZ and PAIR clearly shows that in selected cases these options can replace surgery. Interestingly, almost one-third of the cysts we diagnosed required no treatment but only follow-up. Other interesting findings are: several of the patients referred had non-parasitic lesions; an increasing number of CE patients are migrants from highly endemic countries. In our experience, interdisciplinary assessment, selection of patients, and choice of treatment based on cyst stages, can reduce unnecessary procedures and improve substantially the outcome.
Diarrhoeal Diseases

O26-38
Genotyping of Giardia lamblia in Cuban children
L. Pelayo Durán, H. Wilke, B. Mulder and F. A. Nuñez
1Parasitology, Caudal de la Habana, Institute of Tropical Medicine, Pedro Kouris, Cuba; 2Regional Laboratory for Medical Microbiology and Public Health, Enschede, Netherlands

The intestinal protozoan Giardia lamblia is a cosmopolitan parasite frequently involved in human parasitic gastroenteritis throughout the world. The molecular studies using different genes have classified G. lamblia in different subgroups or genotypes. There are only a limited number of studies performed to relate the genetic characteristics with the variability of clinical outcomes in human giardiasis.

OBJECTIVE The study aimed to identify some clinical and epidemiological characteristics associated in Cuban children infected with different genotypes of G. lamblia.

METHODS A PCR assay targeting to tpi gene was used to genotype Giardia lamblia in human faeces from 16 Cuban children. Mann–Whitney U test.

RESULTS All children infected with genotype B of Giardia had diarrhoea, however this symptom was presented in only five (62.5%) of children with genotype A of Giardia and the duration of diarrhoea was longer in the group of children infected with genotype B (8.1 days) than whom were infected with genotype A (3.8 days) (Man–Whitney U test P < 0.001).

CONCLUSION The present study provides, for the first time, information on the distribution of the genotypes of G. lamblia in Cuba and it is the first study in American continent aimed to correlate the clinical characteristics with the main genotypes of Giardia. In spite of a clear relationship was found between parasite genotype B and a longer duration of diarrhoea; will be necessary further studies with a larger series of fecal samples using preferably genotyping/subgenotyping methods in order to achieve a better knowledge of the distribution of these assemblages in humans with different clinical patterns.

O26-39
Intestinal protozoal infection and HIV in adult in-patients presenting with diarrhoea in a large teaching hospital in Blantyre, Malawi
M. Beadsworth, A. Perez, L. van Lieshout, C. Muthali, A. Watson, T. Hart, N. Beeching and E. Zijlstra
1School of Tropical Medicine, Liverpool, Tropical and Infectious Diseases Unit, Manchester, UK; 2Department of Medicine, College of Medicine, University of Malawi, Blantyre, Malawi; 3Department of Parasitology, University of Leiden, Leiden, Netherlands; 4Department of Medicine, University of Liverpool, Liverpool, UK; 5Department of GU Medicine and Medical Microbiology, University of Liverpool, Liverpool, UK; 6School of Tropical Medicine, Liverpool, UK

OBJECTIVES HIV/AIDS and diarrhoea cause significant morbidity and mortality in the developing world. They are second and fourth commonest communicable diseases causing death. Chronic diarrhoea is an independent marker of immunosuppression. 25% of the world is infected by enteric parasites. However their association with diarrhoea, HIV and degree of immunosuppression remain unclear. As part of a year-long study assessing aetiology and seasonality of diarrhoea in a high HIV prevalent area we assessed these associations.

Aims: To assess prevalence of HIV amongst in-patients with acute and chronic diarrhoea. To assess the relationship between HIV status, diarrhoea and severity of immunosuppression. To assess prevalence of protozoa and association with diarrhoea, HIV and severity of immunosuppression. To assess outcome.

METHODS Between March 2004 and February 2005 all consenting adults with diarrhoea and controls were recruited on 2 days each week. Demographic data, HIV status (CD4 if positive) and stool sampling was undertaken. Wet prep microscopy, modified Ziehl-Neelson for isospora, cryptosporidium and optical white staining for microsporidium were undertaken.

RESULTS Of the 398 patients recruited 388 were included in analysis. Overall 47.7% were male. Median age was 31 (range 15–83). 22.3% presented with acute diarrhoea, 43.7% with chronic and 33.8% were controls. Of those tested 83.6% were HIV positive, 96.4% of chronic diarrhoea were HIV positive (P < 0.001) Overall 17.4% died, 20.5% with chronic diarrhoea, however this symptom was presented in only five (62.5%) of children with genotype A of Giardia and the duration of diarrhoea was longer in the group of children infected with genotype B (8.1 days) than whom were infected with genotype A (3.8 days) (Man–Whitney U test P < 0.001).

CONCLUSION The present study provides, for the first time, information on the distribution of the genotypes of G. lamblia in Cuba and it is the first study in American continent aimed to correlate the clinical characteristics with the main genotypes of Giardia. In spite of a clear relationship was found between parasite genotype B and a longer duration of diarrhoea; will be necessary further studies with a larger series of fecal samples using preferably genotyping/subgenotyping methods in order to achieve a better knowledge of the distribution of these assemblages in humans with different clinical patterns.

O26-40
Brominated polystyrene beads for safe household water purification and storage in India
J. F. Williams, M. Bridges, D. Dunk, J. Santiago, P. Shankar and M. Rao
1HaloSource Incorporated, Bothell, USA; 2Filtrex Corporation, Bangalore, India; 3Eureka Forbes, Aquadiagnostics Inc., Bangalore, India

OBJECTIVES Evaluation of novel brominated polystyrene-hydantoin polymer beads as disinfecting medium for in-home, gravity feed purification of raw water sources.

METHODS Halogen charging of hydantoinylated polystyrene beads with either bromine or chlorine was evaluated as a means of creating potent disinfecting media for incorporation into gravity feed, single-pass water purification devices designed for household use in India. Various experimental configurations were used to compare the efficacy of Br or Cl-powered bead beds in inactivating polio virus and E. coli challenge suspensions, using standard quantitative microbiology methods. Variable input water quality inputs were used to simulate worst-case conditions of turbidity, organic load, hardness and temperatures. The intent was to arrive at device designs and costs that would be optimal for low cost, long-life, in-house purification of water from heavily contaminated sources in a durable, user-friendly format and use pattern. These devices would then be used in health impact studies on diarrhoeal disease incidence rates in user households.

RESULTS Single passes of virus and bacteria-laden input suspensions were effectively inactivated to very high degrees, compatible
Abstracts of the 5th European Congress on Tropical Medicine and International Health


with EPA purification standards, over several thousand liters of challenge water. Dose response and life span data supported the conclusion that Br provided higher potency for larger challenge volumes than did the Cl charged media. Sensory evaluations of output water over the life of the media also showed superior results in Br-treated systems. There were no significant impacts on disinfection by-product (DBP) quantities in output water, with both Br and Halogen systems providing long-term output water with DBP well below EPA and WHO recommended limits, and containing sufficient residual oxidant for valuable protection of stored water. Different configurations were evaluated by householders to arrive at most acceptable use patterns and costs.

CONCLUSION Household water purification with gravity-feed, single-pass treatment of contaminated water using brominated polystyrene-hydantoin beads can be the basis of low-cost, long-life units that produce clear water, free of odor or off-taste, and highly likely to favorably impact diarrhoeal disease rates in user families. Bromine offers efficacy and sensory advantages over chlorine in this application.

O26-41
Characteristics of acute childhood diarrhoea in northern Ghana
K. Reither1, R. Ignatius2, T. Weitzel1, A. Seidu-Korkor3, L. Anyidoho4, E. Saad5, A. Djie-Maletz6, P. Zinell7, F. Amoo-Sakyi7, F. Daniko8, S. Danour9, P. Otchwemah1, E. Schreier1, K. Stark4 and F. P. Mockel6
1Institute of Tropical Medicine Berlin, Charité – University Medicine Berlin, Berlin, Germany; 2Institute of Microbiology and Hygiene, Charité – University Medicine Berlin, Berlin, Germany; 3Ministry of Health, Regional Health Administration, Tamale, Tamale, Ghana; 4School of Medicine and Health Sciences, Tamale, Ghana; 5Northern Region Malaria Project (NORMAP), Tamale, Ghana; 6Robert Koch Institute, Berlin, Germany

OBJECTIVES Acute diarrhoea is a predominant cause of paediatric morbidity and mortality in sub-Saharan Africa. In peri-urban Tamale, northern Ghana, and during the dry season 2005/6, we examined microbiological causes of acute childhood diarrhoea and its clinico-epidemiological aspects.

METHODS The study comprised 243 patients with acute diarrhoea and 124 population control children. Stool samples were collected. Patients were clinically examined, and malaria and anaemia were assessed. (RT)-PCR assays were used to identify rotavirus, astrovirus, norovirus and adenoviruses and culturing methods were applied to detect bacteria. Intestinal parasites were diagnosed by microscopy, stool antigen assays and PCR.

RESULTS The most common symptoms in patients (mean age and 10 months) were watery stools, fever, weakness and sunken eyes. Malaria was present in 15% of the patients and anaemia in 91%; both underweight (22%) and wasting (19%) were frequent. Intestinal micro-organisms were isolated from 77% of patients and from 53% of population controls (P < 0.0001). Rotavirus (55%), adenovirus (28%) and norovirus (10%) were the most common pathogens in patients; intestinal parasites (5%) and bacteria (5%) were comparatively rare. Diarrhoea patients without an identified intestinal pathogen more frequently had malaria (25%) than patients with isolated micro-organisms (12%, P = 0.02). Rotavirus was the only pathogen which occurred significantly more frequently in patients than in the population (odds ratio 7.7, 95% CI, 4.2–14.2), and was associated with young age, fever and watery stools.

CONCLUSION Infection with rotavirus is the major cause of acute paediatric diarrhoea in peri-urban northern Ghana. The high proportion of putative enteropathogens in children without acute diarrhoea suggests prolonged excretion or limited pathogenicity. Sanitation, health education and rotavirus-vaccination can be expected to have substantial impact on childhood morbidity in this population.

Treatment of Malaria: Other Drugs
O26-42
Suboptimal antimalarial treatment and the evolution of virulence: are we shifting the balance?
P. Schneider1, B. Chan2 and A. Read1
1Inst of Immunology and Infection Research, University of Edinburgh, Edinburgh, UK

OBJECTIVES In endemic areas, antimalarial drug treatment often suppresses parasites below levels that cause clinical disease, not necessarily eliminating all parasites. Parasites surviving such drug treatment are likely to experience severe selection pressure. This may result in drug resistance but may also have other, less studied, consequences including changes in transmission stage production and virulence. Such changes, related to the reproductive success of the parasites are of interest from an evolutionary viewpoint. Malaria parasites multiply asexually in the host’s erythrocytes and need to form sexual stages for transmission to the next host. For the parasite, increased asexual multiplication has the benefit of increased transmission potential but also the disadvantage of risking immune attack and host death. It is this balance between pros and cons that determines the optimal level of virulence. My research focusses on the following question: Can suboptimal drug treatment lead to increased virulence? This hypothesis is supported by studies showing that interventions reducing risk of host death (imperfect vaccination, serial passage in animals) selects more virulent parasites and may also apply to suboptimal chemotherapy.

METHODS Apply theories of virulence evolution to suboptimal antimalarial treatment. Assumptions are tested with genetically related virulent and avirulent clones of the rodent malaria parasite Plasmodium chabaudi in mice.

RESULTS Evolutionary theory predicts that suboptimal drug treatment may lead to either increased or decreased virulence. In our pilot experiments, we found that more virulent parasites are less sensitive to drug treatment, which supports the hypothesis that suboptimal chemotherapy can generate natural selection for increased virulence.

CONCLUSION Evolution of increased virulence in response to suboptimal drug treatment is likely. The hypothesis needs further testing to investigate how widespread this evolution of increased virulence is, how it is affected by different treatment regimens and its relative importance compared to the development of drug resistance. We are currently using experimental evolution in the rodent malaria model to confirm the hypothesis using various drugs and parasite clones.

O26-43
Comparison of random vs. ethno-directed research in natural-drug development: antiparasoidal investigation on Indian plants
V. S. S. N. Kantamreddi1 and C. W. Wright1
1University of Bradford, The School of Pharmacy, Bradford, UK

In view of the importance of natural products in drug discovery [1] and that according to WHO, about 80% of the population in...
developing countries depend upon plants for their medicines [2], the present study was designed to assess the value of an ethnomedical approach for the collection of plants for screening rather than a random collection. Because of our special interest in developing antimalarials, the present investigation was carried out on 27 anti-pyretic plants compared with 27 randomly collected Indian plants from forest in the locality of Bhubaneswar, Orissa. A random collection of plant species was carried out without regard for their traditional medicinal uses (if any), and anti-pyretic plants were collected using information obtained from an ethno-botanical survey. *In-vitro* antimalarial activities against chloroquine-sensitive (3D7) and resistant (K1) strains of *Plasmodium falciparum* were assessed using the parasite lactate dehydrogenase assay [3] with chloroquine and artemether as positive controls. Out of 41 methanolic extracts obtained from the antipyretic plants, 33 (80.5%) exhibited antimalarial activities (IC50 ≤ 100 μg/ml), against strain 3D7, representing 22 (93%) of the 27 species. Of these active species, 19 extracts belonging to 14 species were active against strain K1 as well. Seven species, *Alangium salvifolium*, *Barringtonia acutangula*, *Clerodendrum indicum*, *Cassia obtusifolia*, *Poinciana pulcherrima*, *Mimosa pudica* and *Vitex negundo* exhibited low IC50 values (2–33 μg/ml) against both strains, and are particularly worthy of further study. Among 43 methanolic extracts analysed from 27 randomly collected species, 11 (25.6%) extracts from 10 (37%) species were active against strain 3D7, of which 10 extracts belonging to nine plants were active against strain K1. The following five species possessed marked activities (2–31 μg/ml) against both strains, with low IC50 values: *Anogeissus acuminata*, *Glycosmis pentaphylla*, *Phyllanthus reticulatus*, *Sphaeranthus indicus* and *Tarenna zeylanica*, and are of interest for further study. The ethno-directed plant selection approach identified a higher percentage of active species (93%) compared to the random selection approach (37%). However, both the ethno-directed and random selection approaches may serve as useful strategies in the search for biologically active compounds with potential antiplasmodial activity (Table 1).

<table>
<thead>
<tr>
<th>Species/controls</th>
<th>Part/drug</th>
<th>Strain(3D7)</th>
<th>Strain(K1)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>A. salvifolium</em></td>
<td>Bark</td>
<td>2.1 ± 0.2</td>
<td>3.4 ± 0.2</td>
</tr>
<tr>
<td><em>A. acuminata</em></td>
<td>Bark</td>
<td>2.1 ± 0.8</td>
<td>3.2 ± 0.6</td>
</tr>
<tr>
<td><em>C. indicum</em></td>
<td>Fruit</td>
<td>2.8 ± 0.3</td>
<td>17.8 ± 1.3</td>
</tr>
<tr>
<td><em>C. obtusifolia</em></td>
<td>Whole plant</td>
<td>9.4 ± 1.8</td>
<td>33.3 ± 2.1</td>
</tr>
<tr>
<td><em>M. pudica</em></td>
<td>Stem</td>
<td>16.5 ± 0.7</td>
<td>20.4 ± 1.2</td>
</tr>
<tr>
<td><em>S. indicus</em></td>
<td>Whole plant</td>
<td>25.2 ± 2.1</td>
<td>30.8 ± 2.9</td>
</tr>
<tr>
<td><em>V. negundo</em></td>
<td>Leaf</td>
<td>2.8 ± 0.3</td>
<td>17.8 ± 1.3</td>
</tr>
<tr>
<td>Positive controls</td>
<td>Choloroquine</td>
<td>0.02 ± 0.001</td>
<td>0.38 ± 0.03</td>
</tr>
<tr>
<td></td>
<td>Artemether</td>
<td>0.008 ± 0.002</td>
<td>0.014 ± 0.01</td>
</tr>
</tbody>
</table>

In conclusion, the ethnopharmacological approach for the search of new bio-active agents from plant sources has proved to be more predictive than a random collection (graph 1). (Comparison of random vs. ethno-directed activities)

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**REFERENCES**


**O26-44**

A phase 2/3, randomized, double blind, comparative trial of azithromycin plus chloroquine vs. mefloquine for the treatment of uncomplicated *Plasmodium falciparum* malaria in Africa

D. Lewis 1, M. Mulenga 2, P. Magwenyi 1, I. Sagara 3, M. Wasunna 1, A. Odoro 3, A. Se 7, A. Tiono 2, S. Sarkar 2, C. Kityo 1, A. Djinde 3, M. Nambozi 2, R. Juma 5, M. Germain 1, P. Ansah 1, A. Ouedraogo 7, R. Aman 1, G. Kokwaro 1 and M. Dunne 1


**OBJECTIVES**

Azithromycin has demonstrated *in vitro* and *in vivo* activity against *P. falciparum*. This trial is part of a global program assessing the efficacy and tolerability of the combination of azithromycin and chloroquine in the treatment of uncomplicated *falciparum* malaria.

**METHODS**

This was a multi-center, randomized, double-blind study comparing azithromycin (1000 mg or 500 mg) plus chloroquine once daily for three days to mefloquine (MQ) in six countries in Africa. After obtaining informed consent, adults with fever, a positive peripheral blood smear and a positive rapid diagnostic test for falciparum malaria were randomized to one of three treatment regimens: azithromycin (1000 mg or 500 mg) plus chloroquine (600 mg base), once daily for 3 days (AZ1gCQ, AZ500 mgCQ) or MQ (1250 mg divided dose). All subjects were
hospitalized and monitored closely for a minimum of 3 days, until three consecutive blood smears were negative for asexual parasitemia and the investigator deemed discharge from the hospital appropriate. The study participants were evaluated for 42 days with day 28 as the primary time point for analysis. Two interim analyses for review by a Data Safety Monitoring Board were conducted. (www.clinicaltrials.gov, NCT00074841).

RESULTS All treatment regimens were well tolerated. The day 28 efficacy rate in the primary population was 84% and 94% for the AZ1gCQ and SPCQ respectively, with a 95.46% (type-I error rate adjusted for multiple looks into unblinded data by Group Sequential Procedure) confidence interval of the difference of (-22, 79). AZ1gCQ failed to achieve the pre-specified non-inferiority (lower limit of the CI > -10%) to SPCQ. Efficacy response rates varied by region (site) from 71% to 100%. The AZ500 mgCQ treatment group was discontinued for inadequate efficacy (66% clearance through day 28) following the second interim analysis evaluation by the Data Safety Monitoring Board. Subjects who received >=25 mg/kg of azithromycin achieved parasitic clearance on Day 28 of 95.8% (23/24) showing a significant (p=0.0088) azithromycin dose-response relationship in a post hoc analysis when a logistic regression was fitted on the success rate combining the two azithromycin-containing arms. A chloroquine resistant PfCRT haplotype was present in 203/221 (92%) of the baseline specimens tested.

CONCLUSION The combination of azithromycin and chloroquine demonstrated activity against uncomplicated falciparum malaria in India with a significant dose response for the azithromycin component. Trials to determine the optimal dose for the azithromycin component of this combination should be conducted.

O26-46
A phase 2/3, randomized, double-blind, comparative trial of azithromycin plus chloroquine vs. atovaquone-proguanil for the treatment of uncomplicated Plasmodium falciparum malaria in South America
D. Lewis1, G. Carraquillas2, S. Vreden3, G. Utz4, S. Sarkar5, D. Montilla6, R. Montoya7, G. Capella8, L. Duza Sanchez9 and M. Dunne
1Pfizer Global Research and Development, New London, USA; 2CEIS Fundacion Santa Fe de Bogota, Bogota, Colombia; 3Diakonessen Hospital, Paramaribo, Suriname; 4Naval Medical Research Center Detachment, Lima, Peru; 5Pfizer Biostatistics, Mumbai, India; 6Hospital Sant Andreu, Tumaco, Colombia; 7Hospital de Tudo, Tudo, Colombia; 8Hospital San Francisco De Asis, Guayaquil, Colombia

OBJECTIVES Azithromycin has demonstrated in vitro and in vivo activity against P. falciparum. This trial is part of a global program assessing the efficacy and tolerability of the combination of azithromycin and chloroquine in the treatment of uncomplicated falciparum malaria.

METHODS This was a multi-center, randomized, double-blind study comparing azithromycin plus chloroquine to atovaquone-proguanil (A-P) in Suriname (one site) and Colombia (three sites). After obtaining informed consent, adults with fever, a positive peripheral blood smear and a positive rapid diagnostic test for P. falciparum malaria were randomized to one of three treatment regimens: azithromycin (1000 mg or 500 mg plus placebo) or open-label chloroquine (AZ1gCQ, AZ500 mgCQ) or open-label sulfadoxine-pyrimethamine and open-label chloroquine (SPCQ). All subjects were hospitalized and monitored closely for a minimum of 3 days, until 3 consecutive blood smears were negative for asexual parasitemia and the investigator deemed discharge from the hospital appropriate. The study participants were evaluated for 42 days with day 28 as the primary time point for analysis. Two interim analyses for review by a Data Safety Monitoring Board were conducted. (www.clinicaltrials.gov, NCT00074841).

RESULTS All treatment regimens were well tolerated. The day 28 efficacy rate (before PCR correction) was 57% (64/112) and 99% (112/113) for AZ1gCQ and A-P respectively with a 95.01%
The primary endpoint was not achieved. Higher Plasmodium falciparum for 40h, under or not Lapdap is a cheap, new antimalarial drug but its 2 2 with high IC50 for quinine A total of 1238 children aged 6 months to 10 years European Congress on Tropical Medicine and International Health 2007 The Authors 2 © and P. Milligan 18% (109/595) of children treated with Lapdap and there was no evidence that Lapdap caused anaemia in G6PD deficient children. Anaemia with Lapdap was related to high initial parasitaemia and may therefore be reduced by combining Lapdap with artesunate to achieve faster parasite clearance.

O26-48
Fnhe polymorphism in wild isolates of P. falciparum from different continents with a low sensitivity to quinine S. Pelleau 1, P. Lim 2, J. Le Bras 3, S. Corre 4 and R. Jambou 5
1 Institut Pasteur de Dakar, immunologie clinique et parasitaire, Dakar, Senegal; 2 Institut Pasteur de Phnom Penh, Phnom Penh, Cambodia; 3 Hospital Bichat Claude Bernard, Paris, France; 4 Institut Pasteur de Dakar, Dakar, Senegal

Quinine remains a drug of choice to treat severe and chloroquine-resistant malaria. However its mechanism of action is poorly understood. Like mefloquine and chloroquine, sensitivity of parasites to quinine appears to be modulated by proteins such as PfH1 and PCRT expressed in the food vacuole. The SNP PCRT K76T and the amplification of the pfmdr1 copy number have been reported to be associated with a lower sensitivity to quinine but these polymorphisms do not seem to be sufficient to explain the various level of sensitivity observed. Recently, it has been pointed out by QTL analysis (Ferdig et al. 2004) that three loci in chromosomes 5, 7 and 13 are involved in the control of quinine sensitivity. Results from the field and in vitro studies supported the role of fnhe, a gene located in this area and coding for a Na+/H+ exchanger, in modulation of the IC50 to quinine. Studies conducted in Mali highlights again (Djimde et al. 2006, personal communication) an association between the length of the microsatellite ms4760 located in the coding frame of fnhe with the quantity of quinine used in the villages. To further characterize fnhe association with quinine response, we studied 19 wild isolates of Plasmodium falciparum with high IC50 for quinine (>5000 nM), collected among patients suffering from mild malaria attack in Africa and Asia. Five isolates fully sensitive to quinine and 3D7 were used as controls. We first analysed the copy number of the gene present in the genome of the parasites by real-time PCR using beta-tubuline and 3D7 as reference and calibrator. For all the isolates, only one copy of fnhe was found. In a second time we compared expression of the gene by RT-qPCR, in field isolates obtained from patients and cultured in vitro for 40h, under or not pressure of quinine. A dose effect of quinine was observed on mRNA production, in the same time as a retardation of the cell cycle of the parasite. To analyse polymorphism of the gene, a 1500 bp fragment including ms4760 was amplified by PCR for all the samples and sequenced. Length variation of the microsatellite was found. Using heteroduplex approach, the full sequence of fnhe (5915 bp) is under analysis for all the isolates to detect presence of SNP all over the genome. Associations between fnhe polymorphisms and quinine sensitivity will be presented and discussed.

Fungal Diseases/Antibiotic Resistance
O26-49
An outbreak of acute histoplasmosis among members of a naturalistic expedition in Ecuador rain forest
A. Anghelien 1, F. Gobbi 2, G. Monteiro 1, M. Boscolo 1, S. Marocco 1, M. Anselmi 1, A. Rossane 1, C. Savio 2, Z. Bisoffi 1
1 S. Cuore Hospital, Centre for Tropical Diseases, Negrar (Verona), Italy; 2 Amedeo di Savoia Hospital, Clinic of Infectious Diseases, Torino, Italy; 3 S. Cuore Hospital, Laboratory and Microbiology Unit, Negrar (Verona), Italy

BACKGROUND In August 2006 a cluster of a respiratory illness among participants to a scientific expedition to Ecuador was
identified. The index case was initially diagnosed and treated as bacterial pneumonia. A similar presentation occurred in three other subjects, rising the suspicion of an outbreak. Based on epidemiological (all 17 patients had slept in a bat-infested lodge in the Otonga Rain Forrest, and 14/17 patients had visited the Tena caves) and clinical data histoplasmosis was suspected.

**OBJECTIVES** To raise awareness on a potential cause of respiratory disease in travellers.

**METHODS** Cluster description: we contacted all the 26 participants to the expedition for a questionnaire and a clinical examination; chest X-ray or computed tomography, blood tests, ophthalmologic exam were performed if necessary.

**RESULTS** 10/26 subjects participating to the expedition (38.4%) presented with typical symptoms of acute respiratory histoplasmosis (fever, cough, shortness of breath, fatigue, sore throat with oral ulcerations). Six required antifungal treatment (itraconazole), and two were hospitalised; seven individuals complained of abdominal pain, fever, diarrhoea. Without the epidemiological criteria (outbreak, site of exposure, bat infestation) the first three cases were initially diagnosed and treated as flu or bacterial pneumonia. Blood test performed on 16 symptomatic patients showed mild hepatitis in 4/16 (25%), raised CRP in 5/16 (31.3%), no leucocytosis nor leucopenia. Serology for histoplasmosis and antineumoglutaminuria were still underway. X-rays and/or Computerized tomography was performed in 23 cases, showing pathologic findings in 11/23 (nodular pulmonary lesions in all, associated with mediastinal adenopathy in one case, pleural and pericardial effusion in another). Six months after exposure all patients did well, CT scan and/or X-ray showing resolution or improvement.

**CONCLUSION** Histoplasmosis is a deep, potentially serious mycosis that can affect humans through inhalation of airborne spores (Gascón et al. Eur J Clin Microbiol Infect Dis 2005; 24(12): 839-41. Wheat et al: Clinical Infectious Diseases 2000; 30: 688-695). There is a strong association between the presence of bat guano and the contamination from histoplasma capsulatum. Travellers or researchers visiting caves or infested sites are at risk (Morgan et al. Am J Trop Med Hyg 2003; 69(6): 663-9). The flu- or pneumonia-like appearance of the disease and the possible missing of a cluster identification may contribute to under-estimation of histoplasmosis incidence. In patients returning from endemic areas with prolonged respiratory symptoms, clinicians should ask for possible exposure to H. capsulatum. Travel clinics should provide adequate information on this potential occurrence.

**Fungal Diseases/Antibiotic Resistance**

**O26-51** Prevalence and pattern of antimicrobial resistance in *Shigella* spp of acute diarrhoea in Iran

F. Jafari¹, N. Sahebekhtiari², M. Bolfoni³, L. Shokrzadeh¹, M. Yaghoobi¹, M. Nochi¹, S. Salmanzadeh-Ahrabi¹ and M. R. Zai¹

¹National Department of Foodborne Diseases and Acute Diarrhoea, Research Center for Gastroenterology and Liver Diseases, Shahed Beheshti University of Medical Sciences, Tehran, Islamic Republic of Iran; ²Islamic Azad University, Science and Research Branch, Microbiology, Tehran, Islamic Republic of Iran

**OBJECTIVES** The aim of this study was to determine the prevalence and pattern of antimicrobial resistance in *Shigella* spp. in patients with acute diarrhoea in Tehran, Iran.

**METHODS** From April 2004 to September 2005 *Shigella* spp were investigated in stool specimens of 1120 patients with acute diarrhoea by standard method. Antibiotic susceptibility test was done for 14 antimicrobial agents with Kirby–Bauer disk diffusion method.

**RESULTS** In this study the male:Female ratio was 1.4:1 and 66.3% of samples were obtained from children <5 year of age. A total of 157 (14.01%) positive samples of *Shigella* spp, *Shigella sonnei* was the most isolated strain (56.1%) followed by *Shigella flexneri* (30%). *Shigella dysenteriae* and *Shigella boydii* were isolated in 5.1% and 8.3% respectively. All of the *Shigella* spp. was susceptible to ceftriaxone, ciprofloxacin and ceftazidime and the most strains were resistant to tetracycline (95.5%) and some factors connected with coexisting illnesses on the occurrence of pathogens in the oral cavity remains unclear. Aim of this study was to examine and compare prevalence of fungal and protozoan pathogens in oral cavities of patients with some local/general disabilities and assess role of the microorganisms as factors of complications in course of chronic diseases.

**METHODS** Ninety women, 16–50-years old, were categorized into three equal groups involving patients: (i) with advanced local stomatognathic deteriorations, orthodontic treated; (ii) mentally disordered with chronic diseases (epilepsy, fenylketonuria); (iii) general healthy of control group. In each of the groups, younger patients, 18–30-years old, and the older, were analyzed. All patients were assessed clinically. Material of their oral cavity swabs were used for preparation of microscopic wet-mounted and Trichrom-stained slides and for in vitro culture methods on Chromagar–Candida BBL plates to identify fungi and protozoans. Tests F-Fisher and HSD Turkey (P > 0.05) for comparison of prevalence of pathogens in respective patient groups were applied.

**RESULTS** In patients of group I, stomatognathic abnormalities were present, among others: dental huddles, transpositions and prognatism. Pathological changes in gingiva and periodontium, dental caries, lost teeth in patients of group II occurred. Such changes, at various intensities, in patients of control group were found only sporadically. Live, motile protozoans, identified microscopically as Trichomonas tenax and *Entamoeba* gingivalis were more often detected in group II (an average prevalence 66.6%) than of I (23.3%) and III (16%). *Candida albicans* strains were more frequent found in groups I and II (43.3% and 40%, respectively) than III (sporadically). It was clear visible that higher prevalence of fungi and protozoans in older patients was found.

**CONCLUSION** The decreased resistance may be the main factor favoring of appearance of protozoans and opportunistic fungi in the patients with chronic disease. Also, local stomatognathic deteriorations that influence mouth ecology may induce multiplication of Candida albicans strains. Thus, monitoring of oral cavity in aspect of occurrence of fungi is recommended to reduce risk of complications because of disseminated fungal infection.

**Fungal Disease/Antibiotic Resistance**

**O26-50** Fungal and protozoan pathogens in the oral cavity as potential factors of complications in patients with chronic diseases

L. Chomicz¹, J. Piekarczyk², P. Zawadzki³, B. Piekarczyk³, K. Perkowski³ and B. Staroszczyk³

¹Department of Medical Biology, Medical University of Warsaw, Warsaw, Poland; ²2nd Department of Maxillofacial Surgery, Medical University of Warsaw, Warsaw, Poland; ³Department of Orthodontics, Medical University of Warsaw, Warsaw, Poland; ⁴Department of Pharmaceutical Microbiology, Medical University of Warsaw, Warsaw, Poland

**OBJECTIVES** Oral cavity ontocenusis creates an open growth system in which complex interrelations between microorganisms and host occur. Our previous studies showed significant differences in species composition of mouth microorganisms depended on age of the human host, oral health status, specific diet, drug-induced gingival overgrowth, general health condition. Also, it was indicated that various systemic disabilities have different influence on mouth microorganisms. However, to date, effect of...
sulfamethoxazole trimethoprim (91.7%). The most frequent multi
resistance pattern observed among Shigella sonnei strains and was
the combined resistance to (erythromycin, tetracycline, sulfa-
methoxazol trimethoprim) 19 (21.6 %) followed by (erythromy-
cin, tetracycline, sulfamethoxazol trimethoprim, ampicillin) which
was seen in 16 (18.18 %). Among Shigella flexneri all strains were
resistance to three or more antibiotics. In this type of strains one
sample detected with 7 antibiotic (erythromycin, Cefalothin,
tetracycline, sulfamethoxazol trimethoprim, Ampicillin, Amoxicil-
lın – clavulanicacid, Chloramphenicol) resistance pattern.
CONCLUSION Shigellosis is a significant cause of gastroenteritis in
both developing and industrialized countries. An interesting finding
of this study is, Shigella sonnei was the most prevalent (56.1 %)
among Shigella species as it is in developed countries (50.4 %). The
high number of multidrug resistant isolates indicates that a specific
treatment management for Shigella infection is needed.

O26-52
Microbiological aspects of community-acquired pneumonia in a
rural hospital in Zambia
E. J. Nossent1, A. E. Speek1, P. C. Borsboom2 and J. L. Nouwen1
1 Erasmus MC, Rotterdam, Netherlands; 2 Our Lady’s Hospital, Chilonga,
Zambia

OBJECTIVES To study the prevalence of the different causative
bacterial pathogens of community-acquired pneumonia (CAP) and
their resistance patterns and to evaluate the appropriateness of the
treatment of CAP according national and WHO guidelines in Zambia.

METHODS Patients presenting with CAP were interviewed and
physical examinations were performed. All sputa were sent for
culture and resistance testing. Follow-up continued until end of
treatment or hospital stay.

RESULTS A total of 61 patients were included. The case fatality
rate (CFR) was 114/1000. In 10.9% S. pneumoniae and in 63.0% S.
aureus plus one or more Gram negative rods could be cultured:
20.0% of S. aureus strains were methicilin, 40.0% clindamycin
and 28.6% erythromycin resistant. Of the Gram negative rods,
27.2% were resistant to 1st generation cephalosporins, 20.0%
gentamicin and 19.2% to chloramphenicol. The sputa of 65.5% of
the patients who are HIV-positive contained S. aureus and one or
more Gram negative rods. In over 70% of patients the empiric
antibiotic treatment had to be changed according to the results of the
empiric sputum examinations.

CONCLUSION Implementing microbiologic sputum examinations
has a profound impact on improving antibiotic treatment of CAP in
a rural developing country, due to the unexpected high
prevalence of (methicilin resistant) S. aureus and Gram negative
rods as etiological pathogens. A relationship between these
pathogens and co-infection with the HIV-virus seems plausible.
Empiric treatment with a 1st generation cephalosporin, in
combination with gentamicin in case of severe pneumonia, instead
of the national or WHO guidelines, is recommended.

Gender and Health
O26-53
Policy analysis of abortion law reform in Indonesia: dynamics of
state power, human need and women’s rights
C. Surjadi1
1 London School of Hygiene and Tropical Medicine, London, UK

OBJECTIVES This work aims to understand the policy processes and
key influential actors who affect the effort to legalize abortion
in the current dynamic political climate in Indonesia. This study
strived to reach understanding of how favouring and impeding
factors in the three streams (problem recognition, development and
diffusion of policy alternatives, and political context) interact
to impact debate and decision-making on abortion policy and
practices as dictated by law and its reform.

METHODS The study was conducted in Jakarta, Indonesia during
2005 and 2006. The study population was 98 decision-makers,
policy implementers, parliamentarians, religious groups and
reform advocates. The analysis used a combination of Kingdon’s
Multiple Streams framework and Walt-Gilson’s model for health
policy analysis. Purposeful sampling and snowball sampling
methods were applied to gather the study population. The subjects
were analysed using in-depth key informant interview and
triangulation of several data collection methods, including media
and document analysis, and participant-observation.

RESULTS Through a critical analysis of potential problems associated
with multiple players and diverging interests, the study found that opposing stakeholder camps perceive the core problem through different lenses. Although one finds broad consensus that the high maternal mortality rate (MMR) is a major health
problem, they view the role of illicit and illegal abortion in this
problem very differently; as a peripheral issue by opponents of
legal abortion, and as the dominant issue by proponents. While all agree that illicit abortion is a serious problem, consensus fails with
defining the basis of the problem. The opponents of reforms liberalizing abortion frame a moral problem, whereas the
proponents define a problem of women’s rights and access to
healthcare for women. These divergences in views of cause-and-effect and of the very nature of cause create vastly different
concepts of solutions to the problem of excessive MMR. The
ensuing political struggle revolving around proposed amendments
to the health law to develop solutions to an acknowledged
problem thus focuses upon a battle aimed at winning the definition
of the root causes the excessive MMR in Indonesia. A convergence
of the three streams (problems, policy/solutions, and politics) in
this debate is needed to create a window of opportunity for policy
reforms that help solve the problem.

CONCLUSION The findings provide strategies for managing
stakeholders toward a consensus and alignment of positions. The
recommendations may enable key policy advocates to identify and
effectively use potential windows of opportunity in the policy-
making process.

O26-54
A study of menstrual regulation service delivery practices of a
government and non-government clinics in Dhaka City,
Bangladesh
N. M. Hom1
1 James P. Grant School of Public Health, BRAC University, Dhaka,
Bangladesh

In Bangladesh, although abortion is legally restricted, early
menstrual regulation (MR) by vacuum aspiration has been widely
available through public, private and NGOs facilities for over two
decades. This study assessed the quality of MR services delivered
by two MR clinics, one government and one non-government in
Dhaka, Bangladesh through a mixed method approach. For
quantitative data, five structured observations in the government
clinic and twelve in the non-government clinic were conducted on
different steps of MR service using check list scoring tools. For
qualitative data, altogether eight in-depth interviews with provi-
ders and fourteen informal discussions with clients from both
clinics were performed. Survey data analysis was done using excel
software. Study findings revealed that quality of care in MR
The main objective of the study was to assess the aspects of the relationship between clients and counselors in the clinics. Although the counselors were all females, they often displayed insensitive behavior towards the clients. Moreover, clients of both clinics experienced differential care from the providers depending on their economic status. The study also revealed that the clients coming without their husbands found the providers behavior intimidating in the government clinic. A few clients did not want husbands’ involvement due to marital and socio-economic problems but most clients of both clinics wanted their husbands to be counseled for forced intercourse during post-MR period, use of contraceptive methods and emotional support during pre and post MR care. However, the counselors were not providing such counseling. In conclusion, the study found satisfactory clinical skill among the medical staff in both clinics but there is a need for creating gender awareness among the female providers about the female clients’ needs and rights, and husbands’ involvement whenever necessary.

Q26-55 Barriers in access to safe abortion services: perspectives of potential clients from a hilly district of Nepal
A. Bhandari
GTZ, Health Sector Support Programme (HSSP), Kathmandu, Nepal

OBJECTIVES The main objective of the study was to assess the barriers to access and utilization of legal and safe abortion services from the perspectives of potential clients from a hilly district of Nepal.

METHODS It was carried out in Dhading district of Nepal with MWRA (married women of reproductive age, 15–49 years). A mixed research methodology, with qualitative as the core and simultaneous quantitative as supplementary method, was used. In-depth interviews (with eight MWRA), focus group discussions (six groups with 41 MWRA) and informal interviews (with eight key informants) were carried out in the qualitative part; and a cross-sectional survey (72 respondents) and review of hospital records (recent 7 months, 239 clients) were undertaken for quantitative purposes.

RESULTS Despite the legalization of abortion in Nepal in 2002, awareness of legal status of abortion, and availability and cost of safe abortion services in the district is low in the study population. In socio-cultural context, abortion is associated with immoral behaviours and characterized by shame and stigma – more so for unmarried women. It is also considered a sin with repercussions in women’s future lives. Despite this, the view of most women is positive towards liberalization of abortion and abortion rights of women, including unmarried ones. Abortion seeking is not very different across socio-demographic strata. Unqualified providers play an important role in the dynamics of abortion service seeking, acting as referral agents as well as (unapproved) service providers. Distance and lack of road access, and additional costs imposed due to these, such as indirect, opportunity and familial costs, are important deterrents for women of remote villages to seek safe services.

CONCLUSION Lack of awareness, socio-cultural stigma for women, widespread presence of unqualified service providers, and geographical remoteness and inaccessibility are important factors hindering the utilization of safe abortion services available at limited places in geographically challenging hilly districts like Dhading. These barriers need to be addressed through concerted efforts involving different stakeholders.

Q26-56 Public private partnership (PPP) working for rural women's reproductive health in Pakistan
S. Khan
Centre for Health and Population Studies, Lahore, Pakistan

OBJECTIVES In 2006, a case study, sponsored by Society for International Development, Rome, investigated the public private partnership model for provision of quality health care, especially reproductive health, to rural women in Pakistan.

METHODS Fifteen interviews and eight Focus Group Discussions were conducted in rural districts of Lahore city, Pakistan. Interviewed were PPP managers from the Department of Health and the Punjab Rural Support Programme (PRSP) i.e. the private party. Also medical officers, female medical officers and lady health visitors within the PPP, were interviewed. FGDs were conducted with women consumers both inside and outside the health facility including adolescent girls, young males and paramedics including LHVs and lady health workers.

RESULTS On analysing the results, it was evident that the PPP model was ensuring the availability of PHC to the rural poor and the indigent, predominately rural women. The success was based on the kind of strategies adopted by the PPP model and applied at the rural health facility (RHF). These included (i) easy access; (ii) availability of quality medicines and personnel; (iii) affordable services with mutually agreed objectives and methodologies; (iv) a jointly acceptable monitoring and evaluation system; (v) creating a pro-poor environment facilitating easy utilization by poor rural women; and (vi) bridging the gaps between community and public health systems for the un-served and under-served rural populations. Its weakest points were (i) limited provision of reproductive health services for the women, however this was more the fault of the public health system rather than the partnership per se and (ii) poor links with traditional medical services.

CONCLUSION In conclusion it was clear that the PPP promoted Pakistani rural women’s capacity to access PHC.

Q26-57 Understanding induced abortion in Ghana: reasons, methods and outcomes
P. Aniteye, C. Ahiadeke, E. Y. Kwawukume and S. Mayhew
LSHTM, London, UK

Despite improving health statistics Ghana has a surprisingly high maternal mortality rate (MMR) thought to be in large part because of the widespread practice of unsafe abortion. Abortion is also thought to contribute to the declining fertility rate in the country, prompting serious concerns about its use as a family planning method. Access to safe abortion services is in fact legal, but restricted and there is widespread ignorance among providers about the law. Few attempts have been made to understand the practice of abortion in Ghana. The objectives of this study are to identify the characteristics of abortion seekers, reasons for unsafe abortion, methods commonly used and health outcomes.

METHODS Structured interviews were conducted with 131 women who had been admitted to hospital with abortion complications.

RESULTS Of the 131 women interviewed, 78% were single and 78.6% already had at least one child. 87% of women were under age 29 and two thirds were between the ages of 15–24. Most respondents and their partners had basic education and were employed. More than 76% had never used FP. 90% women said their pregnancies were accidental and 69% said they were unwanted. 31% did want the pregnancy but said they terminated it under pressure from others (66%) or because of social and
economic difficulties (34%). The most common methods for inducing abortion were herbs (42%) followed by intrauterine instrumentation (22%), concentrated sugar solutions (15%) and pharmaceuticals (13%). Outcomes included perforated uterus (4.5%), septicamia (3%), hysterectomies (2%) and death (4.5%). While only two respondents stated that they thought abortion was a form of FP, the fact that more than respondents had never used FP suggests otherwise. The primary reason given for non-use of FP was fear of side-effects (41%) followed by lack of knowledge about how FP works (24%).

CONCLUSIONS Findings suggest a two-pronged approach to tackling abortion is needed in Ghana. First, there is a clear unmet need for family planning to prevent unwanted pregnancies and subsequent abortions. The reported fear of side-effects needs to be addressed through education and marketing campaigns. Promoting FP to unmarried women also needs to be a focus. Second, steps must be taken to ensure access to safe abortion services.

AIDS Global Epidemiology

O26-58 Risk of heterosexual transmission of HIV between Surinam, the Netherlands Antilles and the Netherlands

M. Kramer1, M. Cornelissen2, M. Prins3, R. Coutinho1, A. van Sighem1, L. Sabajo4, A. Duits5, C. Winkel6, J. Prins1, M. van der Ende7, R. Kauffman3 and E. Op de Coul2

1Department of Research, Health Service of Amsterdam, Amsterdam, Netherlands; 2Department of Human Retrovirology, Academic Medical Center, University of Amsterdam, Amsterdam, Netherlands; 3National Institute of Public Health and the Environment, Centre for Infectious Disease Control, Bilthoven, Netherlands; 4Academic Medical Center, University of Amsterdam, Amsterdam, Netherlands; 5HIV Monitoring Foundation, Amsterdam, Netherlands; 6Dermatological Service, Paramaribo, Suriname; 7St Elisabeth Hospital, Red Cross Blood bank, Willemstad, Curacao, Netherlands; 8Academic Medical Center, University of Amsterdam, Amsterdam, Netherlands; 9Erasmus Medical Centre, Rotterdam, Netherlands; 10Haga Hospital, Location Leyenburg, The Hague, Netherlands

OBJECTIVES A substantial proportion of HIV-infected heterosexuals in the Netherlands originate from Surinam and the Netherlands Antilles, two former colonies. Unprotected sex while visiting the country of origin and relatively high background prevalence in Surinam and the Antilles (1–2%) seem to be important risk factors for HIV infection. By comparing HIV strains circulating in Surinam and the Antilles with those of Surinamese and Antillean migrants in the Netherlands, we aim to find whether there is evidence for HIV transmission between these groups. Additionally, we aim to study potential HIV transmission to the Dutch heterosexual population.

METHODS Between 2003 and 2005, we collected 56 serum samples from HIV-infected Surinamese and Antillean heterosexuals living in the Netherlands and 72 serum samples from HIV-infected heterosexuals living in Surinam and the Antilles. Three genomic regions were amplified and sequenced: env gp120 C2-V3 region, gag (p17 and partial p24) and pol (protease and half RT). To study potential transmission within the Netherlands, we collected additional pol sequences of 83 heterosexualally infected Dutch patients who are registered in our national observational cohort and who had no apparent relation to Surinam or the Antilles. Sequences were phylogenetically analysed by using the Neighbor-Joining method. For all sequences, epidemiological data was collected concerning country of birth, year of HIV diagnosis, country of infection, and age at diagnosis.

RESULTS A pol tree consisting of pol sequences of persons solely of Surinamese or Antillean ethnic origin shows two Surinamese and three Antillean clusters of related viruses. These clusters included sequences of individuals living in Surinam or the Antilles as well as those who have migrated to the Netherlands and could also be distinguished in env and gag. Although, the bootstrap value was lower in env and gag for three and two of the five clusters, respectively. Based on their history, half of the migrants believed to be infected with HIV in the country of origin. The additional pol tree showing the genetic relatedness of all pol sequences including those of Dutch heterosexual patients, shows no clustering of Surinamese and Antillean patients with Dutch heterosexual patients. All samples of Dutch patients were dispersed among those of Surinamese and Antillean patients.

CONCLUSION Although epidemiological studies show frequent heterosexual relationships between Surinamese, Antillean and Dutch individuals, we find virtually no transmission of HIV between these groups. Transmission mainly occurs within the own ethnic group. Further studies are necessary to gain insight into this discrepancy.

O26-59 Risk factors for HIV-1 infection and high HIV-1 incidence of men who have sex with men, in and around Mombasa, Kenya

E. J. Sanders1, S. Graham2, H. S. Okuku3, E. van der Eerth1, A. Muhamar2, A. Davies1, N. Peshu1, P. Fast3, R. S. McClelland4 and A. Smith5

1Centre for Geographical Medicine Research – Coast, KEMRI/University of Oxford, Kilifi, Kenya; 2University of Washington, Seattle, USA; 3KEMRI, Centre for Geographical Medicine Research – Coast, Kilifi, Kenya; 4IAVI, Medical Affairs, New York, USA; 5Department of Public Health and Primary Care, University of Oxford, Headington, UK

OBJECTIVES To investigate risk factors for prevalent HIV-1 infection and estimate HIV-1 incidences among men who have sex with men (MSM), who report sex with men exclusively (MSME), or with both men and women (MSMW), in and around Mombasa, Kenya.

METHODS Socio-behavioural characteristics signs and symptoms of sexually transmitted diseases (STD) and serological evidence of HIV-1 and syphilis were determined at enrolment into a vaccine preparedness cohort study. Enrolled volunteers receive 3-monthly HIV counselling and testing, and sero-conversions confirmed when both rapid HIV tests were positive.

RESULTS HIV-1 and syphilis prevalence were 44.2% (46/104, 95% confidence interval (CI): 33–52%) and 6.7% (95% CI: 3–13%), respectively for MSM, and 12.2% (18/147, 95% CI: 7–19%) and 1.4% (95% CI: 0.2–5%), respectively, for MSMW. One hundred eighty-six (74%) MSM were paid for sex in previous 3 months, predominantly by local residents (94%); 76 (73%) of MSM, and 45 (31%) of MSMW reported receptive anal sex in past 3 months. Most MSM reported at least one episode of unprotected sex (84% unprotected receptive anal sex, 81% unprotected insertive anal sex) and 41% had not used a condom with any causal partners in the last week. Recent receptive anal sex was strongly associated with prevalent HIV-1 infection; odds ratio (OR) for any receptive anal sex vs. none = 4.3 (95% CI 1.8–10.7), and OR for only receptive anal sex vs. only insertive anal sex = 8.7 (95% CI 1.8–41.0). Risk for prevalent HIV-1 infection increased with age (OR 1.1 per year, 95% CI 1.03–1.17). Injecting drug use was only reported by four MSM. Estimates of HIV-1 incidences were 9.8 (95% CI: 4.1–23.76) per 100 person years observation (PY) in MSM, and 6.5 (95% CI: 2.4–17.3) in MSMW.

CONCLUSION This cohort of Kenyan MSM has a very high prevalence and incidence of HIV-1, likely attributable to high-risk, unprotected anal sex. There is an urgent need for HIV-1 prevention programmes to delivered targeted risk-reduction interventions and STD services to African MSM.
O26-60
Abstract withdrawn.

O26-61
Determinants of late presentation at diagnosis of HIV infection in Venezuela
M. Bonjour1, M. Montagne1, M. Zambrano2, G. Molina1, R. N. Incani3 and A. Tam1
1KIT (Royal Tropical Institute), Biomedical Research, Amsterdam, Netherlands; 2Centro de Atención Integral de Infecciones de Transmisión Sexual y SIDA (CAI-ITS-SIDA), INSALUD (Ministry of Health), Valencia, Venezuela; 3Parasitology, University of Carabobo, Valencia, Venezuela

The scale-up of highly-active antiretroviral therapy in developing countries is slowly improving the prognosis of HIV-infected populations. In Venezuela, a national program offering free HIV diagnosis and treatment was established in 1999. Although the roll-out of the program is rather successful, around 40% of patients present for diagnosis at a later disease stage, indicating that access to care may still be limited. Our study aimed to identify factors influencing delay in HIV diagnosis in Venezuela.

METHODS A case-case approach was used to analyse data collected through a cross-sectional survey at the Regional Reference Centre of Integral Attention for Sexually Transmitted Diseases and HIV/AIDS, Carabobo Region, Venezuela. All patients (n = 225) recently diagnosed with HIV at CAI between May 2005 and October 2006 were included in the study and demographic characteristics, behavioural characteristics and medical details were collected from the patient medical files. Through interviews using a structured questionnaire, detailed data on socio-economic and behavioural factors, including perceived barriers to HIV testing and perceived risk of infection, were collected for 129 of the 225 eligible subjects. ‘Late presentation’ at diagnosis, was defined as patients classified with disease-stage B or C according to the 1993 centers for disease control and prevention (Atlanta, USA) classification compared to patients diagnosed in disease-stage A (‘early presentation’). Principal component analysis was used to create indices for socio-economic status and HIV knowledge, and to categorize variables related to possible barriers to testing. Uni- and multivariate analyses were performed using logistic regression with late presentation as dependent outcome variable.

RESULTS Of the 225 eligible subjects, 91 (40.4%) were defined as late presenters. A similar proportion (51/129) was obtained in the interviewed sub-sample. In univariate analyses, older age (>35 years), lower education level, heterosexuality, not having a fixed partner and lack of knowledge about HIV transmission were associated with late diagnosis (odds ratio >1.7, P < 0.05). Main barriers to early HIV testing were lack of perceived risk of HIV infection, denial of infection, fear, confidentiality doubts, logistic barriers and lack of information on the existence of a free HIV/AIDS program. Principal component and multivariate analysis are in process and results will be presented.

CONCLUSION The identification of factors associated with delay in HIV diagnosis and presentation at a late disease stage will be useful in the development of targeted public health interventions that will increase the likelihood of early diagnosis, and therefore, of the prognosis of people living with HIV/AIDS in Venezuela.

Cysticercosis

O26-62
Evaluation of crude soluble extract, lower molecular weight (10–30 KDa) and excretory secretory antigens of T. solium cysticerci by enzyme linked immunosorbent assay for the diagnosis of neurocysticercosis in children
A. V.Subba Rao1, P. Singh2, N. Khandelwal1, S. Khurana1 and N. Malla4
1Department of Parasitology, Paediatrics, Radio Diagnosis and Imaging, Postgraduate Institute of Medical Education and Research, Chandigarh, India; 2Department of Paediatric Surgery, Postgraduate Institute of Medical Education and Research, Chandigarh, India; 3Department of Radio Diagnosis and Imaging, Postgraduate Institute of Medical Education and Research, Chandigarh, India; 4Department of Parasitology, Postgraduate Institute of Medical Education and Research, Chandigarh, India

OBJECTIVE Assessment of the diagnostic efficacy of enzyme linked immunosorbent assay (ELISA) for the detection of antibody with the use of crude soluble extract (CSE), purified lower molecular weight (10–30 KDa) antigenic fractions and excretory secretory antigen (ES) of cysticercus cellulosae in serum for the diagnosis of neurocysticercosis (NCC) in children.

METHODS Crude, 10–30 KDa and excretory secretory antigens of cysticercus cellulosae were prepared and the diagnostic efficacy of these antigens to detect antibody in serum for the diagnosis of neurocysticercosis in children was evaluated by ELISA. Two hundred and fifty serum samples were collected from 125 clinically suspected and radiologically proven neurocysticercosis and 125 control patients which include patients with seizures but ruled out for neurocysticercosis, patients with other parasitic diseases and apparently healthy children.

RESULTS Among 125 neurocysticercosis patients, 14 (11.2%) are with multiple lesions and 111 (88.8%) are with single CT lesion. The main presenting clinical symptom was seizures (92%) followed by headache, nausea and vomiting. In seizures, focal seizures (74%) were more common. The sensitivity of the ELISA was 33.6%, 61.6%, 26.4% and specificity was 88%, 76.8%, 85.8% with the use of crude, excretory secretory and 10–30KDa antigenic fractions respectively based on 1:800 serum dilution as cut-off dilution to get 95% confidence interval. The sensitivity was 45.4%, 63.6% & 18% in NCC patients with active multiple lesions and 33%, 63.3% and 31% in patients with single active lesion with the use of crude, ES/ and 10–30 KDa antigens respectively.

CONCLUSION Excretory secretory antigen showed significantly higher sensitivity and specificity for the diagnosis of neurocysticercosis in children.

O26-63
Use of recombinant camelid single domain antibodies for the diagnosis of Taenia solium cysticercosis
N. Deckers1, K. Conrath2, K. Kanobana3, B. Victor2, J. Vercruysse3 and P. Dorny4
1Department of Animal Health, Institute of Tropical Medicine, Antwerp, Belgium; 2Department of Cellular and Molecular Immunology, Free University of Brussels, Etterbeek, Belgium; 3Faculty of Veterinary Medicine, Laboratory of Parasitology, Ghent University, Merelbeke, Belgium

Taenia solium cysticercosis is a zoonotic helminth infection in pigs and humans. Serodiagnostic techniques include both antibody and antigen detection assays. However, there are limitations associated to these assays. Antibody detection assays only reflect exposure and not necessarily the presence of an established infection. Antigen detection assays using monoclonal
The objective of the study was to determine the burden of cysticercosis among pigs in the Mbula district, northern Tanzania [1]. However, to date studies on NCC and epilepsy are missing. We interviewed 212 people with epilepsy (PWE) and performed cerebral CT (cCT) scans with i.v. contrast medium administration at Haydom Lutheran Hospital. As controls served 198 consecutive cCTs of individuals without epilepsy. Sera of PWE and lesions highly suggestive of NCC (n = 20), PWE without lesions (n = 20), controls without epilepsy (n = 20) and CSF samples of PWE and lesions highly suggestive of NCC (n = 11) were investigated for anti-cystercial antibodies using the enzyme linked immunosorbant assay (ELISA) and western blot techniques. Based on the Del Brutto criteria [2], cCTs in PWE showed definite NCC lesions in five (2.4%), highly suggestive lesions of NCC in 24 (11.3%) and lesions compatible with NCC in nine PWE (4.2%). This compares to the control group where two people (1.0%) had definite NCC lesions, two (1.0) had lesions classified as highly suggestive and six individuals (2.9%) showed lesions compatible with NCC. Significantly more NCC lesions were found in PWE than in controls (P < 0.001). With cCT scan, serum and CSF analysis, we diagnosed 22 (10.4%) cases of probable and seven cases (3.3%) of definite NCC. In the CT control group, we found two cases (1.0%) with definite NCC and two cases (1.0%) with lesions highly suggestive of NCC. With regard to predisposing factors, we found people, who consumed pork, to have significantly (P = 0.023) more NCC than people, who did not eat pork, close contact with pigs, the absence of latrines and number of people in one household, however, did not show any significant influence on the prevalence of NCC. Our data clearly demonstrates that NCC is a major cause of epilepsy in northern Tanzania.

REFERENCES


Good Governance in the Health System

O26-66

Understanding the impact of decentralisation on reproductive health and reproductive health services

N. Gerein1, C. D. Collins2 and RHD Research Team

1University of Leeds, UK, Nuffield Centre for International Health and Development, Leeds, UK; 2Consultant, Liverpool, UK

OBJECTIVES Decentralisation is a common development strategy in sub-Saharan Africa, but evidence of the effects on service delivery is fragmentary and inconsistent. This 4-year research project in four African countries had an overall objective to find out how decentralisation affects reproductive health (RH) services. The project identified and compared the key features and changes in decentralisation and in RH policies and services, and assessed the extent to which they were inter-related, and beneficial/not beneficial to RH policies. Recommendations for RH and health sector reform policy makers were developed.
Abstracts of the 5th European Congress on Tropical Medicine and International Health

O26-68

Goverance and drug (medicine) control in India: issues and way out

S. Srinivasan and LOCOST

1LOCOST, General Management, Vadodara, India

OBJECTIVES To outline governance issues in policy administration in drug (medicine) control and regulation in India.

METHODS Situational analysis from author’s own manufacture of low-priced medicines for those working with the poor in India, experience of manufacturers and end users. Author has been part of a 25-year long national civil society advocacy effort to highlight governance issues in drug control administration especially in the context of access to medicines and public health needs. Governance issues outlined have to be set right if India’s pharma industry is to be a world leader in affordable medicines. These governance issues are in the area of access, manufacture, quality control, regulation and increasingly the demands thrown in by India becoming an internationally “favoured destination for clinical trials.

RESULTS Looming, if not explosive, health, ethical and political crisis if governance issues continue to be neglected.

CONCLUSION Specific suggestions for turnaround in quality of governance.

O26-69

Civil society participation in health policy formulation: lessons learned from people’s health movement, Gujarat – India

R. Khanna, S. Shah, S. Dand and J. S. Abhiyan

1Society for Health Alternatives, SÀHAJ, Baroda, India; 2SEWA Rural, Jhagadia, India; 3ANANDI, Ahmedabad, India

OBJECTIVES Participation of civil society in the formulation of health policies and programmes is increasingly being recognized as an important aspect of decentralization and good governance in the health sector. This paper describes two initiatives of the Jan Swaasthya Abhiyan (people’s health movement) to work with the
health department in the state of Gujarat, India, to formulate a
GO-NGO partnership policy and a public health act.

METHODS While the formulation of the GO-NGO partnership
policy was spearheaded by the state chapter of the peoples’ health
movement (JSA Gujarat), the public health act was drafted by
representatives of both the national and state JSA. After laying
the context, the paper describes the process of developing these two
documents. The GO-NGO Partnership policy took 2 years to be
finalised. The initial drafting was performed by members of JSA
Gujarat. However, soon it was realized that the drafting itself had
to be performed through a partnership. A working group
consisting of JSA Gujarat members and senior officers of the health
department worked to finalise the policy. At the time of writing
this abstract, the Gujarat public health act is 6 months in the
drafting process.

RESULTS The GO-NGO partnership policy aimed at ensuring
participatory planning and monitoring of health programmes at all
levels – village, primary health centre, district and state – was
adopted by the national health department as a part of the
National Rural Health Mission. The Gujarat public health act
guaranteeing basic health services and right to health care is the
first such act in India and is being keenly awaited by the health
officers at the central government level. The paper describes briefly
the contents of the two documents. Next, the paper analyses the
enabling factors. Proactive and dynamic leadership in the state
health department and the interdisciplinary nature of the JSA
Gujarat and the drafting team are among the enabling factors.

CONCLUSION The paper ends with identifying the challenges for
implementation and some lessons learned. For example, one
section of the GO-NGO policy, the constitution of the State Level
Planning and Monitoring Committee has been altered by the
Minister of Health at the final stage to include a majority of
government representatives, thereby creating an imbalance in the
membership. However, one lesson learned early on in the process
was to have wide ranging public debates on the contents of the
documents, thereby creating opportunities for public pressure,
when necessary.

O26-70
Chikungunya and parliamentary accountability in India
D. V. Mavalankar1 and K. Chaube2
1Indian Institute of Management, Ahmedabad, Public Systems Group,
Ahmedabad, India; 2Indian Institute of Management Ahmedabad, Public
Systems Group, Ahmedabad, India

OBJECTIVES To study how the government of India responds to
questions regarding health asked by members of parliament. This
is to assess parliamentary accountability in India. The study is
done in the context of the massive epidemic of chikungunya fever.
METHODS We have collected questions asked in both houses of
parliament on the epidemic of chikungunya, dengue and other
viral fevers. We analyzed the contents of the questions and the
replies provided by the health ministers. We interpret the replies in
the context of data available from the city of Ahmedabad. In the
analysis we focus on truthfulness, completeness and the spirit
behind the answers given in comparison to the questions.
RESULTS Our analysis shows that answers provided in the
parliament to questions about chikungunya and especially its
mortality are far from the truth. The government claims that there
are no deaths reported directly attributable to Chikungunya inspite
of 1.3 million cases. While in the city of Ahmedabad alone there
have been more than 3000 additional deaths as compared to
previous years during the chikungunya epidemic months. The
answers in parliament do not give any information on the very
poor death and cause of death reporting in India which is the real
reason for very few or no reported deaths due to chikungunya.

CONCLUSION Parliamentary accountability is the backbone of
the democracy. Government on one hand provides several newer
measures like right to information act, e-governance etc but the
constitutional provisions of parliamentary accountability are
systematically neglected as seen by the incomplete, incorrect and
misleading answers given in the parliament in the course of
chikungunya epidemic. We provide a suggestion of opening up the
parliament questions to the public and concerned experts through
posting them on the website before government answers them in
parliament. This will make the parliamentary accountability
stronger and make it more difficult for government to misguide the
parliament and the Nation through incomplete and misleading
information. This would also make parliamentary debates more
open and participative. Given the modern internet technologies
this type of opening up of key debates in health politics is
eminenly feasible and quite cost effective.

O26-71
Are international health policies evidence based? A light shed
from Latin America
J.-P. Unger1, W. Soors2 and P. De Paeppe1
1Public Health Department, Institute of Tropical Medicine, Antwerp,
Belgium

OBJECTIVES To outline the multilateral agencies’ doctrine on
health policy. To explore its empirical basis in Colombia, Costa
Rica, and Chile. Colombia privatized large parts of health
insurance and health care delivery. Costa Rica expanded its
publicly oriented delivery system. In Chile, the dictatorship
promoted the private sector and underfinanced the public sector.
Transition governments did not change the scheme but financed
can public services decently.

METHODS To achieve the first objective, we analysed documents
from WHO, EU and the World Bank. For the second objective, we
traced the countries’ health services results back to their health
policy features. Data were collected through a literature review
and field visits in Costa Rica and Chile.

RESULTS There is a doctrine: multilateral agencies promote disease
control programmes without possibility to integrate them with
curative care, allocating the former to the public and the latter to
the private sector. Colombia applied this policy. Despite a large increase
in health expenditure, more than 40% of the population is still not
covered by health insurance. Real access to health care deteriorated.
Key health indicators are preoccupying. Costa Rica offered compre-
prehensive care with a participative approach through public
services. Efficiency and quality of care can still be improved, but
health services sensitive indicators are outstanding. Costa Rica
spends on health 1/9th of USA and scores better on life
expectancy. Chile has excellent health indicators at a cost of 50% above
Costa Rica. Effectiveness is linked to public services
operations (used by 85% of the Chileans) while inefficiency is due to
Isapres costs (more than 40% of total health expenditure).

CONCLUSION Colombia is one of the few countries where
international doctrine has been fully implemented. As in other
developing countries, inefficient contracting-out can be explained
by government’s weak capacity for control and regulation (not by
a civil war). At odds with international aid policies, community
participation and absence of purchaser-provider split are the
cornerstones of the Costa Rican health policy. Results are
remarkable. Chilean mixed results confirm the adaptation of
public services to developing country conditions and the risks of
privatizing both health insurance and health care delivery.
Leishmaniasis Vaccination and Treatment

O27–1
Immunogenicity and protective efficacy of oral and parenteral T cell epitope based DNA vaccines against visceral leishmaniasis in a mouse model
R. Sachdeva1, N. Malik2 and M. Dubey3
1Parasitology, Postgraduate Institute of Medical Education and Research, Chandigarh, India

DNA vaccination represents a novel preventive strategy for Leishmania infection. Recently, some Leishmania DNA vaccines have been prepared based on different antigens. But these vaccines only encoded the single antigen. In this study, we designed a polytope DNA vaccine encoding multiple T cell epitopes. The protective efficacy of two DNA-based multi-epitope (‘polytope’) vaccines delivered by oral and parenteral routes was checked. We found that the polytopes elicit powerful effector CTL responses and long-lived memory CTL in immunized balb/c mice than the vaccine encoding the single antigen. The immunogenicity and protective efficacy of polytope DNA vaccine and similar DNA vaccine encoding gp63 gene constituting the T cell epitopes was compared. We also found that heat shock protein 70 exhibit an adjuvant activity which was fused with the minigene. It enhanced CTL response to the parasite antigen and therefore overcame the epitope suppression. Therefore, our research contributes to the practicable and feasible aspect of designing a polytope DNA vaccine against visceral Leishmaniasis.

O27–2
Pharmacokinetics of miltefosine in patients treated for old world cutaneous leishmaniasis
1Department of Infectious Diseases, Tropical Medicine & AIDS, Academic Medical Center, Amsterdam, Netherlands; 2Department of Pharmacy and Pharmacology, Slotervaart Hospital, Amsterdam, Netherlands; 3Department of Dermatology, Academic Medical Center, Amsterdam, Netherlands

OBJECTIVES To investigate the pharmacokinetics of miltefosine in patients treated for old world cutaneous Leishmaniasis, we developed a novel, fast and sensitive state-of-the-art liquid chromatography tandem mass spectrometry (LC-MS/MS) assay for miltefosine (M).

METHODS An existing LC-MS/MS analytical assay for a similar alkylphosphocholine compound was modified into a new more reliable assay, which we successfully validated for miltefosine according to the most recent FDA guidelines. From patients treated with M for Leishmania major infections (3 dd 50 mg for 4 weeks), we collected repeated plasma samples during and up to 4 months after treatment and measured the concentration of M ([M]) with the validated assay. Preliminary pharmacokinetic results were obtained by compartmental and non-compartmental analysis of the [M]-time curves.

RESULTS The assay performed well with a linear calibration curve over a validated quantifiable concentration range of 0.004–2 µg/ml (r = 0.9951 or better) using 250 µl of human plasma samples. Intra- and inter-day accuracies in terms of relative error determined at four concentrations (0.004, 0.012, 0.3 and 1.5 µg/ml) ranged from -4.9 to 8.5% and -2.8 to 2.0%, respectively. Intra- and inter-day precisions in terms of relative standard deviation determined for 0.004 µg/ml were lower than 10.7 and 10.6%, respectively. For the other concentrations intra- and inter-day precisions were maximally 7.1 and 5.8%, respectively. Preliminary pharmacokinetic analysis showed a fast increase of [M] to approximately 1.5 microg/ml after the first dose. M accumulated until the end of treatment; mean [M] during the last week of treatment was 30.7 µg/ml (C.I. 95%: 27.7–33.7, n = 27, one exceptional value of 51.6 µg/ml); the mean elimination half life was 9.2 days (C.I. 95%: 8.5–10.0, n = 30) and the extremely slow terminal elimination pointed at a second compartment from which it is slowly released.

CONCLUSION The new assay enables high quality pharmacokinetic studies of M. This study provides the first extensive clinical pharmacokinetic data of M in Leishmaniasis patients. Elimination of M is very slow which benefits efficacy, but has consequences for toxicity and may contribute to selection of resistant parasites.

O27–3
Successful prevention of cutaneous leishmaniasis after an outbreak in a military camp in northern Afghanistan
M. Fischer1, G. Heyl2, R. Hagen1 and J. Bronnert1
1Department of Tropical Medicine, Bundeswehrkrankenhaus Hamburg, Hamburg, Germany; 2Sanitätsamt der Bundeswehr, Munich, Germany

Leishmaniasis is not only a public health but also a significant military problem for all nations with troops in endemic areas. Afghanistan is one of the highest endemic areas worldwide. Referring to WHO records more than 200 000 cases of cutaneous Leishmaniasis occur in Kabul and its surroundings annually. German soldiers have been deployed in Afghanistan since 2002 and in spite of the high incidence in Kabul cutaneous Leishmaniasis was no major health problem with the exception of a few cases. But with the deployment of ISAF troops to the northern part of Afghanistan at the end of 2003, 156 from 881 deployed Dutch soldiers and 16 from 80 German soldiers developed cutaneous Leishmaniasis after an exposure between 3 days and 6 months in a military camp in Masar E Sharif. Clinically the lesions were nodulo-ulcerative and often multiple with lymphatic spread. Diagnosis was confirmed by demonstrating amastigote parasites in skin smears. Further subtyping achieved by PCR methods revealed in nearly all cases L. major as the causative agent.

Treatment was based on intralesional or parenteral application of pentavalent antimonials often supported by the topical application of imiquimod and paromomycin. Cutaneous Leishmaniasis caused by L. major is normally a zoosporidium. Various rodent species such as the ‘great gerbil’ (Rhombomys opimus) are animal reservoirs and are accompanied by sandflies that rest in their burrows. The normal habitat for rodents and sandflies are arid or even semi-desert terrains. The outbreak of cutaneous Leishmaniasis in late 2003 is referred to the construction of sandwells around the camp, where later huge colonies of rodents could be found. Intensive preventive measures, such as the clear away of the colonized soil and the construction of a road-metal surface and stone walls in combination with impregnated uniforms and moskitonets and the application of repellents led to a nearly complete regression of cutaneous Leishmaniasis in Masar E Sharif with only one case from 1300 deployed German soldiers in 2006.
can be rendered immune. This may not be true for every single antigen, and some antigens have been shown to intrinsically induce a Th2 response in mice (i.e. LACK). Using a Th1 inducing adjuvant and/or proper presentation of antigen, a protective Th1 response can be induced. We concentrated on the development of a delivery system (MIDGE vector) comprising an adjuvantive, immune modulating effect to design a vaccine against Leishmania. This approach should work as prophylactic as well as therapeutic vaccine. Our carrier is a minimalistic, immunogenetically defined gene expression (MIDGE) vector, containing only the sequences needed for antigen expression in eukaryotic cells. It does not contain non-essential and potentially dangerous plasmid backbone sequences. Furthermore, MIDGE is a linear, double stranded DNA molecule with covalently closed hairpin-shaped ends. This structure prevents rapid hydrolysis by exonucleases and allows for attachment of other functional molecules. The expression cassette in MIDGE vectors consists of the enhanced early CMV promoter, a chimeric intron, the gene of the antigen protein and the polyA signal of the SV40 large T-antigen. [Figure 1 Schematic diagram of a MIDGE vector] Linking specific peptides to the hairpin loop sequences, one can enhance and modify the type of immune response. Thus, using MIDGE-Th1, a peptide modified MIDGE vector, we have shown that Balb/c mice can be stimulated to produce predominantly a Th1 response against the antigen encoded. MIDGE Th1-vectors encoding several Leishmanial antigens were tested in a mouse model and shown to induce a protective immune response against a live challenge with L. major. In a canine model for visceral Leishmaniasis, a MIDGE-Th1 vector based vaccine was tested. While no sterile immunity could be achieved, most of the dogs immunized with a cocktail of MIDGE-Th1 vectors were able to control the infection. Protected dogs had lower parasite loads than control animals and did not develop a clinical disease.

TB Vaccines and Immunology

O27-5 T cell cytokine responses in patients with active pulmonary tuberculosis from central Africa

J. Nenneh1, H. Winkler2, A. A. Adegnika3, W. Graninger1, P. G. Kremser2 and S. Winkler1

1Department of Infectious Diseases, Medical University of Vienna, Vienna, Austria; 2Medical Research Unit of the Albert Schweitzer-Hospital, Lambaréné, Gabon

OBJECTIVES An understanding of T cell responses that are crucial for control of M. tuberculosis has major implications for the development of immune-based interventions.

METHODS Using flow cytometry we studied the frequency of IFN-γ producing T cells in whole blood and the presence of Th1 cytokines in plasma from patients with pulmonary tuberculosis.

RESULTS A total of 145 patients were included in the study, 39 men and 106 women, mean age 27 years (range 11–63). In 123 cases, the test was positive (119 TB-positive, 4 tuberculin negative). The frequency of IFN-γ producing cells (Mfi) was not different between groups. The Wilcoxon-Mann-Whitney U-test was applied for group differences. Bivariate correlations were done by computing Spearman’s correlation coefficient.

CONCLUSION The overall agreement between the results of QFT-G and SPOT assays is good. A poor overall agreement was seen in the results of the comparison of the QFT-G and SPOT assays separately as well as combined with TST results according to the Dutch guidelines. The results of the gamma interferon tests were not influenced by the BCG vaccination status in our study population. The QuantiFERON-TB GOLD and T spot-TB assays were negative in a surprisingly large proportion of participants within the subset of subjects with a TST ≤15 mm. A large proportion of subjects with QFT values just below the cut-off had clinical or historical indications of TB or M. kansaissi infection, suggesting that the manufacturers cut-off value may be fixed to high.
O27–7

Combined immune parameters and X-ray data in early prognosis of month 2 spumt culture conversion

J. F. Djoba Siawaya1, N. B. Bapel1, H. Veenstra1, M. Kidd2, N. Beyers2, P. van Helden1 and G. Walzl1

1 Biomedical Sciences, University of Stellenbosch Medical School, Tygerberg – Cape Town, South Africa; 2Centre for Statistical Consultation, University of Stellenbosch, Tygerberg – Cape Town, South Africa; 3Department of Pediatrics, University of Stellenbosch Medical School, Tygerberg – Cape Town, South Africa

We investigated 13 healthy community controls and 20 Bactec culture positive tuberculosis (TB) patients treated with directly observed short course anti-tuberculosis chemotherapy. All patients had their postero-anterior and lateral chest X-ray radiography taken at the beginning of chemotherapy and grade for extension of disease according to a standardized method. A full blood count, differential blood count and blood cell phenotype was realized on all blood samples. Serum samples were collected at diagnosis, week 1, 5, 13 and 26 after the initiation of chemotherapy. After the 2-month intensive phase of treatment, 12 patients remained sputum culture positive (slow responders) and eight patients culture negative (fast responders). Soluble intercellular adhesion molecule-1 (sICAM-1), Tumour necrosis factor receptors one and two (sTNFR I and II), Death receptor 5, C-reactive protein (CRP), soluble urokinase plasminogen activator receptor (suPAR), the lymphocyte activation gene-3 (LAG-3), and Granzyme B, were measured in controls and patients serum using immunoassay methods. We observed statistically significant differences between all patients at diagnosis and Controls for CRP, suPAR, LAG-3, sICAM, sTNFRI and DR5 followed by the return toward baseline at the end of anti-tuberculosis therapy. General discrimination analysis and the vector support machine (SVM)-analysis indicated that combined together the selected markers can segregate fast responders from slow responders with high accuracy (80–100% correct classification). This preliminary report suggests that predictive models for differential treatment responses using combinations of host markers hold promise. This is of great interest as markers that can provide an early indication of therapy efficacy and prognosis would have several advantages: facilitate the development and validation of new therapeutic strategy, minimize drug tolerance and resistance due to nonoptimal treatment and accelerate or shorten clinical trials.

O27–8

TB cohort studies in neonates and adolescents: strategies to develop capacity to conduct TB vaccine trials

S. Moyo1, T. Hawkridge1, H. Mahommed1, M. Hatherill1, L. Geiter2, S. Verver2 and G. Hussey1

1 University of Cape Town, Institute of Infectious Diseases and Molecular Medicine, South African Tuberculosis Vaccine Initiative (SATVI), Cape Town, South Africa; 2Aeras Global TB Vaccine Foundation, Maryland, USA; 3KNCV Tuberculosis Foundation, The Hague, Netherlands

OBJECTIVES The overall aim is to build capacity to conduct tuberculosis vaccine trials at the SATVI study site. Specific objectives for the cohort studies are to assess the best method to measure incidence and prevalence of TB infection and disease among neonates and adolescents.

METHODS In a high TB burden area in the Western Cape Province of South Africa, a TB vaccine trial site has been developed. Cohort studies enrolling neonates and adolescents aged 12–18 years respectively started in 2005 and entail 2 years follow-up. Participants are randomly assigned to passive (follow-up via regular health systems and assessment after 2 years) or active (assessment for TB infection and disease every 3 months) case finding. Contacts and symptomatic infants are admitted to a dedicated hospital ward for two nights for full diagnostics including induced sputa and gastric washing. Adolescents undergo a baseline tuberculin skin test (TST), Quantiferon gold in-tube test (QFN-GIT), and questionnaire screen. A TST of ≥10 mm is considered positive. If either the TST or the QFN-GIT test is positive and/or the adolescent has TB symptoms or a household contact with TB, sputum is taken for smear and, if positive, a culture is performed.

RESULTS In the neonatal cohort study 4786 neonates have been enrolled. In the active group more cases of probable tuberculosis have been detected. These were detected earlier than those in the passive group. In the adolescent cohort study to date 6013 adolescents have been enrolled. At baseline, 46% were TST positive and 36% QFN-GIT positive, with 79% agreement between the tests. 27% reported exposure, i.e. living with someone who had TB in the past. QFN had higher sensitivity but lower specificity for TB exposure and TB disease at baseline than TST. Repeat tests at 6 months in a sample of 410 participants showed 10% conversions and 3% reversions in QFN.

CONCLUSION Cohort studies in a TB vaccine trial site can give useful insights into TB case finding and the performance of TB diagnostics.

Tropical Neurology incl. Meningitis

O27–9

Dynamics of meningococcal colonisation and disease in a rural district of Burkina Faso

A. Sie1, J. Leimkugel2, V. Pfluger2, B. Coulbaly1, A. Kapasi2, G. Pluschke2 and T. Junghanss2

1Centre de Recherche en Santé de Nouna, Nouna, Burkina Faso; Section of Clinical Tropical Medicine, University Hospital Heidelberg, Heidelberg, Germany; 2Swiss Tropical Institute, Basel, Switzerland

OBJECTIVES The objective of this study was to describe and analyse in detail the epidemiology of bacterial meningitis in the Nouna Health District.

METHODS Our meningitis surveillance system covered all 25 health posts and the district hospital. Laboratory diagnosis was based on latex agglutination, culture and PCR. Meningococcal carriage surveys were performed within a longitudinal colonisation survey in a sub-region of the district covered by the Nouna DSS and in an outbreak village outside this sub-region.

RESULTS From January 1st until 23rd July 2006, 410 suspected meningitis cases were notified. Overall, 214 CSF samples were collected of which 82 Neisseria meningitidis (72 serogroup A, 4 serogroup Y), 13 Streptococcus pneumoniae and 10 Haemophilus influenzae meningitis cases were confirmed, while 107 of the CSF samples were negative by laboratory diagnosis. The case fatality rate among patients with meningococcal meningitis was 6.25% (5/80) vs. 46.2% (6/13) involved with pneumococcal meningitis and 10% (11/107) involved with negative CSF. In the south of the district 12% (22/180) colonization with serogroup Y meningococci was associated with only a few cases of serogroup Y meningitis. In contrast, 11% (34/316) colonisation of inhabitants of the outbreak village in the south with serogroup A meningococci caused a fulminating serogroup A epidemic.

CONCLUSION Recent outbreaks of W135 and X meningococcal meningitis indicate that several serogroups may develop an
Abstracts of the 5th European Congress on Tropical Medicine and International Health

epidemic potential. The envisioned introduction of a meningococcal serogroup A conjugate vaccine raised concern about coverage of this vaccine and potential serogroup replacements. Our study contributes to an extended data set over space and time which is needed to answer those questions.

O27-10
Outcome of central nervous system tuberculosis: an alternative scoring system
F. Alarcón1, J. Moreira2, J. Rivera1, R. Salinas1, G. Dueñas1 and J. Van den Ende2
1Hospital Eugenio Espejo, Neurología, Quito, Ecuador; 2Institute of Tropical Medicine, Clinical Sciences, Antwerp, Belgium; 3Hospital Metropolitano, Neurología, Quito, Ecuador

OBJECTIVES To compare a scoring system, based on a Spiegelhalter and Knill-Jones methodology,(1) for predicting the clinical outcome of central nervous system tuberculosis (CNSTB) with the traditional British Medical Research Council (BMRC) staging.(2)

METHODS All patients treated between 1989 and 2004 for definitive or probable CNSTB at a reference hospital in Quito-Ecuador were included. The outcome was a five point ordinal scale, rating the severity of neurological sequelae and mortality.(3;4) A multivariate analysis was done to assess the association of predictors with the five point scale. The outcome was further dichotomized and logistic regression analysis was done for four cut off points. A score was built based on the retained logistic regression model and compared with BMRC staging with a ROC curve.

RESULTS Among 310 admitted patients 213 (68.7%) were in BMRC stage II or III. Fifty-seven died (18.3%) and 101 (32.5%) survived with neurological sequelae. In multivariate analysis, with the five point scale as outcome, the associated predictors with poor prognosis were consciousness impairment ($P < 0.0001$), motor deficit ($P < 0.0001$), papilloedema ($P = 0.043$), positive AFB smear or culture ($P = 0.002$), cistern effacement ($p = 0.0003$) and cerebral infarcts ($P = 0.029$). An early start of treatment was associated with good prognosis ($P < 0.0001$). The retained logistic regression model dichotomized the scale between the third and the fourth point discriminating patients who had severe sequelae or died with the others. The associated predictors were consciousness impairment ($P = 0.010$), motor deficit ($P = 0.003$), cistern effacement ($P = 0.006$) and infarcts ($P = 0.015$). The scoring system based on these predictors yielded an area under the curve (AUC) of 0.76 (95% CI: 0.70-0.82), similar to the corresponding AUC of the BMRC which was of 0.72 (95% CI: 0.65–0.78).

CONCLUSION This study provides a new approach to disability and death in CNSTB patients. The Quito Score is easy to apply and could be a sound predictor of poor prognosis. The availability of modern imaging did not improve the ability to predict a bad outcome.

REFERENCES

O27-12
Clinical patterns of an acute West Nile meningo-encephalitis epidemic and the lack of correlation with the poor outcome
B. Circiumaru1 and F. A. Caruntu1
1Infectious Diseases, Matei Balş Institute of Infectious Diseases, Bucharest, Romania

OBJECTIVES Our purpose was to describe and correlate the clinical patterns of a meningo-encephalitis epidemic that evolved in 1996, on the Bucharest area of Romania with the clinical outcome.

METHODS This is a retrospective study, on a few hundred hospitalized subjects, that were admitted in the ‘Matei Balş’ Institute of Infectious Diseases, in the period June–October 1996, with febrile neurological complaints, serologically demonstrated due to the West Nile virus; observation charts were used to map the clinical evolution and the outcome.

RESULTS Several clinical patterns were described: inaugural encephalitis, inaugural meningo-encephalitis, late meningo-ence-
We described the patterns of febrile diseases due to West Nile virus infection during an outbreak, and we conclude that most of symptomatic cases had neurological symptoms, with variable clinical aspects, from slight to severe; the mortality (about 10%) was correlated with the age over 55 years, the prior chronic pathology (e.g. diabetes) and malnutrition; we could not correlate the poor outcome with the clinical patterns described. The recovered patients had not clear neurological complications. This study is not describing the non-hospitalized patients, but there were confident data on febrile illnesses evolving during the same period, in the same geographic region.

Safe Motherhood

O27-13

Maternal mortality in Africa: the contribution of ineffective blood transfusion services

I. Bates, S. McKew, G. Kalanda, N. van den Broek

1 Liverpool School of Tropical Medicine, Liverpool, UK; 2 Royal Liverpool University Hospital, Liverpool, UK

OBJECTIVE Maternal haemorrhage is the leading cause (34%) of maternal deaths in Africa because once bleeding starts death occurs in around 2 h (viz. 10 h for eclampsia, 72 h for obstructed labour). Rapid access to emergency blood transfusion is critical to prevent deaths due to obstetric haemorrhage but there is a shortfall of 40 million units of blood/year in developing countries. In Africa, over 80% of blood comes from family 'replacement' donors; women admitted with haemorrhage have to find a donor from among their family members. This causes significant delays in obtaining blood and puts additional burden on families at a time of emotional and financial stress. We reviewed the literature to quantify, and identify reasons for, maternal deaths due to lack of blood transfusion.

METHODS We extracted information about the number of maternal deaths and near misses directly attributable to lack of timely blood transfusions from published studies. Two authors independently assessed studies for inclusion and collected data using a pre-piloted form.

RESULTS Forty-one studies from 15 countries sub-Saharan Africa provided information about the contribution of haemorrhage to maternal mortality or near misses. These were predominantly retrospective mortality audits and in 20 of these studies, there was a direct association between morbidity/ mortality and lack of blood transfusion. Studies from Gambia (2), Malawi, Nigeria and Tanzania indicated that 184/713 (mean 26%, range 16–72%) maternal deaths could have been prevented by access to emergency blood transfusion. Reasons why blood was not available included inability of patients to pay for blood, lack of blood donors/relative willing to donate, and lack of supplies and transport.

CONCLUSION Our figure of 26% for preventable maternal deaths due to lack of blood for transfusion is probably an underestimate because the contribution of ineffective transfusion services to maternal mortality has not been systematically researched. Centralised collection, testing and distribution of blood facilitates better quality but results in costs of ~$60/unit compared with ~$16/unit from a hospital-based service. Poor families cannot afford to pay the true cost of a transfusion so government subsidies are needed. Examples of ways to conserve transfusion service resources in countries where centralised services are not feasible include encouraging repeat donors from the local community, use of clinical guidelines and logical ordering of pre-donation screening tests. Blood transfusion services are essential to reduce maternal mortality but there is very little research into how they can be delivered and sustained effectively.

O27-14

A confidential enquiry into maternal death and near-miss in Indonesia

L. D’Ambrosio, E. Achadi, J. Hussein, K. Makowicka, T. Rachmawati, D. Suslam

1 Public Health, University of Aberdeen, Aberdeen, UK; 2 University of Indonesia, Salemba, Indonesia; 3 University of Aberdeen, Aberdeen, UK; 4 London School of Hygiene and Tropical Medicine, London, UK

OBJECTIVES We conducted a confidential enquiry into emergency obstetric care provided through the Indonesian village midwife programme. Our objective was to work with local health care providers to assess quality of care at the village-level and identify opportunities for improvement.

METHODS We convened panels of local health care practitioners to review care in fourteen cases of maternal death and severe obstetric complication from West Java. Although the enquiry focused on clinical quality of care, we also investigated factors pertaining to the other major barriers to optimal health care, namely those of the health system and social factors. The reviews were based on transcripts of interviews with healthcare providers and family and community members involved in the care. This allowed an examination of the interface between services and communities, not always reflected in case notes. We also took steps to identify favourable as well as adverse factors in order to recognise positive contributions of providers or users of services, where they occurred. At the end of the case-reviews, recommendations for practice were generated and disseminated.

RESULTS Midwives in villages played a key role in referral, reducing delays in reaching health facilities. Emergency diagnostic skills were accurate. However, midwives were less capable in clinical management of complications. Coverage was poor; midwives were responsible for up to five villages in some locations, presenting serious constraints to availability. Young village midwives were hesitant to provide care unacceptable to women and their families. The reviews revealed that families and communities did not prepare for emergencies with finances or transport, due, in part, to a poorly understood health insurance system. Finally, clear learning impacts from the enquiry were evident. The review panels reported that the enquiry fostered self-reflection, ownership and a great awareness of the needs of pregnant women.

CONCLUSION We recommend that village midwives work with formal and informal providers, present in the community; receive appropriate in-service training for the management of obstetric emergencies and; engage with communities to promote birth preparedness. Our enquiry represents a sustained effort by local health care providers, to learn lessons from adverse events. The practitioners had a unique insight into factors which could affect change and the enquiry provides evidence to achieve contextualised problem solving and improved resource allocation. The method is a diagnostic tool to identify opportunities for improving care, but is also a learning tool for those involved and an agent for change in itself.
O27-15
Preparedness for birth in rural Kyrgyzstan and Tajikistan. Knowledge and perception of women, men and health professionals and the quality of maternity care facilities
O. de Haan1, T. Wiegens2 and W. Boerma2
1Netherlands School Public and Occupational Health, Amsterdam, Netherlands; 2Nävel, Utrecht, Netherlands

OBJECTIVES To get insight in the knowledge, attitude and practices of users and providers of reproductive health services in rural areas. A base line study for the project ‘Services to the People’ which is running till 2010.

METHODS The Standard Tool Kit, developed by the Safe Motherhood Initiative and JHPIEGO, had been adapted and spread under 500 respondents and had five components. Qualitative research: focus group discussions with pregnant women on maternal and infant death causes.

QUANTITATIVE RESEARCH Structured face to face interviews with pregnant women and with men (not necessarily the spouses) on knowledge of danger signs and decisions on service use. Professional Knowledge Questionnaires for providers, to measure clinical competence. Provider Skills Checklist for measuring interpersonal communication and counselling skills. Facility audit on the availability of services, infrastructure and equipment for basic prenatal, natal and postnatal care, with 85 indicators.

RESULTS None of the providers, being obstetricians/gynaecologists, family doctors, midwives and nurses, met international standards on professional knowledge and skills. Of the Tajik women none mentioned all four danger signs during labour. Of the Kyrgyz women only one woman spontaneously mentioned all three key danger signs during the postpartum period and none mentioned all key danger signs during pregnancy or during labour. Of the men in both countries all the scores were zero. Of medical facilities in Kyrgyzstan only half are fully equipped, for Tajikistan this picture is even grimmer: some services score a 0 percent at basic medicines available. Lack of appropriated telecommunication connections makes it even more difficult to provide urgent obstetrical care. Half of the medical facilities need high-quality water supply, light source is mostly available, but in the winter there are often energy breakdowns and planned disconnections of energy, one third of medical facilities does not have separate laboratory.

CONCLUSIONS Tajikistan and Kyrgyzstan are danger places to be pregnant. Neither professionals nor the population are prepared for birth. Main causes for maternal death as hemorrhage and gestosis are even sometimes caused by lack of provider’s knowledge. High maternal and newborn deaths could be partly prevented by skilled providers. However, most of them have not upgraded their competence the last 10–15 years. Introducing evidence based practices, rather than the current obsolete protocols, can substantially reduce the reproductive losses. Providers need urgently training, women’s rights to education and information need to be advocated.

O27-16
Maternal mortality in India: stagnation and hope
D. Mavalankar1, K. Vora1, B. Sharma1, M. Upadhyaya2 and P. Sankar Raman1
1Indian Institute of Management, Public Service Systems Group, Ahmedabad, India

OBJECTIVES To draw out lessons from past program efforts for future direction MH programming.

METHODS To review maternal health situation in India using the available secondary literature- published and unpublished. Discussions with key government officials, international organisations and in participation of review of process of certain maternal health programs.

RESULTS The review of safe motherhood efforts in India shows that in spite of major initiatives taken by the government in last 10 years; significant impact has eluded the country. The challenge is how to make the SM strategies in the second phase of RCH program more successful. For this high priority has to be given to SM with backed with evidence based strategy and detailed micro-level programming. Strengthening EmOC should be the focus of SM strategy, along with skilled care at birth. Given the large size of the country, the project managers and policy makers should focus on effective implementation of selected interventions to reduce maternal mortality rather than trying to do many non-vital activities with little impact on maternal mortality. Monitoring of proper implementation and measuring progress is essential for success. Long standing policy and governance problems of the health system will have to be addressed to ensure effective implementation of SM component of the RCH. It will take at least 10–15 years of consistent, concerted and committed efforts for the program to show results. Some states and NGO efforts are showing the way to progress. The National government has to ensure that sates with high MMR make progress. This needs national and state level political commitment.

CONCLUSION The government must systematically review the past program efforts and focus the future programs clearly on improving EmOC services and skilled birth attendance. This requires consistent policy, systematic programming efforts and regular review to overcome key constraints. Trying to do too many unrelated and non evidence based interventions may not improve maternal mortality reduction.

Safe Motherhood

O27-17
Motorcycle ambulances stationed at rural health centres in Malawi reduce referral time of obstetric emergencies compared with a car ambulance posted at a district hospital
J. J. Hofman1, C. Dzimadzi2, K. Lungu2 and E. Y. Ratsma3
1Malawi College of Medicine, Currently Liverpool School of Tropical Medicine, Child & Reproductive Health Group, Liverpool, UK; 2Educ Consult, Lilongwe, Malawi; 3Malawi Safe Motherhood Project, Blantyre, Malawi

OBJECTIVES The feasibility of motorcycle ambulances for referral of obstetric emergencies from rural health centres to a district hospital was assessed, comparing referral times by use of motorcycle ambulances based at remote rural health centres (HCs) with those by use of a car ambulance based at the district hospital.

METHODS In this descriptive operational research with motorcycle ambulances placed at three rural HCs in Mangochi district, Malawi, data was collected over a 1 year period on obstetric referrals and referral time, as collected from maternity registers and specially designed logbooks and referral forms. Data were entered in the computer and analysed, using excel spreadsheets.

RESULTS Between October 2001 and September 2002, 194 patients were referred, of whom 68 maternity cases. On average two maternity cases and four non-obstetric cases were referred by motorcycle ambulance per month per health centre. Sixty-eight out of 112 obstetric referrals (61%) were transported by motorcycle ambulance and 39% by other means of transport, because sometimes the ambulance, the rider, or fuel was not available, or
because there were more patients to be referred at the same time than the motorcycle ambulance could carry. Referral delay was reduced at least by between 2 and 4 h or between 29% and 75%, depending on the site. There were less uncertainties with regard to delay than with car ambulances stationed at the district hospital, where delays occur in the process of transmitting messages before a car ambulance can depart from the district hospital. Variation in duration of transportation differed according to weather and road conditions, which are worse during the rainy season. However, breakdowns, such as a tyre puncture on the way, were the main delaying factors.

CONCLUSION Motorcycle ambulances can reduce considerably the delay in referring women with obstetric complications from rural HCs to the district hospital, which is the referral point for emergency obstetric complications. Whether this reduction in delay also results in a reduction of maternal mortality or otherwise improvement of outcome of deliveries is difficult to measure as this requires a very large sample.

Safe Motherhood

O27-18 Availability and utilisation of emergency obstetric care services in three districts of Malawi
J. J. Hofman1, E. Kongnyuy2, A. Mushiti2, G. Miyam1, S. Mwalabu2, D. Obrist4, B. Obrist4, J. Armstrong Schellenberg2, 4, O27-19 Comparison of investment and running costs of motorcycle ambulances and a 4WD car ambulance for referral of obstetric emergency cases in rural Malawi
J. J. Hofman1, C. Dzimadzi2, K. Lungu3 and E. Y. Ratsma3
1Child and Reproductive Health Group, Liverpool School of Tropical Medicine, Liverpool, UK; 2Educ Consult, Lilongwe, Malawi; 3Malawi Safe Motherhood Project, Blantyre, Malawi

OBJECTIVES The feasibility of motorcycle ambulances for referral of obstetric emergencies from rural health centres to a district hospital was assessed, comparing investment and running costs between a car ambulance based at a district hospital and motorcycle ambulances based at remote rural health centres (HCs).

METHODS Descriptive operational research with 3 new motorcycle ambulances with sidecars placed at three rural HCs in Mangochi district, Malawi, collecting data over a 1 year period (October 2001 – September 2002) on operating costs and comparing these with operating costs of a new 4WD car ambulance, stationed at the district hospital.

RESULTS Insert table (in 2002: 1 South African Rand = 16 MK) Operating costs of a car ambulance per year, including insurance, road license, fuel, repair and maintenance are approximately 18 times higher than those for a motorcycle ambulance. Correcting for difference in kilometres travelled by calculating costs assuming for both means of transport 10 000 km per year (the annual average per motorcycle ambulance), operating costs of a car ambulance are four times higher than for a motorcycle ambulance.

CONCLUSION The price of one Toyota Landcruiser ambulance equals that of 22 motorcycle ambulances, including two crash helmets, one rain suit, gumboots, foot pump, chain and padlock. However, transport costs from South Africa to Malawi are not included. Assuming transport costs to be 20% of the purchase price, the price of one car ambulance would buy 19 motorcycle ambulances. Motorcycle ambulance (Yamaha AG 200 + sidecar) Car ambulance (Toyota land cruiser) Purchasing costMK 210 240 = (duty free)MK 5 170 800 = (duty free) Comprehensive Insurance per yearMK 11 750 = (duty free)MK 4886.04 (front tyre)MK 1120 =MK 96 475.25 Road licenseMK 210 240 = (duty free)MK 5 170 800 = (duty free) Comprehensive insurance per yearMK 11 750 = (duty free)MK 4886.04 (front tyre) Price of sidecar tyre unknown. MK 11 750 = (x4 tyres)Repair/maintenance costs per yearMK 38 749.30 (MK 3.7 per km)MK 680 752.91 (MK 9.4 per km).

O27-20 Factors affecting home delivery in rural Tanzania
M. Mrisho1, A. Mushiti2, J. Armstrong Schellenberg2, O27-21 Study of physical and psychological stressors on health care workers in a maternity hospital
M. Mrisho1, A. Mushiti2, J. Armstrong Schellenberg2
1Ifakara Health Research and Development Centre, Dar es Salaam, Tanzania, United Republic of Tanzania; 2National Institute for Medical Research – Amani Centre, Muhaza, Amani, Tanga, United Republic of Tanzania; 3London School of Hygiene and Tropical Medicine, London, UK & Ifakara Health Research and Development Centre, Dar es Salaam, Tanzania, United Republic of Tanzania; 4Swiss Tropical Institute, Basel, Switzerland

BACKGROUND Studies of factors affecting place of delivery have rarely considered the influence of gender roles and relations within the household. This study combines an understanding of gender issues relating to health and help-seeking behaviour with epidemiological knowledge concerning place of delivery. METHODS Qualitative and quantitative methods were employed. In-depth interviews, focus group discussions and participant observation were used to explore determinants of home delivery in...
Tropical Medicine and International Health

VOLUME 12 SUPPL 1 PP 25–146 MAY 2007

Abstracts of the 5th European Congress on Tropical Medicine and International Health

southern Tanzania. Quantitative data were collected in a cross-sectional survey of 21,600 randomly-chosen households.

RESULTS Issues of risk and vulnerability such as lack of money, lack of transport, sudden onset of labour, short labour, staff attitudes, lack of privacy, tradition and cultures and the pattern of decision-making power within the household were perceived as key determinants of the place of delivery. Over 9000 women were interviewed about their most recent delivery in the quantitative survey. There were substantial variations between ethnic groups with respect to place of delivery (P < 0.0001). Women who lived in male-headed households were less likely to deliver in a health facility than those in female-headed households (RR 0.86, 95% CI 0.80–0.91). Mothers with primary and higher education were more likely to deliver at a health facility (RR 1.30, 95% CI 1.23–1.38). Younger mothers and the least poor women were also more likely to deliver in a health facility compared to the older and the poorest women respectively.

CONCLUSIONS To address neonatal mortality, special attention should be paid to neonatal health in both maternal and child health programmes. The findings emphasise the need for a systematic approach to overcome health-system constraints, community-based programmes and scale up effective low-cost interventions which are already available.

Treatment of Malaria: ACT III

O27-21
Safety evaluation of artesunate/mefloquine used in African children with uncomplicated P. falciparum malaria

C. Hatzi1, B. R. Beck1, A. Kummerle1, J. L. Heidecker2 and N. Cambon3

1Swiss Tropical Institute, Basel, Switzerland; 2Mepha Ltd, Aesch, Switzerland

OBJECTIVES The ACT mefloquine/artesunate has been widely used in Asia where it has been considered safe and efficacious. The option of this ACT for large-scale application in Africa is currently evaluated by WHO, especially for young children.

METHODS Data from clinical trials in Asia following the WHO protocol for assessment of antimalarial drugs were clustered for adverse events (AEs) and analysed for safety, considering gender, age and mefloquine/artesunate total dose.

RESULTS Data of 854 patients out of six prospective African clinical trials conducted between 2002 and 2006 with the ACT artesunate/mefloquine were analysed. Dosage schemes applied in these studies were consecutively adapted to the WHO policy guidelines changing over the observation period for mefloquine from 15 to 25 mg/kg to the currently recommended mean total dose of 25 mg/kg. Clustering the patients in bodyweight-groups of 10–20 kg, >20–40 kg and >40 kg best suited the current dosage recommendations and were used for analysis. Most patients treated with the 25 mg/kg-mefloquine dose-combination were children (n = 276). An overview of all post-authorisation studies reveals that gastrointestinal and general signs/symptoms of low severity grades (30 %) account for most of the AEs in 1–6 years old children. Neurological, psychiatric and neuro-psychological events (1.7%) included dizziness, insomnia and headache. Some abnormal haematological laboratory values, e.g. low erythrocyte and neutrophil counts, will be discussed in context with the course of the malaria infection and therapy or particularities of African subjects. Observed AEs tend to be less frequent in children than in adults. Neurologic and psychiatric AEs are reported more frequently in the higher age-groups at a reported incidence of 4.6% in children of 7–14 years and 3.4% in adults. Correct detection and assessment of such AEs in young children will be discussed. A recent study with the new FDC of artesunate/mefloquine for small children (Artequin™ Paediatric) indicates that AEs are indeed less frequent in small children than in older ones. Further post-authorisation Safety Monitoring on neurologic and psychiatric AEs is currently underway to confirm that such AEs are in fact less frequent in children than in adults.

CONCLUSIONS The general pattern of AEs in African subjects treated with artesunate/mefloquine is very close to the one reported from other endemic areas. Although detailed information on potential neuropsychiatric data among young African children is not yet available, the use of this ACT appears justified as an alternative to the only ones currently qualified and should bridge the gap until establishment of further FDC-ACTs in Africa.

O27-22
A randomized, investigator-blinded, multicenter, parallel-group study to compare efficacy, safety and tolerability of artemether – lumefantrine dispersible tablet formulation vs. artemether – lumefantrine 6-dose crushed tablets in the treatment of acute uncomplicated Plasmodium falciparum malaria in infants and children: an innovative design

I. Sagara1, S. Abdulla2, Q. Bassa3, M. Hamel4, A. Nahum5, B. Ogutu6, K. Andrian6, M. Cousin7, P. Ibarra de Palacios8

1Malaria Research and Training Center, University of Bamako, Bamako, Mali; 2Ifakara Health Research and Development Centre, Dar es Salaam, United Republic of Tanzania; 3Manhiça Health Research Centre, Maputo, Mozambique; 4Malaria Branch, Center for Disease Control and Prevention/Kenya Medical Research Institute, Kisumu, Kenya; 5Centre de Recherche Entomologique de Cotonou, Cotonou, Benin; 6Walter Reed Project/Kenya Medical Research Institute, Kisumu, Kenya; 7Novartis, East Hanover, USA; 8Novartis, Basel, Switzerland

OBJECTIVES Malaria is primarily a disease of the very young, however specific pediatric formulations are scant. This study was designed to evaluate efficacy, safety, tolerability and pharmacokinetics of a new artemether - lumefantrine pediatric dispersible tablet (DT) formulation for oral suspension in infants and children (≤12 years of age) with body weight of ≥5 kg and ≤35 kg suffering from microscopically confirmed acute uncomplicated P. falciparum malaria.

METHODS The study aimed to demonstrate non-inferiority (using a margin of 5%) of the 6-dose regimen DT vs. the current WHO-supported commercial 6-dose regimen of crushed conventional tablet (CT) at the standard dosage recommendations according to bodyweight. It will compare 14-day and 28-day (primary objective) PCR-corrected parasitological cure rates between the two treatment groups in a total of 890 randomized patients, as well as time to parasite, fever, and gametocyte clearance. It included a futility interim analysis (IA) based on the uncorrected 7-day parasitological cure rate in the first 160 patients randomized. AEs, laboratory findings, vital signs, and ECGs were recorded. Artemether, DHA and lumefantrine plasma levels were also investigated. Eligible patients were to be randomized (1:1) to either treatment group (DT or CT). The 3-day treatment phase was followed by a 39-day observation period. Interim analysis data on 166 patients were recently reviewed by an independent Data Monitoring Board (DMB). Using a pre-specified algorithm for futility (based on an assumed true success rate of 95%), the DMB recommended recruitment proceed. The DMB was also to make recommendations on clinically relevant safety signals. Supportive analysis of 28-day PCR-corrected cure rates will be performed using the per protocol population, and analyses of secondary efficacy objectives will be based on the ITT population.
O27-23
New fixed dose artesunate/sulfamethoxypyrazine/pyrimethamine combination therapies compared to artenether/lumefantrine for the treatment of uncomplicated Plasmodium falciparum malaria across Africa: an open randomized multi-centre trial

I. Sagara1, S. Ruinsa1, I. Adam1, W. Mbacham2, A. Djimde3 and O. Doumba4
1 Department of Epidemiology of Parasitic Diseases, Faculty of Medicine, Pharmacy, and Odonto-Stomatatology, Mali, Malaria Research and Training Centre, University of Bamako, Bamako, Mali; 2Kigali Central University Hospital, Kigali, Rwanda; 3Faculty of Medicine Department Obstet. Gynaecology, University of Khartoum, Khartoum, Sudan; 4University of Yaoundé, Yaoundé, Cameroon; 5Département d’Épidémiologie des Affections Parasitaires (DEAP) Faculté De Médecine de Pharmacie et D’Odonto-Stomatologie (FMPOS), Malaria Research and Training Center (MRTC), Bamako, Mali

OBJECTIVES The efficacy of artemisinin based combination therapies (ACT) has already been demonstrated in a number of studies all over the world. However, it is known that secondary factors like side effects, ease of administration, cost and duration of the treatment can greatly influence the final outcome of any ACT. For this reason, these factors must be handled with equal importance when selecting an appropriate antimalarial treatment. This open randomised multi-centre clinical trial tested the hypothesis that three pills of the fixed dose combination artesunate/sulfamethoxypyrazine/pyrimethamine (As/SMP fdc), administered over 24 h, is not inferior in efficacy to the same drug administered over 48 h and that As/SMP fdc, independently of the duration of its dose interval, is not inferior in efficacy to 24 pills of the 60 h treatment of artemether/lumefantrine (AL, 6-dose) for the treatment of uncomplicated P. falciparum malaria.

METHODS This multi-centre study was carried out between May 2006 and January 2007 in four African countries: Cameroon (Biyem-Assi, Yaoundé), Mali (Samako, Kolle and Bancoumana), Rwanda (Kigali) and Sudan (Alhara Alola, New Halla). Participants at least 6 months of age with uncomplicated P. falciparum malaria were randomly assigned to receive As/SMP fdc 3 pills in 24 h, As/SMP fdc 3 pills in 48 h or AL 24 pills in 60 h. Treatment efficacy was assessed using the 28-day protocol of the World Health Organization.

RESULTS A total of 1260 patients were enrolled (Cameroon: 192; Mali: 261; Rwanda: 539 and Sudan: 319). Adequate Clinical and Parasitological Responses (ACPR) not PCR corrected on day 28 were 96.3%, 97.3% and 97.9% for As/SMP fdc 3 pills in 24 h, As/SMP fdc 3 pills in 48 h and AL 24 pills in 60 h, respectively. Overall, these preliminary results showed an ACPR of 97.2% (not corrected with PCR for reinfection) on day 28. No serious adverse events occurred.

CONCLUSION Both regimens of As/SMP fdc were as effective and safe as AL for the treatment of uncomplicated P. falciparum malaria. Due to its ease of administration and the shortened treatment duration, the fixed dose one-day treatment regimen may improve compliance and therefore may be the preferred choice.

O27-24
Primaquine clears submicroscopic Plasmodium falciparum gametocytes that persist after treatment with sulfadoxine-pyrimethamine and artesunate

T. Bousema1, S. Shkelaj2, C. Drakeley3 and R. Sauerwein4
1 Medical Microbiology 268, Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands; 2Kilimanjaro Christian Medical Centre, Moshi, United Republic of Tanzania; 3London School of Hygiene and Tropical Medicine, London, UK; 4Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands

OBJECTIVES P. falciparum gametocytes may persist after treatment with sulfadoxine-pyrimethamine (SP) plus artesunate (AS) and contribute considerably to malaria transmission. We determined the efficacy of SP + AS plus a single dose of primaquine (PQ, 0.75 mg/kg) in clearing gametocytaemia measured by molecular methods.

METHODS We conducted a two-arm single blind trial in Mnyuzi, an area of hyperendemic malaria in north-eastern Tanzania. Children aged 3–15 years with uncomplicated P. falciparum malaria with an asexual parasite density between 500–100 000 parasites/ul were randomized to receive treatment with either SP + AS or SP + AS + PQ. The main outcome measures were P. falciparum gametocyte prevalence and density by real-time nucleic acid sequence-based amplification (QT-NASBA) during 42 days of follow-up. Haemoglobin levels (Hb) were determined to address concerns about haemolysis in G6PD-deficient individuals.

RESULTS A total of 108 individuals were randomized. P625 QT-NASBA gametocyte prevalence was 88–91% at enrolment and decreased afterwards for both treatment arms. Gametocyte prevalence and density were significantly lower in children treated with SP + AS + PQ. On day 14 after treatment 3.9% (2/51) of the SP + AS + PQ treated children harboured gametocytes compared to 69.7% (32/47) of those treated with SP + AS (P < 0.001). Hb levels were reduced in the week following treatment with SP + AS + PQ and this reduction was related to G6PD deficiency. The Hb levels of all patients recovered to pre-treatment levels or greater within one month after treatment.

CONCLUSION PQ clears submicroscopic gametocytes after treatment with SP + AS and the persisting gametocytes circulated at densities that are unlikely to contribute to malaria transmission. For individuals without severe anaemia, addition of a single dose of PQ to an efficacious antimalarial drug combination is a safe approach to reduce malaria transmission following treatment.

O27-25
Safety and efficacy of methylene blue combined with artesunate or amodiaquine for uncomplicated falciparum malaria: a randomized controlled trial from Burkina Faso

O. Müller1, A. Zoungrana2, P. Meissner3, B. Coulibaly2, S. Traoré3, A. Sie2, L. Walter-Sack2, H. Schirmer2, H. Becher1 and B. Kouyate1
1 Tropical Medicine, Heidelberg University, Heidelberg, Germany; 2CRSN, Nouna, Burkina Faso; 3Heidelberg University, Heidelberg, Germany

OBJECTIVES To study the safety and efficacy of two different methylene blue-based malaria combination therapies, methylene blue-artesunate (MB-AS) and methylene blue–amodiaquine (MB-AQ) were compared to the standard of care, artesunate–amodiaquine (AS-AQ) in Burkina Faso.

METHODS Open label randomised controlled phase II study in 6–10 year old children with uncomplicated falciparum malaria in Nouna town, north-western Burkina Faso. Eligible children of the community were enrolled at the outpatient department of the Nouna District Hospital and sequentially randomized to one of the study arms. Follow-up was for 28 days using the latest WHO protocol on drug efficacy testing.

RESULTS A total of 180 children were enrolled into the study and treated over a 3-day period (61 MB-AS, 58 MB-AQ, 61 AS-AQ). There were no differences between groups with regard to baseline characteristics and there was only one loss to follow-up. There were no deaths and no study-related serious adverse events. MB-containing regimens were associated with mild vomiting and
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O27-26
Access to antimalarial medicines: a ‘Big Pharma’ assets and limitations
F. Bompart1, J.-M. Bouchez1, V. Faillat-Proux1, V. Lameyre1, P. Moneton1 and R. Sebbag1
1Sanofi Aventis, Access to Medicines, Gentilly, France

Within its Access to Medicines program, sanofi aventis has developed an initiative, called Impact Malaria, to mobilize the expertise and resources of the company against malaria. Impact Malaria 4 strategic axes of activity are Research and development of new antimalarial drugs, to anticipate resistances to existing compounds. Improvement of existing drugs to meet the needs and requirements of patients and health care providers. Information on Education and Communication tools to ensure that together with other effective interventions, drugs are appropriately used. Differential pricing policies that give access to high quality drugs to all population segments. The recent registration of the fixed-dose combination of artemether and amodiaquine developed in partnership with the Drugs for Neglected Diseases initiative (DNDi) is an illustration of our work. In this partnership, DNDi made technical contributions, but also, importantly, brought the viewpoint and the weight of civil society, a network of global contributors and the visibility of major Non-Governmental Organizations. Sanofi aventis assets in this partnership are: its expertise in the field of malaria, the know-how needed to improve formulations of existing drugs, to develop and register following international standards and regulations, resources for large-scale production of quality drugs, knowledge of distribution networks and information networks for healthcare providers. However, there are several limitations that affect ‘Big Pharma’s’ capacity to effectively improve access to drugs for the poorest. In the field of malaria, these are primarily: the difficulties of adjusting drug production and demand, complexity of financial mechanisms for drug purchasing, limitations of existing drug distribution networks, informal drug market and the focus of decision-makers on the lowest possible drugs price without consideration for added services. Providing affordable, safe and effective antimalarial drugs is an absolute requirement. However, sustainable control of malaria also requires parallel investments in applied research, training, advocacy, strengthening of public health infrastructure and distribution networks, as well as vector control strategies. Our partnership with DNDi has shown that an alliance between stakeholders from different, and sometimes antagonistic, backgrounds is one way to effectively address some of the complex issues of access to medicines.

Clinical AIDS, Including Opportunistic Infections

O27-27
Predictors of mortality in hospitalised HIV-infected patients in resource-limited setting
F. Castelli1, N. Saleri2, M. Rizzi2, V. Piera2, V. Del Punta3, S. Capone1, G. De Iaco1, S. Rouamba4, E. Sonè5, A. Patroni1, M. Levi2 and J. Simpore6
1Institute for Infectious and Tropical Diseases, University of Brescia, Brescia, Italy; 2Institute for Infectious and Tropical Diseases, University of Brescia, Italy; 3Medicus Mundi Italy, Ouagadougou, Burkina Faso; 4Centre d’Accueil Notre Dame de Fatima, Ouagadougou, Burkina Faso; 5Centre de Recherche Biomolecular Pietro Annigoni, Ouagadougou, Burkina Faso

OBJECTIVES Data on causes and predictors of deaths of HIV patients in Africa are scarce. Aim of our paper is to describe the clinical presentation and risks factors of mortality in hospitalised HIV-infected patients in Ouagadougou, Burkina Faso.

METHODS The study was carried out in a 64-bed AIDS treatment and hospitalisation centre (CANDAF – Centre d’Accueil Notre Dame de Fatima) run by the religious Saint Camille Order in the capital city Ouagadougou. The hospital is equipped with a basic laboratory (parasitological stool examination, malaria smear and biochemistry). Hospitalisation and HAART treatment is free of charge for the patients. Two Italian medical doctors from the University of Brescia and Medicus Mundi Italy, constantly worked in the Centre during the study period. Medical charts of all HIV-infected patients admitted to CANDAF from January 1st, 2004 to August 31st, 2006, were prospectively recorded in the data base. Standardised clinical syndromes at admission and final diagnoses (WHO classification) were recorded, as well as demographic and clinical parameters. Data were entered in a specifically designed Microsoft Access database and analysed by univariate and multivariate analysis.

RESULTS Since January 1st, 2004 to August 31st, 2006, 1071 hospitalised (384 males and 687 females) were recorded. Males were more likely to be in WHO stage IV than female (P = 0.00027) and to have lower CD4 cell counts (111.0/µl vs. 161.1/µl, P = 0.000001). The most frequent clinical syndromes at admission were: GI disorders (661, 61.7%); fever (408, 37.6%); extra-pulmonary TB = 66) respectively. Death occurred in 320 cases (crude mortality rate: 29.9%). At univariate analysis, factors predicting negative outcome were older age, male sex, WHO stage III/IV, fever, wasting/neurological/respiratory syndrome at admission, malaria, tuberculosis. At multivariate analysis, the following parameters were independent predictors of death: older age, fever, wasting or neurological syndrome at admission. Favourable hospitalisation outcome was associated to higher weight or higher platelet count.

CONCLUSIONS Gastro-enteric disorders and fever are the most frequent complaint leading to hospitalization in our setting. HIV-infected men have a later recourse to hospitalization and a worst prognosis compared to HIV-infected females. Older age and thrombocytopenia at entry resulted to be independent negative factor for survival. Early recourse and access to curative health structure may improve survival.
O27-28
Epidemiological and clinical profile of immigrant patients with HIV infection in Alicante, Spain
S. Ezso1, D. Torrus1, C. Navarro1, R. M. Gorís1 and J. Pertilla1
1Internal Medicine, University General Hospital of Alicante, Alicante, Spain

OBJECTIVES To describe the epidemiological and clinical characteristics of immigrant patients with HIV infection attended in a referral centre.

METHODS Retrospective observational study at the department of infectious diseases of the General Universitary Hospital of Alicante (Spain). Inclusion criteria: VIH immigrant patients attended between January 2000 and February 2007 with available clinical history. Descriptive and bivariate analysis was performed.

RESULTS A total of 32 clinical histories were reviewed. 55.8% were males and the mean age was 37 years. The mainly origin was Latino America (44.2%) and sub-Saharan Africa (42.3%) and the mean stay in Spain was 32.8 months. 11 cases had previous diagnosis of HIV infection and seven cases were under antiretroviral treatment. In the 45 cases without treatment the median baseline CD4 count was 275/μl with no difference from origin. 15% had ‘B’ events, and 15% had ‘C’ events, tuberculosis in seven cases. At diagnosis 40% were A2 stage and 31.1% were C3 stage (50% from East Europe). The route of transmission was sexual in more than 90% (67.3% heterosexual and 25% homosexual). HBV coinfection was found in five cases (100% from Africa) and HCV coinfection in six cases. African patients had more risk to have chronic hepatitis (P = 0.032; RR 4.6; 95% IC: 1.06–20.13). 51% began treatment at diagnosis and the other 23% start treatment during follow-up (two cases for gestation and 10 cases by immunologic deterioration). The main treatment combination was 2 NRTI + 1 NNRTI (42.3%). The mean follow-up time was 21.94 months, the mean CD4 count at last control was 449/μl and in 50% (26 cases) the viral load was undetectable. 10 cases had treatment toxicity (23.8%). In 16.7% were a therapeutic failure and in more than 70% were optimal adherence. Seven cases left follow-up (13.5%), mainly sub-Saharan African patients (85.7%) (P = 0.0018; RR: 9.9; 95% CI: 1.1–89.3).

CONCLUSION Sexual is the main route of HIV transmission in immigrant patients. No differences were found in clinical stage between the distinct geographical origins. Chronic hepatitis and loss to clinical follow up are more frequent in African patients.

O27-29
Looking toward the future of HIV prevention: an overview of the current microbicide clinical pipeline
B. Finley1, L. Boyce1, C. Plesca1, P. Harrison1 and F. des Vignes1
1Alliance for Microbicide Development, Silver Spring, USA

OBJECTIVES The microbicide clinical pipeline has undergone significant changes over the past year. This presentation provides a summary of ongoing and planned microbicide clinical trials. It also provides an overview of studies assessing activity of candidates against non-HIV STIs, clinical testing in special populations, contraceptive potential of current candidates, research assessing rectal safety, and candidates recently removed from the clinical pipeline.

METHODS The alliance for microbicide development tracks microbicide candidates through the microbicide research and development database, an online tool updated quarterly with information provided by each candidate’s developer.

RESULTS Within the past year, the microbicide clinical pipeline has decreased from 14 candidates to 11; the status of one candidate previously in clinical development was reassessed and effectiveness trials of two candidates have been stopped. Of the 11 candidates in clinical development, three are in ongoing effectiveness trials. Microbicide candidates are intended to prevent HIV infection through a range of mechanisms of action including vaginal defense enhancement, entry/fusion inhibition, and replication inhibition. While one candidate employs a combination of mechanisms of action, another candidate uses an uncharacterized mechanism. Select STIs, including chlamydia, gonorrhea, and HSV-2 are being assessed as secondary endpoints in two of the three ongoing effectiveness trials. Six of the 11 candidates have enrolled HIV-positive women and/or HIV-positive men in early-stage clinical trials, and 9 of 11 have assessed safety and/or acceptability in men. At least 1 of the 3 candidates currently in effectiveness trials is expected to be contraceptive. In addition, at least 1 of the 3 candidates currently in effectiveness trials is not expected to be contraceptive. Preclinical rectal safety data exists for five candidates, while one candidate is being tested in a phase 1 clinical trial to assess rectal safety.

CONCLUSION For current microbicide candidates, research is being conducted to assess rectal safety, contraceptive potential, and safety and/or acceptability in special populations. Future research will need to address the potential for resistance accompanying use of antiretroviral microbicide candidates and methods for accurately assessing incidence prior to initiation of effectiveness trials. Sound strategies are needed to address questions and challenges in each of these key areas of microbicide development: accurate data must be collected and compiled to enable the microbicide field to make informed decisions regarding future microbicide research.

O27-30
Cellular immune response to Cryptosporidium parvum in Cryptosporidium-HIV co-infected patients
K. Kaushik1, S. Khurana1, N. Malla1 and A. Wanchu2
1PGIMER, Parasitology, Chandigarh, India; 2PGIMER, Internal Medicine, Chandigarh, India

OBJECTIVES Acquired immuno deficiency syndrome (AIDS) is a global emergency with far reaching effects. The gastrointestinal tract is a major target organ in HIV related opportunistic infections, which persists, commonly as diarrhoea. Cryptosporidia are increasingly being recognized as important enteric pathogens in AIDS and other immuno-suppressed patients. The host immune responses that prevent the initial infection by Cryptosporidium, limit its spread and ultimately facilitate its clearance are poorly understood.

METHODS Since data on immune response to Cryptosporidium in HIV patients co-infected with Cryptosporidium are lacking, the present study was designed to assess the cellular immune responses in the HIV patients infected with Cryptosporidium. For this PBMCs separated from the patients were proliferated in the presence of Cryptosporidium parvum crude soluble antigen (CCA) and proliferation was measured by counting the thymidine incorporation into the cells.

RESULTS PBMCs from the Cryptosporidium infected patients (both HIV infected and non-infected) showed high proliferation against CCA as compared to Cryptosporidium non-infected subjects.
CONCLUSION Specific cellular immune response was found in patients (both HIV-infected and non-infected) against Cryptosporidium parvum.

Diagnostics of Communicable Diseases

O27-31 Detection of parasite DNA in stool samples by multiplex real-time PCR: a potential diagnostic tool to study the epidemiology of multiple intestinal parasites


1Parasitology, Leiden University Medical Center, Netherlands; 2Welcome Trust Research Laboratories, Blantyre, Malawi; 3College of Medicine, University of Malawi, Blantyre, Malawi; 4Academic Medical Center/Emma Children’s Hospital, Amsterdam, Netherlands; 5Liverpool School of Tropical Medicine, Liverpool, UK

OBJECTIVES Studying the epidemiology of intestinal protozoa and helminthic infections traditionally relies on microscopic stool examination. Although costs of microscopy are generally low, this approach has several important disadvantages. Sensitivity and specificity are highly dependent on the skills of the microscopist. Moreover, multiple sample examination is often required, as well as laborious staining procedures to visualize the opportunistic protozoal infections. Here we describe a number of multiplex real-time PCR assays to detect parasite DNA in stool samples collected under field conditions.

METHODS Real-time PCR’s were developed for the species specific detection of a wide range of parasites, including Giardia lamblia, Cryptosporidium parvum/hominis, Entamoeba histolytica, Enterocytozoon bieneusi, Encephalitozoon spp., Isospora belli, Ancylostoma duodenale, Necator americanus, Strongyloides stercoralis, Schistosoma mansoni and S. haematobium. Multiple targets were combined into multiplex real-time PCR’s, including an internal control for the detection of possible inhibition of the amplification by faecal contaminants. High numbers (n > 100) of negative and positive DNA controls and well-defined stool samples were used to evaluate sensitivity and specificity of the assay for each detected parasite species. The performance of the real-time multiplex PCR as a diagnostic tool in epidemiological and clinical research is illustrated by two independent studies. Faecal samples were collected in Blantyre, Malawi in order to evaluate (i) the association between protozoal infections and diarrhoeal complaints in relation to HIV-1 status and CD-4 counts of adult hospitalized patients (n = 333); (ii) the contribution of hookworm infection in the aetiology of severe anaemia in small children (n = 841).

RESULTS All assays achieved 100% specificity and high sensitivity when performed on DNA controls and well defined stool samples. Comparable PCR results were seen when samples were mixed with ethanol and stored at tropical temperatures. High numbers of parasite positive stool samples were seen in both studies from Malawi, with Enterocytozoon bieneusi being the predominant parasite in HIV associated diarrhoea cases and Ancylostoma duodenale in anaemic children. Species specific cycle threshold values showed significant association with some of the clinical parameters, including CD4 counts and anaemia status.

CONCLUSION The described PCR approach shows promise for species specific detection of parasite DNA in faecal samples, although uncertainties remain for the interpretation of the (semi-)quantitative output as an indicator of disease. The simple faecal sample collection procedure and the high throughput potential may provide a powerful diagnostic tool to study species-specific distribution patterns or to monitor (clinical) intervention programs.

O27-32 Laboratory diagnosis of melioidosis during the Tsunami disaster

R. M. Hagen1, M. Fischer1, J. Bronnert1, A. Turnwald-Maschner1, A. Indra2 and M. Mueller1

1BWK Hamburg, Fachbereich Tropenmedizin am Bernhard-Nècht-Institut, Hamburg, Germany

OBJECTIVES Melioidosis is an infectious disease of tropical areas especially in Southeast Asia caused by Burkholderia pseudomallei. The diagnosis remains difficult and B. pseudomallei has to be handled under BSL3-conditions in European laboratories. We could establish a reliable diagnosis based on culture with selective media (ASA, BPSA and BCA) and biochemical identification (Api 20NE) in combination with confirmative cELISA and real-time PCR for a reliable diagnosis. The aim of our study was to evaluate this strategies during the tsunami disaster when severe cases of tsunami-related melioidosis occurred affecting both tourists and locals.

METHODS Swabs from different sites and sputa were cultured on blood and two different selective culture media (ASA and BPSA). Material from residents treated in the German field hospital and on bord of the naval hospital carrier ‘Berlin’ were sent following IATA regulations. B. pseudomallei strains from different geographical origins served as controls. Sample preparations obtained from the swabs as well as colonies suspected to be B. pseudomallei were inactivated to perform a cELISA with a monoclonal antibody and a LC real-time PCR assay targeting the flic gene. Confirmation was done by Api 20NE in parallel.

RESULTS We could isolate and identify B. pseudomallei strains from five tourists and two local patients. These clinical isolates all showed a characteristic morphology on the ASA and BPSA culture media as well as a typical biochemical profile. All preparations and isolates were tested positive in the cELISA and the real-time PCR assay.

CONCLUSION We recommend the use of the classical selective culture media ‘Ashdown Agar’ or alternatively the commercially available ‘Burkholderia Cepacia Agar’ for the isolation of B. pseudomallei from clinical material in combination with the Api 20NE as ‘gold standard’. In addition, rapid and reliable tools i.e. cELISA or real-time PCR assay should be used to obtain a presumptive diagnosis and the enable an effective antibiotic treatment without time loss.

O27-33 Detection with microscopy, quick-tests and real-time PCR and molecular identification of Cryptosporidium spp. in Dutch patients

M. van de Biezen-Brinkman1, D. Vastert-Koop2, M. Lawa3, H. Wilks2 and B. Mulder3

1Department Parasitology, Laboratory for Medical Microbiology and Public Health, Enschede, Netherlands; 2Laboratory for Medical Microbiology and Public Health, Enschede, Netherlands

OBJECTIVES Cryptosporidium frequently causes watery diarrhea in both immunocompetent and immunocompromised patients
According to the existing textbooks, in an earlier study we found that the majority of positive Cryptosporidium samples were found in mushy stools from children younger than 10 years and that Cryptosporidium remains largely underdiagnosed in current routine diagnostic practice in the Netherlands. We compared four different diagnostic methods for the detection of Cryptosporidium in mushy faeces from children with acute or chronic diarrhea sent in for bacteriological or parasitological examination.

METHODS Microscopic examination on stained faecal samples (IHK-stain), Crypto-stripTM (Coris Bioconcept), immunocass STATfTM (Meridian Bioscience) and real-time PCR for the detection of Cryptosporidium were compared. From mid August to mid October 2006, 200 mushy faeces from children up to 6 years were included. 75 were sent for bacteriological examination and 127 triple faeces test (TFT)-samples, were sent to the parasitology department, representing a more chronic form of diarrhea. For molecular differentiation of C. hominis and C. parvum we sequenced the Cryptosporidium outer wall protein (COWP)-gene.

RESULTS Thirty faces where found positive for Cryptosporidium in real-time PCR, 28 where confirmed by immunocass STATfTM, 19 by Crypto-stripTM (Coris Bioconcept) and 14 by microscopy. Using real-time PCR as a reference method the sensitivity of microscopy, Crypto-stripTM and immunocass STATfTM were 64%, 63% and 93% respectively while the specificity always exceeded 98%. From the total of 30, 12 Cryptosporidium samples could be identified; 11 were identified as genotype Cryptosporidium hominis and one as Cryptosporidium parvum.

CONCLUSION Immunocass STATfTM is a very specific and sensitive method for the laboratory detection of Cryptosporidium in faeces. Immunocass and the Crypto-stripTM are very specific but less sensitive methods, in our hands. Examination of mushy stools from children till 6 years, sent only for bacteriological examination, for the presence of Cryptosporidium yields additional positive samples (40%) which would otherwise not have been detected. The majority of all Cryptosporidium were identified as Cryptosporidium hominis, as could be expected in children after the summer period.

O27-34
Detection of L. pneumophila by nested PCR-RFLP and ELISA on urine specimens in pregnant women with respiratory infections and comparison of two tests
S. Motahari1, L. Chamani Tabriz2, M. J. Tehrani2, H. Zeerati3, M. Kargar1 and S. Asgar4
1Reproductive Biotechnology Research Center, ARI, Reproductive Infections, Tehran, Islamic Republic of Iran; 2Monoclonal Antibody Research Center, ARI, Reproductive Immunology, Tehran, Islamic Republic of Iran; 3School of Public Health/Tehran University of Medical Sciences, Epidemiology and Biostatistics, Tehran, Islamic Republic of Iran; 4Microbiology, Azad University of Jahrom, Jahrom, Islamic Republic of Iran

OBJECTIVES Pneumonia during pregnancy can induce serious consequences to mother and fetus so its diagnosis and therapy is very important. There is no published investigation on legionella infection prevalence during pregnancy. It is known that in patients with Legionelllosis, bacterial LPS and DNA excretes in urine for extended periods of time so combination of PCR and ELISA would be the best diagnostic tool.

METHODS This is a cross sectional study on 95 pregnant women with respiratory infection during winter to summer 2006. Presence of legionella infection was confirmed by nested PCR-RFLP and ELISA antigen detection test on urine specimens. Data analyzed by SPSS: 13.

RESULTS The average age of participants was 25 (15–41 years old). The most prevalent clinical features were: fever (22.1%), chills (35.8%), cough (56.8%), headache (54.7%), diarrhea (8.4%) and abdominal pain (38.9%). PCR was positive in 21 cases (22.1%) confirmed by nested PCR-RFLP. ELISA was positive in four (4.2%) patients. PCR was positive in 71.4% of patient with fever and 81.1% among patients without fever (P < 0.001). PCR was positive in 44.1% of patient with chills vs. 9.8% in patient without chills (P < 0.001). There was statistic relation with test results and abdominal pain (P < 0.05), previous liver or renal problems (P < 0.01) but no relation with other signs and symptoms. ELISA results were significantly related to fever and chills (P < 0.001).

CONCLUSION It seems that there is a considerable prevalence of this infection in studied population (22.1%). In our study ELISA was less sensitive than PCR (P < 0.05). PCR and ELISA on urine sample are suitable to detect different Legionella species and can provide results in a few days. It will be a great help in diagnosis and treatment of pneumonia especially during pregnancy. This study supported by Reproductive Biology Research Center, Avesina Research Institute, Iran.

Diagnostics in Communicable Diseases

O27-35
Comparison of indirect micro-immunofluorescence test and ELISA for detection of IgG antibodies against tick-borne spotted fever Rickettsiae
G. Dobler1, M. Faulde2, M. Pfeffer3, S. Essbauer4 and R. Wölfel5
1Department of Virology and Rickettsiology, Bundeswehr Institute of Microbiology, München, Germany; 2Department of Zoology, Bundeswehr Central Institute, Koblenz, Germany; 3Department of Bacteriology, Bundeswehr Institute of Microbiology, München, Germany

OBJECTIVES Tick-borne rickettsial diseases are recognized as emerging infections throughout many parts of the world. So far the standard method for detection of anti-rickettsial antibodies is indirect micro-immunofluorescence (MIFT). However epidemiological studies are hampered because the MIFT is labor-intensive and time-consuming. Recently ELISA assays became commercially available. But only few data on sensitivities and detection limits of these ELISA assays are known. The possible value of MIFT and ELISA for epidemiological studies was investigated in an Afghan population sample.

METHODS A total of 139 serum samples collected from inhabitants of Northern Afghanistan were tested for anti-rickettsial IgG antibodies using a commercial MIFT and were compared to commercial Rickettsia IgG ELISA (both PanBio, Brisbane, Australia) conducted according to the manufacturer’s instructions. Positive sera in MIFT were diluted for endpoint titration.

RESULTS Around 26/139 sera (18.7%) gave a positive reaction by MIFT with titers >1:32. By ELISA only 10/139 sera (7.2%) reacted positive. All sera positive by ELISA were also reactive in MIFT (1005 concordance). However 16 sera positive in MIFT were not recognized by ELISA. Sera positive by ELISA exclusively exhibited titers in MIFT of ≥1:128.

CONCLUSION Our results show for the first time a high prevalence of antibodies against rickettsia of the tick-borne spotted fever group in Northern Afghanistan. By convention rickettsial infection is presumed with IgG antibody titers ≥1:64. According to our data 18.7% of the population tested showed anti-rickettsial IgG antibodies of ≥1:64 as evidence of recent or past infection with
rickettsiae of the spotted fever group. Our comparison data show that MIFT is much more sensitive than the tested commercial ELISA. By ELISA only sera with IgG titers of ≥1:128 could be detected. Consequently, the ELISA in its present form cannot be recommended for epidemiological studies. The usefulness of the ELISA used in this study for the detecting of acute rickettsial infections remains to be determined.

Public Private Partnership

O27-36
A comparative study of cost and quality of care of malaria treatment in public and private health facilities in Nigeria: a case study of Lagos state

I. Arsoyibo
Health Economics, University of Capetown, Capetown, South Africa

OBJECTIVES The study explored the cost and quality of malaria care in public and private health facilities at the primary health level in an urban community in southern western Nigeria

METHODS A pre-tested questionnaire was administered to patients attending either public or private health facilities to estimate the direct and indirect cost of accessing healthcare services. Providers cost were estimated from providers by using interviews and review of financial records to assess the total and unit cost of such services. Structural quality (adequacy of equipment and staff mix) and process quality (interpersonal relationship, use of treatment guidelines and algorithms) were assessed using structured checklist, observation and proxies such as patients’ satisfaction.

RESULTS The study showed that the unit cost of providing malaria care per month was about $12 in the public facility and $30 in private health facility while seeking health care cost about $7 for public attendees and $10 for private attendees per episode of malaria. Furthermore, a higher proportion of the patient cost consists of 65% of indirect cost while direct cost makes up about 35%. While physical access to the private and public facilities was not a problem, prolonged waiting time, poor staff mix, poor interpersonal relationship, lack of privacy and non availability of fees structures to the patients were observed problems in public facility and private facility fared better in this regard. However, both facilities performed poorly in the technical aspect of quality with the non adherence to treatment guidelines and the use of clinical algorithm in management of malaria cases.

CONCLUSION Based on the findings of the research include incorporation of public-private partnership in the on-going revitalization of the primary health care services with the inclusion of certain incentives such as improved training opportunities in the field of malaria diagnosis for health professionals at the primary level in public and private sector.

O27-37
PPM DOTS for TB control: panacea to reach the Millennium Development Goals?

P. De Paepe1, J.-P. Unger1 and W. Soors1
1Public Health Department, Institute of Tropical Medicine, Antwerp, Belgium

OBJECTIVES To assess the evidence base for the heavy promotion of PPM DOTS (public private mix DOTS) by the WHO.

METHODS A review of available publications on PPM DOTS.

RESULTS Since a few years, WHO is promoting a new modality of disease control for tuberculosis, PPM DOTS. It involves private sector providers in TB control, mainly by training them to detect cases, asking them to notify cases and providing them with TB drugs for free. The Global Plan to stop TB states that ‘introducing or scaling up PPM DOTS is an integral component of the new Stop TB Strategy and the Global Plan to stop TB’. PPM DOTS started in India, and many Asian countries followed suit. Africa then adopted it, for instance in Kenya. And recently we noticed WHO-PAHO has even started promoting PPM DOTS in Latin America. We analyse if there is sufficient evidence base for the strikingly strong promotion of PPM DOTS by WHO. WHO mentions in all its publications on PPM DOTS two Indian projects found to be cost-effective. But these two projects took place in special conditions, involving free consultations by private doctors and a medical not-for-profit college. WHO states that cure rates improve with PPM DOTS. When it states that detection rates increase, one wonders if formerly unnoticed cases give a false image. On the other hand, it is well known that deprived patients hardly consult private doctors, and certainly not in the sustained way necessary for PPM DOTS. Many countries have reached excellent results in TB control with public systems: Peru, Oman, Morocco, Syria, Chile and Vietnam are among them.

CONCLUSION Evidence seems to point towards strengthening public health systems as the most cost-effective way of tuberculosis control. Proposing PPM DOTS as an important strategy for TB control overstretches research validity.

REFERENCES

O27-38
Scale-up of services for HIV/AIDS, tuberculosis and malaria control: the contribution of global fund-suppored programs, as of December 2006

M. J. Sempala1, I. Katz1, R. Komatsu1, P. Banai1, J. Cutter1, P. Schumacher1, E. L. Koenenromp1, B. S. Schwardtlander1 and D. Low-Beer1
1Performance Evaluation and Policy Department, The Global Fund to Fight AIDS, Tuberculosis and Malaria, Vernier, Switzerland

OBJECTIVES The Global Fund, an international public/private partnership dedicated to attracting and disbursing additional resources to prevent and treat HIV/AIDS, tuberculosis and malaria, has become a primary financier of the world’s fight against these diseases. Harmonizing donor funding upstream in a common, unied fund, with programs owned by countries based on mutual accountability, it supports local efforts with US$6.8 billion committed across 136 countries. We reviewed the contribution of Global Fund-supported programs to the global delivery of key interventions, from 2001 through 1st December 2006.

METHODS Service delivery results routinely reported by grant recipients, in the context of progress review and performance-based funding, were aggregated across the portfolio.

RESULTS As of 1 December 2006, Global Fund-supported programs delivered 18 million insecticide-treated mosquito nets (ITNs); 770 000 people were receiving life-extending antiretroviral
treatment, and a joint total of 1.2 million people have been put on HIV treatment in programs to which the Global Fund and/or PEPFAR, the United States President’s Emergency Plan for AIDS Relief, are contributing. Global Fund-supported programs have also treated over two million people for tuberculosis under the DOTS strategy (directly observed treatment, short course). A range of other essential interventions are furthermore being supported, such as spraying homes of people living at risk of malaria with effective insecticides, malaria treatment, and voluntary counseling and testing for HIV. The delivery of results relies on a network of partnerships including recipient governments, donors, civil society, private sector, foundations and technical partners. The majority of Global Fund financing is aligned with country planning cycles and integrated in national programmes, which use existing national monitoring and evaluation systems, budget execution and financial reporting procedures.

CONCLUSION Countries appear to be able to use global financing, from Global Fund and other donors, flexibly and effectively to support services and systems and to rapidly scale-up key interventions for populations most in need. Challenges for the coming years include consolidation and expansion of the funding to match global need, securing longer-term donor commitments that will allow recipient programs to ensure continuity in services, and demonstration of impact on disease burden.

Leishmaniasis Epidemiology, Diagnosis and Clinical Features

O27-40
Diagnostic tests for kala-azar at primary care level: a multi-centre study of the frieze-dried DAT, rK39 strip test and katex in east Africa and the Indian subcontinent

M. Boelaert1, S. El-Safi2, A. Hailu3, M. Mukhtar4, S. Rijal5, S. Sundar6, M. Wasunna6, A. Aseffa7, J. Mburu8, J. Menten9, P. Desjeux10 and R. Peeling11

1Institute of Tropical Medicine, Department of Public Health, Antwerp, Belgium; 2Khartoum University, Department of Microbiology and Parasitology, Khartoum, Sudan; 3Addis Ababa University, Department of Microbiology, Immunology and Parasitology, Addis Ababa, Ethiopia; 4B.P. Koirala Institute of Health Sciences, Department of Medicine, Dharan, Nepal; 5Banaras Hindu University, Institute of Medical Sciences, Varanasi, India; 6Kenya Medical Research Institute, Centre for Clinical Research, Nairobi, Kenya; 7Armbruer Hansen Research Institute, Addis Ababa, Ethiopia; 8Institute of Tropical Medicine, Clinical Trial Unit, Antwerp, Belgium; 9Institute for One World Health, Divonne, France; 10WHO, Diagnostics R&D, PDE, UNICEF/UNDP/World Bank/WHO Special Programme for Research & Training in Tropical Diseases, Geneva, Switzerland

OBJECTIVES Three rapid tests for Visceral Leishmaniasis (VL), a Direct Agglutination Test (FD-DAT), a rK39 dipstick test (rK39) and a urine latex antigen test (KAtex) are candidates for field use. Diagnostic accuracy of the three tests was compared in a multi-centre study in the two most affected regions: East-Africa and the Indian subcontinent.

METHODS Between 2002 and 2005 all clinically suspect patients presenting at health facilities in five participating countries, namely Ethiopia, Kenya, Sudan, India (Bihar state) and Nepal, were prospectively recruited to reach a sample size of 310. Tissue aspirates for parasitology, a 7.5 ml venous blood sample for serological tests (5 ml in children) and a 5-ml urine sample were taken. Direct microscopic examination of tissue smear, the DAT, the rK39 dipstick and the KAtex urine test was performed. Sensitivity and specificity with 95% credible intervals were estimated by latent class analysis with Bayesian estimation methods.

RESULTS In the Indian subcontinent, both the FD–DAT and the rK39 strip test reached the target profile of >95% sensitivity and >90% specificity, but not so in East-Africa. Sensitivity of the FD DAT was high in Ethiopia and Kenya but lower in Sudan, while its specificity was below 90% in Kenya. Sensitivity of the rK39 was below 80% in the three countries, and its specificity was only 70% in Ethiopia. The urine antigen test showed moderate to very low sensitivity in all 5 countries.

CONCLUSION FD DAT and rK39 can be recommended for clinical practice in the Indian subcontinent. In East-Africa, their clinical use should be carefully monitored. More work is needed to improve existing formats, and to develop better VL diagnostics.
Abstracts of the 5th European Congress on Tropical Medicine and International Health

O27-42
Application of QT-NASBA in cutaneous leishmaniasis patients in Brazil and Suriname

W. van der Meide¹, H. Schallig², R. Lai A Fat³, L. Sabajo³, J. Guerra⁴, L. Coelho⁴, R. Hu³, G. J. Stolting⁵ and W. Faber⁶
¹KIT Biomedical Research, Amsterdam, Netherlands; ²Academic Hospital, Paramaribo, Suriname; ³Dermatology Service, Ministry of Health, Paramaribo, Suriname; ⁴Fundação de Medicina Tropical do Amazonas, Manaus, Brazil; ⁵Academic Medical Center, Amsterdam, Netherlands

OBJECTIVES Currently available diagnostic methods for cutaneous leishmaniasis (CL) have a relative low sensitivity or do not obtain reliable results for parasite quantification. One optimal detection and quantification assay would also be ideal for the monitoring of treatment schedules. Current treatments are not always successful and new drugs and treatment schemes need to be evaluated. In this study, Quantitative Nucleic Acid Sequence Based Amplification (QT-NASBA) technology has been used to detect and quantify Leishmania parasites in skin biopsy samples.

METHODS The assay is based on the detection of small subunit ribosomal RNA (18S rRNA), and 136 clinical samples were tested. The study population for treatment evaluation comprised of Surinamese (n = 24) and Brazilian (n = 43) inhabitants who were clinically confirmed with cutaneous leishmaniasis (CL) by direct microscopic identification of Leishmania amastigotes in Giemsa-stained smears, histopathological examination or PCR. Two-millimetre skin biopsies were collected before and at the end of treatment with pentamidine and meglumine antimoniate (Glucantime). All samples were tested in QT-NASBA.

RESULTS Test evaluation revealed that QT-NASBA had a sensitivity of 95% and a specificity of 100% and that a wide range of numbers of parasites in skin biopsy samples could be quantified (5–1 000 000 parasites per biopsy sample). The number of parasites in a lesion is determined before and after treatment with QT-NASBA and so far the results indicate that these data can be used to assess the outcome of treatment.

CONCLUSION In conclusion, the QT-NASBA is a highly sensitive and specific method that allows quantification of Leishmania parasites in skin biopsies. This may provide an important tool for therapy monitoring of CL patients. Supported by The Netherlands Foundation for the Advancement of Tropical Research (W96-210).

O27-43
Appearance of post-kala-azar dermal leishmaniasis (PKDL) during chronic course of visceral leishmaniasis (VL) in an AIDS patient undergoing immune reconstitution: a case report

N. Cesarani¹, A. De Bona¹, D. Ratti¹, S. Bossolasco¹, P. Cinque¹, M. Guffanti¹, A. Lazzarin¹, G. Gaiera¹ and Tropical Diseases Group
¹IRCCS H San Raffaele, Infectious Diseases, Milan, Italy

OBJECTIVES Post-kala-azar dermal leishmaniasis (PKDL) is a possible complication of visceral leishmaniasis (VL) characterised by a macular, maculo-papular and nodular rash, rarely observed in HIV infection. We describe a case of PKDL during immune reconstitution in a multi-drug resistant AIDS patient.

METHODS A 40-year-old man, HIV-positive since 1985, with a history of CMV infection, iatrogenic insulin-dependent diabetes mellitus, Hodgkin’s lymphoma, chronic bacterial otomastoiditis and chronic fungal pansinusitis, recurrent bacterial pneumonia and a complete deficiency of G6PD, multiple drug allergy, Wolff-Parkinson-White syndrome. He was diagnosed with VL in May 1996 while still naive for HIV-therapy and treated with multiple courses of liposomal amphotericin B (L-AmB). He suffered many relapses, always treated with L-AmB, started a single course of therapy with miltefosine in July 2005 and afterwards continued with maintenance therapy with L-AmB. Due to a new relapse, he started for the first time in November 2006 an association therapy with L-AmB (5 mg/kg, day 1–5, then weekly for 5 courses) + miltefosine 100 mg/daily, with a significant reduction in parasite load. Since 1998, the patient experienced multiple HAART regimens, always with poor compliance; the latter (darunavir, ritonavir and lamivudine), started in January 2006 obtained a moderate but significant immunovirologic improvement. In January 2007, multiple papular skin lesions appeared on trunk and arms; a punch biopsy on the right arm demonstrated the presence of Leishmania spp. amastigotes while low levels of parasitic DNA were also detectable in blood. We optimised the dosage of miltefosine (150 mg/daily) always in association with L-AmB (5 mg/kg every 15 days), reducing after the former to 100 mg/daily due to mild renal failure. A slight improvement of skin lesions was observed during therapy, the clinical and parasitological follow-up is still ongoing.

RESULTS The pathogenesis of PKDL is largely unknown but it seems to involve a wide number of immune mechanisms and the activity of various cytokines. The persistence of Leishmania parasites in the skin, following the apparently successful treatment of the latter VL relapse, together with the significant improvement of the HIV-infection leading to an immune reconstitution status, was probably the cause of the appearance of PKDL in this patient.

CONCLUSIONS Post-kala-azar dermal leishmaniasis appeared at a time of relative improvement in immunovirological and parasitological control of these two chronic infections and during suppressive association therapy of VL in multitreated patient. This support the importance of immune reconstitution in the pathogenesis of the disease.

O27-44
A simple method for isolation of lesion-derived amastigotes of Leishmania major from balb/c mice; employing its surface bound immunoglobulins

A. Mirjalili¹
¹Razi Vaccine & Serum Research Institute, Biotechnology, Karaj, Iran, Islamic Republic of Iran

OBJECTIVES Isolation techniques for amastigote stage of L. major are mainly based on the size of amastigote, using various filters, or the density and size using Percoll gradient centrifugation techniques. Despite the advantage of isolating a pure form of amastigote by these techniques, they have several disadvantages: (i) They are time-consuming and need 2–3 h continuous laboratory work especially filtering the suspension through different filters or making Percoll gradient tubes. (ii) They need special filters with different pore sizes (3, 5, 8 μm) for Glaser technique, and high-speed centrifugation for Percoll gradient procedure. One of the important properties of lesion-derived amastigote is thought to be the attachment of various
host proteins including immunoglobulins on the surface of amastigote. In this study, the presence of immunoglobulins on the surface of lesion-derived amastigotes was detected by Western blotting using three different peroxidase conjugated anti-heavy chain antibodies and peroxidase conjugated anti-mouse IgG antibody. Then, a new technique was developed for isolation of lesion-derived amastigotes.

METHODS This technique simply consists of a microbiological volume 12 suppl 1 pp 25–146 may 2007

In this retrospective cohort study, we included all HIV-1-infected women treated with a nevirapine containing HAART regimen at the AMC, Amsterdam, or at the EMC, Rotterdam, in whom nevirapine plasma concentrations were measured as part of routine patient care. Excluded were patients using co-medication with known interaction with nevirapine, and patients with nevirapine plasma levels <0.5 mg/l, reflecting serious non-compliance. The nevirapine plasma concentrations of pregnant patients were compared with the first available plasma concentrations of non-pregnant patients. If available, NVP plasma concentrations of the same woman during and outside pregnancy were compared. Univariate and multivariate linear regression analyses were used to identify and adjust for confounding factors.

RESULTS A total of 197 women were included in the analysis: 45 pregnant and 152 non-pregnant women. For most pregnant women the nevirapine concentration was determined during the second (44.4%) or third (42.2%) trimester. NVP concentrations were lower in pregnant women (median 5.2 (IQR 3.9–6.8) vs. 5.8 (IQR 4.3–7.7 mg/l, Mann-Whitney, P = 0.08). In 20 pregnant women, plasma nevirapine levels were also measured before or after pregnancy. The mean concentration during pregnancy was 4.8 mg/l, outside pregnancy this was 5.8 mg/l (paired T-test, P = 0.073). The proportion of patients with an adequate plasma NVP concentration (>3.0 mg/l) was not significantly lower in pregnant women (94.1% vs. 91.1%, P = 0.50). In the multivariate analysis pregnancy (B = -0.90, P = 0.046) and African descent (B = 1.13, P = 0.005) were the only parameters significantly associated with the plasma concentration of nevirapine.

CONCLUSION Nevirapine plasma concentration levels are lower during pregnancy, but this rarely results in subtherapeutic plasma concentrations. Therefore, the standard NVP dosage can be used in pregnancy. This holds especially for patients with an African ethnicity, because being of African descent probably compensates for the lowering effect of pregnancy on nevirapine concentrations.
O27-47
Rolling out HAART in relation to adherence: opportunities and challenges available to health facilities and providers in Uganda
A. W. Nakanyienda1, D. Akurut1, R. Kwasa2 and T. Ogutu3
1Busoga University, Humanities, Jinja, Uganda; 2Protecting families against HIV/AIDS, Kampala, Uganda; 3Jinja Regional Referral Hospital, Pharmacy, Jinja, Uganda

INTRODUCTION Although Uganda is a success story to emulate in sub-Saharan Africa (Green, 2003), there is growing concern about sub-optimal adherence to ART as significant barriers to HIV/AIDS care.

PURPOSE The purpose of the study was to identify factors that facilitate or constrain adherence to ART among adults in Uganda.

METHODS The study was conducted during May and June 2005 at two facilities providing ART. The bulk of the data were based on mainly qualitative methodologies. Data were mainly gathered using FGD guide, adherence tool, semi-structured interview (SSI) guide, exit interview guide, key informant interview guide, observation guide and pharmacy stock records. The use of various pre-tested instruments increased the validity of results. After transcribing and cleaning, textual data were converted to rich text format and analysed using Nudist Nvivo. Quantitative data were analysed using SPSS. A total of 200 people participated in the study including ARV users, community members and health workers. Systematic sampling was used to select the final sample. Ethical approval and permission for the study were provided by the MoH including ARV users, community members and health workers.

RESULTS Findings reveal that ARVs are provided free of charge in the facilities studied. However, related costs (including user charges and transport expenditures) as well as treatment fatigue, heavy workloads, long waiting times, side effects, hunger, discrimination and stigma and lack of appropriate counselling, were reported as obstacles to optimal adherence to ART.

CONCLUSION Consistent with its overall achievement in its approach to HIV/AIDS, Uganda has made a good start in scaling up ART and this is widely appreciated. However, Uganda appears to be moving very quickly to scale up access to ARVs without addressing critical issues such as the factors listed above. We anticipate that it will be impossible to scale up access to ART in Uganda if many patients become resistant to first-line ARVs and more expensive second-line medicines are needed instead. The above factors are already impeding adherence and some patients are dropping out of treatment as a result. Therefore, ART programmes in the country need to be designed in ways that address these factors.

Education in International Health

O27-48
Teaching health research skills in Ghana: evaluation of a course designed by in-country health professionals
1Liverpool School of Tropical Medicine, Liverpool, UK; 2Komfo Anokye Teaching Hospital, Kumasi, Ghana; 1Komfo Anokye Teaching Hospital, and School of Medical Sciences, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana; 2School of Medical Sciences, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana

BACKGROUND In developing countries, the ability to conduct locally-relevant health research and high quality education are key tools in the fight against poverty. The objective of our study was to evaluate the effectiveness of a novel UK accredited, learner-designed research skills course delivered in a teaching hospital in Ghana.

METHODS Study participants were 15 mixed specialty health professionals from Komfo Anokye Teaching Hospital, Kumasi, Ghana. Effectiveness measures included process, content and outcome indicators to evaluate changes in learners’ confidence and competence in research, and assessment of the impact of the course on changing research-related thinking and behaviour. Results were verified using two independent methods.

RESULTS Fourteen of fifteen learners gained research competence assessed against UK Quality Assurance Agency criteria. After the course there was a 36% increase in the groups’ positive responses to statements concerning confidence in research-related attitudes, intentions and actions. The greatest improvement (45% increase) was in learners’ actions, which focused on strengthening institutional research capacity. 79% of paired before/after responses indicated positive changes in individual learners’ research-related attitudes (n = 53), 81% in intention (n = 52) and 85% in action (n = 52). The course had increased learners’ confidence to start and manage research, and enhanced life-long skills such as reflective practice and self-confidence. Doing their own research within the work environment, reflecting on personal research experiences and utilising peer support and pooled knowledge were critical elements that promoted learning.

CONCLUSIONS Learners in Ghana were able to design and undertake a novel course that developed individual and institutional research capacity and met international standards. Learning by doing and a supportive peer community at work were critical elements in promoting learning in this environment where tutors were scarce. Our study provides a model for delivering and evaluating innovative educational interventions in developing countries to assess whether they meet external quality criteria and achieve their objectives.
developed, including collaborative community projects (safe garbage disposal, communal bath house, water drainage system).

Approach: We integrate family health information into the public health education materials by introducing systematic data collection in a database. This database can produce demographic data and prevalence and incidence information. Subsequently, public health education materials based on the local context can be developed. This effort facilitates integration of practice into theory and of different modules within the same curriculum. Database design: The relational database is developed with Epi-Info software as a single-user system for students. For staff a batch procedure is available to merge student files. Analysis of the aggregated data provides a general picture of the public health situation in this neighbourhood. Implementation: Basic skills in Epi-Info software existed. However, additional training was required to successfully use the database. In 2007, 60 first year students started with data-entry at household level (n = 180). In the next phase (2008) data-entry will include data on individual family members. These are used to create the new public health materials. As participating families are not yet randomly selected, generalisation of overall results needs careful consideration.

CONCLUSION Although this resource poor environment challenges our efforts, the family health programme has great potential to contribute to public health content in the medical curriculum. Developing this database stimulates students' awareness about the relation between individual health status and public health.

O27-50
Blended learning: the management of medicines in international health
R. Huss1, R. Summers1, K. Wiedenmayer2 and T. Schwering3

INTRODUCTION E-learning is any form of learning that uses electronic media for imparting content and communication. One option is web-based training with tutoring and networking of learners. This provides a unique opportunity where participants who are separated by geographical distances can learn together as a cyber group. Blended learning combines e-learning with a face to face seminar. The online course has a structure of seven thematic modules. Other parts of each module are a case scenario, exercises, a chat, a multiple choice test and several case studies. During the face to face seminar, the students develop a project proposal to improve medicine management.

OBJECTIVES 1. To present the results of external and internal evaluations for continuous course improvement. 2. To analyse the potential of peer to peer and work-based learning. 3. To describe the output of the courses in terms of trained students and their satisfaction.

METHODS An external participatory evaluation was conducted after the first intake of the online and face to face course. Internal participatory qualitative and quantitative evaluations have been organized during the next three course cycles. The course team has summarised the findings and established a plan of action for course improvement. The online course requires of each student to work on 20 problem-based individual exercises which are linked to the national context and the work environment. There are additional tasks of one virtual group exercise to develop a standard treatment guideline, seven thematic chats and the presentation of a case study. The contact seminar requires the development of a project proposal as individual and group work.

RESULTS The first course round led to an improvement of the globalization module, exercises to strengthen interactivity and the accreditation with the Troped network. Next, the topics of antimicrobial resistance and the promotion of medicines were introduced. The next round led to improved assessment criteria for the exercises. Each time the course content was updated. A total of 134 participants from 31 countries started and 92 completed the e-learning course. A total of 36 students participated in the face to face seminar. Interactive learning between the students has improved from cycle to cycle due to the exercise design and facilitation. The student satisfaction was generally high.

CONCLUSION Online learning allows students from different low and high income countries to learn from each other and to link their learning experience with concrete work problems. It requires several course cycles to develop an adequate approach.

O27-51
Strengthening public health laboratories: the integrated capacity development training program for laboratory specialists
L. Lee1, A. Pierson2, A. Berger1, M. Youssef1, S. Cognat1, C. Mathiot1, S. Menna1, G. Rodier1, P. Dubois1 and WHO Lyon Office Training Support Programme1

INTRODUCTION Laboratory systems having little involvement in surveillance activities, insufficient diagnostic capacity, and inadequate development of local resources. To address this short fall, the WHO Lyon Office designed and implemented an integrated capacity development training programme for laboratory specialists that targets the strengthening of public health laboratories for disease surveillance in resource-limited countries.

METHODS The training is based on country level assessments of the needs of national laboratories, and consists of a 2-year training programme having three training sessions incorporating into the curriculum the important elements of progress monitoring and follow-up. A major feature of the programme is that trainees spend a majority of their time applying learned skills. As a result the training offers participants immediate field experience using concepts and practices learned in the classroom – a distinct improvement over the ‘in-and-out’ training methods used in the past.

RESULTS Since 2001, 29 countries from African, Middle East and Eastern Europe regions have participated in the programme, which has proven valuable in strengthening laboratory network and external quality control, and in building local capacity. Here, we describe the main features of the training programme and findings from training data and surveys.

CONCLUSION Despite some positive progress in strengthening of national public health laboratories, resource-limited countries continue to face enormous development challenges. The data highlights the need for advocacy at the national level to ensure that adequate resources are allocated for public health laboratory development in resource-limited settings.
Quality of Care

O27-52
Human resource development and the needs of specific populations
M. Dieleman1 and A. van der Kwaak1
1Royal Tropical Institute, KIT Development, Policy and Practice, Amsterdam, Netherlands

BACKGROUND Poor performance of healthcare providers leads to low accessibility of services, inappropriate care and harmful practices. Especially the poor and marginalised groups are most affected as they have the least power to act against performance problems. Recently patients’ perspectives on quality of care has received more interest. The World Development Report 2004 mentions the importance of ‘putting the poor at the center of service provision’ to make services work. However, few studies have been conducted into healthcare needs of vulnerable groups. From 2001–2006, studies were carried out in various countries investigating patients and providers perspectives in relation to quality of care. In this paper, study findings of perspectives both by providers and patients are linked to human resource management and quality of care.

OBJECTIVES To discuss the issues and indicators determining quality of care from providers’ and patients’ perspective in order to formulate strategies for quality improvement.

METHODS Desk study of studies and literature review on performance, from providers’ and patients’ perspectives.

RESULTS Poor people define poverty as lack of income, instability, worry, shame, sickness, humiliation and powerlessness (WB, 2002). From the studies, it becomes clear that healthcare providers need to understand the impact of poverty on people’s lives and how to be responsive to their specific needs. But healthcare providers themselves face problems in their work, causing absenteeism, low motivation, job dissatisfaction and inadequate knowledge, skills and attitudes. Managers need to address the determining factors of performance problems so as to create an enabling environment. The literature shows that at health-system level changes in payment systems, decentralization, community participation and accountability mechanisms have made a positive impact. At facility level positive experiences have been gained with quality assurance interventions, performance-based incentives, supportive supervision, and improvement of leadership and management. These strategies need to be directly linked to the needs and perspectives of poor people, by their active involvement in management and accountability and through the formulation of specific indicators.

CONCLUSION Human resource management should take perspectives and needs of providers and patients into account in order to improve the performance of health services and make them more responsive to the needs of patients, in particular the poor and vulnerable. For this, innovative gender sensitive HR packages are needed.

O27-53
Definition and implementation of actors map for TB patient care (PC) in peripheral health services in Burkina Faso
R. Zerbo1, P. Huygens1, K. M. Drabo1, B. Kafando1, F. Assogba1, J. Macq2, J.-B. Ouedraogo1 and B. Dujardin1
1Centre National de Recherche et de Sûreté en Santé en Afrique (CNRS/DRF/FORESA) – Burkina Faso, Ouagadougou, Burkina Faso; 2Université Libre de Bruxelles, ESP-Politiques et Systèmes de Santé, Brussels, Belgium; 3Direction Régionale de la Santé de Plateau Central, Ouagadougou, Burkina Faso.

OBJECTIVES TB patient care (PC) of chronic pathologies, such as tuberculosis, is as much of interest for the health system actors as for research programmes in public health and social sciences. The knowledge of actors concerned by these pathologies is necessary to take efficient collective and concerted measures within the framework of PC and disease control. This thinking is relevant for the improvement of health services organization in peripheral services that are generally located in rural or semi-urban zones.

METHODS A socioanthropological exploratory diagnostic study has been made by the FORESA project in the sanitary districts of Bousse, Ziniaré, and Zorgho belonging to the Sanitary Region of the Central Plateau in Burkina Faso. In total, 127 individual interviews and 24 focus groups have been realized between February and April 2006. The data qualitative analysis has been realized using ATLAS.ti.

RESULTS The exploratory study analysed patients’ therapeutic attitudes and B. Dujardin.

METHODS Desk study of studies and literature review on human resource management should take perspective of care providers and patients are linked to human resource management and quality of care.

RESULTS Human resource management should take perspective of care providers and patients are linked to human resource management and quality of care.

CONCLUSION Human resource management should take perspectives and needs of providers and patients into account in order to improve the performance of health services and make them more responsive to the needs of patients, in particular the poor and vulnerable. For this, innovative gender sensitive HR packages are needed.

O27-54
Introduction of improved quality management in basic reproductive health services: an example from Southern Sudan
J. Bitzer1
1Difaem – German Institute for Medical Mission, Tübingen, Germany

OBJECTIVES The purpose of this study was to introduce quality management (QM) in Basic Reproductive Health Services and to assess the value of QM procedures. The hypothesis was that ‘QM’ procedures influence the health care outputs positively.

METHODS This was a prospective intervention study. The study sample consisted of 94 health staff including TBAs of a Primary Health Care Programme at southern Sudan. Our methods included document review, statistical analyses of health information system data, direct observation, structured interviews with staff and patients, key stakeholders interviews and focus group discussions as well as capacity building for Sudanese staff. After development and testing of an appropriate QM Model, we measured changes in the health care processes and outputs. The study was conducted between March 2004 and June 2006.

RESULTS The number of standards increased significantly as well as the utilization of the services. The organizational access was improved through reorganization of different services. The relevance to need could be improved through the implementation of delivery services at one remote health centre. Furthermore with a reduced total project budget more people are served now. The human resources have been identified as the most important factor.
O27-55 Effectiveness of supportive supervision in improving the performance of National Immunization Programme (NIP) in Georgia

N. Zakareishvili¹, M. Djibuti¹, N. Rukhadze¹, G. Gotsadze¹, A. Zoide¹ and J. Cohen²
¹Caritio International Foundation, Tbilisi, Georgia; ²University of Toronto, Faculty of Pharmacy, Toronto, Canada

OBJECTIVES The objective of the proposed research was to document the implementation and effectiveness of a model of ‘SUPPORTIVE’ supervision in improving performance of the immunization programme at the district level in Georgia. Hypothesis was tested if as a result of the introduction of the intervention package, there will be detectible improvement in the performance of immunization programme.

METHODS The project has designed and tested a set of interventions to ensure that personnel of the Center of Public Health carry out their supervisory activities through personal contact on a regular basis to guide and support supervised staff responsible to provide immunization services at community level to become more competent in their work. The package of interventions is being implemented within 15 districts selected randomly out of nation’s 67 districts. Another 15 districts were selected to serve as controls. Both study and control districts were selected randomly matched by immunization programme performance indicators, geographical location, population density etc. The effectiveness of the intervention package was assessed with a post-pre quasi-experimental research design. Measurements were assessed at the baseline and end of the 1 year intervention. Improved service delivery outcome indicators for the effectiveness of the intervention package pertained to immunization coverage, contraindications/refusals rate, and vaccine wastage. Individual staff level outcome indicators pertained to motivation, knowledge and attitude towards various components of Human Resource Management including supportive supervision. Quantitative as well as qualitative data analysis was done. The primary analysis produced descriptive statistics and compared the intervention and control districts, pre- and post-test. Univariate analysis compared improved service delivery and individual-level outcomes pre/post-test within intervention districts, as well as between treatment groups. Subsequently, a more robust analysis was performed using multivariate regression to account for potential confounders. Qualitative data from the health facility and CPH staff focus groups were analysed.

RESULTS The supportive supervision was successfully implemented, supportive supervision functioned as intended and significant improvements in the performance of immunization programme occurred after the implementation of the intervention. All performance indicators (Immunization coverage, contraindication/ refusals and vaccine wastage) for National Immunization Programme within the study districts have improved substantially and research details will be presented.

CONCLUSION Supportive supervision is an important tool in improving Health Workers performance, which have also been proved in our study for the National Immunization Programme.

O27-56 Measuring quality from clients’ perspectives – an experience from rural India

A. Sinha¹, D. K. Pal², P. Kasa³, R. Tiwari¹ and A. Sharma²
¹R D Gardi Medical College, Community Medicine, Ujjain, India; ²Department of Community Medicine, NSCB Medical College, Jabalpur, India

OBJECTIVES 1. How can we evaluate quality of selected reproductive and child health services? 2. What are the clients’ perspectives of quality of these services in a rural district of Central India?

METHODS A descriptive (Cross-sectional) population based study at village level in rural setting. Participants: 840 clients, entry criteria – all eligible users of reproductive and child health services from government set-up; exclusion criteria – unwillingness to participate and those who violate the entry criteria. Clients were interviewed with the help of a structured proforma and a unique scoring system was developed to quantify quality of care. Indicators for coverage and Quality of Care for various reproductive and child health services, Client Satisfaction.

RESULTS The quality of evaluated services ranged from very poor to poor despite good coverage at certain points.

CONCLUSION The observations showed a huge gap between coverage and quality of the selected services and highlighted the associated key operational issues. One of the key issues was client satisfaction with the health care provider which needs to be addressed at all possible levels.

Reducing Health Related Stigma

O27-57 Stigma and social participation among people with disability in South Sulawesi, Indonesia

W. H. van Brakel¹, I. van der Vliet², J. Schuller², S. Siwan³, D. Dahlan³, K. Beise¹, L. K. Wardhant³, S. Asapa⁴, M. van Elteren⁵ and Rapid Disability Appraisal Study Group
¹Royal Tropical Institute, DEVILeprosy Unit, Amsterdam, Netherlands; ²VUMC, Amsterdam, Netherlands; ³Department of Public Health, Hasanuddin University, Makassar, Indonesia; ⁴Netherlands Leprsy Relief Indonesia, Makassar, Indonesia; ⁵Pasit Latihan Kusta Nasional, Makassar, Indonesia; ⁶Provincial Health Office Sulawesi Selatan, Makassar, Indonesia

OBJECTIVE To assess perceived stigma and social participation among people with disability in South Sulawesi, Indonesia. Data were collected as part of a study to validate a new Rapid Disability Appraisal (RDA) toolkit.

METHODS A cross-sectional household survey was conducted in five rural sub-districts. Door-to-door screening was carried out, using a 10-question disability screening questionnaire. In households, where a person with disability (PWD) was found, interviewers asked permission to interview this person. Informed consent was asked before the RDA interview. The RDA toolkit comprises a series of items on personal and environmental factors, a child disability questionnaire, the WHODAS 12-item scale to measure activities, the 18-item Participation Scale and the 3-item Jacoby perceived stigma scale. Besides the RDA interviews, in-depth interviews and focus group discussions were held with PWD as well as community members. Only the results of the RDA instruments are included in the current report. Profiles of participation and perceived stigma score are presented and compared with scores from community controls from the same
villages. Multivariate logistic regression was done to study factors associated with participation and stigma.

RESULTS A total of 331 PWD and 50 controls were included in the study. The median age was 41 and 37, respectively; the percentage women was 52% among PWD and 64% among controls. Despite the higher percentage among the controls, the median number of years of study was 2.5 among PWD and 6 among controls. Median monthly family income was Rp 200,000 less among PWD (40%). According to the Participation scale, 60% of PWD had participation restrictions, of which 27% were more severe. Among PWD, 21% reported to feel that people felt uncomfortable with them, treated them as inferior or avoided them because of their disability. Multivariate analysis showed three factors that increased the risk of participation restriction, activity limitation, living in a temporary shelter, and stigma, while being married and having primary education decreased this risk. People were more likely to perceive stigma if they had participation restriction, activity limitation, non-formal education (as opposed to being illiterate), and when they were not married.

CONCLUSIONS Participation restrictions and perceived stigma were common experiences among people with disability in South Sulawesi, Indonesia. People with disability had much less education and a much lower family income and were much less likely to be employed or married. As a result, they suffer even more hardship than other poor people in the region.

O27-59 Protection of human rights and mainstreaming of HIV-positives: a case study
D. Kahiresset
Rural Organisation for Poverty Eradication Services (ROPEs), Non Governmental Organisation, Bangarupallam, India

Currently, there are 5.2 million HIV-positives living in India. India has the second highest number of HIV-positives in the world. The Indian Constitution guarantees certain fundamental rights viz. right to work, social security, health, equality between men and women, privacy, education and information, marry and found a family, liberty, freedom of movement and the right not to be discriminated. But, all the HIV-positives in India are denied most of these human rights irrespective of caste, creed, colour, religion, social age. This human rights deficit is increasing the spread of HIV infection among the marginalized groups. They are denied their basic necessities. They are not permitted to work. Thus, they are finding it difficult to eke-out their livelihood. HIV-positive children are also denied these basic rights. In the present paper, an attempt is made to explain how a Non-Governmental Organization (NGO) has succeeded by its strategies in protecting the human rights of HIV-positives and also bringing them into the mainstream.

OBJECTIVES Eliminate all types of stigma and discrimination against the HIV-positives and restore fundamental rights guaranteed by the Constitution bring all the HIV-positives into the mainstream, and make all the HIV-positives to live happily and peacefully like any other Indian citizen.

METHODS The present programme was initiated by an NGO with the help of trained social workers in 25 villages located in Andhra Pradesh, where there were 403 HIV-positives (41 children and 362 adults) who were denied their human rights and discriminated at all levels. Programme Interventions: Information, education and communication on HIV and human rights; distribution of literature on HIV and human rights; group discussions; community education and mobilization; one-to-one meetings; meetings; workshops; enactment of plays; folk media; social support; involvement of government officials; and legal aid.

RESULTS As a result of the concerted efforts of the NGO, the HIV-positives are able to enjoy now all the fundamental rights without any discrimination in hospitals, schools, temples, work place, community etc. They now enjoy social security, equal pay for equal work, etc. They are now able to marry and found a family. Thus, much of the discrimination against HIV-positives is eliminated in society and they are brought into the mainstream. Lessons learned: The interventions used in this study would go a long way not only in restoring/protecting the human rights of HIV-positives but also help to bring them into the mainstream to lead a peaceful and happy life, wherever HIV-positives are denied their rights.
O27-60
Subverting STIs and stigmatization: the ANEDS as a solution to STI transmission among and stigmatization of intravenous drug users
M. Daniel1
1Oxford University Department of Public Health and Primary Care and The STRIDE Charitable Fund, Inc., Cambridge, MA, USA

OBJECTIVES This study aimed to quantify the extent and range of stigma borne by intravenous drug users (IDUs) and their friends and family as a result of drug-use, HIV, and hepatitis C (HCV) status. The study also examined the projected impact and acceptability of the automated needle-exchange and disposal system (ANEDS), a machine designed in concept by the author which is intended to increase access to clean needles and syringes. Currently, access is limited partly due to limited hours of and proximity to Needle and Syringe Exchange Programmes (NSEPs) but primarily due to the fact that IDUs fear discriminatory repercussions of being seen by the community at these centers and thus 70–80% of them do not use the NSEPs. This significantly contributes to rates of HIV and HCV transmission due needle-sharing.

METHODS A prospective interview-based study was conducted with a respondent-driven sample of IDUs (n = 100) and friends and family of IDUs (n = 200). Data were supplemented with a key informant study of a random sample of NSEP workers (n = 50) and community perceptions were judged by a random sample (n = 50) of the general community. A projected-impact model for the ANEDS was conducted using data available from the Manipur State AIDS Control Society.

RESULTS Data revealed nearly universal stigmatization and discrimination against IDUs on the basis of drug use and HIV status. Discrimination occurred across a broad range of activities causing loss of job, salary, school admission or place of residence, impaired marriageability, and social ostracism sometimes escalating to demonstrative violence. Importantly, this study reveals that such stigma, particularly which impacts social interactions such as marriage, extends to relatives of IDUs and HIV-positive individuals. There was no data reflecting stigma for HCV status and concurrently limited knowledge of the disease, suggesting an important point of sensitive education-based intervention. Data from the projected-impact study for the ANEDS revealed that an intervention involving the placement of 900 machines in Imphal, Manipur’s capital city, such that IDUs would not have to travel more than 200 m to exchange injecting equipment, achieves a benefit-cost ratio of 250:2:1.

CONCLUSIONS IDUs and their friends and family suffer wide-ranging and significant discrimination from associations with drug-use and HIV though not with HCV, presumably due to demonstrated limited knowledge of the disease. As this very real stigma prevents use of NSEPs and consequently increases needle-sharing, a public health imperative exists to seek life- and cost-saving interventions such as the ANEDS.

O27-61
Migrant workers and health risks: Bangladeshi migrant workers in Hong Kong and Malaysia
A. Ahsan Ullah1
1City University of Hong Kong, Asian and International Studies, Hong Kong, China

Migrant workers are always vulnerable to various forms of discrimination with varied degrees at the country of destinations, which worsens when they are tagged with ‘illegal’. The study explores the extent of health problems of migrant workers and the plan to visit a doctor. Questionnaire survey was done on 126 migrant workers from Hong Kong and Malaysia. An overwhelming majority of the migrants suffered from diverse health problems and only a few of them visited clinics. Majority had unsafe sex. Most of them stayed in unhygienic environment. A significantly higher percentage (P < 0.000) of the HKRs visited clinics compared with the MRs. There is a significant difference (P < 0.503) in the sufferings of STDs between two groups. Data further show that migrants in Malaysia had suffered from diseases with a significantly higher frequencies (P < 0.003) compared with the HKRs. However, there is significant difference (P < 0.503) in the sufferings of STDs between these two groups of migrants. The lack of family care, and the estrangement from the family have exposed them to the forms of diseases, especially the STDs. However, the overall condition of the HKRs is better than that of the MRs. This might be linked to the income benefits of the HKRs which was significantly higher (P < 0.000) compared with the MRs.

Health Related Stigma

O25-14
Immigration, health and scientific discourse in Spain
L. Otero1, T. Blasco1 and B. Sanz1
1Instituto de Salud Carlos III, Nacional Center of Tropical Medicine, Madrid, Spain

OBJECTIVE The aim of this study was to approach the discourse developed in the scientific literature produced by Spanish researchers regarding immigrants. The hypothesis is that these studies do not consider factors that are important in order to know the real health situation of the immigrant population.

METHODOLOGY These data are part of a qualitative and quantitative research to analyse the following categories of discourse: 1) Study population; 2) Age; 3) Sex; 4) Gender; 5) Ethnic group; 6) Socio-economic situation; 7) Disease; 8) Culture.

RESULTS A total of 146 papers were reviewed. The diseases that were mostly associated with the immigrant population were infectious diseases (tuberculosis, HIV) The majority of the papers dealt exclusively with adults (72.7%); the data distribution by sex is used only in 5.8% of the papers; articles that have a gender perspective are only about prostitution or abortion; socio-economic factors (residence permit, housing, etc.) were considered in 19.1% of the studies; the category ‘ethnic group’ is never used; immigrant populations are classified according to the region of origin; cultural differences to explain health inequalities are used in 30.1% of the papers.

CONCLUSIONS The papers we analysed respond mainly to health problems that have a potential effect in public health. There is an important absence of research related to the health of immigrant children; gender perspective should be included in the studies in order to have more information about women’s health and to avoid the inequity in health due to gender discrimination. Socio-economic factors related to immigrant health should be analysed more often, and health studies should offer answers to improve the health of the population as a whole. Cultural differences should not be used as the only factor to explain health differences between the immigrant and the native population.

Harmonization and Global Partnerships: The Changing Face of Aid Architecture?

O27-62
Achieving the health Millennium Development Goals (MDGs) through improved health financing and policy
F. Goodwin1
1European Public Health Alliance, Brussels, Belgium

OBJECTIVES The European Network for Global Health brings together 14 European NGOs to press for a greater European
contribution to achieve the Millennium Development Goals (MDGs), particularly the three health related MDGs. The first annual report of the network will highlight the gap in funding between Europe’s commitments and its actual spend on the health sector in developing countries. Future work of the network will build upon this initial contribution of the quantity of finance and extend it with analysis of the quality of Europe’s development assistance.

METHODS The first report of the network estimates the gap between the commitments of European governments and their financial contributions to securing those commitments. The next 4 years of the project will build upon this first assessment of the financing of development cooperation. Future analysis will also examine how this cooperation should change so as to better serve the attainment of the MDGs. This focus on improving the quality of assistance will add to the networks continued call to deliver the quantity of assistance previously promised.

RESULTS The first report of the network will underscore the continued gap between European government’s commitments and their expenditure on health in developing countries. The need to address this gap will be a feature of the networks message over the coming years. In addition, three issues have been identified as crucial components to improving the quality of development cooperation to attain the MDGs: strengthening health systems; research and development needs and gender issues. Working groups have been established within the network to facilitate the analysis in each of these areas.

CONCLUSIONS These three working groups will seek to liaise with those active in these three key areas. For 2007–08 priorities for work will focus on defining the most essential elements of health systems and how these can be strengthened. In addition the identification of key areas for investment in research and development for new products to address diseases of poverty will be central to the work of the ENGH in 2007–08. The network will therefore look to forge alliances across the research community to facilitate its work in general and the output of the research and development working group in particular.

O27-63 Feasibility of SWAp in the post-Soviet context – evidence from Tajikistan
T. Mirzoev1, J. Newell1 and A. Green1
1University of Leeds, Nuffield Centre for International Health and Development, Leeds, UK

BACKGROUND External aid forms a major contribution towards health systems development in many developing countries. A former soviet republic, Tajikistan, is not an exception. The country, experiencing gradual transition from relief to development phase, is in search of an adequate response to lack of coordination of external aid and fragmentation of health systems development. Sector wide approaches (SWAp)s emerged in the 1990s as one option to increase the effectiveness of external aid to the country and to develop government leadership of the health system development process. Health sector SWAp{s} are implemented in a number of developing countries including those in transition, but very little is known as to whether approach is feasible in the former soviet context.

OBJECTIVES To assess the feasibility of health SWAp in the former soviet context using the context of Tajikistan as a case study and focusing on the main elements or key prerequisites for implementing SWAp in the health sector.

METHODS Analysis of secondary data (both published and unpublished) complemented by observation of series of meetings and semi-structured interviews with key informants from central government and donor organisations.

RESULTS Tajikistan has been one of the most neglected republics both economically and politically. Furthermore, political crisis and sharp economic decline in mid 1990s threw the country several years back in its development. Currently there is no solid capacity for leading the sustainable partnership with development partners and Tajikistan does not appear to fulfil most prerequisites for implementing health SWAp, namely: robust health policy, expenditure and institutional frameworks, sustainable dialogue with development partners, harmonised implementation framework and agreed operational procedures.

CONCLUSION At a first glance, health SWAp is not feasible within the current context of Tajikistan. However, the implementation of SWAp is usually preceded by several years of capacity building and maintaining the dialogue with development partners. The Tajik government should make an appropriate decision and initiate dialogue with development partners well in advance. It appears that the other former soviet republics, in contrast with Tajikistan, do not have major barriers for implementing health SWAp. Health policy development and analysis is a core for government-donor coordination and one feasibility of adapting the concept of SWAp to the post-soviet context is through implementing a limited number of its elements.
quality of care) are two factors that risk to cause the demotivation of SWAp stakeholders. Study supported by a grant from the Belgian Co-operation Directorate through a research group (GRAP-SWAP) for Health Sector Wide Approach in Sub-Saharan Africa.

**Q27-65**

The public health sector in the 21st century: putting health systems strengthening in perspective

J. Koot and R. Peeperoor

1Public Health Consultants, Amsterdam, Netherlands; 2Royal Netherlands Embassy, Dar es Salaam, Tanzania, United Republic Of

**OBJECTIVES** The paper discusses developments in the health sector in Sub-Sahara Africa, especially comprehensive and selective primary health care, health sector reforms and global health initiatives. The paper puts these developments in the wider context of government reforms, decentralisation and government financing. The paper defines challenges and steps towards effective management of health services, and health systems strengthening in particular.

**METHODS** The paper analyses mechanisms for health services management, like devolution/deconcentration, privatisation, delegation and contracting. Factors for success and failure are identified. Human resources management and human resources development in health are discussed in the wider context of government policies. The paper studies practices of financing and budgeting in health, in relation to government and donor policies.

**RESULTS** Many studies and policy documents look at the health sector in isolation, considering the Ministry of Health as the principal actor, determining policies and practices in health service delivery. In reality, there are many other players in and outside the health sector, who have as much or even more influence and impact on service delivery: other ministries, local government entities, training institutions, private providers, donors and non-governmental organisations. The ‘black box thinking’ about health systems has confused, rather than clarified the debate. The authors argue that critical analysis of roles and responsibilities, especially of those players outside the health sector, is necessary to guide action and break away from the circular debate about selective vs. comprehensive health care or, in today’s discourse, disease control vs. health systems strengthening.

**CONCLUSION** Health systems strengthening starts with clear demarcation of roles and responsibilities of the various players in and outside the health sector. The core businesses of the Ministry of Health must be defined as policy making and planning, legislation and regulation, quality assurance, monitoring and evaluation, external relations and fund raising. The ministry must take up its role as initiator, communicator and, where necessary, controller. The ministry should lift the claim to be the main implementer, and rather seek effective collaboration with players that are better placed for that role. The paper proposes mechanisms for such collaboration.

**Q27-66**

Has GAVI changed aid donor responses? The case of Norway

K. Sandberg

1University of Oslo, Section for International Health, Trondheim, Norway

**OBJECTIVES** A study of GAVI efforts to introduce new vaccines from 1999 to 2005 has found that donor countries went from being reluctant players on the outskirts of the Children’s Vaccine Initiative in the late 1990s to become strong supporters of GAVI. Given that the objectives of the two initiatives are fairly similar, what can account for this change? This led to questions about how internal political processes regarding global health initiatives play out among various domestic constituencies in donor countries, determining the official response.

**METHODS** This is an offshoot from a qualitative study of the formation and effectiveness of GAVI, based on 21 interviews with decision-makers from GAVI partner agencies, donor country representatives, observers, and a review of published and grey literature. The findings are also based on public statements and observations of interactions between domestic constituencies at GAVI-related meetings in Norway.

**RESULTS** The data show a divide between the political leadership which initiated support to the alliance, and the bilateral aid agency set to administer it. The political leadership has emphasized the importance of being a player in global initiatives that pioneers new aid mechanisms. The bilateral aid agency maintains weight on the perspective from recipient countries, ongoing sector processes and support for primary health care. They are often named the ‘traditionalists’ in aid delivery. At the same time, universities and other research institutes involved with vaccine development have emphasized GAVI’s potential as a vehicle for new vaccines and immunization-related technologies. The bilateral aid agencies became key representatives of donor countries within GAVI once it was established. They have been influential, for instance in developing the health systems strengthening investment case. In this way, the bilateral aid agency initiated a modification of GAVI’s approach, suggesting a change in its position on global vaccine initiatives rather than a change in policy response.

**CONCLUSION** The data suggest that donor countries are not unitary actors, but an arena where objectives of global initiatives are negotiated and even contested. There are nevertheless limitations to the data, since they emerged as a spin-off of a larger study from a group of informants selected to represent a broader topic. Still, it can serve as an exploratory study, and a basis for discussing the possibilities for doing research on similar issues related to aid architecture in recipient countries with a focus on the negotiated response of health aid actors and recipient country governments.

**Mental Health**

**Q27-67**

Transition of adult mental health services in Ukraine, 1991–2006

O. Golichenko, P. de Graaf, W. van de Graaf and B. Gerretsen

1ICF ‘International HIV/AIDS Alliance in Ukraine’, Kyiv, Ukraine; 2European Forum for Primary Care, Utrecht, Netherlands; 3Consultant, Amsterdam, Netherlands; 4Royal Tropical Institute, Coordinator NTUC-MIH, Amsterdam, Netherlands

**OBJECTIVES** The purpose of the paper is to analyse the process of transition of mental health services (hereinafter MHS) from hospital-based to community-based services in Ukraine from 1991 to 2006.

**METHODS** Literature review (in English, Ukrainian and Russian); eight interviews with international stakeholders based in the Netherlands and Ukraine; e-mail communication with experts with long-term experience in the field of mental health in Ukraine and NIS region; case-study of transition of MHS in Lithuania. Analytical frameworks used in the thesis can be divided into three groups – theories on MHS delivery, framework of MHS analysis and theories on the process of transition from community-based to hospital-based model of MHS.
RESULTS Indicators of transition developed and measured: 1991–2001 hospital level, 1991–2000 community level, 2001–2006 hospital level, 2001–2006 community level are periods and levels of transition. There have been no changes from 1991 till 2006 in the structure of MHS delivery on system level, however, there are some changes on the grassroots and hospital levels, in the form of pilot community care services projects. The reasons of slow transition are described. Mental health reforms in Central Europe and Baltic states are more advanced than in Ukraine.

CONCLUSION Slow progress in the change of MH service delivery to a system which takes into consideration the psychological and social dimensions of mental health is happening because there are two processes of transition taking place: on community level, during the first period of transition (1991–2001), and hospital level, during the second period of transition (2001–2006), and the link between two levels of transition is very weak. Existing analytical frameworks on MHS and process of transition suggest that transition of MHS is the result of the interplay of internal and external factors which originate from internal and external sources on the levels of the society, state institutions and international organizations. Stewardship of the Ministry of Health of Ukraine is needed for a sustained development of MHS. Thesis recommends to develop community care centers at health system level and appropriate human resources for it as well as to integrate MHS at primary health care in order to stimulate the development of the process of transition in Ukraine. There is a need to develop partnerships on the level of communities, countries and intergovernmental mechanisms with countries of Central Europe, Baltic states and Ukraine in order to enhance the development of community MHS in Ukraine.

O27-68
Mental health scenario in Orissa
H. Dutta1 and B. Panda1
1Orissa Voluntary Health Association, NGO, Bhubaneswar, India

OBJECTIVES 1. To identify socio-economic and psychosocial factors leading to migration. 2. To assess whether migratory population have more mental health problems than general population. 3. To identify causes of mental health problems among the migratory population

METHODS Multistage Stratified Random Sampling method would be adopted. The three districts of Khurda, Ganjam and Bolangir were selected as these three districts have highest number of migratory population. The sample size was drawn using proportional allocation in the selected districts. We have interviewed total of 547 samples in Ganjam, Bolangir and Khurda districts of Orissa. We have also interviewed key mental health care providers, key NGO functionaries, and taken few case studies to supplement the information gathered through schedules. We have interviewed recently returned Interstate migrants at their places of origin. Intrastate migrants were interviewed in their place of migration. General population was interviewed at their normal place of residence.

RESULTS • 24.35% and 24% of respondents among interstate and intrastate migrants are currently ill while among general population 21.79% are currently ill. So percentage of currently ill respondents is more in case of migrants than for general population. • Among currently ill persons 49.22% have fever while 14.06% have gastric. Few people are also suffering from rheumatism, malaria, diarrhoea, skin diseases, tuberculosis, hydroxyl, headache, anaemia, typhoid, hernia, jaundice, stone in kidney, filaria, blood pressure, and piles. • The mean GHQ scores for interstate migrants, intrastate migrants and general population is 3.197, 2.406 and 2.123 respectively. Thus the mental health status of the interstate migrants is the worst among the three groups. The mental health status of intrastate migrants is worse than the general population but better than that of the interstate migrants. • 35.75% of interstate migrants have GHQ score above 3 while 23.83% of them have GHQ score above 4. • 29.71% of intrastate migrants have GHQ score above 3 while 15.43% of them have GHQ score above 4.

Treatment of Malaria: ACT II

O27-69
Efficacy, safety, and tolerability of dihydroartemisinin-piperaquine (Arteki®) for the treatment of uncomplicated falciparum malaria in the Peruvian Amazon region
A. Erhart1, U. D’Alessandro1, A. Bernasoni1, T. Grande1, D. Gamboa2 and A. Llanos-Cuentas3
1Institute of Tropical Medicine, Parastisology, Antwerp, Belgium; 2Institute of Tropical Medicine ‘Alexander von Humboldt’, Parastisology, Lima, Peru

OBJECTIVES To compare the efficacy of dihydroartemisinin-piperaquine with mefloquine-artsunate, the current first line treatment in Peru.

METHODS A randomised open label clinical trial was carried out between July 2003 and July 2005 in a rural area south of Iquitos, the largest city of Peruvian Amazon region. A total of 522 patients with P. falciparum uncomplicated malaria were recruited, treated (260 on mefloquine-artsunate and 262 on dihydroartemisinin-piperaquine) and followed up for 63 days.

RESULTS PCR-adjusted adequate clinical and parasitological response was extremely high for both drugs (99.2% for mefloquine-artsunate and 97.7% and for dihydroartemisinin-piperaquine) [RR: 0.98, 95% CI (0.96-1.01), P = 0.28]. No early treatment failure was observed. Gametocyte clearance was faster in the mefloquine-artsunate group (28 days) than in the dihydroartemisinin-piperaquine (35 days). However, dizziness, anorexia, insomnia, and anxiety were significantly higher in the mefloquine-artsunate group (P < 0.01).

CONCLUSION Dihydroartemisinin-piperaquine is as effective as mefloquine-artsunate in treating uncomplicated P. falciparum malaria but it is better tolerated and much cheaper (1 USD) than mefloquine-artsunate (18.65 USD on the local market). Therefore, it should be considered as a potential candidate for the national antimalarial drug policy in Peru.

O27-70
Efficacy and safety of artesunate plus amodiaquine (AS+AQ) in routine use for the treatment of uncomplicated malaria in Casamance, Southern Senegal
P. Brasseur1, P. Agramame2, O. Gaye2, M. Vailland3, W. R. J. Taylor4 and P. Olliaro4
1IRD, Dakar, Senegal, Dakar, Senegal; 2Laboratoire de Parasitologie-Mycologie, CHU Amiens, Amiens, France; 3Faculté de Médecine, Université Clermont Anta Diop, Dakar, Senegal; 4CRP-Santé, Luxembourg, Luxembourg; 5Oxford University Clinical Research Unit, Hanoi, Vietnam; 6UNICEF/UNDP/WB/WHO Special Programme for Research & Training in Tropical Diseases (TDR), Genève, Switzerland

BACKGROUND There are no data on the long term use of an artemisinin combination treatment in moderate or high transmission areas of Africa.

METHODS Artesunate plus amodiaquine (AS+AQ) was used to treat slide proven falciparum infected patients of all ages in the Oussouye district, Casamance, Senegal over 6 years (2000–2005). Efficacy, by Kaplan Meier survival analysis (n = 966), and safety
(adverse event rates, haematology and biochemistry) were determined over 28 days. Loose tablets dosed on bodyweight were used during 2000–2003 (n = 731) and a commercially available co-blister was used during 2004–2005 (n = 235). Treatment was supervised during 2000–2004 and unsupervised in 2005.

**RESULTS** Annual crude (non-PCR corrected) cure rates remained stable over the study period (range 88.5–96.7%); mean 94.6% (95% CI 92.9–95.9). There was no statistically significant difference between years, products used, or how it was administered. All 36 LTFs occurred in patients under 16 years of age of whom 20 were aged between 6–10 years. Using a Cox proportional hazard model, the contribution to hazard of failure was borderline for year (P = 0.06) but significant for the total daily dose of AS (P = 0.004, hazard of failure = 0.993 (0.988; 0.998) and for year 2004 vs. reference year 2000 (P = 0.003, hazard ratio = 4.496, 95% CI 1.661–12.168). Nine, co-blister treated patients (9.9% of all patients) withdrew because of drug related adverse events; seven had gastrointestinal complaints of whom two were hospitalised for vomiting. By day (D) 28, the mean total bilirubin (n = 72), AST (n = 94) and ALT (n = 95) values decreased. Three patients had D28 AST/ALT values >40 and <200 IU/L. Changes in white cell counts were unremarkable (n = 87).

**INTERPRETATION** AS+AQ in combination was highly efficacious and well tolerated in this area and justifies the decision to use it as first line treatment. Long term monitoring of safety and efficacy should continue with this valuable ACT.

**O27-71**

**A randomised trial comparing efficacy and safety of artemesunate–amodiaquine given as combined or individual therapies for the treatment of acute, uncomplicated Plasmodium falciparum malaria in children in Burkina Faso**

S. B. Sirima1, A. B. Tono1, A. Gansane1, A. Diarra1, A. Ouedraogo1, A. T. Korate1, C. Morgan1, J. R. Kiechel1 and R. W. Taylor2

1Centre National de Recherche et de Formation sur le Paludisme, Osagadougou, Burkina Faso; 2Cardinal Systems, Paris, France; 3Drugs for Neglected Diseases Initiative (DNDi), Geneva, Switzerland; 4Oxford University Clinical Research Unit, Oxford, UK

**OBJECTIVES** Increasing drug resistance to monotherapy malaria treatments has led to the WHO recommending artemisinin based combination treatments as first-line treatment. The loose combination of artemesunate and amodiaquine as a suitable treatment for malaria, were treated for 3 days with a single dose of artemesunate (AS), amodiaquine (AQ) and amodiaquine (AQ, 67.5 mg) (AS/AQ: Coarsucam®) to the individual drugs administered together (AS 30 mg + AQ 153 mg: Artesunax® + Flavoquine®). The dosing regimen was defined according to the patient’s age and weight at inclusion.

**METHODS** This randomised, controlled, open-label, parallel-group study compared the efficacy and safety of 3 day regimens of an oral fixed-dose combination therapy of artemesunate (AS, 25 mg) and amodiaquine (AQ, 67.5 mg) (AS/AQ: Coarsucam®) to the individual drugs administered together (AS 30 mg + AQ 153 mg: Artesunax® + Flavoquine®). The dosing regimen was defined according to the patient's age and weight at inclusion.

**RESULTS** A total of 750 patients aged between 6 months and 5 years old were enrolled in the study, 375 in each treatment group, of whom 626 (83.5%) completed the study. The primary efficacy endpoint was the polymerase chain reaction corrected parasitological cure rate at day 28. In the Per protocol data set this was found to be the same (92.1%) in both treatment groups and the non-inferiority of AS/AQ compared with AS+AQ was shown to be non-inferior and higher cure rates. The PCR-corrected parasitological cure rates at day 28 were 95.7%, AS/AQ vs. 96.0%, AS+AQ, with a 90% confidence interval for the difference of (-0.023, 0.028) AS/AQ was shown to be non-inferior to AS+AQ in terms of all secondary efficacy endpoints measured including the time to treatment failure and the presence of parasitaemia, gametocytes and fever. There was no significant difference in the number of patients reporting treatment-emergent adverse events in each group (33.9% AS/AQ compared with 37.2% AS+AQ, P = 0.40).

The proportion of these adverse events thought to be possibly or probably related to the study drug was only 2.4% AS/AQ vs. 1.9% AS+AQ. Biochemical and haematological profiles were in conformity with current knowledge of short-term amodiaquine and artesunate treatment tolerability.

**CONCLUSION** The fixed dose combination performed well with similar efficacy and safety to the loose combination. These data support the use of this new fixed dose combination of artesunate and amodiaquine as a suitable treatment for Plasmodium falciparum malaria.

**O27-72**

**Open-label, stratified study on the efficacy, safety and pharmacokinetic characteristics of two paediatric formulations of artesunate/mefloquine (Artequin®) in African children with acute uncomplicated P. falciparum malaria**

M. K. Bouyou-Akotet1, M. Ramharter2, M. Masika Mafumbi3, S. T. A. Gagnon2, M. Pamba Mphindou2, M. A. Missinou2, S. Issifou2, J. L. Heidecker5, N. Cambou1, P. W. Kremers6 and M. Kombo4

1Faculty of Medicine, Université des Sciences de la Sante, Department of Parasitology-Mycology, Libreville, Gabon; 2Albert Schweitzer Hospital, Medical Research Unit, Lambarene, Gabon; 3Mepha Ltd, Aesch, Switzerland

**OBJECTIVES** In line with the evaluation of the large-scale application of the ACT artemesunate/mefloquine by the WHO also for Africa in the currently recommended mean total dose of 12/25 mg/kg, pharmacodynamic and pharmacokinetic characteristics as well as acceptability of the co-blister artemesunate/mefloquine (Artequin® 300/750) and the new fixed-dose co-formulation (Artequin® Paediatric 50/125) were investigated for the treatment of uncomplicated Plasmodium falciparum malaria in Gabonese children.

**METHODS** Children stratified according to body-weight (10–20 kg: group A; >20–40 kg: group B), suffering from uncomplicated P. falciparum malaria, were treated for 3 days with a single daily dose of Artequin® Paediatric or Artequin® 300/750, respectively. Efficacy was assessed by the 28-day cure rate (primary outcome), 14-day cure, time to parasite clearance (PCT), time to fever clearance (PCT), parasite reduction rate (PRR) and gametocyteny. Safety and tolerability assessment consisted of monitoring and recording clinical and biological adverse events. Acceptability of drug intake was assessed by swallowability. Pharmacokinetic characteristics of dihydroartemisinin/mefloquine were assessed in the first 12 children of each group eligible for PK analysis.

**RESULTS** Seventy-one children were enrolled, 41 in group A and 30 in group B. Three patients were excluded from efficacy evaluation (one repeated vomiting, two protocol deviations). The 28- and 14-days cure rates were 100% for both treatment groups (PP analysis). Mean PCT was shorter in treatment group B (30.8 ± 9.3 h) than in treatment group A (34.1 ± 12.6 h). The median FCT was approximately twice as long in group A (23.3 h) than in group B (12.3 h). Gametocyte reduction rate was 100% in both groups on day 28. Approximately 1/3 of the patients...
O27-73
Randomised, comparative study of the efficacy and safety of artesunate amodiaquine co blister (Arsucam™) administered as a single daily dose vs. two daily doses in the treatment of Plasmodium falciparum malaria attack
J. L. Ndoye1, B. Faye1, P. Brasseur2, M. Cissé3, T. Kueté4, A. Same-Ekobo5 and O. Gaye6
1University Cheikh Anta Diop, Dakar, Parasitology, Dakar, Senegal; 2Research for Development Institute, UR 077, Dakar, Senegal; 3Ministry of Health, Medical District of Oussouye, Dakar, Senegal; 4University of Yaoundé, Parasitology, Yaoundé, Cameroon

Arsucam™ is a co blister presentation of artesunate and amodiaquine, with a once daily dosing regimen. The number of tablets to be taken (particularly in adults), suggested that tolerability might be improved by allowing patients to divide the daily dose.

OBJECTIVES The primary endpoint of this randomised, comparative, open-label multicentre study conducted in Senegal and in Cameroon in 2005 was to demonstrate the non-inferiority of Arsucam™, as a single dose intake vs. two daily doses. A secondary endpoint was to compare the tolerability of the two dosing regimens.

METHODS Any subject with malaria attack confirmed by parasitemia was randomly allocated in one of the two regimens, with dosage based on bodyweight range, after informed consent. All products were administered by an authorised person. Investigating physicians and biologists were unaware of treatment allocation. A 3-day treatment period and 14-day follow-up period was performed. The primary endpoint was the adequate response to treatment on D14 (WHO definition). The two-sided 90% confidence interval of the difference was calculated on ITT population; the acceptance limit for non-inferiority was 3%.

Tolerability was evaluated by incidence of adverse events.

RESULTS A total of 316 patients, adults and children weighing more than 10 kg, were included in the study. The two patient groups were strictly comparable on D0. PCR corrected adequate responses to treatment were similar for the two treatment regimens on D14 (99.4% in the one daily dose group vs. 99.3% in the two daily doses group). Statistical analyses demonstrated the non-inferiority of administering Arsucam™ as two intakes. Arsucam™ was well tolerated in both groups. Main reported AEs were gastrointestinal disorders (2.5%) and pruritus (2.5%). Safety profiles were similar in both groups, and no unexpected AE was reported.

CONCLUSION This study confirms the efficacy and good tolerability of Arsucam™ administered in one or two daily doses.

O27-74
Optimized age-based dosing regimens of the new fixed-dose combinations artesunate–amodiaquine and artesunate–mefloquine for the treatment of uncomplicated falciparum malaria
D. Terlouw1, L. Ribeiro2, W. R. Taylor2, P. L. Olliaro3 and F. O. ter Kuile1
1Liverpool School of Tropical Medicine, Child and Reproductive Health Group, Liverpool, UK; 2Drugs for Neglected Diseases Initiative, Geneva, Switzerland; 3World Health Organization Special Programme for Research and Training in Tropical Diseases/ Product Research and Development, Geneva, Switzerland

OBJECTIVES The regulatory development of drug regimens is based on body weight dosing. However, in practice, antimalarial treatment is often based on age resulting inevitably in some patients receiving doses outside the therapeutic range. We developed a novel methodology to design practical age-based dose regimens that maximise efficacy and minimise toxicity for the treatment of uncomplicated malaria and used this for two new fixed-dose combinations of artesunate/amodiaquine in Africa (AS/AQ) and artesunate/mefloquine in Latin America (AS/MQ).

METHODS Target doses for the individual drug components were 4 mg/kg (AS), 10 mg/kg (AQ) and 8 mg/kg (MQ) daily for 3 days (12, 30 and 24 mg/kg total respectively). We compared the proportions of patients predicted to receive doses within predefined therapeutic ranges for mefloquine (5–11 mg/kg/day), amodiaquine (7.5–15 mg/kg/day) and artesunate (2–10 mg/kg/day) for a range of age-dose categories, using representative weight-for-age reference databases (Brazil n = 43 366 and sub-Saharan Africa n = 88 054).

RESULTS The proportions of African patients predicted to receive adequate therapeutic doses were 83.4% AQ and 99.9% AS using paediatric (p) and adult (a) tablet strengths of 25/67.5 and 100/270 mg AS/AQ and five age-dose categories: 0–2 month (1p), 2–11 month (1p), 1–5 year (2p), 6–13 years (1a), and ≥14 years (2a). The figures for MQ and AS in Brazilians were 89.8% and 99.0% respectively, with tablets containing 25/50 and 100/200 mg AS/MQ and four age-dose categories: 0–11 month (1p), 1–5 years (2p), 6–11 years (1a), and ≥12 years (2a).

CONCLUSION This method is a useful tool for designing user friendly dosing regimens for drug registration and programmatic use. AS/AQ was recently launched for use in sub-Saharan Africa using the above age-based regimen. Work is ongoing to develop regional age-based dose regimens for AS/MQ targeted for South America, sub-Saharan Africa and Southeast Asia.

Geographical Dermatology
O27-75
Incidence of pediculosis in an area of high transmission is dependent on pediculicidal treatment of family members: an experimental study
D. Pilger1, J. Heukelbach2, A. Khakban3, F. Araújo Sales de Oliveira4, G. Fengler2, A. J. Monteiro5 and H. Feldmeier6
1Charité – University of Medicine, Campus Benjamin Franklin, Institute for Microbiology and Hygiene, Berlin, Germany; 2School of Medicine, Federal University of Ceará, Department of Community Health, Fortaleza, Brazil; 3Mandacaru Foundation, Fortaleza, Brazil; 4Federal University of Ceará, Department of Estatística e Matemática Aplicada, Fortaleza, Brazil; 5Federal University of Ceará, Departamento de Estadística e Matemática Aplicada, Fortaleza, Brazil

OBJECTIVES To assess the effect of treatment of household members with pediculicides on the incidence of head lice infestation in children living in an endemic area.

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METHODS We conducted an observer-blinded intervention study in children 5–15 years in a resource-poor community in the city of Fortaleza, Brazil. Children were recruited when coming back from a holiday camp where they had participated in a clinical trial against head lice. The absence of pediculosis capitis was verified by wet combing before enrolment. The households of the participants were randomized into two groups. In the intervention group, all family members were treated with ivermectin (or in single cases with permethrin), in the control no treatment of family members was performed. Treatment of household members was carried out one day before the children came back from the holiday camp, and repeated after 10 days. The children were examined for the presence of *P. humanus capitis* every 3 days for a period of 48 days.

RESULTS In total, 132 individuals (64 in the intervention group; 68 in the control group) were included in the study. The two groups did not differ in sex and age distribution, family size and family income. The median inflation-free time was 24 days (interquartile range: 11–45 days) in the intervention group and 14 days (11–25 days) in the control group (P = 0.02). After 30 days, re-infestation rates were 56.2 % and 79.4 % in the intervention and control groups, respectively. Kaplan-Meier analysis with log rank test yielded a significant difference in the incidence of head lice infestation between both groups (P = 0.02; Figure).

CONCLUSION This is the first study assessing the incidence of head lice infestation and the effect of treatment of household members in a hyperendemic area. Our data show that re-infestation with head lice occurs rapidly in the household, but that transmission in the community is also high.

Q27-76
Growing urbanization and parasitic skin diseases in slums of big cities
Heukelbach J

Growing urbanization in developing countries has led to an increased agglomeration of underprivileged people on limited space, with devastating consequences for human health. The parasitic skin diseases scabies, pediculosis, hookworm-related cutaneous larva migrans (CLM) and tungiasis occur particularly in the slums of big cities. In this presentation, the factors leading to polyparasitism and high parasite load in urban slums in Brazil will be discussed, and our experience with different control and prevention measures and their sustainability will be presented.

METHODS Questionnaires were sent to all 54 medical posts of the Medical Mission in the interior of Suriname. For every patient with lesions suspect for CL a questionnaire needed to be filled in by the health worker. Sixty-seven questionnaires were returned from 18 of the 54 medical posts. From January 2006 until March 2006 we visited six medical posts in the interior. Twenty-eight patients with lesions suspect for CL, selected by the health worker, were questioned, examined, photographed and 2-mm skin biopsies were taken. In Paramaribo 37 suspected CL patients were included at the Dermatology Service and the Academic Hospital. In addition, in these cases, the diagnosis was confirmed by skin smears. In the Netherlands PCR was performed on all skin biopsies in order to confirm the diagnosis and to determine the Leishmania species.

OBJECTIVES Cutaneous leishmaniasis (CL) is widespread in Suriname. Little is known of its epidemiology. The last reports show a mean annual incidence of 4.9 per 1000 inhabitants for the interior and 0.66 per 1000 inhabitants in the whole country between 1979 and 1985. Only Leishmania Viannia guyanensis is described as causative parasite. However, risk factors seem to be increasing due to gold mining activities and migration of illegal workers. Also different clinical manifestations are seen, suggesting that other Leishmania species are involved. This study aims to estimate the incidence of CL for the interior, the geographical distribution and to detect the infecting Leishmania species in Suriname in 2006.

METHODS We conducted an observer-blinded intervention study in children 5–15 years in a resource-poor community in the city of Fortaleza, Brazil. Children were recruited when coming back from a holiday camp where they had participated in a clinical trial against head lice. The absence of pediculosis capitis was verified by wet combing before enrolment. The households of the participants were randomized into two groups. In the intervention group, all family members were treated with ivermectin (or in single cases with permethrin), in the control no treatment of family members was performed. Treatment of household members was carried out one day before the children came back from the holiday camp, and repeated after 10 days. The children were examined for the presence of *P. humanus capitis* every 3 days for a period of 48 days.

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Q27-76
Growing urbanization and parasitic skin diseases in slums of big cities
Heukelbach J

Growing urbanization in developing countries has led to an increased agglomeration of underprivileged people on limited space, with devastating consequences for human health. The parasitic skin diseases scabies, pediculosis, hookworm-related cutaneous larva migrans (CLM) and tungiasis occur particularly in the slums of big cities. In this presentation, the factors leading to polyparasitism and high parasite load in urban slums in Brazil will be discussed, and our experience with different control and prevention measures and their sustainability will be presented.

Many aspects of urban slums lead to high prevalence of parasitic skin diseases: poor housing, overcrowding, lack of hygiene, insufficient water supply, low level of education, infected animals living in close bonds to humans, lack of resources, and limited access to health care. If available, treatment options for scabies and pediculosis (mainly benzyl benzoate and sulphur compounds) are poorly accepted by the population, with consequently low adherence to treatment. Our data show that mass treatment with an oral broad-spectrum antiparasitic compound such as ivermectin is a better solution. On the other hand, community control of CLM, a zoonotic disease, would need reduction of the intestinal helminth load in the animal population. However, the dog and cat populations are abundant, and many animals stray around. In the case of tungiasis, sustainable control is more complex and would need – in addition to the control of the human, dog and cat reservoirs – reduction of the rat population. Off-host stages of the flea causing tungiasis survive for a prolonged time in the environment and are responsible for maintaining high attack rates. To protect severely infested individuals at least temporarily from continuous reinfection, we applied a repellent on the feet. Incidence and pathology was reduced to an insignificant level. However, attack rates rose up again few weeks after discontinuation of the applications. To attain sustainable reduction of the four major parasitic skin diseases in the urban slum environment, an integrated approach is needed, aiming at reduction of human and animal reservoirs and better housing, besides a strong commitment from health policy makers.
Abstracts of the 5th European Congress on Tropical Medicine and International Health

RESULTS The diagnosis CL was confirmed in 58 of the 65 cases by PCR. The greater part of the species was identified as L. Viannia guyanensis. Most new CL patients were found in the middle part of Suriname, along the Suriname River. The clinical incidence is estimated between 0.4 and 3.9 per 1000 inhabitants for the interior.

O27-78
Clinicopathological study of neurofibromatosis type 1 – an experience in Nigeria
O. Odebode1
1Surgery, University of Ilorin Teaching Hospital, Ilorin, Nigeria

OBJECTIVES This study was designed to evaluate the clinical and pathologic pattern of Neurofibromatosis Type 1 (NF-1) among Nigerians and to emphasize the place of histological examination in complementing the usual set of clinical criteria for the diagnosis of this genetic disorder.

METHODS A retrospective case study of 98 clinically diagnosed NF1 patients whose dermal mass lesions (neurofibromas) were excised and processed for histological diagnosis over a period of 22 years (1980–2001) at the University of Ilorin Teaching Hospital (UITH), Ilorin, Nigeria.

RESULTS There were 98 patients: 60 males and 38 females (ratio 3:2) aged 1–99 (mean ± SD = 3.4 ± 1.7) years. All patients had neurofibromas which were benign in 95 (96.9%) and malignant in three (3.1%) patients while 94 (96%) patients had café-au-lait spots. Benign neurofibromas were clinically cutaneous [50(51%)], subcutaneous [37(37.8%)] and plexiform [8(8.2%)]. Site distribution of the neurofibromas includes the extremities (50%), trunk (20.4%), head and neck (19.4%), and multiple sites (10.2%). Three patients presenting with neurofibrosarcomas were aged 4, 23 and 27 years respectively. Their deaths were responsible for the mortality rate of 3.1% recorded in this study.

CONCLUSION In our setting, neurofibromatosis type 1 is commoner among males with highest density of neurofibromas over the extremities.

O27-79
Immigrant and travelers’ dermatology
A. Sethi1
1Dermatology, University of Chicago, Chicago, USA

OBJECTIVES To outline common dermatologic diseases seen in immigrants and travelers in the West

METHODS Cases seen in a dermatology clinic setting in University hospital based academic centers

RESULTS Infectious dermatologic diseases are being commonly seen in the West due to travel and immigration (e.g., leprosy, leishmaniasis, myiasis).

CONCLUSION Uncommon infectious dermatoses should be kept in mind as well taking a pertinent travel history in immigrants presenting to clinic.

Mathematical Modelling of Disease Control Programmes

O27-80
A household structured model for directly transmitted tropical infections; a special reference to leprosy
E. A. J. Fischer1, A. Meima1, J. H. Richards2 and S. De Vlas3
1Department of Public Health, Rotterdam, Erasmus MC, University Medical Center Rotterdam, Netherlands

OBJECTIVE Household structured models have been presented before (e.g. Ball et al. 1997). The time scale of the infection and the epidemic nature of most of these models are not met for all diseases. The assumption, that changes in household do not occur during the infection period, is not valid for infections with a long sub-clinical, and infectious period. We study the importance of household transmission for such an infection, and do not assume stable households.

METHOD We developed a microsimulation model that explicitly models the creation and change in households. We used this model in the context of leprosy, as this is a disease with a long infectious period. We calibrated the model for Bangladeshi data and simulated two deviant scenarios with on average small and on average large households.

RESULTS The household scenarios had average household sizes of approximately 2.8, 4.4 and 7.7. We were able to calibrate the infection parameters for an incidence of 10 per 10 000 in the population with intermediate household size. Using the same calibrated parameter values, the incidence in the population with the largest households was almost six times higher than that of the small households.

CONCLUSION Household structure and dynamics should be taken into account for directly transmitted infections with a higher rate of within household transmission and with a generation time on the demographic time scale.

O27-81
Modeling the effective reproduction number for Plasmodium vivax malaria
H. Nishiura1
1Department of Medical Biometry, University of Tubingen, Tubingen, Germany

OBJECTIVES Vivax malaria in temperate zones shows clear seasonality reflecting the population dynamics and other entomologic characteristics of the vector, Anopheles spp., which hibernates during the winter season. Supporting the stability of its endemicity, it has been demonstrated that the incubation period of vivax malaria in the temperate zone is likely, in part, to be prolonged.

METHODS For example, the maximum likelihood estimates of mean short- and long-term incubation periods for Korean vivax malaria are 26.6 days and 48.2 weeks, respectively. Whereas this information would facilitate understanding of the ecological characteristics (e.g., malaria evolution), the incubation period is also useful to estimate the time-specific transmission potential (i.e., the effective reproduction number, R0). I developed a method to estimate the effective reproduction numbers for vivax malaria by year and month. Given that the malaria cases in year t is infected either in the same year t or previous year t-1, the expected number of cases can be given by a convolution equation. Likelihood-based approach was employed to estimate the reproduction number.

RESULTS Although the effective reproduction number was rather high during first 2–3 years of the epidemics investigated (e.g., R0 > 50), the estimate has declined below unity immediately after the control measures were instituted. Seasonal changes in the risk of transmission were realized as the transmission potential of malaria relative to month. The qualitative pattern of the seasonal forces appeared to be consistent with that of population dynamics of Anopheles sinensis.

CONCLUSION The significance of estimating R0 for malaria lies in the practical implications on the evaluation of control program. The obtained estimates reasonably allowed epidemiologic interpretation of the malaria trend.
O27-82
Individual-based spatiotemporal simulation of SARS transmission in Chinese hospitals
J. Zhou1, J. Gong1, W. Cao2 and W. Li1
1State Key Laboratory of Remote Sensing Science, Institute of Remote Sensing Applications, CAS, Beijing, China; 2Beijing Institute of Microbiology and Epidemiology, State Key Laboratory of Pathogen and Biosecurity, Beijing, China

OBJECTIVES. Most studies of the spatiotemporal transmission of SARS using GIS have been placed on the distribution mapping of disease data and large-scale spatiotemporal distribution of SARS during the 2003 epidemic. However, there has been less effort in the study on the spatiotemporal distribution of SARS on a microscale. This paper employs multi-agent and virtual geographic environmental technologies to explore the characteristics of SARS transmission in Chinese hospitals.

METHODS. A new spatiotemporal transmission model of SARS in hospitals was designed based on simulating individual persons. The behavior of medical workers, patients and their visitors in hospitals, and the differences between two transmissions routes considered in the model bring different results of the SARS transmission in hospitals. The relationship between infection source, transmission route and susceptible person was described by a multi-agent approach.

RESULTS. The integration of a virtual geographic environment platform and agent technology was realized, and a prototype system was built to simulate the spatiotemporal transmission of SARS in hospitals. A simulation was carried out to analyze the transmission of SARS in a virtual 3D hospital, which was built according to a real hospital. An experiment considering the influences of person particular behavior and environment factors on SARS transmission was conducted.

CONCLUSION. The integration approach of VGE platform and intelligent agent can be helpful for modeling the spatiotemporal transmission of SARS by a visual mode.

O27-83
Modeling the tuberculosis diagnostic process to predict the impact of new diagnostic technologies
S. J. de Vlas1, J. Cunningham2, R. A. Ahmad3, M. Perkins4 and N. J. D. Nagelkerke5
1Erasmus MC, Department of Public Health, Rotterdam, Netherlands; 2WHO, Tropical Disease Research (TDR), Geneva, Switzerland; 3Department of Public Health, Faculty of Medicine, Gadjah Mada University, Jogjakarta, Indonesia; 4Foundation for Innovative New Diagnostics (FIND), Geneva, Switzerland; 5Department of Community Medicine, United Arab Emirate University, Al Ain, United Arab Emirates

OBJECTIVES. Inadequate diagnostic tools and weak health systems contribute to poor TB case detection in many high burden countries. New diagnostic technologies are being developed which might improve both the speed and level of detection. We have constructed a mathematical model to describe the diagnostic process and predict the impact of new diagnostics across different geographic settings (here: Indonesia and sub-Saharan Africa).

METHODS. The model encompasses TB biology, steps of the diagnostic process and the organization and utilization of health care services. Innovatively, the model separates pulmonary disease into four stages, each linked to the performance of multiple diagnostic tests. Clinical symptoms and health seeking behavior are also functionally related to these stages. Moreover, HIV and its association with pulmonary TB have been included. Individual behavior and the properties of the health system can be flexibly defined according to country specific data.

RESULTS. Model-predicted sensitivity and specificity of standard diagnostics – i.e. smear microscopy and chest X-ray vs. culture as gold standard – were within the range reported by various field studies. Also, the natural history of untreated smear-positive TB cases closely mimicked data from the pre-treatment era. For the Indonesian context, replacing chest X-ray by culture or a future nucleic acid amplification test (NAAT) as second-line diagnostic will result in a 5–10% reduction of TB-related death, but only when assuming that doctors would more often refer for second-line testing and always consider a positive test result conclusive for treatment. Replacing standard smear microscopy by a point-of-care (POC) test with equal diagnostic performance as culture but 0% dropout would lead to a much higher impact (about 25% reduction of TB-related death). A similarly large effect of POC (30% reduction) is expected in a sub-Saharan context with an impoverished health system. Using POC as a rapid test to refer for confirmative testing by smear-microscopy would result in about half this impact (15% reduction), but this effect would largely disappear (only 3% reduction) if doctors do not refer false-negative POC cases for smear-microscopy. Active case finding using POC followed by smear-microscopy will also have a high impact (20% reduction), but at the same time lead to high rates of over-treatment.

CONCLUSION. New diagnostics can have a substantial impact on TB case finding and treatment, mainly through reduction of delay and thereby dropout. The eventual impact also depends heavily on possible changes in doctors’ decisions.

Zoonoses
O27-84
Zoonoses in urban and peri-urban areas of Kampala, Uganda
K. Maka1, C. Waiswa2, E. Frew1, M. Eister1 and S. Welburn1
1Centre for Infectious Disease, College of Medicine and Veterinary Medicine, University of Edinburgh, Midlothian, UK; 2Faculty of Veterinary Medicine, Makerere University, Kampala, Uganda; 3Centre for Infectious Disease, College of Medicine and Veterinary Medicine, University of Edinburgh, Edinburgh, UK

OBJECTIVES. In developing countries, cities are rapidly expanding and peri-urban livestock farming has an important role to feed growing city populations. However, it also carries risks of zoonoses (Fynn 1999). This study tests the hypothesis that the incidence of zoonoses is high in peri-urban areas of Kampala, Uganda.

METHODS. Peri-urban areas were determined by classifying areas according to their distance from Kampala city into three urbanicity groups (urban, peri-urban and rural) according to the sociological way. The hospital was selected because all of the interviewed villages had access. Case-control studies of these diseases were conducted from records between January 2006 for the evidence of spatial clustering using SaTScan (version 7.0.1). Controls were selected from fracture patients matched against cases for sex, age group, month of diagnosis.

RESULTS. Eleven villages were classified into peri-urban and the mean of the distance from city centroid was 12.3 km (95% CI: 7.0–17.6). The distances from the centroid to 3 urbanicity groups were significantly different (F2,84 = 49.43, P < 0.001). Number of daily cattle per village was the biggest in peri-urban (mean 318, urban 6.34 and rural 24.5, P < 0.001). Brucellosis, 82 epilepsy, 79 abdominal tuberculosis, and 104 GI infections were matched with controls. The patients of all diseases
were scattered within urban and peri-urban areas. Disease clusters were found only for brucellosis (6.34 km radius, \(P = 0.001\)) and GI infections (5.66 km radius, \(P = 0.002\)). The clusters overlapped and included the hospital in urban area.

**CONCLUSION** The overlapped clusters suggested patients exhibiting acute symptoms go to the closer hospital. The risk of zoonoses was not consistent with large cattle population in peri-urban areas. Therefore, understanding food distribution networks in urban and peri-urban areas is more important for the disease control.


Q27-85

**Toxocariasis as an important and serious health problem in nomad children of Chaharmahal and Bakhtiary province of Iran, 2006**

K. Manouchehri Naeini\(^1\), R. Nabavi\(^1\) and N. Zebardast\(^1\)

\(^1\)Mycology and Entomology, Parasitology, Faculty of Medicine, Shahrekord University, Shahrekord, Islamic Republic of Iran

**OBJECTIVES** Rural residence, low socioeconomic status and a close association with puppies were strongly associated with the seroprevalence of *T. canis* infection. The life style of nomads living in this area caused to suppose that the rate of infection may vary in this community compared with other population groups. Therefore, the study was carried out to determine the seroprevalence of *T. canis* infection among the nomad children living in this area and to investigate the correlation of the infection with sex, history of dog ownership and the status of the population residency whether in settled or migrating families.

**METHODS** Twenty-seven and five nomad children under 10-year-old of the province were selected by a randomly cluster sampling method and their sera were collected and examined by the ELISA kits (IgG) purchased from DRG Company, Germany. A questionnaire form contained some demographic and other information including clinical and laboratory data was also filled for each of the participants.

**RESULTS** A total of 140 sera out of 275 (50.9%) were positive for *T. canis* IgG antibodies, where the positive rate was 49.4% and 52.7% in the males and females, respectively (\(P = 0.42\)). The seropositivity among children that had a close contact with dogs was 50.7% while the rate was 51.3% in none exposed subjects (\(P = 0.84\)). The rate of seropositivity for the parasite was also 50.2% and 70% in the resident and migrating nomad children (\(P = 0.22\)).

**CONCLUSION** Toxocariasis is a prevalent zoonotic infection in nomad children of this area and should be considered as an important potential risk for developing of clinical disease and its serious complications. Therefore, control measures should be directed toward the reduction of infection in sheep-dogs through periodic deworming of the animals and prevention of human infections by health education programs and improvement of living standards e.g. nutrition status among nomad children.

Q27-86

**Molecular detection of spotted fever group rickettsiae including emerging pathogens in ticks from Morocco**

M. Sarih\(^1\), C. Socolovschi\(^1\), N. Boudebouch\(^1\), M. Hassar\(^1\), P. Parola\(^1\), D. Raoult\(^1\)

\(^1\)Research Department, Pasteur Institute, Casablanca, Morocco

**OBJECTIVES** Our aim was to detect and characterize *Rickettsia* sp. in hard ticks collected in Morocco, using polymerase chain reaction (PCR) and sequence analysis of amplified products, and to discuss their potential threat for human and animals.

**METHODS** A total of 370 ticks, including seven species from four genera, were collected from 2002 to 2006 from domestic animals and vegetation in the Taza region (Northeast of Morocco). These were tested by molecular methods for the presence of rickettsiae by targeting citrate synthase gene.

**RESULTS** Specific sequences of the rickettsiae were detected in 101 ticks (27% of tested ticks). We identified six different rickettsiae of the spotted fever group, including five pathogens: *Rickettsia aesculimannii* in *Hyalomma marginatum marginatum* (8.6%), *R. massiliae* in *Rhipicephalus sanguineus* (4.7%), *R. slovaca* and ‘*Candidatus R. raoultii*’ (*Rickettsia* sp. RpA4) in *Dermacentor marginatus* (54.5%), ‘*R. monacensis*’ and *R. belvettica* in *Ixodes ricinus* (64.3%). Finally, an incompletely described rickettsia has been detected in 78 of 113 (69%) of *Haemaphysalis* ticks.

**CONCLUSION** We report in this work for the first time the identification of four more SFG pathogenic Rickettsiae in Morocco including *R. massiliae*, *R. slovaca*, ‘*Candidatus R. raoultii*’ (*Rickettsia* RpA4) and ‘*R. monacensis*’.

Q27-87

**High seroprevalence of antibodies against *Coxiella burnetii*, the causative agent of human Q fever, in young Ghanaian children**

R. Kobbie\(^1\), S. Kramme\(^2\), S. Adjei\(^1\), O. Adjei\(^1\), B. Fleischer\(^2\) and J. May\(^1\)

\(^1\)Infectious Disease Epidemiology, Hamburg, Bernhard Nocht Institute for Tropical Medicine, Germany; \(^2\)Bernhard Nocht Institute for Tropical Medicine, Central Diagnostic Unit Medical Microbiology, Hamburg, Germany; \(^3\)Kumasi Centre for Collaborative Research in Tropical Medicine, Kumasi, Ghana

**OBJECTIVES** To assess the seroprevalence of Q fever antibodies in young African children living in a rural area with intense perennial malaria transmission.

**METHODS** Two-hundred and nineteen randomly selected 2-year-old children, participants of a registered trial on intermittent preventive treatment of infants (IPTi), and 159 healthy adults from the same nine neighbouring villages of the rural Afigya Sekyere district, Ashanti Region, Ghana, were included in this cross-sectional study. Measurements of *Coxiella burnetii* phase 1 + II IgG and IgM antibody titers were performed with immunofluorescence assays (IFA) applying the manufacturer’s instructions.

**RESULTS** Around 16.9% (37/219) of the young children, as compared to 9.9% (15/152) of healthy adults were seropositive for Q fever when applying a phase II IgG cut-off titer of 1 : 64. More individuals in the children's group had high antibody-titers indicating recent disease which was also confirmed by the presence of IgM antibodies. There was no cross-reactivity related to clinical *P. falciparum* malaria episodes or asymptomatic *P. falciparum* parasitaemia.

**CONCLUSION** Our results show that a large percentage of young children living in rural areas of Ghana have detectable antibody-responses to *C. burnetii*. The study indicates that human Q fever might be another, yet neglected cause of feverish diseases of children under the age of 5 years in sub-Saharan Africa. We suppose that these children become exposed to *C. burnetii* very early in life, that they are prone to develop acute Q fever, which is clinically indistinguishable from *P. falciparum* malaria. This might very frequently result in unnecessary receipt of expensive antimalarials. In the context of limited resources this might be an important information.
O27-88
Incidence and prevalence of IgG antibodies against Rickettsia of the spotted fever group in traveller returning from tropical and subtropical countries
G. Dobler1, S. Essbauer1, M. Pfeffer2 and R. Wöllf1
1Department of Virology and Rickettsiology, Bundeswehr Institute of Microbiology, München, Germany; 2Department of Bacteriology, Bundeswehr Institute of Microbiology, München, Germany

OBJECTIVES Rickettsiae are a group of obligate intracellular bacteria causing various forms of typhus and spotted fever worldwide. Several forms of rickettsioses are classified as emerging infections and some of them have a potential for biological weapons. Except for some case reports, however only few data are available on the incidence and prevalence of rickettsial infections in travellers returning from tropical and subtropical countries.

METHODS We tested 37 serum pairs and 126 single sera from patients with fever and additional constitutive symptoms returning from tropical and subtropical countries for IgG antibodies against spotted fever and typhus group rickettsiae. For testing commercial indirect immunofluorescence tests were used. Sera were screened at a dilution of 1:32 and in case of positive reaction they were titrated.

RESULTS Eight patients (three serum pairs and five single sera) reacted against Rickettsia typhi. One of the serum pairs showed significant increase of antibodies demonstrating acute infection. The single sera exhibited antibody titers from 1:32 up to 1:128. These results were classified as past infection. 24 patients (seven serum pairs and 17 single sera) showed positive antibody titers >1:32 against Rickettsia conorii. Four serum pairs differed significantly (4-fold increase of titer) and were therefore classified as acute infection. Four of the 17 single sera exhibited antibody titers of >1:256 and were therefore also grouped as acute or recent infections. Our data show that 1/153 (0.6%) acutely ill patients with fever returning from the tropics or subtropics had evidence evidence for an acute infection with rickettsiosis of the typhus group. 8/153 patients showed evidence of acute tick bite spotted fever. 7/153 (4.6%) patients showed evidence of past infection with rickettsiosis of the typhus group. 13/153 patients (8.5%) showed serological evidence of past infection with rickettsiosis of the spotted fever group.

CONCLUSION Rickettsiosis proved to be a frequent cause of fever in travellers returning from tropical or subtropical countries and should there be included into the differential diagnosis in patients with fever.

TB-HIV Co-Infection
O27-90
Laboratory diagnosis of TB in TB and HIV endemic settings and the contribution of real time PCR for MTB in bronchoalveolar lavage fluid
G. Kibiki1, B. Mulder2, A. Van der Vel1, N. Sam1, M. Boeree3, A. Van der Zanden1 and W. Dolmans
1KCMC Hospitals/ KCM – College, Internal Medicine, Moshi, United Republic of Tanzania; 2Laboratory for Medical Microbiology and Public Health, ENSCHEDE, Netherlands; 3Department of Internal Medicine, Division General Internal Medicine, University Nijmegen Medical Centre St Radboud, Nijmegen, Netherlands; 4Department of Medical Microbiology, Kilimanjaro Christian Medical Centre, TAZANIA, United Republic of Tanzania; 5Department of Pulmonary Diseases and University Lung Centre Derrherswald, University Nijmegen Medical Centre St Radboud, Nijmegen, Netherlands; 6Department of Medical Microbiology and Infection Control, Gehe Hospitals, Apeldoorn, Netherlands

OBJECTIVES To evaluate the diagnostic accuracy of various TB diagnostic methods in HIV infected patients in endemic setting using culture for MTB of bronchoalveolar lavage fluid (BAL) as the gold standard. • To correlate qPCR cycle threshold (CT) values to the MTB culture results. • To retrospectively evaluate the development of active TB in patients with positive qPCR/culture negative who never received TB treatment.

METHODS We evaluated 120 HIV-infected Tanzanian patients with chest infection for the diagnostic accuracy of smear for AFB, culture and real-time PCR (qPCR) using sputum and bronchoalveolar lavage fluid (BAL), and MycoDot® serological test. We correlated qPCR cycle threshold (CT) values to the TB culture results. Retrospectively we evaluated the development of active TB in patients with positive qPCR/culture negative who never received TB treatment.

RESULTS Fifty-six patients could not produce adequate sputum. Sputum AFB smears and the serological test had sensitivities of 66.7% and 0%, respectively. Culture of BAL identified 28 TB patients. qPCR was positive in 73 patients, 27 of which were also TB culture positive (96.4% sensitivity and 52.3% specificity of the qPCR using CT cut off value of 40). Using 32 as a CT value, the qPCR had a sensitivity of 85.7% and specificity of 90.9% to diagnose TB in BAL. No patients with positive qPCR but negative culture developed active TB in 18-months of follow up.

CONCLUSION We found that around half of the patients could not produce (adequate) sputum. Microbiological diagnosis of TB using sputum as recommended by the WHO for resource-poor settings was inefficient and missed the majority patients with TB. The TB serological test had very limited value in TB/HIV co-infection. TB culture was limited by delay in MTB growth. qPCR of BAL was limited by low specificity. CT value of 32 improved the specificity to over 90%. A prospective follow up study of qPCR in sputum and BAL is warranted in a TB/HIV resource-poor setting.
identified using reversed line blot hybridisation and 16S DNA sequencing.

RESULTS Only in 47% of the 187 diagnosed TB cases, M. tuberculosis was cultured. In another 19% of the cases, exclusively NTM were cultured, whereas from 12% of the TB cases a combination of M. tuberculosis and NTM was isolated. In the remaining 29% of cases, in which TB was diagnosed clinically, no mycobacteria were cultivable. HIV positivity was found significantly correlated with the isolation of NTM from sputum and inversely correlated with the isolation of exclusively M. tuberculosis from the sputum (P < 0.05).

CONCLUSION We conclude that basing the diagnosis of tuberculosis on symptoms, sputum smear and/or chest X-ray may lead to significant numbers of false-positive cases of tuberculosis in Zambja, due to the increased prevalence of HIV and inaccuracies in the diagnosis of TB.

O27-91
Differential diagnosis of mycobacteria in clinical specimens of HIV-infected patients at an infectious diseases hospital, São Paulo, Brazil
E. Boccardo1, M. Eiras1, S Sousa2, Co-infection TB/HIV – IER
1Instituto de Infectologia Emilho Ribas, Ambulatório, São Paulo/SP, Brazil; 2Instituto de Infectologia Emilho Ribas, Laboratório Clínico IER, São Paulo/SP, Brazil

OBJECTIVES Tuberculosis (TB) remains a major infectious disease and causes high morbidity and mortality worldwide. The objective of this research was to evaluate the positivity of the bacteriological diagnosis of mycobacterial agents in our laboratory, including AIDS patients co-infected with TB.

METHODS From January 2005 to December 2005, a total of 4833 clinical specimens were analysed (sputum, biopsies, bone marrow, CSF, urines, pleural effusion and blood). All specimens, except blood and bone marrow, were subjected routinely to smear examination for acid-fast bacillus (AFB) and cultured in MGIT-960 automated system. Blood and bone marrow were cultured in BACTEC-9240. Identification of mycobacteria isolated was carried out by Accuprobe. The average time needed for detection of mycobacteria was 15 days.

RESULTS Out of 4833 samples, 326 (6.74%) were positive by culture for mycobacterial agents. Among the culture positive specimens, 275 (84.3%) were from HIV-positive patients, and 208 (63.8%) were collected from male. From 326 culture positive specimens, 206 (63.2%) were isolated from sputum and 67 (32.5%) were also positive by microscopic examination (AFB smear-positive specimens). Of the 326 culture positive specimens, 261 (80%) were culture positive for Mycobacterium tuberculosis and 65 (20%) were culture positive for non-tuberculous mycobacteria (NTM). From NTM, Mycobacterium avium complex (MAC) was the most prevalent pathogen (83%), followed by M. kansasii (12.4%) and M. abscessus (4.6%).

CONCLUSION Our results showed that HIV/TB association has significantly increased throughout the years. Non-tuberculous mycobacteria infections remains a significant problem in HIV-positive patients, specially caused by MAC. Sensitivity of direct mycobacterial observation was lower than culture. Bacterial culture positivity is the gold standard test for TB. BACTEC-960 system has ability of quick detection of new cases of TB. Appropriate isolation facilities is required to improve diagnosis and to promote limitation of the disease.

O27-92
Barriers and opportunities for introducing HIV testing among TB patients in Jogjakarta, Indonesia: Barriers and Enablers
Y. Mahendradhata1, R. A. Ahmad2, P. Lefevre1, M. Boele1 and P. Van der Stuyf1
1Institute of Tropical Medicine Antwerp, Antwerp, Belgium; 2Gadjah Mada University, Yogjakarta, Indonesia

OBJECTIVES WHO recommends HIV testing among TB patients as an entry point to integrated TB–HIV care. The National Tuberculosis Control Programme in collaborations with several stakeholders conducted anVCT among TB patients in Jogjakarta province, Indonesia in 2006 involving 1044 TB patients. At the same time, we offered Voluntary Counselling and Testing (VCT). We aimed to investigate: (i) the reasons why TB patients decide to accept or to refuse HIV testing; and (ii) how healthcare workers perceive the introduction of HIV testing in TB patients.

METHODS We interviewed 32 TB patients based on an in-depth interview guide. Four Focus-Group Discussions (FGDs) were conducted with first line healthcare workers. Three specialist physicians and three district disease control managers were interviewed using an in-depth interview guide. Both the interview and FGD guide covered pros and cons of HIV testing among TB patients, the perceptions surrounding it and obstacles to its implementation. All interviews and FGDs were recorded using a digital recorder and transcribed. Data analysis was conducted using the QSR* N7 software.

RESULTS TB patients’ refusal of anonymous HIV test was related to fear of needle pricks and health workers not explaining well. Patients’ acceptance was associated with appreciation of its potential benefits. Patients’ interest in VCT services was related to belief that VCT will lead to better health and risk perception. Fear of stigmatization surrounding HIV testing was an issue among Indonesian TB patients although much less than had been generally anticipated and it does not seem to play a major role in refusal of VCT service. Health workers support the idea of HIV testing on condition that their safety is ensured and that the benefits to patients are clear and real. The additional workload caused by HIV testing was more a concern in hospitals than by first line healthcare workers. District disease control managers and chest and internal medicine specialists would like to see a clearer link between HIV testing and HIV care.

CONCLUSION Introduction of HIV testing among TB patients in the Indonesian TB programme should be accompanied by interventions to: (i) ensure effective communication between health workers and patients; (ii) strengthen human resource numbers, particularly in the hospitals; (iii) strengthen local HIV care and treatment services and (iv) ensure an effective linkage from HIV testing of TB patients to HIV care.

O27-93
Treatment access by TB /HIV coinfected patients: the case of Malawi
T. Chilipane Banda1, B. Nhlenea Simwaka1, R. Chimzizi1 and I. Makwiza Namakhoma2
1Research for Equity and Community Health (REACH) Trust, Research, Lilongwe, Malawi; 2Research for Equity and Community Health (REACH) Trust, Lilongwe, Malawi; 3Malawi National TB Control Program, Lilongwe, Malawi

OBJECTIVES In Malawi over 70 per cent of TB patients are HIV positive. According to the ART treatment guidelines in Malawi, all TB patients who are living with HIV qualify to be on ART treatment. Currently the Ministry of Health through the HIV/AIDS unit is rapidly scaling up provision of ART. The aim of this
study was to assess the extent to which TB and HIV/AIDS integration has enhanced access to ART by TB/HIV co-infected patients from an equity perspective.

METHODS The study was conducted using both quantitative and qualitative methods. The quantitative methods used 2006 routine ART data to assess the proportion of TB patients who have been enrolled on ART covering the entire nation. The qualitative methods used individual in depth interviews to understand the challenges that TB patients face in accessing ART treatment in urban Lilongwe district.

RESULTS Results show that 17 per cent of all HIV/AIDS patients were started on ART because of TB. The TB and ART programmes are parallel vertical programs with different structural arrangements. This has negative consequences on TB patient who are required to report to two different clinics. The impact on patients includes incurring of direct costs in form of transport and food and also opportunity costs of accessing the services. Patients have to make two separate visits for each appointment with long waiting times before being attended.

CONCLUSION Although Malawi has progressed in scaling-up of ART and integration of TB and HIV, the current arrangement creates a lot of challenges in the monitoring of TB patients referred to ART. TB recoding forms currently do not have HIV variables, making it difficult to determine proportion of TB patients who are on ART. Furthermore, a horizontal integration of TB and HIV services is essential to reduce the socio-economic burden of illness on their households.

Ethics in Health

O27-94 Conducting fieldwork with outreach groups on female commercial sex workers in a metropolitan area in the United Kingdom: ethical challenges

Z. Yin¹, D. Baxter¹ and T. Threadgold²

¹University of Manchester, Medicine, Manchester, UK; ²Manchester Action on Street Health, Manchester, UK

OBJECTIVES This paper has three core aims. First, to explore how ethical considerations that are inevitably encountered in research on female commercial sex workers (FCSWs) are addressed. Secondly, to identify possible strategies concerning research ethics challenges that may be employed during the process of fieldwork. Thirdly, to document possible strategies that can be used to overcome these ethical challenges.

METHODS This paper draws upon interviews with 92 female commercial sex workers in a metropolitan area as well as the work of others in the United Kingdom.

RESULTS Specified guidelines for ethical considerations are embedded in the strategies provided.

CONCLUSION In the conclusion, this paper links ethical challenges and strategies discussed with debates which have highlighted possible myths, stereotypes or misunderstanding on FCSWs.

Dengue I: Networks and Epidemiology

O28-1 Estimation of the force of infection for dengue

H. Nishiura¹

¹Department of Medical Biometry, University of Tübingen, Tübingen, Germany

OBJECTIVES Whereas epidemiologic risks of dengue hemorrhagic fever (DHF) have been explored for more than 30 years, transmission dynamics of dengue are yet to be clarified. In particular, there have been only a few statistical studies that examined the observed data. Force of infection (FOI) permits estimate of the transmission potential, and thereby, provides us with an estimate of critical coverage of vaccination required for the eradication.

METHODS This study develops a model to estimate the force of infection based on limited data on DHF incidence, and attempts to clarify age-specific risk of DHF following secondary infection with a heterologous strain. There are two key data sources: (i) age-specific DHF incidence with time and (ii) age-specific number of DHF due to primary and secondary infections (i.e., DHF cases with an explicit determination of primary or secondary infection by means of virological confirmation).

RESULTS Using a simple Bayesian method, age-specific conditional probability of DHF (i.e., given dengue haemorrhagic fever) is obtained. Further, using the probability and observed DHF incidence with explicit likelihood procedures, the maximum likelihood estimates of the age-independent FOI and a decay parameter for short-lived cross-protective immunity against heterologous strains are obtained.

CONCLUSION The estimates allow for clarifying age-specific risk ratio of DHF following secondary infection. The obtained estimates suggest that previous studies significantly underestimated transmission potential of dengue in endemic countries.

O28-2 Emergence of dengue and dengue haemorrhagic fever in Kerala state (South India): impact of climate change on Aedes albopictus skuse as the sole vector

B. K. Tyagi¹

¹Centre for Research in Medical Entomology (ICMR), Madurai, India

OBJECTIVES A long-term entomo-epidemiological investigation (2002–05) was carried out in Kerala to determine the impact of climate change and increased anthropocentric activities responsible for the emergence of Aedes albopictus-induced dengue and DHF.

METHODS Five districts viz, Trichur, Ernakulum, Idukki, Kottayam and Trivandum in Kerala state, south India situated in three altitudinally different physiographic zones, were selected for the survey. Climatic data from these zones were obtained from different sources and analysed with respect to the abundance and distribution of dengue vectors. Ovitraps were used to determine the breeding potential of Aedes albopictus in different physiographic situations far away from its cradle in highland forested ecosystem. The collected mosquito vectors, viz; Ae. aegypti and Ae. albopictus, were screened for the presence of dengue virus through ELISA. The adult mosquitoes emerged from the field collected mosquito immature were also screened for the virus regulation through transovarial mode (TOT).

RESULTS Aedes aegypti, the principal vector in India, was but insignificantly prevalent (4.4%) mostly along the coastal belt of urban areas. On the contrary, Ae. albopictus, the Asian tiger mosquito originally preferring sylvatic habitat, was predominantly prevalent (69.7%) amongst the 26 species so far sampled throughout Kerala, particularly the mountainous Western Ghat region. Aedes albopictus bred prodigiously in a large variety of natural and artificial breeding sites, especially the latex collecting cups and cocoa pods. There is a clear indication of interspecific competition between Ae. aegypti and Ae. albopictus for breeding sites, and the latter is observed to displace the former from most of its domain. As a result, Ae. albopictus has
established in even urban environment near the coastal belt. Dengue virus has been isolated only from Ae. albopictus by enzyme-linked immunosorbent assay (ELISA) technique from a total of four pools of febrile adult females as well as two pools from those adults reared from the field-collected immature specimens.

CONCLUSION It is propounded that in Kerala, both the dengue virus and its vector Ae. albopictus have disseminated from the highland forested areas of Kottayam district to lowland areas in recent times. Certain new methods to control the vector in Kerala are discussed.

O28-3
Comparison of an enzyme-linked immunosorbent assay for detection of nonstructural 1 (NS1) glycoprotein and an antibody based ELISA for the diagnosis of dengue in Vietnam
L. P. Hoang1, D. K. T. Thai2, T. T; T. N. Tran1, T. G. Phan1, Q. H. Le1, Q. B. Tran1, V. N. Nguyen1 and P. J. de Vries2
1Department of Tropical Diseases Cho Ray hospital, Ho Chi Minh City, Vietnam; 2Department of Infectious Diseases, Academic Medical Center, Amsterdam, Netherlands

OBJECTIVES To compare dengue NS1 antigen – ELISA for dengue and to compare this to antibody ELISA based sero-diagnosis.

METHODS Paired acute and convalescent serum samples were obtained from 531 patients with acute undifferentiated fever who presented at primary facilities in Binh Thuan province, southern Vietnam. NS1-antigen ELISA and the IgM-capture and IgG ELISA based diagnosis were compared.

RESULTS Dengue NS1 antigen was found in 57 of 531 (10.7%) acute sera, taken after a median of 0.9 days of fever. Cut off values for antibody ELISA and thresholds for defining seroconversion were adapted to achieve maximum agreement with the NS1-antigen test. The kappa value was 0.574 with corresponding positive and negative predictive values for acute (primary or secondary) dengue of 63% and 95% respectively. Discordant results were mainly found in patients diagnosed with acute secondary dengue but who had a negative NS1-antigen test and in a few patients without acute dengue who had repeatedly very high NS1-antigen test results.

CONCLUSION The Platelia™ Dengue NS1 Ag test can be used for early sero-diagnosis of dengue virus infection, but positive predictive value is limited; unexpected high antigen concentrations are rare but need further study.

Diagnostics Malaria, HIV and TB

O28-4
Does the introduction of malaria antigen tests improve clinical care? results from a randomized study in Burkina Faso
J. Van den Ende1, C. Lodemann1, A. Angebien1, T. Haididou Pha2, S. Bienvenu Sinna1, K. Van den Ende3, F. Gobbi1, G. Baraca2 and Z. Bizzof2
1Institute of Tropical Medicine, Clinical Sciences, Antwerp, Belgium; 2Centre for Tropical Diseases, S. Cuore Hospital, Negrar (Verona), Italy; 3RSS/Centre Muraz, Bobo Dioulasso, Burkina Faso; 4MLAL/Unidea An Ka Here So, Bobo Dioulasso, Burkina Faso; 5Clinic of Infectious Diseases, Amedeo di Savoia Hospital, Torino, Italy

INTRODUCTION Conventional (microscopical) malaria diagnosis requires an important investment, skilled technicians and regular maintenance and supervision. We wondered whether the introduction of a Rapid Diagnostic Test (RDT) might improve clinical diagnosis in feverish patients in a rural setting in Burkina Faso.

METHODS The field study was carried out in 10 peripheral health centres of Bobo Dioulasso and Banfora at the end of the dry season (May 2006), when the malaria transmission is lowest. Febrile patients were randomised either to be treated conventionally (i.e., on a presumptive basis), or after a RTD for malaria (Paracheck®). RTD results were compared with thick films, which were read in a reference laboratory. We recorded the clinical diagnosis before RTD and after.

RESULTS Correlation between RTD and thick film was fairly good (OR 53.5; CI 26.8–106.8). In the RTD aided group 334/405 (82.5%) of patients where put on malaria treatment, against 357/448 (79.7%) in the ‘clinical diagnosis only’ group (RR 1.03; CI 0.96–1.10). 232 patients (80%) with a negative RTD were treated as malaria cases, seven patients (6.2%) with a positive RTD were not treated for malaria. In patients submitted to RTD significantly less second diagnoses were made than in the ‘clinical diagnosis only’ group (RR = 0.8; IC 0.79–0.95). This decrease in alternative diagnosis was consistently present in patients with higher (>1000/microlitre), lower and absent parasitaemia. Clinical diagnosis of malaria before knowing the negative result of RTD was changed in 12 of 279 cases. (18.5%).

CONCLUSION Malaria treatment did not differ according to the use of antigen tests. Moreover, introduction of RTD might have a deleterious effect if positive, since cases with low parasitaemia will not be explored for possibly life-threatening diseases. If negative, clinical officers make also less alternative diagnoses, which is an unintelligible observation. Training in clinical reasoning including interpretation of laboratory results should be organized for all clinical officers.

O28-5
Malaria diagnostics centre for excellence: results from training and pilot microscopy certification
P. Oloa1, B. Oguta1, C. Adambol2, R. Onkkel1, J. S. Odera1 and C. Oder2
1Centre for Clinical Research, Kenya Medical Research Institute, Malaria Diagnostics Centre of Excellence, Kisumu, Kenya; 2Walter Reed Army Institute of Research, Silver Spring, MD, USA

BACKGROUND Microscopy error impacts malaria prevention and treatment trials, as well as the assessment of new diagnostic tests. As few as 1% false positive results can lower observed protective efficacy by 15% or more in clinical trials.

METHODS To ensure valid clinical trials results we established a Malaria Diagnostics Centre for Excellence in 2003 in Kisumu, Kenya. Standardized training and objective testing methods are now in place as a component of an initial and a refresher training course. Participants must have a diploma in clinical laboratory medicine and at least one year of experience as malaria microscopists. Trainees have been from nine African countries, with pilot certification conducted within Kenyan Institutes.

RESULTS Training results have revealed substantial improvement, while cut offs for certification are higher than what we anticipated. Recent training results, as well as the results from the pilot certification effort, will be presented in detail. The role of malaria microscopy relative to rapid diagnostic tests and other new technologies in the clinical and clinical research settings will be reviewed.

CONCLUSIONS Malaria microscopy can be substantially improved with training and certification of technicians. Its role in the European Congress on Tropical Medicine and International Health
era of many new diagnostic tests remains to be fully determined. Highly accurate malaria microscopy is required for the evaluation of new diagnostic tests.

O28-6
Loop-mediated isothermal PCR (LAMP) for the diagnosis of falciparum malaria
D. Paris1, M. Imwong1, M. Faiz2, M. Hasan3, E. Bin Yunus2, K. Silamut1, S. Lee1, N. Day1 and A. Dondorp1
1Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; 2Faculty of Tropical and Internal Medicine, Chittagong Medical College, Chittagong, Bangladesh

OBJECTIVES A recently described Loop-Mediated Isothermal PCR (LAMP) enables molecular diagnosis of Plasmodium falciparum malaria in settings with limited technical resources. We evaluated this technique as a diagnostic tool in the setting of a tertiary referral hospital in Chittagong, Bangladesh, in comparison with microscopic examination of a peripheral blood film, an HRP2-based Rapid Diagnostic Test (RDT), and nested PCR, which served as the ‘gold standard’

METHODS DNA extraction for the LAMP assay was done either by conventional methods (LAMP-DNA-ext) or by simple heating of the blood sample (LAMP-heat). Turbidity and pellet formation after centrifugation, denoting positive test results, were either assessed visually (LAMP-eye) or by performing gel electrophoresis (LAMP-gel). A total of 115 patients with clinical suspicion for malaria on admission were included, of which 67 (58%) had falciparum malaria by nested PCR.

RESULTS The sensitivity and specificity (95% CI) of the ‘LAMP-DNA-extract’ assay were 76.1 (68.3, 83.9) and 89.6 (84.0, 95.2), similar to microscopy. The ‘LAMP-heat-eye assay, requiring a minimum of technical instruments demonstrated 79.1 (71.7–86.5) and 58.3 (49.3–67.3) respectively, using gel electrophoresis for assessment (LAMP-heat-gel) improved this to 76.1 (68.3–83.9) and 83.3 (76.5–90.1). Specificity (95% CI) of microscopy and RDT were high with 100% (100–100%) and 100% (100–100%), with sensitivities of 73.1 (65.0–81.2) and 77.6 (70.0–85.2), when compared with nPCR.

CONCLUSION In contrast with a previous report, the performance of the LAMP technique, without the use of a real-time turbidometer, compares to conventional microscopy and requires further optimization to make this promising technique a suitable simple molecular method for the field setting.

O28-7
An anti-idiotypic chicken polyclonal antibody recognized by a mouse monoclonal antibody directed against the MSP-1 recombinant protein of Plasmodium yoelii
L. Spencer1, I. Justiniano2 and N. Zerpa2
1Universidad Simon Bolivar, Cell Biology, Caracas, Venezuela; 2Fundacion Instituto de Estudios Avanzados, Biocience, Caracas, Venezuela

OBJECTIVES One of the most important and well studied parasite surface proteins at the stage of the life cycle is merozoite surface protein-1 (MSP1). Plasmodium MSP1 undergoes proteolytic processing into several fragments, of which only the C-terminal 19 kDa fragment (MSP1-19) remains on the merozoite surface during invasion of a new erythrocyte. We have produced an anti-idiotypic antibody in chicken (IgY), that is capable of recognizing a monoclonal antibody (Mab) B6 (IgG2a) raised against the recombinant protein MSP-1-19 of Plasmodium yoelii.

METHODS The Mab B6 was inoculated in ISA Brown chickens and isolated from egg yolk by Polyethylene glycol precipitation. IgY was evaluated by enzyme-linked immunosorbent assay (ELISA) and Western blots.

RESULTS The IgY obtained was recognized by Mab B6 in an ELISA. However, no recognition was obtained by Western blots from SDS-PAGE prepared under reducing or non-reducing conditions. These results suggest that the epitope recognized by this Mab requires a specific conformational structure for the interaction between Mab and IgY. Also, hyper-immune sera from mice infected with Plasmodium yoelii (7 and 60 % of parasitaemia) were used in ELISA tests using post-immune IgY as antigen, showing differential recognition in comparison to pre-immune IgY. Using this antibody, we have been able to obtain a mimicked antigen-like MSP-1 response.

CONCLUSION The results of this study show that IgY anti-MabB6 mimics the epitope of MSP-1 recognized by MabB6 and hyper-immune sera of infected mice demonstrating that this IgY could be used as an antigen for diagnosis of malaria.

Military Medicine

O28-8
Doxycycline–chloroquine vs. doxycycline-placebo for malaria prophylaxis in nonimmune soldiers: a double-blind randomized field trial
R. Michel1, S. Bardot2, B. Queryrias1, J.-P. Boutin1 and J.-E. Touze2
1Departement d’Epidemiologie et de Sante Publique, Institut de Medicine Tropicale du SSA, Marseille Armees, France; 2Pharmacie Centrale des Armées, Orléans, France; 3Direction Centrale du Service de Santé des Armées, Paris, France

OBJECTIVES: To compare tolerability and efficacy of doxycycline–chloroquine versus doxycycline as malaria prophylaxis.

METHODS In 2004 and 2005, a double-blind, placebo-controlled randomized field trial was designed. Participants were French army soldiers deployed from four to six months in Côte d’Ivoire or Gabon. Compliance was assessed using self-reports in standardized notebooks and dosage of doxycycline in unexpected blood samplings. Adverse effects were weekly reported in the same notebooks. Efficacy was assessed through the incidence density of malaria.

RESULTS A total of 936 volunteers were included in the data analysis. The compliance rate was 86.6% and was similar in the two groups. Our data suggested a higher biodisponibility and elimination half life time of doxycycline when combined with chloroquine. Proportions of subjects developing at least one adverse effect was similar in the two groups. The proportion of nausea or vomiting was higher in the doxycycline–chloroquine group. Overall, 15 cases of Plasmodium falciparum malaria cases were diagnosed: eight cases in the doxycycline group and seven in the doxycycline–chloroquine group. The efficacy of the two chemoprophylaxis regimens of the trial was similar. Yet, one can expect an increase of efficacy of the combination against Plasmodium vivax, what would be interesting in French Guiana where almost 4000 French soldiers are posted and 187 Plasmodium vivax malaria cases declared to the French military epidemiological surveillance system in 2005.

CONCLUSION In summary, the addition of chloroquine to doxycycline seems interesting for many reasons: in areas where chloroquine is not used left, reversions of Plasmodium falciparum resistance have been reported, no significant decrease of tolerability of the doxycycline–chloroquine was observed compared to doxycycline alone in our study, pharmacological studies did not show any competition between doxycycline and chloroquine, the combination efficacy has been described in
malaria therapy and one can expect an increase of efficacy of the combination against \textit{Plasmodium vivax}.

**O28-9**

\textbf{Behavioural and environmental determinants of malaria in French army during 4 month missions in Africa}


1 \textit{Institut de M\'edecine Tropicale du Service de Sant\'e des Arm\'ees, Parasitology, Marseille Arm\'ees, France}

Malaria is one of the major threats faced by troops deployed in tropical Africa, particularly during military operations. Chemo prophylaxis, insecticide impregnated bed net, long-sleeved battledress and repellent are used in the French army as anti malaria protective devices. The risk of clinical malaria and the level of exposition to malaria transmission of troops (n > 1200 individuals) deployed in tropical Africa (Senegal, C\'ote d\’Ivoire, Chad, Gabon, Central Africa Republic and Djibouti) have been evaluated by epidemiological survey of clinical attacks and by the comparison of the IgM and IgG immune responses against 12 pre-erythrocytic \textit{P. falciparum} antigens before and at the end of the mission. The incidence of clinical attacks and of infections have been analyzed according to personal (age, rank, knowledge, previous experience of missions in endemic areas), behavioural (activities during night, use of anti-vectorial devices and observation of chemo prophylaxis) and environmental determinants. Environmental factors have been evaluated using remote sensing methods (e.g. NDVI estimated by satellites) and epidemiological data bases. Serological data suggest that most anti-vectorial devices (except repellents) are effective to prevent infections. The permanent use of treated bed net and long-sleeved battledress during the nights were associated with more than 60\% adjusted protective efficacy. Serological and clinical data show that environmental factors are the most important determinants of malaria risk and these predictive factors are assessable using remote-sensing data and epidemiological data bases that are freely accessible. The observance of the chemoprophylaxis is the second most important determinant factor of the incidence of clinical malaria. The irregular intake or the premature arrest of the chemoprophylaxis are associated with more than an half of the clinical malaria cases during or after the mission.

**O28-10**

\textbf{Outbreak of chikungunya fever on La Reunion island: serological results of a military cohort study}

B. Queyraux1, M. Grandadam2, R. Michel1, H. Tolou2 and J. P. Boutin1

1 \textit{Epidemiology and Public Health Department, French Forces Institute of Tropical Medicine, Marseille, France}; 2 \textit{Virology Department, French Forces Institute of Tropical Medicine, Marseille, France}

OBJECTIVES A major outbreak of chikungunya fever has spread out in La Reunion island (southwestern Indian Ocean) since the beginning of 2005. In January 2007, the cumulative estimated global incidence was 266 000 (35\%). In June 2006, the French Forces Institute of Tropical Medicine performed a retrospective cohort study among the 737 military policemen distributed over the island. It is one of the first assessments of seroprevalence following this massive outbreak.

METHODS Each volunteer has completed a questionnaire and has given a blood sample. Antibodies (IgM and IgG) directed against Chikungunya virus were tested using MAC-ELISA and IgG-capture assays, with three different ways: using unwarmed serum, warmed serum and plasma.

RESULTS The number of participants was 662 (87.4\%). Most of them were male (94.7\%), the mean age was 39.4 years. Our first results showed a global incidence of reported Chikungunya fever of 23.9\% (158/662) between January 2005 and June 2006. Gender and age were not related to illness. Seroprevalence of anti-Chikungunya virus IgM and IgG was respectively 9.5\% and 18.0\%. Global seroprevalence (i.e. positivity for IgM and/or IgG) on June 2006 was 19.3\%. Better results were obtained with plasma, the results with unwarmed serum were less sensitive. Incidence of asymptomatic forms (i.e. seropositivity without self-reported illness) was 3.2\%. This result is consistent with the assumption that the rate of asymptomatic forms is low with Chikungunya infection.

CONCLUSION This low rate of asymptomatic forms in our cohort suggests that the estimated incidence from the reported cases is very close to the real incidence of Chikungunya infection. So, the herd immunity can be assessed with the estimated incidence rate of clinical cases. On La Reunion island, two-thirds of the population were not infected and remain susceptible to the virus. So, due to this low herd immunization level, the threat of a new major outbreak is real.

**O28-11**

\textbf{Importance of serological antibody testing for reconnaissance of areas of military missions}

G. Dobler

\textit{Dept. of Virology and Rickettsiology, Bundeswehr Institute of Microbiology, M\'unchen, Germany}

OBJECTIVES Armed forces of European countries are increasingly engaged in areas with different climatic conditions and/or hygienic standards than usually found in Europe. The troops are therefore in risk to become infected with unusual pathogens. Often pre-mission medical reconnaissance is not available to evaluate the epidemiologic risk of infectious diseases as missions often take place in areas where no such information is available at all.

METHODS During an sero-epidemiological investigation 140 human sera from residents without any travel history of the Northern Afghan city of Kundoz were tested for prevalence of antibodies against various viruses (dengue virus, West Nile virus, tick-borne encephalitis virus, Sindbis virus, Sandfly Naples virus, Sandfly Sicilian virus, Crimean Congo virus, hantaviruses and rickettsiae. For testing commercial ELISA assays (where available), indirect immunofluorescence (commercial and in-house) and neutralization test (where applicable) were used.

RESULTS The results show evidence for circulation of West Nile virus (22.1\%), of dengue virus (3.6 \%), of sandfly fever virus Naples (9.2\%), Sindbis virus (2.1\%), Crimean Congo hemorrhagic fever virus (4.2\%) and hantaviruses (5.7\%). Antibodies against rickettsiae of the spotted fever group (19.5\%) and of the typhus group (49\%) were also detected.

CONCLUSION These results for the first time during the last 40 years give evidence on the existence of several arboviruses and rickettsiae in northern Afghanistan. The existence of some of the arboviruses and rickettsiae tested in this study was even not known to the governmental infectious disease experts.

Knowledge on the circulation of these pathogens is a prerequisite for prophylaxis against these pathogens. Serological testing antibodies in local population proofed to be a useful tool for the detection of pathogens in unknown epidemiological situations.
O28-12
Medical support during EUFOR DR Congo: in-theatre experiences and follow-up, first results
R. M. Hagen, M. Fischer, J. Bronnert, D. Wiemer, A. Krueger and T. Harbaum
BWK Hamburg, Fachbereich Tropenmedizin am Bernhard-Nocht-Institut, Hamburg, Germany

OBJECTIVES The aim of the medical task force during the military mission EUFOR DR CONGO was to provide an adequate treatment as early as possible for the deployed troops to assure the stabilisation and evacuation of severe ill patients to an appropriate level of care. The deployment of 780 soldiers during the first six months required intensive preventive preparations in regard to tropical environment, prevailing infectious diseases and limited medical standard in the Democratic Republic of Congo.

METHODS For this purpose briefings were regular held to sensitize the troops for major health risks like vector- and waterborne diseases and STD. In addition, a well defined vaccination schedule was applied to assigned military personnel. In Kinshasa as well as in Libreville (Gabon) field hospitals were maintained during the deployment containing surgical capabilities as well as laboratory facilities. Medical doctors specialised in infectious diseases and hygiene provided an appropriate in-theatre management on both locations. MEDEVAC aircrafts were in stand-by to evacuate critical ill patients. An evaluation team was deployed to monitor the vector pressure. After redeployment of all troops, soldiers were followed up by their GP and standardized laboratory examinations were performed to exclude possible acquired infectious diseases. In addition, clinical symptoms and possible side effects of the chemoprophylaxis were documented.

RESULTS During the mission and the follow-up period of 3 months no case of Malaria or other tropical infectious disease occurred. Four patients with required intensive care and one with a renal failure were evacuated.

CONCLUSION Preventive means in combination with medical facilities under European standards tailored to mission resulted as expected by assuring physical fitness and readiness of the deployed troops. The continuous presence of an infectious disease consultant has proved to be effective in order not only to treat but to prevent tropical diseases.

O28-13
Health care in adverse circumstances, experiences from Zabul and Uruzgan provinces in Afghanistan
T. Loginova¹ and L. Bazeliuk²
1Necrological hospital ‘Sociotherapy’, Kiev, Ukraine; 2Drop-in-Center, Kiev, Ukraine

OBJECTIVE To draw lessons from implementing primary health care in two southern provinces in Afghanistan.

METHODS The study gives an overview of developments in health policies and practices in Afghanistan since 2001. It describes the health care programmes in Zabul and Uruzgan provinces. The study assesses successes and failures of the programmes, applying criteria developed by Carlson et al. for health and education in difficult environments (DHID Health Systems Resource Centre, 2005). The study used David Korten’s ‘model of fit’ (Korten, 1985) to assess relations between the organisations, the health care programme and the beneficiaries.

RESULTS Afghanistan started almost from scratch in development of health care after the Taliban regime was removed. The Ministry of Public Health initiated an innovative way of stewardship: the ministry formulates policies and defines packages of care; the ministry contracts non-governmental organisations for implementation of health services and monitors their performance. The non-governmental organisations have the freedom to implement health services, according to local opportunities. The local population is poor and lives in a disadvantaged position in remote and infertile areas, with a poor infrastructure. Schools and health facilities are scarce. The population in general holds conservative views on society. The women face limited rights on education and health services. The population disallows contacts between male health workers and female patients. Disruptions by insurgents are frequent; travelling in rural areas is dangerous. Because of threats of Taliban, rural areas are no-go areas for government officials. Under these circumstances it is difficult to recruit female staff and to mobilise female community health workers. It is problematic to open new health facilities in the rural areas. Despite these constraints Afghan NGOs have managed to increase coverage of both curative and preventive health services, with the exception of supervised deliveries. Critical success factors were maintaining strict neutrality and close contacts with traditional leaders in the provinces. Building trust between NGOs and local communities was crucial. The NGOs built strong internal support structures for health services. In addition, guaranteed funding and flexibility from the donor side contributed to the success.

CONCLUSIONS Under difficult circumstances, it was possible to expand health services in two southern provinces in Afghanistan. The government policies allowed NGOs to take full responsibility for health service delivery in the provinces. The NGOs maintained strict neutrality and used traditional structures in the society to build trust and gain access. Increase in health coverage was achieved.

O28-14
Arrangement of social aid and medical care to IDUs in a specific district of Kyiv
1. Loginova¹ and I. Bazeliuk²
1Necrological hospital ‘Sociotherapy’, Kiev, Ukraine; 2Drop-in-Center, Kiev, Ukraine

OBJECTIVE To improve the IDUs access to HIV voluntary counselling and testing (VCT). This work is carried out in place of IDUs ‘accumulation’ – by subdivisions of the narcological hospital ‘Sociotherapy’ (where IDUs get medical treatment), departments of Criminal Correctional Inspection (where probationers are registered) and NGO ‘Drop in Center’. The Correctional Inspection provided a premise for HIV voluntary counselling and testing using quick tests. In case of positive results the client is sent to the AIDS Center for in-depth clinical and immunological examination and prophylactic follow-up. Such type of social and medical aid is on demand and convenient for the clients – testing is anonymous, confidential and free of charge, undergoes in friendly environment without moralizing and disapproval of their behaviour.

RESULTS Increase of VCT importance as the tool for HIV prevention; quick determination of serostatus; ability to provide results during first client’s visit for counselling and enrolment; intervention programs (Harm Reduction Program, Substitution Therapy, adherence to ARV program & ARV treatment; increased number of tested clients; bigger number of HIV-positive persons has been identified for appropriate treatment and social support.

CONCLUSION Within the current period 28% of HIV positive persons has been detected out of the total examined IDUs. VCT in
place convenient for IDUs encourages them for safer behaviour; examination of sex and drug partners; expands the possibility of IDUs participation in rehabilitation programs, substitution and ARV therapy (in case of HIV+ status).

O28-15
Challenging health systems with community’s perceptions and expectations through socioanthropological feed-back data
P. Huynens, J. Macq, S. Laokri and B. Dujardin
Université Libre de Bruxelles, Politiques et Systèmes de Santé dans les Pays en Développement, Bruxelles, Belgium

OBJECTIVES FORESA3 is an operational research programme aiming at improving health care making it more sensitive to patients’ expectations and needs. Taking TB as an entry-point to criticize health systems in four West African countries implementing ‘patient-centred approach’ (PCA), the project ultimately research dysfunctions and strategies to overcome them.

METHODS Qualitative operational research has been used, questioning health practitioners and other actors on results obtained in the field by a multidisciplinary team of socioanthropologists and public health specialists about access to TB care and prevention. 160 semi-structured interviews were conducted in the 4 sites together with direct observation. Participatory methods of group discussions were also used. Data were transcribed in French and analysed using Atlas-ti.

RESULTS The method proved efficient in stimulating reflexivity on health practices and interactions amongst health workers and politics. In the field, new synergies were created with the civil society, notably between traditional healers and health workers. However, the extension to be given to the well-known concept of PCA was found variable according to the actors. Causes of resistances to change attitudes and practices amongst Health Workers will be elicited from the data.

CONCLUSION Restitution of socioanthropological feed-back data from the civil society about their perceptions and expectations of the ‘patient-centred approach’, often demonstrates controversies according to the actors. Arena of discussions around PCA often tells us more about the motivations of ‘holders’ criticizing or establishing the legitimacy of powers around the stake of patients ‘wellbeing’.

O28-16
From informers to transformers: a new role for women health volunteers in Tabriz City, Iran
M. R. Sheikh1, D. E. Tarin1, E. H. Behdad2, and P. S. B. Rifkin3
1World Health Organization, Tehran, Islamic Republic of Iran; 2National Public Health Management Center, Tehran, Islamic Republic of Iran; 3London School of Economics, Social Policy, London, UK

OBJECTIVES To test the hypothesis (in a pilot project): Health Volunteers are more able to support community participation and empowerment for health improvements by facilitating communities to define and solve their own problems than by only providing information on health problems.

METHODS A research team from the National Public Health Management Center in Tabriz was constituted and a 3 day workshop was held to present participatory approaches to this team and Provincial and Municipal Health Managers. The Principal Investigator trained Women Health Volunteers (WHV) for one of the urban health centres to use methods of mapping, matrix priority setting and a visioning matrix (all visualisation methods) to do a participatory needs assessment with the families for which the WHV were responsible. The needs assessment resulted in a list of priority activities which each group undertook with support from the health center to address the identified problem.

RESULTS Each group identified and took action to address the problem they chose. The most striking example was a group who decided to do morning exercises to improve the health of women over 50 in a park which was taken over by drug addicts. Regular activity by these women removed the addicts from the park. In addition, the women requested further information and meetings from the WHV on health topics relevant to older women. Their husbands supported meetings to discuss drug problems with the male youth in the area.

CONCLUSION It is possible to enable local people to identify and act upon their self defined needs with support of local health staff. More research is needed however to assess how the pilot can be scaled up and how initial enthusiasm can be sustained.

O28-17
Skill sets for successful engagement of communities in research for health
H. Jeene1, S. De Haan2, R. Jordi3, K. Khan4, V. Kimotho4, J. Njoka5 and V. Varshney6
1African Medical and Research Foundation AMREF, Nairobi, Kenya; 2Council on Health Research for Development - COHRED, Geneva, Switzerland; 3Industrial Health Research Group - IHRG, Capetown, South Africa; 4Aga Khan University, Karachi, Pakistan; 5University of Nairobi, Nairobi, Kenya; 6Centre for Science and Development, New Delhi, India

INTRODUCTION Community members are often not recognised as a potential human resource in health research. The contextual knowledge that communities have, and indeed wisdom, is a reason for ensuring their full participation, certainly where resources seem poor.

MATERIALS AND METHODS A working group on Civil Society participation in research for health analysed a number a case studies where communities had either set the research agenda, were actively participating in research, and/or were involved in translating research into policy and action.

RESULTS AND DISCUSSION It was found that relatively small scale technical and methodological support was essential in all case studies. The successful case studies had in common that the community human resource could be potentiated to a large degree through the transfer of a modest set of skills. This skills set was fairly uniform across the case studies from Africa and South Asia. This set of skills is however not part of routine university research methodology curricula. As a result academic researchers often under-utilise the human resource potential in the study communities and use methodologies that are more exhaustive than participatory, and more costly as potential human resources in the community are not utilised to their full potential. An outline of skill sets required for academicians, development workers, health staff and local decision makers will be presented.

CONCLUSIONS The development of modules on community research for health, both for inclusion in academic curricula, and for use in Continuous Professional Development (CPD) has high potential for mobilising more human resources for research for health. The relevance of this in resource poor settings is high.
Leptospirosis

O28-18
Sero-epidemiology and serological follow-up of anti-leptospiral IgG in children in southern Vietnam

1Academic Medical Center, Division of Infectious Diseases, Tropical Medicine and AIDS, Amsterdam, Netherlands; 2Department of Virology, Cho Ray Hospital, Ho Chi Minh City, Vietnam; 3Binh Thuain Provincial Malaria and Goiter Center, Phan Thiet City, Vietnam; 4Cho Ray Hospital, Tropical Diseases Clinical Research Center, Ho Chi Minh City, Vietnam

OBJECTIVES To investigate the sero-epidemiology and persistence of IgG antibodies against Leptospira among children in rural southern Vietnam.

METHODS Serum samples from 262 primary school children (7–13 years of age), taken in 2003–2005 were analysed with a commercially available enzyme-linked immunosorbent assay (ELISA).

RESULTS Sero-conversion was observed in 10.4% (22 of 211, 95% CI 5.6–26.7) of the children, corresponding to an annual incidence of 0.87% (95% CI 0.80–0.92). None recalled a disease suggestive of severe leptospirosis. In 61% (31 of 51, 95% CI 47.1–73.0) of the children with detectable Leptospira IgG antibodies in 2003, these were still detectable 2 years later.

CONCLUSION Leptospira IgG antibodies may develop and persist for years in children who do not recall recent manifestations suggestive of severe leptospirosis. The results of cross-sectional surveys uncover the dynamics of waxing and waning antibody concentrations and point at a large burden of clinically non-significant Leptospira infections in southern Vietnam. This also causes background reactivity for serological testing and thus necessitates collection of paired sera for demonstration of seroconversion to diagnose acute leptospirosis.

O28-19
Survival of pathogenic leptospires in fresh water
F. Aviat1, S. Rocheress-Roulet2, J. Bellin2, C. Lefur3, A. Kodo3 and G. Andre-Fontaine1

1Ecole Nationale Vétérinaire de Nantes, Unité de Bacteriologie Medecale et Moleculaire des Leptospires, Nantes Cedex, France; 2Ecole Nationale Vétérinaire de Lyon, Immunologie-Microbiologie-Pathologie Infectieuses, Lyon, France

Leptospirosis is an important infectious disease in humans with a worldwide distribution. Many studies show fresh water is very important when leptospirosis outbreaks expand. It is interesting to study the behaviour of pathogenic leptospires in fresh water and in particular their survival and preservation of virulence.

OBJECTIVES The aim of this assay in vitro was the study of pathogenic leptospires survival, strain 564 serovar Icterohaemorrhagiae, in natural mineral waters.

MATERIAL AND METHOD Five natural mineral waters were chosen according to their pH and mineral contents. One millilitre of strain 564 culture was inoculated into 150 ml of each filtered mineral water. Aliquots of each preparation was stored at 4°C, room temperature and 30°C. Leptospirosis survival in mineral waters has been followed over 20 months. Every month cultures and pH were realized for each condition. One month later, cultures were observed to detect possible multiplication of survivor leptospires. The preservation of virulence for strain 564, after reinoculation from mineral waters, was checked on gerbils highly susceptible animal model.

RESULTS Leptospirosis survival was different from one to another mineral water. The longest survival was 10 months at 4°C, 14 months at room temperature and 20 months at 30°C. When pH was basic, leptospires didn’t survive but acid pH has not perturbed the pathogenic leptospires multiplication whatever temperature. On 13 and 20 months, two water reisolates were tested on gerbils. They died on third day after injection.

CONCLUSION This original work showed that survival and keeping virulence of leptospires was possible in mineral waters although conditions were unfavourable. Leptospiroses could survive many months in natural waters with different mineral characteristics and pH even acid. Which mechanisms are responsible for pathogenic leptospiroses survival in drastic conditions? These data confirm that leptospirosis is a waterborne disease with a major risk for human in tropical areas.

Filariasis

O28-20
A rapid health impact assessment of the African Programme for Onchocerciasis Control (APOC)
W. A. Stolk1, L. J. Veerman1, S. J. De Vlas1 and J. D. F. Habbema1

1Erasmus MC, Department of Public Health, Rotterdam, Netherlands

BACKGROUND Onchocerciasis is an important cause of visual impairment, blindness, skin lesions and severe itching. The African programme for onchocerciasis control (APOC, 1995–present) operates in 15 countries, aiming to eliminate onchocerciasis as a public health problem by yearly mass treatment with ivermectin.

OBJECTIVE To assess the impact of APOC thus far on skin and eye problems and the burden of disease (DALYs) and to predict its impact for the next 10 years.

METHODS We categorized the population in the APOC area according to type of onchocerciasis, pre-treatment endemicity level, and number of treatment rounds by the end of 2005. Using mathematical simulation, we estimated the impact of APOC on the prevalence of infection and disease in each category. We then calculated and aggregated the expected number of people with infection and disease and estimated the annual number of DALYs lost. All reported numbers are standardized to the size of the population in 2005.

RESULTS Before the start of APOC, respectively 25% and 75% of the 88.5 million target population lived in areas with savannah and forest/mixed type of onchocerciasis; 5%, 30%, 33% and 31% respectively lived in non-, hypo-, meso- and hyperendemic villages; 27%, 17%, 16% and 41% respectively had 0, 1–3, 4–6 and 7–9 rounds of CDTI. Overall, the prevalence of troublesome itch, blindness and low vision were about 15.3%, 0.4% and 1.1%. By the end of 2005, these numbers were reduced by about 60%, 28%, and 16% respectively. The annual DALY-loss was 1.7 million before APOC, but was about halved by 2005. With continuation of APOC and especially by inclusion of the 27% APOC population not yet treated in 2005, the annual DALY loss may be reduced to <15% of its pre-APOC level by 2015.

CONCLUSION The APOC strategy has a strong impact on the prevalence of itch. The rate of reduction in blindness and low vision are lower, because of the irreversibility of these consequences of onchocerciasis. The burden of onchocerciasis-related disease in DALYs was almost halved by 2005 and can be reduced to <15% of the pre-APOC burden, if the programme continues successfully in the next 10 years. Estimates of the pre-APOC prevalence of clinical manifestations are subject to uncertainty, due to limited data availability and high variability between studies. The same problems hamper validation of the model predictions. Field studies are required to confirm the results of this rapid impact assessment.
O28-21
Prevalence and density of microfilaria in a Loa loa endemic zone of Gabon
The Authors

OBJECTIVES Microfilaria (mf) has been shown to be the major determinant to the transmission and fatal side effect during chemotherapy in loasis. In order to map blood born filaria in Gabon, and to study the distribution of microfilaria.

METHODS A survey was organised in different parts of the country based on randomly chosen villages. 1825 individuals were selected based on this approach. A direct examination of 10 µl of blood, followed by a parasite concentration technique on 1 ml of blood was performed systematically on each sample collected between 9:00 a.m. and 3:00 p.m.

RESULTS It appeared that the overall prevalence of microfilaria was 33%; with 25% of Loa loa; 12% of Mansoumella perstans, and 3% mixed L. loa and M. perstans infection. Males were more often infected than females (299 vs. 157; χ² = 70.63, d.f = 1, P < 0.001). The prevalence was variable according to the area, with L. loa being more prevalent in the west coast (33.5%, n = 313) compared to the equatorial region (n = 584, 26%; P = 0.01), the extreme north (n = 589, 22.2%, P < 0.001), and the extreme south (n = 339, 20.3%, P < 0.001). Furthermore, the prevalence was significantly higher around equator when compared to the northern (P < 0.001) and southern (P = 0.05). Age did affect the prevalence in the southern area (P < 0.04). In contrast, the prevalence of individuals with heavy microfilaria loads (mf > 5000/ml) was similar in all area examined (P = 0.05).

CONCLUSION These results suggest that the density of microfilaria at an individual level is not dependent on geography, age, or sex. Therefore the risk of side effects in case of mass chemotherapy might be similar in any area of the country.

O28-22
Assessment of the prevalence of Onchocerca volvulus infection in Damba district, province of Uige, Angola
The Authors

BACKGROUND The presence of foci of Onchocerca volvulus transmission in Angola has been already documented by APOC (African Programme for Onchocerciasis control), but the definition of the endemcity level in the different regions has yet to be achieved. In six areas of the country only has the CDTI (Community Directed Treatment with Ivermectina) project been approved. In the Damba district, situated in the Northern Province of Uige, a collaboration between the Ministry of Health and the Italian NGO CUAMM-Medici per l’Africa has been underway for 4 years. The finding of a high prevalence of subcutaneous nodules, dermatologic and also ocular lesions prompted the medical team to perform a REMO (Rapid Epidemiological Mapping of Onchocerciasis, WHO/TDR) in collaboration with the Health Province of Uige and with the National WHO office.

OBJECTIVES To map for the first time the prevalence of onchocerciasis in the Damba district, Province of Uige, Northern Angola.

METHODS The survey was carried out following the classical REMO method. Briefly, based on favourable geo-climatic criteria for simulid habitat, 13 high-risk and six low-risk communities were selected. In each community, 50 adult males (age 20–60 years, resident in the area for at least 10 years) were randomly selected and clinically screened for nodules, skin lesions and blindness. Based on the prevalence of nodules, the communities were classified as hyper, meso and hyperendemic.

RESULTS In 12 high-risk communities accepting to participate, 271/596 subjects overall (45.5%) had subcutaneous nodules; eight of them were classified as hyperendemic (prevalence >40%). In five low-risk villages the prevalence of nodules was 43/252 subjects or 17%; two were mesoendemic (prevalence 20%–40%) and three hypendemic (<20%).

CONCLUSION We found a high prevalence of onchocerciasis in several communities, justifying to start a community control program (CDTI). A previous RAPLOA had been carried out in the same province in 2004, but only in 12% of the 17 endemic villages (with negative results). This assessment should now be completed in the remaining villages before CDTI according with the recommendations of the expert Committee on areas of co-endemicity (O. volvulus and L. loa infection), in order to avoid the risk of severe meningoencephalitis following ivermectin administration (Boussinesq M et al. Relationships between the prevalence and intensity of Loa loa infection in the Central province of Cameroon. Annals of tropical medicine and parasitology, 2001, 95, 495–507).

Health Financing and Community Insurance in SS Africa

O28-23
Performance agreements in Costa Rica’s primary care
The Authors

OBJECTIVES To identify if and how Performance Agreements (Compromisos de Gestión) hamper service delivery at primary care level in Costa Rica. Introduced since 1996 and conceptualized as a purchaser-provider split within Costa Rica’s main provider (CCSS, Caja Costarricense de Seguro Social), Performance Agreements aim at improved service delivery by gradually replacing historical financing by payment for performance.

METHODS In-service observation, key informant interviews and focus group discussions during four field visits (2004–2006) to the Alto Arazu region of Costa Rica conducted by a team from the Antwerp Institute of Tropical Medicine (Jean-Pierre Unger, Pierre De Paepe and Werner Soors) in co-operation with the regional medical division of the CCSS.

RESULTS The following effects of performance agreements (PA) were detected at primary care level: a handful of PA items consumes on average 36% of all available consultation time; the coincidence between registered and observed examination and diagnosis activities is lower in PA than in other consultations; consultation time dedicated to note taking only is higher in PA than in other consultations. Indicators of patient-centered care score lower in PA than in other consultations. Between 43% and 90% of the population refers difficulties to access medical care for needs or demands not covered by the PA. CONCLUSION Performance Agreements in Costa Rica indeed hamper service delivery. Negative effects on both quality of care and access to care were identified. Moreover, the poor are the first to be directly affected, as they have little options (they can wait, go to an emergency ward, or forego consultation). In the end they might suffer even more, as middle class is pushed toward the private sector, thus eroding solidarity. To avoid the disintegration of its...
To assess the impact on health services from the IMF programmes constrain government spending in 135

The ‘removal of user fee policy’ in rural areas in 4 2 and A. Rietsema
Out of pocket health expenditure decreased by 62%
The studies identify a number of ways in which IMF
ª 3
Utilization of services in districts where user fees were
2007 The Authors
Desk reviews and country casestudies (Sub-Saharan
Present the institutional set-up and discuss the results
tracking system’ will be used to decide on further expansion of the
health need to be developed. A national ‘service utilization
tors (e.g. community involvement, waiting time and staff motiva-
institutions) are being tracked and analysed in Southern Province.
METHODS A literature review on user fee policies was done. Health
service data were analysed over a two-year period before
policy implementation and compared to data for the period after
user fees were removed (April–December 2006). Semi-structured
staff interviews, facility observations and district reports were used
to assess quality.
RESULTS Utilization of services in districts where user fees were
removed has increased by >50%, but shows substantial variation
in place and time. Utilization in districts with continuation of user
fees remained nearly unchanged, indicating that user fee removal
did initially increase access to health care. The increase in staff-
workload together with the removal of bonus payments resulted in
burn-out, de-motivation and staff attrition. Drug consumption
increased and drug shortages occurred frequently, leading to a
reduction in access where people were forced to buy drugs
elsewhere. User fee revenue used to be retained at facility level and
was essential to maintain quality in times of shortages. Activities
previously funded through user fees could no longer be imple-
mented (e.g. maintenance, supplementary drugs and support staff)
or were funded from other sources, leading to unplanned grant
expansion and increase in debt. The simultaneous reduction in
district funding due to the appreciation of the local currency
aggravated the negative effects. Involvement of community
partners reduced, because Neighbourhood Health Committees
previously decided on the use of medical revenues.
CONCLUSION The ‘removal of user fee policy’ in rural areas in
Zambia in 2006 was partly based on a study by the University of
Ctinga province. Utilization of health services increased as expected,
Zambia. Utilization of health services increased as expected,
although further analysis will determine if this was mainly due to
increased access for rural poor or to ‘trivial use’. The negative
effects on the health system such as increased staff workload,
increased drug consumption leading to drug shortages and reduced
quality were foreseen, but recommended compensation measures
were not taken. Innovative ways to keep communities involved in
health need to be developed. A national ‘service utilization
tracking system’ will be used to decide on further expansion of the
policy.

Performance-based financing and changing the district health
system: experience from Rwanda
R. Soeters 1, C. Habineza 2, P. B. Peerenboom 3 and A. Rietsema 4
1 Consultant to Cordaid, Den Haag, Netherlands; 2 Cordaid, Kigali, Ru-
da; 3 Consultant to Cordaid, Doetinchem, Netherlands; 4 Cordaid, Den
Haag, Netherlands
OBJECTIVES Document experiences with performance based
contractual relationships in Cyangugu province, Rwanda.

METHODS Present the institutional set-up and discuss the results
of two household surveys and of a World Bank study in Cyangugu
province.
RESULTS Out of pocket health expenditure decreased by 62%
from USD 9.05 to USD 3.45. The percentage of respondents
declaring that user fee payments had been ‘catastrophic’ decreased
from 2.5% in 2003 to 0.7% in 2005. The proportion of women
delivering in a health facility increased from 25% to 60%. Family
planning acceptance increased 5.4–11.6%. An unexpected result
was that to expand their production, health facility managers
created 120 new jobs for skilled and previously unemployed
workers.
CONCLUSION Evidence from low-income Asian countries shows
that performance-based financing (as a specific form of contract-
ing) can improve health service delivery more successfully than
traditional input financing mechanisms. The experience from
Rwanda demonstrates that performance-based financing is a
feasible strategy in sub-Saharan Africa too. Performance-based
financing requires at least one new actor, an independent well
equipped fundholder organization in the district health system
separating the purchasing, service delivery as well as regulatory
roles of local health authorities from the technical role of contract
negotiation and fund disbursement. In Rwanda, local community
groups, through patient surveys, verified the performance of health
facilities and monitored consumer satisfaction. A precondition for
the success of performance-based financing is that authorities must
respect the autonomous management of health facilities competing
for public subsidies. These changes are an opportunity to
redistribute roles within the health district in a more transparent
and efficient fashion.

Health sector budgets and IMF macroeconomic policies
E. Verheul
1Wemos, Amsterdam, Netherlands
OBJECTIVES IMF programmes constrain government spending in
order to achieve and/or maintain macroeconomic stability. Studies
by Wemos (2006) and the Centre for Global Development (2007)
assessed whether and how the macroeconomic policy framework
in IMF programmes unduly limit health sector budgets, and
therefore constrain the scaling up of health expenditures necessary
for achieving the health millennium goals.
METHODS Desk reviews and country casestudies (Sub-Saharan
Africa).
RESULTS The studies identify a number of ways in which IMF
programmes restrict the potential to increase public sector budgets,
including for health. IMF fiscal policies limit government
expenditure, while the rationale provided for these policies is at
best sketchy. No evidence was found that social trade-offs were
analysed. Feasible policy alternatives (that would allow higher
spending levels) were usually not explored. Spending limits on
public sector wages, an element in many IMF programmes, proved
to be ineffective instruments and have adverse consequences for
the health sector facing severe human resource crises. The
disconnect between macroeconomic and social policy making is
aggravated by a lack of capacity in Ministries of Finance to analyse
alternative policy choices and Ministries of Health to present
prioritised and costed sector plans. In addition, IMF programmes
predict aid levels to decrease in the medium term, contrasting
global commitments to substantially increase aid.
CONCLUSION The current ‘way of doing business’ needs to
change, in order to achieve the health MDGs and strengthen health
systems in Africa. Macroeconomic and fiscal frameworks should be based on MDG-based sector plans, linking long-term development goals with short-term macroeconomic stability concerns. Donors should scale-up aid levels and harmonise their programmes. Capacity building to analyse, plan and budget should be enhanced at all government levels. Civil society monitoring and advocacy is paramount.

**Schistosomiasis I1: Epidemiology and Diagnostics**

**O28-27**

*Present status of urinary schistosomiasis in Iran*

G. Mowlavi, J. Massoud, A. Mansoorian, A. Nikkhoo and A. Kejbafzadeh

1 Medical Parasitology Tehran, Tehran University of Medical Sciences, Islamic Republic of Iran; 2 Tehran University of Medical Sciences, Tehran, Iran, Islamic Republic of Iran

**INTRODUCTION**

Urinary Schistosomiasis has been known to endemic in southwestern Iran since decades ago. It was, until recently one of the major public health problem for the only endemic province of Khuzestan, with the highest rate of 8.3% (40 000–50 000 infected individuals) in epidemic periods (in 1970). The success of the interventions which were based on case finding, the treatment of the infected individuals, and the chemical and environmental control for Bulinus truncates is obviously prominent in current monitoring.

**OBJECTIVES**

As the country is approaching elimination phase for urinary schistosomiasis, the national committee within the Ministry of Health has encouraged its affiliated centers for more studies on different aspects of disease transmission. The present study has carried out to determine the present status of urinary schistosomiasis in Khuzestan province as well as finding the new habitats for Bulinid snails.

**METHODS**

Urine examinations were drawn from villagers residing in the areas, mainly among school children (80%), using both centrifugation and visible haematuria technique for schistosome ova. During a sequential visit by our team urine specimens were collected between 10:00 am and 14:00 pm for almost 4 years. Each person was given a prenumbered bottle in the field, and the name of the person including age and sex was entered against the appropriate number on a form kept by the investigating team.

**RESULTS**

Up to now a total of 3400 persons have been examined. The present results indicate that, in the Khuzestan region, the transmission of *Schistosoma* haematobium is being successfully interrupted as none of the samples were found to be positive.

**CONCLUSION**

The plan for the future is to continue monitoring transmission, by passive surveys in local health centers and active case-finding among schoolchildren, and to continue snail sampling and focal mollusciciding. Total elimination appears to be possible if the health authorities in neighboring areas can be persuaded to adopt a similar strategy of integrate control.

**O28-28**

*Schistosomiasis in African infants and pre-schoolers*

R. Stothard

1 Natural History Museum, Zoology, London, UK

**OBJECTIVES**

From the perspective of preventive chemotherapy control, schistosomiasis in infants and preschool children has been largely overlooked. In this talk I will review the existing literature and comment upon data obtained from directed field surveys undertaken in Uganda, identifying the barriers to use of praziquantel (PZQ) within the younger child.

**METHODS**

A total of 155 mother and child pairs, from 12 shoreline villages on Lake Victoria in Uganda, were examined for intestinal schistosomiasis. Diagnosis relied upon a combination of parasitological sampling (Kato-Katz thick smears and formol-ether concentrations of three consecutive stool samples) and urine dipsticks which detect circulating cathodic antigen. Water contact patterns of the participants were assessed using an interrogative questionnaire.

**RESULTS**

The prevalence of intestinal schistosomiasis within this sample of children aged between 5 and 36 months was approaching 50%. It was found that *Schistosoma mansoni* was the dominant helminth and that infected children were 3.6 (95% CI 0.9–14.1) times more likely to have an infected mother.

**CONCLUSION**

Infants and preschool children within high transmission locations are at certain risk of schistosomiasis. While such younger children would benefit from administration of PZQ, there are presently constraints which would limit its use.

**O28-29**

*Multiplex real-time PCR for the (semi)-quantitative detection of Schistosoma mansoni and S. haematobium in stool samples collected in northern Senegal*

R. ten Hove, J. Verweij, K. Vereecken, K. Polman, L. Dieve and L. Van Lieshout

1 Leiden University Medical Center, Parasitology, Leiden, Netherlands; 2 Institute of Tropical Medicine, Parasitology, Antwerp, Belgium; Centre Santé de Richard Toll, Richard Toll, Senegal

**OBJECTIVES**

Epidemiological studies on schistosomiasis traditionally rely on the detection of parasite eggs in stool or urine by microscopy. We developed a multiplex real-time PCR assay for species specific (semi)-quantitative detection of *Schistosoma* infections as a possible alternative or additional tool for diagnosis of schistosomiasis in stool samples collected under field conditions.

**METHODS**

Specific primers and Taqman probes were designed on cytochrome-c oxidase sequences of *S. mansoni* and *S. haematobium*, and together with primers and probe for the detection of an internal control optimized as a multiplex real-time PCR. The PCR was technically evaluated with DNA isolated from individual adult *Schistosoma* worms and a wide range of non-related parasitic, bacterial and negative controls (*n* = 150). For comparison of the multiplex real-time PCR with *Schistosoma* egg excretion 176 stool samples were analysed collected from 88 individuals living in a remote village in northern Senegal endemic for both *Schistosoma* species. All individuals participated in a large cross-sectional population based study and were selected for PCR analysis on the basis of microscopic examination of at least two stool and two urine samples representing a wide range of egg excretion. Stool sample aliquots were mixed with ethanol within 24 h after production and stored and transported at local temperatures for several weeks before DNA isolation and PCR was performed at the laboratory.

**RESULTS**

The multiplex real-time PCR for the detection of *S. mansoni* and *S. haematobium*-specific DNA in human faecal samples showed 100% specificity while sensitivity was comparable to Kato-Katz stool examination, both for single and duplicate stool samples. In addition, a high number of *S. haematobium* infected individuals showed *S. haematobium*-specific DNA in their stool samples. A significant correlation was demonstrated between the Cycle threshold-values of the species-specific PCRs and the microscopically determined intensity of infection, being either the counted number of *S. mansoni* eggs in stool or *S. haematobium* eggs in urine.

**CONCLUSION**

The described PCR approach shows promise for species specific (semi)-quantitative detection of *Schistosoma* DNA
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in faecal samples. The simple sample collection procedure and the high throughput potential may provide a powerful diagnostic tool for epidemiological studies on schistosomiasis in remote areas, with possibilities for extension to other helminths or protozoa, using additional molecular targets.

O28-30
Specific adaptations in the outer-surface of adult Schistosoma mansoni and binding of circulating antigens to host lipoproteins

J. J. Van Hellemond1, H. Sprong2, J. F. H. M. Brouwers1 and A. G. M. Tiels1
1Biochemistry and Cell Biology, Utrecht University, Utrecht, Netherlands; 2Membrane Enzymology, Utrecht University, Utrecht, Netherlands

OBJECTIVES • Characterization of the lipid and protein composition of the outer-surface membranes of blood-dwelling schistosomes in order to detect tegument-specific factors involved in host-parasite interactions. • Study of the binding of schistosomal antigens to host lipoproteins and their effect on the immune system of the host.

METHODS • Isolation of tegumental membranes followed by identification by mass spectrometry. • In vitro and in vivo studies on GPI-anchored schistosomal antigens.

RESULTS Characterization of the proteome of the tegument of adult schistosomes resulted in the identification of 43 tegument-specific proteins, of which over 20% showed no homology to any other sequence present in the databases. Characterization of the lipidome resulted in the identification of many tegument-specific lipids, of which lysophosphatidyl-serine was demonstrated to activate toll like receptor two on dendritic cells, a process that results in the induction of a regulatory T-cell response. GPI-anchored schistosomal antigens (such as Sm200) circulate on host lipoproteins, which subsequently (i) are endocytosed via the LDL-receptor by non-immune cells, and (ii) are bound by host antibodies that then allow endocytosis of lipoproteins by immune cells via the Fc-receptor pathway, resulting in induction of apoptosis in neutrophils.

CONCLUSION The tegumental outer-surface membrane of adult schistosomes is the host-parasite interface and contains many tegument and schistosome-specific proteins and lipids. These compounds of the parasite are involved in manipulation of their host for their long term survival. Transfer of parasite antigens and immunomodulating lipids to host cells via host lipoproteins disrupts lipid homeostasis in immune cells, promotes neutrophil apoptosis and probably induces aberrant antigen presentation, resulting in an inefficient immune response of host.

The Pathology of Malaria

O28-31
Impact of HIV-1 infection on the hematological recovery after a clinical malaria attack

J. P. Van Geertruyden1, M. Mulenga2, V. Chalwe1, M. Nambozi2, D. Mukwamataba1, R. Colebunders1 and U. D’Alessandro0
1Parasitology, Institut voor Tropische Geneeskunde, Antwerp, Belgium; 2Clinical Sciences, Tropical Disease Research Centre, Ndola, Zambia; 3Universiteit Antwerpen, Antwerp, Belgium

OBJECTIVES Anemia is often associated with malaria and also the most frequent cytopenia in HIV-infected individuals. We compared hematological recovery in HIV-malaria co-infected with HIV negative malaria patients who successfully cleared parasitaemia.

METHODS We treated and followed up for 45 days, 971 adults (HIV+e651; HIV-320) with non-severe clinical malaria in Ndola, Zambia. Main outcome was hemoglobin (Hb) change after successful antimalarial treatment. Risk factors were analyzed in a multivariate linear regression model.

RESULTS At enrolment, HIV-1 infected patients had lower mean Hb compared to HIV-1 uninfected (122.6 g/l vs. 135.4 g/l; P < 0.001) and in HIV-1 infected, Hb was associated with CD4 cell count (P = 0.001). Fourteen days after antimalarial treatment, mean Hb decreased by 5.2 g/l (95% CI, -7.2 to -3.1; paired t test, P < 0.0001) in HIV-1 positive patients and by 3.7 g/l (95% CI, 5.1–2.2; paired test, P < 0.0001) in HIV-1 negative patients. HIV-1 was a risk factor (P < 0.001) for Hb decrease. Between day 14 and 45, Hb increased in both HIV-1 negative (+ 6.8 g/l; 95% CI, 4.8–8.9; paired t test, P = 0.0001) and HIV-1 positive patients (+ 2.8 g/l; 95% CI, 0.1–5.3; paired t test, P = 0.007). Hb increment tended to be lower in HIV-1 positive than in HIV-1 negative patients (P = 0.06). Evaluating the total 45 days period Hb did not recover in HIV-1 positive patients (1.2 g/l; 95% CI, 4.22–+ 1.71; paired t test, P = 0.66) and differed (P = 0.01) from the HIV-1 negative group (+3.45 g/l; 95% CI, 1.36–5.54; paired t test, P = 0.0001). After adjustment, age, Hb values at baseline, female gender and HIV-1 infection all negatively influenced the Hb recovery at day 45. The hematological recovery was not associated with CD4 cell count (P = 0.68).

CONCLUSION HIV-1 infected malaria patients had a slower hematological recovery after successful parasite clearance compared to non HIV infected, Malaria preventive measures should be a priority for this vulnerable group.[Mean Hb (SEM) by HIV-1 status ] [Mean difference Hb (SEM) by HIV-1 status ].

O28-33
Transferrin polymorphism influences the risk of severe malarial anaemia in Gabonese children

J. B. Lekana-Douk1, D. Parzy2, P. C. Nze Obiang1, D. Prieur2, P. Mouidi4, N. Obiang1, F. Fumoux3 and M. Kombila1
1 Département de Parasitologie-Mycologie et Médecine Tropicale, Université des Sciences de la Santé, Libreville, Gabon; 2Université de la Méditerranée, UR1P Institut de Médecine Tropicale Service de Santé des Armées Le Pharo, Unité de Pharmacogénétique des Maladies Parasitaires, EA 864, Marseille, France; 3 Université de la Méditerranée, Unité de Pharmacogénétique des Maladies Parasitaires, EA 864, Marseille, France

OBJECTIVE Severe malarial anaemia (SMA) is one of the most complications of severe malaria in African children. Although the factors that determine the patient outcome of malaria have not been completely defined, host genetics factors are implicated. SMA is often associated with iron deficiency, but explorations of soluble transferrin revealed controversial data. Several studies have involved transferrin polymorphisms in pathogenesis of diseases associated with iron deficiency. Here, we investigated the effect of polymorphisms of transferrin and TLR1 (transferrin receptor 1) in malaria pathogenesis.

METHODS A total of 194 Gabonese children (38 with uncomplicated malaria, 117 with mild malarial anaemia and 39 with SMA) were recruited. Polymorphisms were analysed using PCRRFLPs.

RESULTS The mean age of children with SMA was 27.7 months confirming that SMA is associated with young age (P < 0.05). Transferrin C3 allele characterized by G258S mutation (A879G transition in exon 7), is associated with the development of SMA (10.3% vs 0%, P < 0.05). This is consistent with observations showing that C3 allele increased the risk of haemolytic anaemia. The C2 allele, characterized by amino acid mutation P570S (T1815C transition in exon 15) is associated with the decreasing of the risk of development of SMA (25.6% vs. 2.6% and 10.8%, P < 0.05). Frequencies of C2 and C3 alleles are respectively 2% and 13% in the population of the study. Polymorphism of TLR1
(S142G) is not associated with the development of SMA and polymorphisms of transferrin exons 4, 8 and 12 were not detected. **CONCLUSION** The present study is the first that investigate the influence of transferrin on the pathogenesis of SMA and reports the association of transferrin polymorphisms with the risk of SMA in Gabonese children. Further studies in a larger population and family based analysis are required.

**O28-34**

**Matrix-metalloproteinases MMP-8, MMP-9 and their tissue inhibitors TIMP-1, TIMP-2 in children with Plasmodium falciparum malaria**

A. Dietmann\(^1\), R. Helbok\(^2\), P. Lackner\(^1\), M. Reindl\(^1\), P. Kremser\(^2\) and E. Schmutzhard\(^1\)

\(^1\)Clinical Department of Neurology Medical University Innsbruck, Innsbruck, Austria; \(^2\)Department of Parasitology University of Tubingen, Institute of Tropical Medicine, Tubingen, Germany

**OBJECTIVES** *Plasmodium falciparum* causes the most severe form of human malaria, which kills 1.5–2.7 million people every year. The exact mechanisms leading to cerebral malaria are still not fully understood. Especially the role of the blood-brain-barrier breakdown is an important point in the pathogenesis of neurological complications. In the present study, the proteolytic enzymes matrix metalloproteinases 8 and 9 and their tissue inhibitors 1–2 were analysed in the sera of Gabonese children with *Plasmodium falciparum* malaria with a special focus on cerebral malaria and severe malaria with convulsions.

**METHODS** Serum levels of MMP-8, MMP-9, TIMP-1 and TIMP-2 from children with cerebral malaria (n = 7) and severe malaria (n = 41) were compared with serum levels from children with uncomplicated malaria (n = 43), infectious diseases other than malaria and convulsions (n = 8), and healthy controls (n = 14). Levels were analysed using enzyme-linked-immunosorbtent-assays (ELISA) for total MMP-8, MMP-9, TIMP-1, and TIMP-2 on admission to hospital, 24 hours after admission and follow up after 6 (±2) weeks and correlated with the clinical course of patients.

**RESULTS** MMP-8 and TIMP-1 levels were significantly elevated in cerebral and severe malaria. MMP-9 levels showed no significant elevation in disease, but a strong correlation to MMP-8. TIMP-2 levels were lower in study groups than in healthy controls. The MMP-9/TIMP-1 ratio was lowest in cerebral and severe malaria patients, and decreased development during course of disease, a slightly increase was observed for TIMP-2.

**CONCLUSION** MMP-8 and TIMP-1 indicated severity of disease. Raised TIMP-1 levels and low TIMP-2 levels support the hypothesis of a TIMP-1-predominant pattern in acute inflammatory disease. Even if we could not demonstrate elevated MMP-9 levels in cerebral or severe malaria, the strong correlation of MMP-8 and MMP-9 suggests participation of both MMPs in the pathogenesis of malaria.

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**Dengue II: Immunology and Clinical Aspects**

**O28-36**

**Acute dengue: possible correlation with NS1 antigen profiles and disease severity**

K. T. D. Thai\(^1\), C. Tromp\(^1\), N. Van den Esch\(^1\), T. T. T. Ng\(^2\), H. L. Phuong\(^3\), N. V. Nam\(^1\), P. T. Giao\(^4\), L. Q. Hung\(^5\), G. J. Van Doornum\(^6\) and P. J. de vries\(^6\)

\(^1\)Academic Medical Center, Division of Infectious Diseases, Tropical Medicine & AIDS, Amsterdam, Netherlands; \(^2\)Department of Virology, Cho Ray Hospital, Ho Chi Minh City, Viet Nam; \(^3\)Tropical Diseases Clinical Research Center, Cho Ray Hospital, Ho Chi Minh City, Vietnam; \(^4\)Binh Thuan Provincial Malaria and Goiter Center, Phan Thiet city, Vietnam; \(^5\)Department of Virology, Erasmus Medical Center, Rotterdam, Netherlands

**BACKGROUND** Circulating non-structural (NS1) antigen can be detected in blood during acute dengue. It is not clear whether NS1 or its antibodies contribute to development of antibody-dependent enhanced infection or to protection by virus neutralization.

**OBJECTIVES** To investigate the time course of dengue NS1 antigen concentrations in patients with acute dengue and explore its relationship with disease severity.

**METHODS** Between April and June 2003, 37 patients with acute undifferentiated fever were investigated. Dengue diagnosis was **OBJECTIVES** To study for association of CLAG9 with severe and cerebral malaria in Thai patients.

**METHODS** About 7 kb of CLAG nine gene including 5' UTR was sequenced in 32 parasite samples from patients infected with *Plasmodium falciparum* to screen for polymorphisms. Only polymorphisms with the minor allele frequency >10% were further analyzed in all 480 blood samples including mild (204), severe (166) and cerebral malaria (110) using allele-specific PCR, PCR-RFLP, PCR-artificial RFLP and direct sequencing. Allele frequencies at each polymorphism were compared between the three groups of patients to see whether there is significant difference.

**RESULTS** There were 23 polymorphisms identified in CLAG9 including 18 SNPs and 5 microsatellites polymorphisms. Of these, 11 polymorphisms including -942T/C in 5'UTR, 824T/C in intron1, 1412G/C in exon2 with the change of amino acid K/N, 2140(AT)7-8/18 and 2201TG in intron4, 2341G/C and 2385C/G in exon5 with the change of S/T and D/N respectively, 2487(AT)10-12/9 in intron5, 2585G/C in exon6 with the change of T/R, 4773G/C and 5184A/C in exon9 with the change of V/L and K/Q respectively were analyzed further in all samples. A haplotype block with complete LD (D\(^1\) and \(r^2 = 1\)) was found between 2201TG, 2385G/A, 2487(AT)10-12/9 and 2383C/G. Comparing allele frequency between mild, severe and cerebral malaria patients showed significant differences between mild and severe malaria at -942T/C (OR = 2.103, \(P = 0.007\)), 2140(AT)7-8/18 (OR = 1.881, \(P = 0.016\)), 2341G/C (OR = 1.819, \(P = 0.034\)) and haplotype block of 2201–2585 (OR = 2.002, \(P = 0.006\)). The results demonstrated that parasite carrying CLAG9 with -942C, 2140(AT)18, 2341C and haplotype GA(AT)9G genotype was associated with severe malaria. As strong LD was observed among these polymorphisms, we could not determine which polymorphism was the primary cause of severe malaria.

**CONCLUSION** The present study showed that the genetics of CLAG9 was contributed to severe malaria. Although the role of CLAG9 in the pathogenesis of severe malaria has not been known, CLAG9 has been postulated to involve in mechanism of cytoadhesion. CLAG9 2385S located at the end of exon5 may alter RNA splicing process which may contribute to the regulation of gene expression or may encode the variant form of protein with altered function. Therefore, the biological significance of CLAG9 in pathogenesis of severe malaria should be further studied.
confirmed with a commercially available IgM capture and IgG ELISA (using E/M dengue specific antigens, Focus Diagnostics Inc., Cypress, CA, USA). Acute sera of all patients were also tested for the presence of NS1 antigen (Platelia™ Dengue NS1 Ag – ELISA, Bio-Rad Laboratories, Inc., Hercules, CA, USA). When positive, all samples were detected at 12, 24, 36, 72 h and 21 days later were tested.

RESULTS Of 37 patients, 12 were diagnosed with acute dengue with antibody ELISA, two with primary and 10 with secondary dengue. Patients with dengue had lower white blood cell counts, and higher plasma aspartate aminotransferase levels than patients without dengue. In five dengue patients, dengue NS1 antigen was detectable. Patients with persisting high NS1 antigenemia during the first 24 h after presentation, had a prolonged illness and more severe symptoms, compared to those who cleared NS1 antigen within the first day, but this did not reach statistical significance.

CONCLUSION Data suggest that high levels of dengue NS1 antigen are associated with prolonged illness and possibly also with disease severity.

O28-37
Health-related quality of life among dengue/dengue hemorrhagic fever patients in central Brazil
1 Public Health Department, Public Health/Federal University of Goias, Instituto of Tropical Medicine and Goiania, Brazil; 2 Brandeis University, Schneider Institute for Health Policy, Boston, USA

OBJECTIVES To assess the health-related quality of life among ambulatory and hospitalized dengue/dengue hemorrhagic fever (DF/DHF) patients.

METHODS This investigation was conducted in Goiania city (1.2 million inhabitants), Central Brazil, as part of a multicountry study on dengue disease burden. Potential participants were identified from daily official case notifications, laboratory records, and hospital visits in outpatient and inpatient facilities from both public and private sectors, from March through June 2007. Participants or their legal surrogates were interviewed once around 15 days of the onset of symptoms. Health-related questions included modules developed by WHO World Health Survey and EuroQOL. Impact on health was assessed by comparing self-reported overall health before and during the illness episode, by the number and quality of days affected, number and severity of mental and physical health domains affected. This report is based on the 410 participants with laboratory-confirmed DF/DHF. Ethical approval from local IRB and signed informed consent was obtained prior to the study.

RESULTS A total of 301 eligible ambulatory cases (52% private sector) and 109 hospitalized cases (48% private) were interviewed. Females, adults, and DHF cases represented 60%, 81%, and 16% of the participants, respectively. Self-reported mean (SD) days of fever and overall dengue episode were 4.6 (2.6) and 10.6 (3.5) among outpatient and 5.7 (2.7) and 14.6 days (4.7) among inpatient participants, respectively. Most participants reported 'good' or 'very good' general health status prior to the disease. During the illness episode, however, the majority still felt 'bad' or 'very bad' about 10 days after the onset of symptoms. The most frequent complaints were difficulty in vigorous activities, in performing daily activities and physical distress. Almost half of the inpatients and one fourth of the outpatients reported difficulties with self-care. On a 100 point-scale, where 100 corresponded to perfect health, mean (SD) quality of life was markedly impaired: 20 (16) among outpatient and 16 (11) among inpatient participants.

CONCLUSION This study demonstrates the prolonged duration of physical/mental impairment and poor quality of life among adult dengue patients. It reveals constraints in several physical and psychological domains both during and after the dengue acute episode. Financial support: Pediatric Dengue Vaccine Initiative and Pronex/CNPq/Sectec (#23234156).

O28-38
A newly engineered dengue antigen is immunogenic when expressed by a live attenuated measles vaccine
S. Brandl1, M. Lucas2, H. Bedouel3, C. Combredet, M.P. Frenkel1, A. Moris1, P. Després4 and F. Tangy1
1 Institut Pasteur, Laboratoire de Génomique Virale et Vaccination, Paris, France; 2 Institut Pasteur, Unité Postulante Interactions Moléculaires Flavivirus-Hôtes, Paris, France; 3 Institut Pasteur, Prévention et thérapies moléculaires des Maladies Inrmaines, Paris, France; 4 Institut Pasteur, Groupe Virus et Immunité, Paris, France

OBJECTIVES To design a new Dengue virus (DENV) tetravalent vaccine derived from pediatric measles vaccine.

METHODS To this purpose we first focused on the design of a newly engineered DENV antigen by using the envelope domain III (EDIII) that contains neutralizing and non cross-reactive epitopes fused or not with different peptides from the Membrane (M) protein from DENV. As a proof of concept preclinical immunogenicity data obtained in mice after immunization with measles vectors expressing the DENV1 sub-immunogens will be presented. Kinetics of expression of surface costimulatory molecules CD80, CD86, CD83 and CD40 analyzed by flow cytometry and of 23 cytokines and chemokines secretion by monocyte derived dendritic cells (DCs) detected by Luminaex will also be exposed.

RESULTS Only the recombinant measles vector that expressed the EDIII fused to a peptide coding a fragment from the M protein raised neutralizing and non cross-reactive antibodies directed against DENV1 EDIII. This recombinant virus also promoted earlier maturation of DCs and enhanced the production of 11 cytokines and chemokines by these cells.

CONCLUSION Based on these results, five tetravalent antigens coding the four EDIII from DENV1, 2, 3, 4 and a peptide from the M protein were designed and inserted into single recombinant measles vectors. These recombinant viruses were produced and are under evaluation in mice.

O28-39
Inflammatory gene expression changes in children with severe dengue virus infection
1 Department of Internal Medicine, Slotervaart Hospital, Amsterdam, Netherlands; 2 Department of Pediatrics, Dr Kariadi Hospital, Semarang, Indonesia; 3 Institute of virology, Erasmus Medical Center, Rotterdam, Netherlands; 4 Academic Medical Center, Center for Experimental and Molecular Medicine, Amsterdam, Netherlands

OBJECTIVES The host response to dengue virus infection is characterized by the production of numerous cytokines, but the overall picture appears to be complex. Different observations suggested that immunoparalysis may be involved. The role of toll like receptor (TLR) activation was never investigated in human patient samples before. This study aimed to elucidate these various topics by gene expression profiling of whole blood samples measuring mRNA levels from 50 genes encoding inflammatory proteins simultaneously.

METHODS Whole blood mRNA from 56 Indonesian children with severe dengue virus infections was isolated on day 0, 1, 2, 7 and 30 after hospital admission. mRNA was analyzed in a single...
reaction by multiplex ligation-dependent probe amplification (MLPA) and levels were related to the day of defervescence.

RESULTS The gene profile showed up-regulation during infection of 10 genes including interferon (IFN)-gamma, interleukin (IL)-12a and macrophage inhibitory factor (MIF), which were implicated in dengue pathogenesis before. Concurrently however, the nuclear factor (NF) kappaB pathway was down-regulated together with downstream effector genes encoding IL-1beta, IL-8 and TNF-alpha. Moreover, up-regulation of genes related to the NFkappB pathway was correlated with parameters of disease severity. The only TLR up-regulated during infection was TLR7, whereas TLR1 and TLR2 were down-regulated. The role of TLR4 was not clear from this study.

CONCLUSION Together, these data suggest that the *in vivo* host response to severe dengue virus infections is characterized by a general antiviral response including up-regulation of IFN-gamma and TLR7 synthesis whereas down-regulation of the NFkappB pathway suggests a functional state of concurrent immunoparalysis in circulating leukocytes.

**O28-40**

**Incidence of primary dengue virus infections in Southern Vietnamese children and reactivity against other flaviviruses**


1Academic Medical Center, Division of Infectious Diseases, Tropical Medicine & AIDS, Amsterdam, the Netherlands; 2Department of virology, Cho Ray Hospital, Ho Chi Minh City, Viet Nam; 3Binh Thuan Provincial Malaria and Goster Center, Phan Thiet City, Viet Nam; 4Cho Ray Hospital, Tropical Diseases Clinical Research Center, Ho Chi Minh City, Viet Nam; 5Department of Virology, Erasmus Medical Center, Rotterdam, the Netherlands

OBJECTIVES To study the incidence of asymptomatic primary dengue infections among children and reactivity against other flaviviruses.

METHODS A total of 216 children who had no dengue specific IgG antibodies during a sero-survey in 2005, were re-examined 23 months later, in 2007, to determine if seroconversion had occurred. Dengue specific IgG was demonstrated with ELISA and reactivity patterns against other flaviviruses were assessed by using immunofluorescence assay (IFA).

RESULTS Sixty-six children showed seroconversion for dengue virus specific IgG; the true annual incidence of primary dengue was thus 17.3% (95% CI: 13.8–21.4). Japanese Encephalitis virus (JEV) specific IgG antibodies were detected by IFA among three (4.6%) samples that showed seroconversion in the dengue ELISA, due to cross-reactivity.

CONCLUSIONS Our findings highlight the high incidence of dengue among Vietnamese children; infections with JEV are rare.

**O28-41**

**Adult dengue shock syndrome with severe gastrointestinal bleeding, prolonged renal failure/induced hypertension and nosocomial MRSE pneumonia**

R. H. H. Nelwan1, E. Susil2, A. Ranil, A. Mudalili3, I. Alwi4 and H. Gunawan5

1Tropical & Infectious Disease, Faculty of Medicine University of Indonesia, Jakarta, Indonesia; 2Nephrology and Hypertension, Faculty of Medicine University of Indonesia, Jakarta, Indonesia; 3Gastroenterology, Faculty of Medicine University of Indonesia, Jakarta, Indonesia; 4Haematology and Oncology, Faculty of Medicine University of Indonesia, Jakarta, Indonesia; 5Cardiology, Faculty of Medicine University of Indonesia, Jakarta, Indonesia; 6Pulmonology, Metropolitan Medical Center Hospital, Jakarta, Indonesia

Dengue Shock Syndrome is the most difficult condition to treat in the hospital very often with fatal ending. We will describe an adult case that survived.A 33 years old Indonesian male was referred to a peripheral hospital for an acute onset 5 day fever and severe hematemesis- melena. The patient arrived with feeble pulse and blood pressure on palpation only, decreased body temperature, cold extremities, felt very weak but was still conscious. Two infusion lines were installed for a massive dose of crystalloid solution. The pulse and blood pressure stabilized but there was still vomiting with fresh blood clots and total renal shut down. His laboratory findings were Hb 7.1 g/dl, Leuc 15,000/ul, Thromb 100,000/ul, SGPT 1287u/l, SGOT 3212u/l, ureum 141 mg/dl, creatinine 6.68 mg/dl, CRP 27.515 mg/l, D-dimer 200 mg/ml. Chest X-ray was normal. Blood Dengue IgM/IgG were both positive. PCR 500 cc was given, also oral sucralfate, intravenous omeprazole, tranexamic acid and carbazochrome sulfonate. One gram ceftriaxone was added. As treatment failed Fresh Frozen Plasma, vit K and esomeprazole IV 5 times daily and also somatostatin was administered at day 4 as Hb was still 6.1 gm/dl and PCR had already been given on average 700 cc/day for 3 days. Thrombocytes dropped to 32,000/ul so that a thrombopheresis was done. On day seven Hb 10.9 g/dl; SGOT 90 u/l, SGPT 156 u/l, CRP near normal. Since creatinine increased daily hemodialysis was performed while the patient was on total parenteral nutrition. On day 13 blood pressure increased to 165/110 mmHg but urine started to be produced. The patient was given 5 mg amlodipine besylate. On day 18 the patient complained of dyspnkea and expectorated bloody sputum. His CRP shot up to 73, 588 mg/ml, and so did creatinine (11.8 mg/dl). His chest X-ray showed pneumonia and bilateral pleural effusion. The sputum was positive for MRSE and he was put on appropriate antimicrobials and relieved from dyspnea by pleural puncture (350 cc). He was also given ethamsylate, aminophyllin, salbutamol and guaiphenesin. This nosocomial pneumonia resolved 10 days later while the patient was still on twice weekly hemodialysis. On day 24 his BP/HR was still not normal and ramipril/ carvediol was given and finally after an ECHO was done changed to 40 mg telmisartan and 12.5 mg twice daily metoprolol tartrate on which he remained even after discharge 10 days later. He had to continue ambulatory hemodialysis twice weekly. One month later he was still on once weekly hemodialysis and on antihypertensive treatment.

**Hepatitis**

**O28-42**

**Thrombocytopenia and/or leucopenia in chronic hepatitis C with and without schistosomal liver disease**

A. A. H. Hassan1, A. H. Serwah2, M. M. Awad3, N. R. Wissa2 and A. S. Al Makdad4

1Suez Canal University, Tropical Medicine, Ismailia, Egypt; 2Suez Canal University, Medicine, Ismailia, Egypt; 3Suez Canal University, Clinical Pathology, Ismailia, Egypt

OBJECTIVES To estimate the prevalence of thrombocytopenia and/or leucopenia (T &/or L) in patients with HCV chronic hepatitis and to investigate the responsible mechanisms in patients with and without schistosomal liver disease (Sch-LD).

METHODS A total of 193 consecutive adult patients fulfilling the criteria of chronic HCV liver disease were included after exclusion of other causes of CLD and bleeding. Clinical examination, CBC, LFTs, stool analysis and abdominal US were performed for all patients. Anti-platelet antibodies (APAB), Thrombopoietin (TPO), and Schisto-Ab-IHAT were measured & bone marrow (BM) aspiration was done for patients with Sch-LD.

RESULTS One hundred and three patients (53.4%) had (T &/or L), 23.8% had thrombocytopenia, 29% had both thrombocytopenia...
and leucopenia and 0.5% had isolated leucopenia. Sch-LD was diagnosed in 36 cases (35%) of them. Among (T and/or L) cases APAB was +ve in 33.4% and 64.4% had high level of serum TPO and there was no difference between Sch-LD +ve and –ve cases. A statistically significant weak negative correlation was found between TPO and APAB (r = -0.42, P < 0.001). Meanwhile, a statistically significant strong positive correlation was revealed between bone marrow cellularity and megakaryocytosis (r = 85%, P < 0.001), but no significant correlation was found between BM cellularity and either TPO or APAB. These correlations held true irrespective of Sch-LD status. The BM was found to be hypo-cellular in 47.4% and hyper-cellular in 38.8% with no significant difference according to Sch-LD status. Splenomegaly was present in 92% but only about 25% could be defined as having hypersplenism.

CONCLUSION The mechanism of thrombocytopenia and/or leucopenia in HCV-CLD appears complex and multifactorial. Hypersplenism contributes 25% of cases. APAB and bone marrow inhibition might be the more plausible mechanisms. Sch-LD does not appear to affect prevalence or mechanisms of (T &/or L) in HCV-CLD patients.

O28-43

Population based hepatites A, B and C sero-survey and genotyping in central west region of Brazil

M. Turchi1, C. Marcelli, R. Oliveira1, F. Silva1, R. Aires1, B. Bariani1, F. Souto1, J. Fontes1, V. Azevedo Silva1, J.I. Aguizar1, J.I. Barros1, G. Santos1, U. Montarroyos2, C. Braga1, R. Cardoso3, R. Ximenes4 and L. Pereira6

1IFESP/Federal University of Goias, Goiânia, Brazil; 2Health State Secretariat of Mato Grosso, Cuiaba, Brazil; 3Health State Secretariat of Mato Grosso do Sul, Campo Grande, Brazil; 4Federal University of Mato Grosso do Sul, Campo Grande; 5University of Sao Paulo, Sao Paulo, Brazil; 6State University of Pernambuco, Recife, Brazil

OBJECTIVES To estimate the seroprevalence of hepatites A (HAV), B (HBV) and C (HCV) and genotypes for HBV and HCV in Central-West region/Brazil.

METHODS This study is part of a national survey on hepatitis infection in Brazil. A household investigation was carried out among participants from 5 to 69 years old in 2004/2005. Sample was representative of the ensemble of the three state capitals (cities of Goiânia; Cuiaba and Campo-Grande; ~2.5 million inhabitants), for age-groups and stratified by capital with a uniform sampling fraction. Census tracts, blocks and households were drawn with probability proportional to size and selected subjects. A household interview was done and blood samples collected. Serology for HAV, HBV and HCV (ELISA) and genotyping for HBV and HCV were performed in reference laboratories. Ethical approval by regional and national committee and signed informed consent were obtained.

RESULTS A total of 4017 participants, age-group 5–9 (n = 310), 10–19 (n = 1804) and 20–69 (n = 1903) were investigated. Hepatitis A prevalence (IgG) was 32.3% (95% CI 27.1–37.8) and 55.9% (95% CI 50.2–60.9) for 5–9 and 10–19 age-groups, respectively. Exposure for HBV (anti-Hbc) was 1.3% (95% CI 0.8–1.9) among participants aged 10–19 and 12.7% (95% CI 11.2–14.2) for the older subjects. Carrier prevalence (HbsAg) ranged from 0.2% to 0.7% according to age groups. HBV-DNA identified genotypes D, A and F. The overall anti-HCV prevalence was 1.1% (95% CI 0.6–1.6) among participants aged 10–19 and 1.9% (95% CI 1.4–2.7) for older age-group. HCV-RNA genotypes 1, 1b and 3a were identified.

CONCLUSION This household survey detected high prevalence of HAV infection among children with evidence of early viral exposure. Central-West region of Brazil was classified as low HBV endemicity region, probably due to HBV vaccination offered by the national routine immunization program. High level of anti-HCV prevalence was detected among adolescents and different genotypes circulating at population level. Sponsors: Brazilian Ministry of Health, Pan-American Health Organization, State and Municipal Health Secretariat.

O28-44

Genotyping and population-based seroprevalence of hepatites A, B and C virus infection in the northeast region of Brazil


1Federal University of Pernambuco, Internal Medicine, Recife, Brazil; 2Ministry of Health, LACEN, Distrito Federal, Brazil; 3Parasitology, Aggen Magalhães Research Center, Recife, Brazil; 4Public Health, Federal University of Pernambuco, Recife, Brazil; 5Tropical Medicine, Federal University of Pernambuco, Recife, Brazil; 6Tropical Medicine, Federal University of Paraíba, João Pessoa, Brazil; 7Internal Medicine, Federal University of Paraíba, João Pessoa Brazil; 8Public Health, Federal University of Ceará, Fortaleza, Brazil; 9Public Health, Federal University of Pernambuco, Recife, Brazil; 10Health State Secretariat of Alagoas, Maceió, Brazil; 11Health Public Health, Secretariat of Maceió, Maceió, Brazil; 12Internal Medicine, Federal University of Rio Grande do Norte, Natal, Brazil; 13Public Health, Federal University of Rio Grande do Norte, Natal Brazil; 14Internal Medicine, Federal University of Bahia, Salvador, Brazil; 15Health Public Health, Federal University of Bahia, Salvador, Brazil; 16Internal Medicine, Federal University of Maranhão, São Luís, Brazil; 17Public Health, Federal University of Maranhão, São Luís, Brazil; 18Internal Medicine, Federal University of Pernambuco, Recife, Brazil; 19Immunology, Aggen Magalhães Research Center, Recife, Brazil

OBJECTIVES To estimate the seroprevalence of hepatites A, B and C and genotypes for HBV and HCV in the northeast region of Brazil.

METHODS A population-based survey was carried out in the northeast (2004/2005), as part of a national survey which is being conducted in all regions of Brazil. The sample was representative of the ensemble of the nine state capitals in this region and for each age group considered. The sample was stratified by capital with a uniform sampling fraction. In each capital census tracts and, then, blocks were drawn with probability proportional to size; subsequently a systematic sample of households was drawn and their residents selected. The study was approved by regional and national ethical committees and signed informed consent was obtained.

RESULTS A total of 4,180 individuals were investigated. Hepatitis A seroprevalence (anti-HAV IgG) was 41.50 (95% CI: 35.80–47.36) in the age group 5–9 and 56.60 (95%-CI 51.15–61.92). Seroprevalence of anti-Hbc ranged from 2.12% (95%-CI 1.51–2.88) in the age group 10 to 19 to 11.62 (95% CI 6.10–13.16) in the age group 20–69; seroprevalence of HbsAG was 0.11% (95% CI 0.01–0.39) in the age group 10–19 and 0.48 (95% CI 0.22–0.91) in the age group 20–69. HBV-DNA genotypes A and F were identified. Seroprevalence of anti-HCV was 0.94 (95% CI 0.55–1.50) in the age group 10–19 and 1.88% (1.30–2.61) in the age group 20–69. HCV-RNA genotype 1, 1b, and 3a were identified.

CONCLUSION This population based survey indicates that a large proportion of HAV infection in Northeastern Brazil occurs in early childhood. The low HBV endemicity is probably related to the
incorporation of the hepatitis B vaccine into the infant/adolescent immunization programme. The prevalence of anti-HCV of 1.88 corresponds to approximately 111 757 people who have been infected with HCV in this region. Sponsors: Brazilian Ministry of Health, Pan-American Health Organization.

**O28-45** Impact of traditional rites and immunisation programme on the epidemiology of Hepatitis B in Ghanaian children

C. Kreuzberg1, S. Erhardt2, P. Appiah-Thompson3, M. Lüdgehetmann1, S. Polywka1, H. -H. Feucht1, O. Ajdei4, A. W. Lohse1, J. May3 and P. Buggisch1
1Department of Internal Medicine, University Medical Center Hamburg-Eppendorf, I., Gastroenterology, Infectious Diseases and Bernhard-Nocht-Clinic for Tropical Medicine, Hamburg, Germany; 2Bernhard-Nocht-Institute for Tropical Medicine, Clinical Research Unit, Hamburg, Germany; 3Kumasi Centre for Collaborative Research in Tropical Medicine, Kumasi, Ghana; 4Department of Medical Microbiology, University Medical Center Hamburg-Eppendorf, Virology and Hygiene, Hamburg, Germany; 5Bernhard-Nocht-Institute for Tropical Medicine, Infection Epidemiology Group, Hamburg, Germany

**BACKGROUND** Hepatitis B is highly endemic in sub-Saharan Africa. Routine childhood vaccination was introduced in most countries. However, free vaccination is only available for infants.

**OBJECTIVES** Our study aimed at detecting risk factors for transmission of Hepatitis B in previously not vaccinated children and examining efficiency of the vaccination program in children in rural Ghana.

**METHODS** Children and adolescents aged 6 months–18 years attending monthly weighing sessions in Agona District, Ashanti Region, Ghana were recruited and screened for tribal marks, history of blood transfusion, as well as socioeconomic and educational factors. Blood samples were tested for Hepatitis B (HB) markers and immune response to HB vaccine.

**RESULTS** A total of 377 children (182 male, 195 female and mean age 6 years) were recruited. 12.2 % (46/377) had anti-HBc antibodies. 38.7% (27/46) of them developed a chronic infection resulting in an overall HBs Ag prevalence of 7.2% (27/377). However, only 51.9 % (14/27) of the HBs Ag positive carriers had a detectable viral load. HB virus (HBV) genotypes were almost exclusively E except genotype A in one case. In children not vaccinated the estimated risk of HB infection adjusted for family clusters increased threefold in children with tribal marks (OR 3.3, 95% CI 1.2–9.2, P < 0.02). In 3.0 % (3/101) of the children who were expected to be immunised we still detected HBs Ag although 78.2% (79/101) even had protective anti-HBs antibody levels.

**CONCLUSION** In the rural Ashanti region of Ghana traditional rites remain an important route of transmission of HBV in children. Furthermore, our results suggest that even with good vaccination coverage, prevalence of Hepatitis B will remain high probably due to vertical transmission. We conclude that additional implementation of routine HBs Ag screening in pregnancy followed by immunisation at birth is warranted.


L. Kasraian1 and A. Torab1
1Ibto Research Center, Shiraz, Islamic Republic of Iran

**OBJECTIVE** Evaluating trends in blood donors infectious disease rates is essential for monitoring blood supply safety and donor screening effectiveness.

**METHODS** Cross-sectional survey data from all blood donors who referred to Fars blood transfusion service from 2002 till end of first half of 2005. Then we reviewed (507 531) demographic characteristic and the number of HBS HIV HCV.

**RESULTS** Prevalence of HIV between 2002 till first half of 2005 in order were and prevalence of HBS were 0.57, 0.52, 0.53, 0.39 and prevalence of HCV were 0.19, 0.13, 0.09, 0.16 the prevalence of this infection was more in first, male and married blood donors (P < 0.05) and not related to age (P > 0.05).the prevalence of HBS was less in 2005. the prevalence of HCV not significant change over the time.

**CONCLUSION** Incidence rate of this infection in Fars blood donors is less than normal population and didn’t change over time that may be due to effective donor selection and the lower prevalence rate of HBS & HCV in donor population.

**Immunology and Biology of Malaria**

**O28-47** Role of TLRs in protection against malaria

1Department of Internal Medicine, University Medical Center Hamburg-Eppendorf, I., Section Tropical Medicine and Infectious Diseases, Hamburg, Germany; 2Department of Immunology, Bernhard-Nocht-Institute for Tropical Medicine, Hamburg, Germany; 3Department of Immunology and Biochemical Microbiology Research Center Borstel, Borstel, Germany; 4Max-Planck-Institute of Immunobiology, Metzachroff Laboratory, Freiburg, Germany; 5Technical University of Munich, Institute of Medical Microbiology, Immunology and Hygiene, Munich, Germany

**OBJECTIVES** Host innate immunity is important for early parasite control but also contributes to disease pathology. Plasmodial glycosylphosphatidylinositol (GPI) is considered to contribute to malaria pathology by inducing pro-inflammatory cytokines. GPI has been shown to be recognized by Toll-like receptors. However, it is unclear whether TLR-signaling also contributes to parasite clearance.

**METHODS** In a murine malaria model, the role of the TLR cascade for parasite clearance and for initiating innate and cell mediated immunity was analysed. Mice deficient for TLR2, TLR4, TLR9 as well as TLR-combinations and the intracellular adaptor protein MyD88 were infected with non-lethal *Plasmodium yoelii*. Moreover, additional MyD88-dependent receptors of the IL-1/TIR receptor family were analyzed. Parasitaemia and survival were assessed. On day 6 post infection Cytokine levels were measured in serum and in cultured spleen cells after 48 h stimulation with anti CD3. To assess T cell stimulation, respective activation markers were assessed by flow cytometry.

**RESULTS** MyD88/- mice showed significantly higher parasite loads. MyD88/- mice had significantly lower levels of IL-12 and IFN-gamma. IL-18 levels did not differ significantly between cases and controls. In contrast to MyD88/– mice, activation of CD4 + T cells was significantly increased in TLR2/4/9/- mice compared to controls.

**CONCLUSION** MyD88 plays an important role in eliminating blood stage parasites. This may be reflected by its role in IL-12 production as well as IL-18 recognition. While TLRs do not seem to play a role in direct parasite control they may contribute to immune tolerance as infection proceeds.
METHODS A matched case-control study among 870 Ghanaian children (290 severe malaria patients, 290 asymptomatically infected children, and 290 healthy controls) was conducted in the hyperendemic area of Tamale, northern Ghana. Three functional and three regulatory MBL2 polymorphisms were typed by PCR-RFLP.

RESULTS A missense mutation resulting in low MBL activity (MBL2 C) was found in 35% of healthy controls. It was more common in asymptomatically infected children (42%, \( P = 0.01 \)), and even more so in patients with severe malaria (46%, \( P = 0.007 \)). MBL2 C heterozygosity was associated with increased odds of infection [odds ratio (OR), 1.6; 95% CI, 1.1–2.1], severe malaria (OR, 1.7; 95% CI, 1.2–2.4), and of severe anaemia in particular (OR, 2.3; 95% CI, 1.4–3.8). These effects were pronounced in the youngest children. The case fatality rate did not differ with MBL2 genotype. The population attributable fraction of severe malaria by the proband susceptible MBL2 C allele was 17%.

CONCLUSION The MBL pathway of the complement system appears to be a critical determinant of susceptibility to malaria. In northern Ghana, the MBL2 C variant, very common at a prevalence of 30–40%, increases the odds of \( P. falciparum \) infection and severe malaria. This is especially true for the most common manifestation in this highly endemic area, severe anaemia, and in the youngest children.

O28-50 Mixture models for analysis of immune responses in epidemiological studies

D. Liu1, J. Iversen2 and P. Milligan1

1Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, London, UK; 2Medical Research Council Laboratories, Banjul, Gambia

OBJECTIVES In immunoenpidemiological studies it is often of interest to consider both the concentration of antibodies, and the proportion of individuals with detectable concentrations (responders). But statistical analysis of the concentrations is complicated by the presence of zero values (antibody titres less than the assay sensitivity), as well as by left-censoring. We describe a new method using a mixture model which allows test sensitivity to be estimated from the data and does not require a fixed detection limit to be specified. The method is illustrated using data on antibody responses to malaria bloodstage antigens MSP1-19 and AMA-1 from a study of ethnic differences in malaria risk in The Gambia.

METHODS Antibody responses to MSP1-19 and AMA-1 in plasma samples from 658 adults and children over 6 months of age, from a cross-sectional survey in three ethnic groups at the end of the dry season in The Gambia, were measured using ELISA. Mixture models were used to compare the proportion of responders and the mean concentration of antibodies, between ethnic groups, allowing for effects of left-censoring. We assume that detection depends on the concentration and on the assay sensitivity which was estimated from the data. Mixed models were estimated by a Gibbs sampling procedure. Results were compared to those obtained when an alternative model, which assumed a fixed detection limit, was used.

RESULTS The mean concentration of total IgG to MSP1-19, and the proportion of responders, was higher in the Fula ethnic group and significantly lower in the Temne ethnic group. The prevalence of MSP1-19 responders was higher in the Fula ethnic group. These effects were similar for AMA-1.

O28-49 Mannose binding lectin deficiency and severe malaria

F. P. Meckenhagen1, V. Holmberg2, F. Schuster2, E. Dietz2, J. C. Sagurrua Visconti1, S. D. Anemana4 and U. Benzie1

1Charité – University Medicine Berlin, Institute of Tropical Medicine Berlin, Berlin, Germany; 2Department of Bacteriology and Immunology Haartman Institute, University of Helsinki, Helsinki, Finland; 3Charité – University Medicine Berlin, Institute of Biostatistics and Clinical Epidemiology, Berlin, Germany; 4Ministry of Health, Regional Health Administration Takoradi, Takoradi, Ghana

OBJECTIVES Both susceptibility to and manifestation of malaria are subject to inter-individual variation. Genetic disposition to a large extent contributes to this. Mannose-binding lectin (MBL) is a serum protein which initiates innate immune responses to microbial pathogens by binding to non-self surface oligosaccharides. MBL deficiency is the most common congenital immunodeficiency and has been shown to predispose to infections, particularly in children and immune compromised. Its role in malaria, however, remains unclear. We examined the influence of six polymorphisms of the MBL2 gene on \( P. falciparum \) infection and severe malaria.

METHODS and U. Bienzle

The mean concentration of total IgG to MSP1-19, and the proportion of responders, was higher in the Fula ethnic group and significantly lower in the Temne ethnic group. The prevalence of MSP1-19 responders was higher in the Fula ethnic group. These effects were similar for AMA-1.

O28-48 Plasmodium falciparum infection causes pro-inflammatory priming of human toll-like receptor responses

M. McCall1, M. Nexte1, R. Hermansen1, T. Jansen2, D. Golenbock3, A. v. d. Ven1 and R. Sauerwein1

1Medical Microbiology, Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands; 2General Internal Medicine, Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands; 3Division of Infectious Diseases and Immunology, University of Massachusetts Medical School, Worcester, USA

OBJECTIVES Toll-like receptors (TLRs) are a major group of pattern recognition receptors that are crucial in initiating innate immune responses and are capable of recognising Plasmodium ligands. The objective of this study was to examine modulation of human TLR-responses by \( P. falciparum \) (P.f.).

METHODS We have investigated \textit{ex vivo} Toll-like receptor responses during acute experimental \( P. falciparum \) infection in 15 malaria-naive volunteers. We have further explored the modulation by P.f. of human PBMC responses \textit{in vitro}.

RESULTS TLR-4 responses in whole blood \textit{ex vivo} stimulations were characterised by significantly \((P < 0.01)\) up-regulated pro-inflammatory cytokine production during infection compared to baseline, whereas TLR-2/TLR-1 responses demonstrated increases in both pro-inflammatory and anti-inflammatory cytokine production. Responses through other TLRs were less obviously modified by malaria infection. The degree to which pro-inflammatory TLR responses were boosted early in infection was partially prognostic of clinical inflammatory parameters during the subsequent clinical course. Although simultaneous co-stimulation of human PBMCs with P.f. lysate and specific TLR stimuli in \textit{vitro} did not induce synergistic effects on cytokine synthesis, PBMCs started to respond to subsequent TLR-4 and TLR-2 stimulation with significantly \((P < 0.05)\) increased TNF \( \mu \) and reduced IL-10 production following increasing periods of pre-incubation with P.f. antigen. In contrast, pre-incubation with preparations derived from other parasitic, bacterial and fungal pathogens strongly suppressed subsequent TLR responses.

CONCLUSION Taken together, \( P. falciparum \) primes human Toll-like receptor responses towards a more pro-inflammatory cytokine profile both \textit{in vitro} and \textit{in vivo}, a characteristic exceptional amongst micro-organisms.
Leprosy

O28-51 Magnetic resonance imaging used for diagnosing osteomyelitis in leprosy patients with neuropathic feet with clinical signs of mild inflammation

E. Slim1, X. Illarramendi2, M. Maas3, E. P. Sampaio4, J. A. C. Nery5, E. N. Sarno2 and W. R. Faber5
1 Academic Medical Center, Rehabilitation Medicine, Amsterdam, Netherlands; 2Leprosy Laboratory, Oswaldo Cruz Institute, Fiocruz, Rio de Janeiro, Brazil; 3Academic Medical Center, Radiology, Amsterdam, Netherlands; 4Academic Medical Center, Dermatology, Amsterdam, Netherlands

The present study was performed to further explore the imaging spectrum of neuropathic feet in a defined group of leprosy patients.

OBJECTIVES MRI findings were studied in patients with longstanding ulcers and/or localized cellulitis but without clinical suspicion of osteomyelitis. As far as we know such type of patients have not been studied using MRI.

METHODS All patients underwent the MRI protocol consisting of: sagittal T-STIR (4 mm) T1-W, T2-W images and coronal T1 FATSAT imaging before and after intravenous contrast administration. MRI signs for detecting osteomyelitis were used as described in the diabetic literature.

RESULTS A total of 15 neuropathic feet from nine patients were included. The forefront was predominantly affected, 91% clinically and 93% on MRI. Claw toes and bone absorption in the forefront and soft-tissue abnormalities diagnosed clinically were confirmed on MRI examination in 100% of the feet. Cellulitis diagnosed clinically was confirmed on MRI in 33% of the cases. Although none of the neuropathic feet were clinically suspected for osteomyelitis, MRI signs for osteomyelitis were found in 27% of the feet. In 3 feet with clinical signs of cellulitis, the osteomyelitis was related with a superficial ulcer.

CONCLUSION An important discrepancy between the clinical and the MRI findings was found with regard to osteomyelitis. These MRI findings in this defined group of patients may influence decision making during the follow-up since osteomyelitis requires a more aggressive medical approach to prevent further complications.

O28-52 Difficulties perceived by primary health care professionals regarding the decentralisation of the leprosy elimination programme in Paraíba State, Brazil

M. da Silveira Mendes1, M. Maia Cantidio1, J. I. Pontes de Aquino2, L. Cavalcante Trindade3, G. Pereira Campos4, D. Hinder5 and J. Heukelbach1
1Programa de Saúde da Família Uniao, Joao Pessoa, Brazil; 2Complexo Hospitalar Clementino Fraga, Joao Pessoa, Brazil; 3Secretaria Estadual da Saude, Joao Pessoa, Brazil; 4Leprosy Relief Association, Natal, Brazil; 5Department of Community Health, School of Medicine, Federal University of Ceará, Fortaleza, Brazil

OBJECTIVES To identify factors on the Primary Health Care (PHC) level associated with the ineffective decentralisation of the Leprosy Elimination Program in northeast Brazil.

METHODS We conducted an operational research study in Joao Pessoa, a capital city in northeast Brazil, on knowledge, attitudes and practices regarding leprosy. Self-applied structured questionnaires were distributed to all PHC professionals (physicians and nurses), working in the Family Health Programme.

RESULTS In total, 234 questionnaires were returned and included in data analysis (response rate = 67%). Only 133 (57.1%) of PHC professionals felt qualified to diagnose leprosy clinically, and 78 (33.8%) to treat a patient with Multi-Drug Treatment (MDT). Interestingly, 60 (32.4%) considered the state reference centre to be solely responsible for diagnosis and treatment of leprosy. Only 74 (32.6%) stated that MDT was available in their health centre. In total, 161 (69.7%) had undertaken training workshops on leprosy control. However, the training did not improve their perceived difficulties in the diagnosis and management of leprosy cases, even those without complications: 79.9% of the trained, and 83.3% of the non-trained professionals sent new cases for confirmation of diagnosis to the reference centre; 93.9% of the trained and 96.9% of the non-trained perceived difficulties in treating leprosy reactions, and 72% of trained and 85% of non-trained difficulties in assessing the patients’ disability grade. Benefits of training included improvement in the detection of new cases and in the education of family members.

CONCLUSION PHC professionals did not feel sufficiently qualified to diagnose and treat straightforward leprosy cases. As a result, many patients were transferred to the reference centre without necessity. To guarantee an effective decentralisation of the Leprosy Elimination Programme, PHC professionals should be trained considering their needs, and standards for the referral and counter-referral of leprosy patients should be established. In addition, logistical problems, such as the availability of MDT in the PHC centres, must be addressed.

O28-53 Rural towns are a risk factor for leprosy: Study of the spatial distribution of leprosy in a district in northwest Bangladesh

E. A. J. Fischer1, D. Pahan2, S. Chowdhury3 and J. H. Richards4
1Department of Public Health, Erasmus MC, University Medical Center Rotterdam, Rotterdam, Netherlands; 2The Leprosy Mission Bangladesh, Rural Health Program Nilphamari, Bangladesh

OBJECTIVE Leprosy has an uneven spatial distribution indicating heterogeneity in underlying risk factors. We aim to describe spatial and spatio-temporal patterns of leprosy incidence. Furthermore, we try to determine the risk related to the proximity of geographic features, like towns, rivers, water, roads and railroads.

METHODS A retrospective study was conducted in which the spatial distribution of leprosy in a high endemic district in northwest Bangladesh was determined. We traced back the houses of patients detected between 1989 and 2003. The risk of proximity to towns, leprosy clinics, water, roads and railroads was estimated using Poisson regression models. The spatial scan statistic and the related space-time scan statistic were used to identify high incidence clusters of leprosy.

RESULTS The incidence rate of leprosy was four time higher in and around towns compared to 10 kilometers or more from a town. A relationship with water was also identified. Proximity to roads, railroads and clinics was not related to risk of leprosy. Several high incidence clusters were identified both in space and time in the southern part of the district showing the heterogeneous distribution of leprosy.

CONCLUSIONS In rural areas, towns amplify the incidence of leprosy. Leprosy is non-uniformly distributed over the district and this was not explained by population density differences.
Abstracts of the 5th European Congress on Tropical Medicine and International Health

O28-54
The uncomplicated neuropathic foot in leprosy patients: a clinical and radiological follow-up study
E. Slim1, A. F. Hoeksma2, M. Maas3 and W. V. R. Faber4
1Rehabilitation Medicine, Academic Medical Center, Amsterdam, Netherlands; 2Rehabilitation Medicine, Jan van Breemen Institute/Slootervaart Ziekenhuis, Amsterdam, Netherlands; 3Radiology, Academic Medical Center, Amsterdam, Netherlands; 4Dermatology, Academic Medical Center, Amsterdam, Netherlands

An MRI study in 2000 on 10 leprosy patients with neuropathic feet, but without clinical complications such as ulcerations, osteomyelitis or Charcot deformities (so-called uncomplicated neuropathic foot), revealed abnormalities in nine of these patients, with degradation, interruption of subcutaneous fat and effusion/synovitis, all located in the first metatarsophalangeal (MTP) region.

OBJECTIVES Since these MRI abnormalities may precede clinical complications of the foot, a follow-up study in these patients was performed.

METHODS New evaluation of the neuropathic foot was based on a clinical examination and an MRI.

RESULTS Four patients were lost to follow-up. The average follow-up period was 4.6 years. The MRI findings in the MTP one region at the start of the study disappeared in three patients, but were still present in two other patients. In six patients new MRI findings were found, without clinical signs of ulcerations, osteomyelitis or Charcot deformity. No relationship could be found between the MRI findings located in the MTP region at the start of the study and the development of foot ulcers, callus or skin fissures in the MTP 1 region during the follow-up period.

CONCLUSION The results of this study show that MRI findings of interruption and infiltration of the subcutaneous fat of uncomplicated neuropathic feet in leprosy patients do not necessarily have any clinical implication for the development of foot problems in the future.

O28-55
The relationship between detection delay and impairment in leprosy control: a comparison of patient cohorts from Bangladesh and Ethiopia
N. Van Veen1, A. Meima1 and J. H. Richards1
1Erasmus MC, University Medical Center Rotterdam, Public Health, Rotterdam, Netherlands

OBJECTIVES To examine the quantitative relationship between detection delay and impairment in two different leprosy patient populations

METHODS Leprosy patients from two study cohorts (BANDS and AMFES) who reported voluntarily were included in the analysis. Data on detection delay, WHO impairment status, type of leprosy, age and sex were analysed using descriptive statistics and multivariable logistic regression analysis to identify significant risk factors for impairment and to quantify the relationship between detection delay and impairment status at intake.

RESULTS Detection delay was an independent risk factor for impairment at presentation in multivariate analysis. AMFES reported more impairment at detection than BANDS. In multivariable analysis, this difference was significant among PB patients (51% in AMFES vs. 15% in BANDS), but not in MB patients (56% in AMFES vs. 45% in BANDS). In fact, for every delay category PB patients from AMFES had much higher proportions of impairment than PB BANDS patients. Impairment rates in MB patients from AMFES were higher in every delay category, but the differences between the two cohorts were much smaller compared to PB patients.

CONCLUSION Our analysis confirms earlier findings that with longer delays, the risk of impairment at presentation increases. With the same reported delay, however, the proportion impaired can vary considerably between different patient populations, in particular for PB leprosy. Delay can therefore not simply be used as a general or absolute performance indicator for programme evaluation. Achieving short delays remains important in general, but understanding and addressing the underlying mechanisms of delay specific to a patient population adds substantially to the effectiveness of leprosy control.

O28-56
Effectiveness of neurolysis in reducing disabilities in patients with leprosy, Rondônia State, Brazil
M. d. J. Freitas de Alencar1, E. de Freitas Cabral2, C. Ribeiro de Oliveira2, R. C. Garcia Amaral2, A. Novaes Ramos1 Jr., P. A. M. Schreuder1 and J. Meulekamp1
1Department of Community Health, School of Medicine, Federal University of Ceará, Fortaleza, Brazil; 2Secretaria de Saúde do Estado de Rondônia, Policlinica Oswaldo Cruz, Porto Velho, Brazil; 3Secretaria de Saúde do Estado de Rondônia, Programa de Controle de Hanseníase e Tuberculose, Porto Velho, Brazil; 4Netherlands Leprosy Relief, Rio de Janeiro, Brazil

OBJECTIVES To describe the effectiveness of surgical decompression (‘neurolysis’) in leprosy patients with severe neuritis and no improvement of function or pain after high dose corticosteroid therapy.

METHODS We realized a retrospective study in leprosy patients with neuritis of ulnar, median, common peroneal and posterior tibial nerves who received neurolysis in the reference hospital in Rondônia State (Brazil), 2000–2003. We collected data concerning sensory and motor loss of the affected peripheral nerve trunks, before and after neurolysis. To assess semi-quantitatively the degree of sensory and motor deficiencies, ordinal scores based on the clinical evaluations were used.

RESULTS Of the 118 individuals operated on 297 peripheral nerve trunks, 96 (81.4%) patients were classified as borderline, 21 (17.8%) as lepromatous, and one patient as tuberculoid leprosy. The median of the semi-quantitative score of the sensory deficiency reduced significantly for the ulnar, median and posterior tibial nerves (all \(P < 0.001\)). In total, 90% of the patients with severe sensory deficiency before surgery presented with improved sensitivity after neurolysis. The clinical classification and the period between the first episode of neuritis and surgery did not modify the chance of improvement. Of the 10 patients that were operated 48 months after the first episode of reaction involving the ulnar nerve, five improved, four did not present any change, and one worsened. Similar to the sensory evaluation, the median motor score of the ulnar and common peroneal nerves improved significantly. Almost 60% of the patients operated on the common peroneal nerve presented more muscle strength after surgery.

CONCLUSION The sensibility and muscle strength improved significantly after surgery in most patients, even after a prolonged period of neuritis. Corticosteroid therapy remains the standard treatment of severe leprosy neuritis, but in case of unsuccessful treatment, neurolysis may be indicated. Appropriately designed controlled studies are overdue.

HIV: Prevention and Resistance to Treatment

O28-57
Novel delivery system for microbicides
A. Shams1
1The Scripps Institution of Medicine and Science, San Diego, USA

INTRODUCTION The AIDS pandemic is the worst health crisis in human history. With no cure or vaccine in site, a huge effort is
required for prevention. Despite all our efforts to promote the condom, the AIDS pandemic continues to spread unchecked particularly in women. Unfortunately microbicides, Nonoxynol-9, Cellulose Sulphate, and even Lemon juice increased the risk of HIV transmission when compared to placebo. It would appear that any minimal cumulative irritation by microbicides, to cervical cells, can increase the entry of HIV.

**OBJECTIVE**: (i) to shield the cervix -the main portal of entry to the STIs/HIV from the deleterious effects microbicides and the HIV; (ii) to store and deliver the microbicide for a prolonged time only on the vaginal side, and to meet the HIV virus head on as soon as it is deposited into the vagina.

**MATERIALS AND METHODS**

The FemCap is the newest cervical barrier approved in Europe and United States. The FemCap covers the cervix – the portal of entry for bacteria and viruses- and the site of chemokine receptors for the HIV virus (CCR-5 and CXCR-4). The FemCap is designed with a unique delivery system that stores and delivers the microbicide on the vaginal side. ACIDFORM microbicide has a unique bioadhesive and acid buffering properties that maintains the vaginal ecology and yet kills most of the STIs microorganisms including the HIV. Ten adult women applied ACIDFORM mixed with Gentian violet dye into FemCap’s groove, and inserted the FemCap into their vaginas. The cervix and vagina of all women were photographed before, during, and 6 h after removal of the FemCap that was loaded with ACIDFORM/Gentian violet.

**RESULTS**

The bulk of the microbicide/Gentian violet came out with the device with no staining detected over the cervix, while all the vaginal walls were very lightly coated with the Gentian violet stain.

**CONCLUSION**

This research has demonstrated that the use of the FemCap in combination with ACIDFORM can deliver the microbicide on the vaginal side and yet spares the cervix from the deleterious effects of microbicides. This ensures protection to the cervix and immediate and sustained contact of the microbicide with the HIV upon deposition into the vagina.

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**O28-58**

**Immunological assessment of pregnant HIV-infected women at St Camille Medical center, Ouagadougou, Burkina Faso**

F. Castelli, V. Pietra, J. Simpore, S. Pigatte, N. Belem, D. Sa, A. Pini, S. Capone, L. R. Tomasoni, S. Caligaris, and G. Carosi

1 Institute for Infectious and Tropical Diseases, University of Brescia, Brescia, Italy; 2 Institute for Infectious and Tropical Diseases, University of Brescia, Ouagadougou, Burkina Faso; 3 Centre de Recherche Biomoléculaire Pietro Asinogom, Ouagadougou, Burkina Faso; 4 Centre Medical Saint Camille, Ouagadougou, Burkina Faso

**OBJECTIVES**

To assess the immunological status of HIV-infected women during and after pregnancy in order to obtain clues on the optimal timing of starting HAART in pregnant women in resource-limited settings.

**METHODS**

All pregnant women attending St Camille Medical Centre (SCMC) in Ouagadougou in the period June 2002–May 2006 were offered opt-in Voluntary Counselling and Testing (VCT) by rapid tests. HIV-infected women undergo clinical and immunological evaluation to assess the need for starting HAART according to 2003 WHO guidelines or to receive ART prophylaxis only.

**RESULTS**

A total of 334 pregnant women have been screened HIV-infected during the study period. Clinical and immunological stage were as follows: WHO stage I (n = 170) = severe immunodepression (< 200 CD4/μl); n = 34; advanced immunodepression (200–349 CD4/μl); n = 47; moderate immunodepression (> 350 CD4/μl); n = 89; WHO stage II (n = 121) = n = 50; n = 37; n = 34 respectively; WHO stage III (n = 40) = n = 28; n = 7; n. 5 respectively; WHO stage IV (n = 3) = n = 3; n = 0; n = 0 respectively. All women complying with WHO-2003 recommendations have been administered HAART. For 97 women in stage I/II for whom HAART was not indicated according to 2003 guidelines (CD4+ > 200/μl CD4+ count was available also 4–6 months after delivery. A significant improvement compared to pregnancy values was observed in those women with moderate/none immunosuppression during pregnancy (n = 57; mean = 607 vs. 539, P < 0.001), but not for those with advanced immunodepletion (n = 40; 359 vs. 283; P = ns). However, 21/40 of the latter group had CD4 + cell count >350 cells/μl after pregnancy and none showed clinical progression.

**CONCLUSIONS**

As many as 87.1% of our pregnant women are in WHO stage I/II. Of them, 58.8% have CD4 + count below 350/μl, thus confirming the need for immunological determination to assess HAART timing. A significant post-delivery increase in CD4 + count was observed in WHO stage I/II pregnant women for whom HAART was not indicated according to both 2003 and 2006 WHO guidelines (CD4 ≥ 350/μl).
Poster abstracts

Access to Drug and Treatment Adherence

PA 1
Household survey on utilization of medicines in selected communities in South Africa

K. Pelzer, G. Mohlala, N. Phaswana-Mafuya, S. Ramlagan, K. Zuma, and N. Mbelle
HSRC, Pretoria, South Africa

OBJECTIVES The aim of this study was to examine the prevalence of drug use, and how morbidity, use of health services, self-evaluated health, demographic pattern and lifestyle characteristics influence drug use in a general population.

METHODS Cross-sectional community survey. The sample included 480 households randomly selected from two provinces (Western Cape and Limpopo).

RESULTS Results showed that 29% of the medicines used were not prescribed by a health professional. The number of households keeping antibiotics were (11.3%), analgesics (26.8%), steroids (1.0%), and vitamins (6.0%). Most respondents (62.1%) indicated that they had obtained medicines free of charge, while 25.1% paid in the range of 1 to 25 Rand and 12.8% paid above 25 Rand for their medicines. Most participants indicated that they have access to a health facility within 10 km of their residence where they could obtain medicines, and could be reached within 30 min, while it would cost less than 5 Rand for transport to reach the facility. On the management of childhood diarrhoea most respondents (63%) indicated that they would first give oral rehydration solution (ORS) while 22% said they would start by taking the child to a health professional.

CONCLUSION Our findings suggest a need for improved access to health facilities to help reduce the use of self-medication and thus improve on rational drug use at household level, pharmaceutical care and patient counselling.

PA 2
Achievements of the access to medicine index project

W. Leereveld
Access To Medicine Index Foundation, Haarlem, Netherlands

OBJECTIVES The pharmaceutical industry is specifically recognized in the UN Millennium Development Goals as an actor that contributes to their ultimate realization. As manufacturers of life-saving drugs and innovators of new treatments, pharmaceutical companies can play a significant role in their sphere of influence. What is this role? how far does it extend? and how should it evolve to address the lack of access to treatments to disadvantaged people? Phase 1 of a unique multi-stake holder study has completed to determine how best to evaluate pharmaceutical companies’ strategies and performance on improving the access to medicines for those in need in developing and developed countries. The aim of the Access To Medicine Index is to build a rational, yet aspirational framework to analyze pharmaceutical companies’ responses to the access challenge and to encourage continuous improvement.

METHODS Study Structure An online questionnaire was created, which was then sent to over 200 worldwide experts on the access to medicine subject. Open feedback was gathered from a wide range of stakeholders including NGOs, academia, consultants, investors and government officials on pharmaceutical company practice. Subsequently two round tables were conducted in London and New York, to discuss and refine a framework to assess pharmaceutical companies’ performance.

RESULTS The study to date has determined that pharmaceutical companies should be involved in eight specific areas, with discussions concluding that the following criteria and weightings should be used to best evaluate company performances. Weightings have been assigned to each of the eight criteria based on stakeholder discussions that add up to 100%.- Access to Medicines Management (20%): Accountability for ATM, responsibility, implementation of ATM policies, collaboration with all stakeholders and transparency in reporting.- Policy Influence & Lobbying (10%): Disclosure of policy positions, activities and funding to ensure consistency.- R&D in neglected diseases (20%): R&D investment in neglected diseases in-house and in collaboration with public institutions.- Patent & Licensing (15%): Patent relaxation policies and voluntary license agreements.- Equitable Pricing (15%): Assessment of pricing mechanisms for all markets and transparency.- Drug Donations (10%): Compliance with the WHO guidelines on drug donations and performance of donation programs.- Philanthropic Activities (5%): Capacity building and training of health care professionals.- Ethical promotional and Marketing Activities (5%): Marketing practices and adherence to ethical criteria in medicinal drug promotion.

Amoebiasis

PA 3
Detection of Mycobacterium tuberculosis strains with MIRU-typing, spoligotyping, and RFLP methods, isolated from Ethiopian patients

R. Ramazanzadeh1, R. McNerney2, and H. Traore2
1Kurdistan University of Medical Science, Microbiology, Sanandaj, Iran, Islamic Republic of Iran; 2London School of Hygiene and Tropical Medicine, London, UK

OBJECTIVES Distribution of tuberculosis in local or global population has been detected by use of molecular epidemiology techniques such as restriction fragment length polymorphism (RFLP), spoligotyping, and variable number tandem repeat (VNTR) typing methods.

METHODS In these study 22 strains of the Ethiopian patients has been studied by RFLP, VNTR, and Spoligotyping methods.

RESULTS The discriminatory power of RFLP, VNTR, and Spoligotyping has been detected 97%, 97%, and 23%, respectively.

CONCLUSION In conclusion with considering that VNTR has high discriminatory power in PCR-based technique and can be used as alternative method for typing M. tuberculosis isolates.
PA 4
Incidence of cmaA2 gene in Beijing and non-Beijing strain of M. tuberculosis isolated in TB patients
R. Ramazanzadeh¹, N. Amir Mozafari², and P. Farmia³
¹Faculty of Medicine, Kurdistan University of Medical Science, Microbiology, Sanandaj, Iran, Islamic Republic of Iran; ²Iran University of Medical Science, Tehran, Iran, Islamic Republic of Iran; ³Shabab Beheshti University of Medical Science, Faculty of Microbiology, Tehran, Iran, Islamic Republic of Iran

OBJECTIVES The aim of this study was to investigate the prevalence of cmaA2 gene in M. tuberculosis strains isolated and typed by spoligotyping. The associated risk factors among patients with different nationalities residing in Iran were also determined.

METHODS The study population involved a total of 439 patients that referred to the NRITLD, the referral tuberculosis center in Iran; during March 21st 2003 to March 21st 2004. The isolated M. tuberculosis strains have been characterized by performing susceptibility tests against four first-line antituberculosis drugs and were then subjected to spoligotyping characterization. PCR was used for detection of cmaA2 gene and its nucleotide sequence was also determined.

RESULTS Spoligotyping of M. tuberculosis strains resulted in 140 different patterns. One hundred twenty two (87.1%) of these spoligotype isolates were unique and reported for the first time. The remaining 18 (12.8%) spoligotype patterns were previously reported from other geographical regions of the world. Haarlem family was most prevalent than other genotype. Interestingly, 6.3% of the strains belonged to the Beijing family. Antibiotic resistances were higher in those isolated from the Afghani patients. The cmaA2 gene was detected in M. tuberculosis clinical isolates but not in saprophyte strains such as M. kansasi. The other risk factors such as sex and age were also contributing factors to the diseases state. The results showed that multi drug-resistances were more prevalent in bacteria isolated from Afghani TB patients residing in Iran. In addition, spread of M. tuberculosis strains belonging to the Beijing family among Iranian patients has to be considered seriously. This study confirmed the widespread existence of cmaA2 gene in almost all the clinical isolates. It is also important to undertake studies to identify which factors are the most significant to consider in tuberculosis control program.

PA 5
Differential diagnosis of hepatic abscess through Entamoeba histolytica IgG ELISA antibodies
A. E. Pinilla¹ and M. C. Lopez²
¹Universidad Nacional de Colombia, Internal Medicine, Bogota, Colombia; ²Universidad Nacional de Colombia, Public Health, Bogota, Colombia

OBJECTIVES Analyze the utility of IgG ELISA in etiologic diagnosis of hepatic abscess.

METHODS Prospective study in Colombian patients with hepatic abscess was made since 2002 until 2006. The literature has reported that the kinetic specific anti-E. histolytica IgG antibodies may persist for several years. Also, the IgG ELISA and immunodifusion test has been questioned in tropical countries. For this reason, this project researches the usefulness of the ELISA for IgG antibodies and immunodifusion test kinetic for the etiologic diagnosis of liver abscess.

RESULTS Two cases are presented. The first patient is a man with 65 years old with diabetes mellitus who presents abdominal sepsis and fever, he has a pyogenic hepatic abscess which presents negative IgG ELISA and immunodifusion test for Entamoeba histolytica but positive hepatic drain culture for Escherichia coli and Fusobacterium spp. The second, is a case which presents the results of the follow-up during 44 months of the IgG antibodies of a 69 year old patient from Choco (Colombia), who consulted with two week symptoms of fever and abdominal pain in the right upper quadrant; the diagnosis of amebic liver abscess was achieved through the clinical features, liver ultrasound, IgG ELISA and immunodifusion with the response to treatment with metronidazole. The kinetic of ELISA IgG behaves in the following way: it was positive during the first 32 months, at the beginning the absorbance was 1.3 (cut-off point 0.34) instead of the observance declined quickly in the first year and half, it remained positive until 32 months and it was negative at the end with ELISA absorbance 0.25, in 44 months.

CONCLUSIONS The ELISA to IgG antibodies and immunodifusion is usefulness for etiologic diagnosis of hepatic abscess, if it is negative discard the amebic etiology. Besides, the kinetic of ELISA IgG could be positive from months to less years.

PA 6
Prevalence of Entamoeba histolytica and Entamoeba dispar in Gonbad city, Iran
A. Haghighi¹, E. Nazemallahi Mojarad², M. Azimi Razi², F. Mesgarian³, and M. R. Zali⁴
¹Shabab Beheshti University of Medican Science, Department of Parasitology and Mycology, School of Medicine, Tehran, Iran, Islamic Republic of Iran; ²Shabab Beheshti University of Medican Science, Research Center for Gastroentrology and Liver Diseases, Tehran, Iran, Islamic Republic of Iran

OBJECTIVES The aim of this study was represented the distribution of E. histolytica and E. dispar in urban and rural areas of Gonbad city in the north of Iran.

METHODS From February 2005 to July 2006, five hundred and fifty one fecal samples were collected from primary health care centers of Gonbad city. The samples were examined by light microscopy (direct smear, lugol, and trichrom staining) to differentiate E. histolytical/E. dispar complex from other non-pathogenic intestinal amoebae and PCR was used to differentiate E. histolytica from E. dispar.

RESULTS The E. histolytica specie was detected in 2 of 551 analyzed stool samples (0.36%). E. dispar species was observed in 20 samples (3.63%) and both species of Entamoeba were detected in 1 sample (0.18%).

CONCLUSION Microscopy is not a sensitive and reliable technique for diagnosing intestinal amebiasis as well as differentiation of E. histolytica from E. dispar. It is now known that most of human cases of infection with E. histolytica/E. dispar are actually E. dispar. E. dispar is non-pathogenic, and requires no treatment. Because of this, differential diagnosis of the pathogen E. histolytica from the commensal E. dispers is of the utmost importance.

PA 7
Entamoeba histolytica and Entamoeba dispar infection frequency detected by PCR among patients with gastrointestinal complaints in Zahedan city, Iran
A. Haghighi, A. Salimi-Khorashad, and B. Kazemi
Shabab Beheshti Medical University, Parasitology and Mycology, Tehran, Iran, Islamic Republic of Iran

OBJECTIVES Differential diagnosis of Entamoeba histolytica and Entamoeba dispar has great clinical and epidemiological importance. The prevalence of these two enteric protozoan parasites in most part of Iran is, as yet, unclear.

METHODS Microscopy methods (direct smear, formalin ether concentration and xenic culture) and PCR technique were used for
diagnosis of the enteric parasites in this study, with emphasis to Entamoeba histolytica and Entamoeba dispar protozoa in patients with gastrointestinal complaints. A total of 1562 stool samples were examined from July 2004 to January 2006 in Zahedan city, South East of Iran.

RESULTS Four hundred and seventy seven (30.5%) of the patients were infected with one or two intestinal parasites. The most prevalent protozoa were Giardia lamblia (10.1%), Entamoeba coli (10%), Blastocystis hominis (2.2%), Chelomastix mesnili (1.7%), Trichomonas hominis (0.7%), Entamoeba histolytica/Entamoeba dispar (0.5%), and Iodamoeba butschlii (0.45%). From eight (0.5%) microscopy positives Entamoeba histolytica/Entamoeba dispar samples, six (0.4%) were identified as E. dispar by PCR techniques, while Entamoeba histolytica species was not detected at all.

CONCLUSION PCR of two microscopy positive Entamoeba isolates were negative, perhaps due to the PCR error, lack of DNA or any other morphologically identical Entamoeba species like Entamoeba moshkovskii. Although Zahedan city is located in a tropic area near the border of Afghanistan, with poor hygiene; the prevalence of E. histolytica and E. dispar in comparison with the other parasites and infectious diseases are unexpectedly low.

PA 8
A route of genotyping of Entamoeba histolytica: t-RNA gene studies
1Gallblane Military Medical Academy, Ankara, Turkey; 2Division of Parasitology, Ankara, Turkey; 3Harran University, Department of Microbiology, Sanliurfa, Turkey; 4Stanford University, Department of Infectious Disease, Palo Alto, USA; 5Yuzuncu Yil University, Department of Parasitology, Van, Turkey; 6University of Virginia, Departments of Medicine, Microbiology, and Pathology, Division of Infectious Diseases, Charlottesville, USA

OBJECTIVES Entamoeba histolytica infections can be asymptomatic or cause invasive disease characterized by colitis and liver abscess. The molecular basis for this variability in outcomes is not clear. This provides an opportunity to determine whether the genotype of the parasite influences the clinical manifestations of E. histolytica infection. We have investigated polymorphisms in tRNA genes flanked - short tandem repeats (STRs) - in E. histolytica isolates from infected individuals in Turkey.

METHODS In the present study, a total of 17 patients (three had no symptoms, 13 had diarrhea/dysentery, and one had developed liver abscess by E. histolytica, as diagnosed by an amoebic stool antigen detection, E. histolytica II kit, TechLab, Inc., Blacksburg, VA, and real-time PCR) were used. Genotypes were determined using six tRNA-linked polymorphic markers. Nested PCR was performed with E. histolytica-specific tRNA linked STRs primers. Initial primers located entirely in tRNA genes, while the nested PCR primers included A-T rich regions flanking the tRNA genes.

RESULTS We identified 12 different genotypes among 17 isolates when the genotypes of the six loci were combined with the all isolates. Nested PCR had a success rate of >95% at all six loci. We observed a significant degree of STR polymorphism among E. histolytica strains obtained from fecal samples even the strains isolated from a restricted area.

CONCLUSION Strain identification is an easy, sensitive, and stable technique for investigating the relationship between parasite genotype and clinical outcome. Although the number of isolates from Turkey was too small to illustrate an ultimate conclusion the presence of a high degree of genetic polymorphism in the tRNA-linked markers is important. Also, results demonstrate the value of the research of the prototypes of spread of amebiasis.
PA 11

Investigation of the prevalence of amoebiasis and determination of Entamoeba spp. with polymerase chain reaction (PCR) and enzyme immunoassay (EIA) in Izmir province, Turkey

H. Dagcî, O. Kurt, M. Demirel, I. Ostan, N. Azizi, A. Mandracioglu, M. Tanyuksel, and M. Ak
Ege University School of Medicine, Parasitology, Izmir, Turkey

OBJECTIVES Discrimination of the pathogen Entamoeba histolytica from the non-pathogen Entamoeba dispar is not possible with microscopic but with molecular methods, such as EIA and PCR.

METHODS The aim of this study was to assess the prevalence of amoebiasis in Izmir province and determine the Entamoeba species with PCR and EIA. A total of 2047 people were selected by cluster sampling and they were visited in their dwellings, completed an inquiry form and submitted stool samples. All stool samples were examined with wet-mound, formalin ethyl acetate concentration and trichrome staining, followed by inoculation in Robinson’s medium for culture. Stool samples found to be positive for E. histolytica or E. dispar in any of these methods, were further analyzed with PCR and EIA for the identification of species. The statistical analysis investigating any relation between the parasites and both personal and environmental factors, was done with SPSS® 11.5, with the assessment of t-test, ANOVA and chi-square.

RESULTS Fifty-nine of 2047 (2.8%) stool samples were found to be positive for E. histolytica or E. dispar. Among these 59 samples, E. histolytica was determined in 14 (0.7%) with PCR and 5 (0.2%) with E. histolytica antigen-specific ELISA (EIA). E. dispar was diagnosed in 31 of 59 (5.1%) samples with species-specific PCR. Fifty-four of 59 (2.6%) samples found to be negative in EIA were then considered as E. dispar. Demographic examination of the study group revealed a statistically significant difference between the prevalence of Entamoeba spp. and other intestinal parasites and in people living in shanty houses (P < 0.01), recently immigrated to Izmir (P < 0.01), having no social security (P < 0.05) and living with a crowded family (P < 0.01).

CONCLUSION To our knowledge, this study is important that it is the first community-based prevalence study of amoebiasis in the West of Turkey, with an aim to identify E. histolytica and E. dispar. Amoebiasis was found to be a significant health problem, mostly among people with lower socioeconomic status in Izmir province.

PA 12

Detection and identification of Entamoeba species by reverse line hybridization in stool samples from Hué, Vietnam

J. J. Verweij1, E. A. T. Brienen1, J. Blessmann2, A. Le Van3, and E. Tannich2
1 Leiden University Medical Center, Parasitology, Leiden, Netherlands; 2 Bernhard Nocht Institute for Tropical Medicine, Hamburg, Germany; University of Hue, Medical College, Hue, Vietnam

OBJECTIVES Classically, diagnosis of E. histolytica is based on the finding of characteristic cysts and/or trophozoites in faecal preparations. E. histolytica cysts and those of non-pathogenic amoeba species are differentiated based on their appearance and size of the cysts. However, since the recognition that non-pathogenic Entamoeba dispar and Entamoeba moshkovskii are morphologically identical but represent separate species, alternative techniques for an accurate diagnosis have to be explored. In this study faecal Polymerase Chain Reaction and Reverse Line Hybridization Blot technique were used for the diagnosis of intestinal Entamoeba infections. Results were compared with those of microscopy.

METHODS DNA samples and results from microscopy of approximately 500 stool samples from Hué, Vietnam were available. Polymerase Chain Reaction and subsequent Reverse Line Hybridization Blot (RLB) was performed to identify E. histolytica, E. dispar, and a range of other Entamoeba species and genetic variants.

RESULTS The DNA samples from Hué, Vietnam showed hybridization with the specific probes of a large variation of Entamoeba species and genetic variants. Samples that showed hybridization with E. histolytica showed less mixed infections with other Entamoeba species as compared with E. dispar positive samples. More detailed comparison of DNA hybridization and microscopy will be presented at the meeting.

CONCLUSION DNA based methods have proved to be specific and sensitive and therefore microscopy is no longer the only ‘gold standard’ of parasite identification. These techniques can be used as additional standards in diagnosis, epidemiology and quality control in amoebic infections. The lack of other Entamoeba species in E. histolytica-positive samples may indicate that E. histolytica outgrows non-pathogenic Entamoeba species. However, this phenomenon deserves further investigations.

PA 13

Effects of chlorpromazone and rokitamycin in mice experimentally developed amoebic meningoencephalitis by Naegleria fowleri

J. H. Kim1, A.-H. Yang1, K.-J. Choo1, A. Song1, H.-J. Sohn1, K.-I. Imm2, and H.-J. Shin1
1 Ajou University School of Medicine, Microbiology, and Molecular Science & Technology, Suwon, Korea, Republic of; 2 Yonsei University College of Medicine, Parasitology, Seoul, Korea, Republic of

OBJECTIVES Free-living ameba, Naegleria fowleri, leads to a potentially fatal infection known as primary amebic meningoencephalitis (PAME). Amphotericin B is an agent with established clinical efficacy in the treatment of PAME in humans, but therapy with this drug is often associated with adverse effects on the kidneys and other organs, and all persons treated with amphotericin B have not been survived. In an attempt to identify other useful drugs for treating PAME, we investigated the activity and efficacy of nine kinds of antibiotics.

METHODS Nine kinds of antibiotics, neomycin, hygromycin, zeocin, erythromycin, roxithromycin, clarithromycin, rokitamycin, chlorpromazine, and miltefosine were tested. Firstly, the in vitro cytotoxic effect of nine antibiotics on cultivating N. fowleri trophozoites was observed. After we selected antibiotics which were
shown the in vitro cytotoxicity against N. fowleri, we investigated the in vivo efficacy of selected antibiotics in treatment for PAME.

RESULTS In results, hygromycin, roxithromycin, rokitamycin, chlorpromazine, and miltefosine induced 100% cytotoxicity against N. fowleri at 8 days post treatment. In experimental PAME, mice treated with hygromycin showed the prolonged survival period, but their mortality was 100%. Otherwise, survival rate of mice treated with roxithromycin, miltefosine, chlorpromazine and rokitamycin showed 20%, 50%, 70% and 70% at 28 days post treatment, respectively. Otherwise, the number of times for drug administration was an important factor, and effects of drug treatment were best at 3, 7, and 11 days intervals in all cases.

CONCLUSION Finally, chlorpromazine and rokitamycin may be useful therapeutic agents for PAME as showing the strong effects in vitro and in vivo.

PA 15

Epidemiology of E. histolytica and E. dispar infections in a non-endemic area (Parma, Italy) during 2003–2006
A. Calderaro, C. Gorrini, S. Peruzzi, G. Piccolo, G. Dettori, and C. Chezzi
University of Parma, Department of Pathology and Laboratory Medicine, Section of Microbiology, Parma, Italy

OBJECTIVES Since E. histolytica is morphologically indistinguishable from E. dispar, a reassessment of the worldwide prevalence of amoebic infection based on methods able to differentiate the two species was strongly recommended by World Health Organization (Tanyuksel and Petri, 2003). The area in which our laboratory is located (Northern Italy) has seen in recent years an increase of people travelling to tropical countries, a significant flow of immigration and the adoption of children from the same areas which has led to a parallel increase in imported tropical infections. The aim of this study was to assess the occurrence of E. histolytica and E. dispar infection among the patients with suspected intestinal parasitosis presenting to University Hospital of Parma as diagnosed by the combination of traditional and molecular methods (PCR and Real-Time PCR) (Calderaro et al., 2006).

METHODS During 2003–2006, 7281 clinical samples belonging to 306 patients (a total of 511 samples – 496 faeces, 7 liver abscess samples, 8 intestinal biopsies - belonging to 306 patients).

RESULTS Eight patients (2.61%) proved to be infected by E. histolytica (3 with amoebic liver abscess and 5 with amoebic dysentery; 5 with imported amoebiosis and 3 with the disease acquired in Italy) and 22 by E. dispar (7.18%).

CONCLUSION Though rare, the detection of E. histolytica infections in a non-endemic area like Italy emphasizes that our country needs to expand its range of parasitology laboratories with adequate molecular diagnostic assays. Moreover, a parasitological check-up on arrival in Italy for adopted children and adult immigrants from developing countries to identify carriers of faecal–oral transmitted infections like amoebiasis might be useful to enhance the individuals’ health by treating intestinal parasitic infections as well as to protect the public health of the community.

PA 16

Genotyping of E. histolytica strains detected in Parma (Italy): preliminary results
A. Calderaro, C. Gorrini, G. Piccolo, S. Peruzzi, G. Dettori, and C. Chezzi
University of Parma, Department of Pathology and Laboratory Medicine, Section of Microbiology, Parma, Italy

OBJECTIVES AND METHODS Current understanding of the epidemiology of amoebiasis still lacks the knowledge of what determines the outcome of E. histolytica (Eh) infections. It is possible that one of the determining factors resides in the genotype of the parasite. In this study we used a recently described PCR assay based on short tandem repeat (STR)-containing loci linked to tRNA genes (Ali et al., 2005) to investigate the extent of genetic diversity among Eh strains from clinical samples of patients with amoebic colitis or liver abscess. Nineteen samples (faeces, liver abscess and intestinal biopsy samples) belonging to 8 patients with amoebiosis (5 intestinal, 3 extraintestinal) were analysed.

RESULTS AND CONCLUSION On the basis of the variability of the number of STRs at the six loci, all strains had unique genetic fingerprints (except for 2 strains from the faeces of 2 patients belonging to the same family), reflecting a high degree of polymorphism in the population studied. Interestingly, in a patient for whom sample from both faeces and liver abscess was available, the strains from the two types of samples had different genotypes. This suggests a possible role of the genotype in determining tissue tropism, a hypothesis that certainly needs to be confirmed on a significant number of strains from faeces and abscesses of individuals with extraintestinal disease.

Sequencing of the amplification products at all 6 loci for all the strains analysed is in progress in order to confirm genotype assignment which was done primarily on the basis of the estimated PCR product sizes in agarose gel. A genotyping study in Bangladesh (Ali et al., 2007) has suggested that the parasite genome plays a role in determining the outcome of infection with Eh. It is important to know whether this observation can be replicated in other parts of the world. To investigate this, extensive sample collections from additional geographical areas are needed. Therefore, though not inferred from a large population of Eh strains, we are confident that the results of the present study, when taken together with genotyping data produced on an increasing number of strains isolated from asymptomatic and symptomatic patients in different geographical areas, could contribute to a deeper understanding of the link between Eh genotype and the outcome of infection.

PA 17

Targets of the E. histolytica transcription factor URE3-BP
C. Gilchrist1, D. J. Baba1, M. Leo1, A. Hochreiter1, S. K. Connell1, Y. Zhang2, L. Lockhart1, C. Evans1, O. Crasta1, B. W. S. Sobrã1, G. Ehrenkaufer1, U. Singh3, B. J. Mann1, and W. A. Petri Jr1
1University of Virginia, Department of Medicine, Charlottesville, USA; 2Virginia Bioinformatics Institute, Blacksburg, USA; 3Stanford University School of Medicine, Departments of Internal Medicine and Microbiology, Stanford, USA

The E. histolytica transcription factor URE3-BP is a potential regulator of two E. histolytica genes: hgs5, one of the genes that encode the heavy subunit of the Gal/GalNac inhibitable lectin, and the ferredoxin gene fdx1. A one-hybrid screen of E. histolytica proteins identified the protein URE3-BP as capable of binding to the sequence TATTCGATT (URE3), a motif present in both promoters. Chromatin immunoprecipitation experiments con-
firmed its interaction with both the hsl5 and fab13 promoter DNA and antibody interference assays demonstrated specific calcium-dependent binding of URE3-BP to the motif (Gilchrist et al. 2003). Precise mapping of the URE3 element was performed by electrophoretic mobility shift assays and the motif matrix T[acg][g][T][C][C][T][a][g]T is found significantly more often in promoters (chi-square analysis P > 0.001).

OBJECTIVES To identify other E. histolytica genes regulated by this transcription factor we have used both bioinformatics and transcriptome profiling.

METHODS A custom array (E._his_1a520285) was designed representing both ORF and selected UTR regions. Arrays were performed using RNA isolated from ameba either inductively expressing a calcium insensitive mutant of URE3-BP (EF (2) mutURE3-BP) or a control construct. The data from this experiment was normalized using the gcRNA program and statistical significance was determined by the use of SAM. The regulatory DNA of the modulated transcripts was then searched for potential URE3 motifs.

RESULTS The microarray results indicate that expression of the dominant positive URE3-BP led to a pattern of mRNA change; 1) the decrease in several enzymes involved in long chain fatty acylCoA synthetase concurrent with an increase in lecithincholesterol acyltransferase levels, suggesting a net increase in triglycerol synthesis; 2) a decrease in many enzymes involved in transcription and translation; 3) downregulation of many of the proteins which could be incorporated into filopodia-like projections. The URE3 matrix was not found in many of the promoters modulated by the expression of EF(2)mutURE3-BP. A possible explanation is that URE3-BP does not act directly on these promoters. We compared the list of genes to the list of transcripts downregulated in ameba within the intestine, as the URE3-BP transcript was significantly downregulated within the in vivo environment. This allowed us to identify 11 co-regulated transcripts, which include those with a possible signaling function, a single-stranded DNA binding protein and a protein kinase (TMK103). Ten of the 11 genes contained a match to the URE3 matrix in either the 5’ or 3’ sequences.

CONCLUSION The modulation of these transcripts may be important in the host environment.

PA 19

In vitro effect of extracts and essential oils of Iranian Allium sativum (garlic) and Thymus vulgaris on trophozoites of Entamoeba histolytica

M. Behnia1, A. Haghigh2, H. Komeylizadeh3, S. J. Seyyed Tabaei4, and A. Abadi4,
Parasitology and phytotherapy
1Science and Research Branch, Islamic Azad University, Parasitology, Tehran, Iran, Islamic Republic of Iran; 2School of Medicine, Shahed Beheshti Medical University, Parasitology and Mycology, Tehran, Iran, Islamic Republic of Iran; 3School of Pharmacy, Shahed Beheshti Medical University, Chemistry, Tehran, Iran, Islamic Republic of Iran; 4School of Medicine, Shahed Beheshti Medical University, Parasitology and Mycology, Tehran, Islamic Republic of Iran; 5School of Medicine, Shahed Beheshti Medical University, Community Medicine, Tehran, Iran, Islamic Republic of Iran

OBJECTIVES From the beginning of this decade and with the revival of the phytotherapy, biological researches about herbal medicines have been in progress. On the other hands side effects of herbal medicines are nothing or very rare. Our objective was to determine the antiamoebic activity of essential oils, hydro alcoholic and hexanic extracts from Allium sativum and Thymus vulgaris. Some studies have proven antimicrobial properties of these plants.

METHODS Essential oil isolated by steam distillation using a Clevenger-type apparatus. Hydro alcoholic and hexanic extracts were obtained by maceration of plants with ethanol/water (60:40) and hexan respectively for 14 days at room temperature (25 °C). Anti-amoebic activity was determined over cultures of Entamoeba histolytica (HM-1:IMSS) in Diamonds modified TYI-S-33 medium. Microscopic counting of trophozoites after their incubation in the presence of different concentrations of crude extracts and essential oils were made in order to determine the cytocidal and cytostatic activities respect to control cultures and metronidazole. Data were analyzed using two-way analysis of variance (ANOVA).

RESULTS In this study after 24 h: the minimal inhibitory concentration (MIC) of T. vulgaris hydro alcoholic, hexanic extracts and essential oil of it were 4, 4 and 0.7 mg/ml; and the MIC of A. sativum hydro alcoholic, hexanic extracts and essential oil of it were 60, 60 and 0.4 mg/ml, respectively. After 48 h: the MIC of T. vulgaris hydro alcoholic, hexanic extracts and essential oil of it were 3, 3 and 0.7 mg/ml; and the MIC of A. sativum hydro alcoholic, hexanic extract and essential oil of it were 60, 3 and 0.3 mg/ml, respectively. The MIC of metronidazole after 24 h and 48 h were 2 and 1.5 µg/ml, respectively. In all experiments the results are significantly different from control (P < 0.01).

CONCLUSION The results indicated that these plants inhibited growth of E. histolytica at low concentrations, therefore T. vulgaris and A. sativum have some anti-amoebic components (T. vulgaris including thymol, carvacrol, borneol and linalool; A. sativum including allin, aljene and other organosulfides) that antimicrobial properties of these were proven. On the other hand, considering that the use of this type of infusion apparently does not produce secondary effects, it is important to characterize and purify the compound responsible for the detected anti-amoebic activity, with the purpose of identifying a new drug that could be more powerful and less toxic.Keywords Entamoeba histolytica, Thymus vulgaris, Allium sativum, herbal medicine

PA 20

Analysis of the repeated region of chitinase gene in Entamoeba invadens isolates

G. Garcia1, F. Ramos1, A. Valadaz1, P. Morran1, E. Gonzalez1, A. Limon1, J. Yañez2, P. Gaytan2, and C. Ximenész1
Faculty of Medicine, Autonomous University of Mexico, Experimental Medicine, Mexico, D.F., Mexico; 2Institute of Biotechnology, Autonomous University of Mexico, Cuernavaca, Morelos, Mexico

OBJECTIVES Our interest in the present study is to analyze the polymorphism of the repeat region in chitinase gene in Entamoeba invadens to be compared with homologous regions present in Entamoeba histolytica and E. dispers.

METHODS We have sequenced and analyzed the polymorphism of the chitinase gene in Entamoeba invadens isolates from Mexican turtles and IP and PZ axenic strains using the Byg Die System and the terminator cycle sequencing fluorescence method.

RESULTS Our partial results revealed that no one of the chitinase sequences analyzed had differences in the repeated region.

CONCLUSION: The chitinase and other polymorphic genetic loci have been used as a tool for genotyping of strains, and they
represent an important advance for studying differences in virulence, tissue tropism and organ tropism by the parasite. Moreover we can use these different genotypes in order to understand the transmission, the distribution and the spread mechanisms of Entamoeba strains. Our results suggest that this loci can not be use in genotyping studies in E. invadens as has been used in E. histolytica and E. dispar species. Therefore it will be necessary to look for other markers for genotyping studies. On the other hand, as the polymorphism of the repeated region present in E. dispar and E. histolytica chitinase genes is very different from the no-polymorphic repeated region from E. invadens chitinase gene, it would be interesting to determine if this difference has any effect in encysting process in the axenic culture.

ACKNOWLEDGMENT The present work was partially supported by grants number: DGAPA IN206405, PAPIIME PE-200105, PAPIIT IN226806-3, PAPIIT IN227006-2, CONACYT 52424-Q.

PA 21 Epidemiology of amebic liver abscess in Mexico: the case of Sonora
O. Valenzuela1, P. Moran2, K. Cordova3, N. Corrales3, A. Cardoza3, N. Gomez2, A. Gomez2, and C. Ximenes2
1University of Sonora, Chemical and Biological Science Department, Mexico, D.F., Mexico; 2Faculty of Medicine, Autonomous University of Mexico, Experimental Medicine, Mexico, D.F., Mexico; 3University of Sonora, Chemical and Biological Science Department, Hermosillo, Sonora, Mexico; 4Centro Medico Nacional Siglo XXI, IMSS, Hospital de Pediatría, Mexico, D.F., Mexico

OBJECTIVES The purpose was to evaluate the dimension of E. histolytica invasive infection through a reliable analysis of incidence of ALA based on the hospital discharges incidence rates in this community. The period studied was January 2000 to December 2005.

METHODS The present work is an ecological study of trends of morbidity of ALA occurred in the period from 2000 to 2005. The analysis of morbidity data of amebic liver abscess in Mexico shows that in some of states incidence rates are remarkable high. One of these is Sonora, a large Northwest state with one of the highest incidence rates for ALA in 1995 and in 2002 (26.97 and 12.57 cases/100,000 inhabitants respectively). The major frequency of ALA was observed between 20 and 59 years old individuals. The population incidence rates evaluated and reported in the present work for 2000–2002 were 7.14, 8.40 and 7.79 respectively, in contrast with the official data by federal entities of 5.34, 6.94 and 12.57/100,000 inhabitants. Apparently there is a sub-valuation in the 2000–2002 period. Considering patients’ place of residence in Sonora at the time of admission, a geographical relation was observed, 75% of ALA outcomes occurred in 5 from 72 counties in Sonora. All of these are geographically close to Hermosillo.

CONCLUSION In summary, our investigation highlights the importance of this pathology in our country. This fact stresses the need for a strategy to study the specific risk factors that determine the epidemiological behavior of E. histolytica invasive infection in this particular state.

ACKNOWLEDGMENTS The present work was partially supported by the Grants number: IN-206405-3, IN-226806-3 and IN-227006-2 from PAPIIT; PE-200105 from PAPIIME and 52424-Q from CONACYT.

PA 22 Epidemiology and genetic diversity of Entamoeba histolytica in Spain
M. J. Gutierrez-Cisneros, M. Flores, T. Garate, A. Blanco, and I. Fuentes
ISCIII, Parasitology, Madrid, Spain

OBJECTIVES To study the epidemiological characteristics of human amebiasis cases, diagnosed at Servicio de Parasitología CNM-ISCIII, as well as the genetic diversity of Entamoeba histolytica clinical strains.

METHODS Twenty cases were diagnosed, between January 2005 and December 2006, using a nested PCR, targeting the SSUrDNA region. Genetic diversity was determined by nucleotide sequencing of one protein-coding (SREHP) and non-coding regions ( locus 1–2 and S-Q), also obtained by a nested-PCR with DNA extracted from stool specimens and the aspirated pus of liver abscesses.

RESULTS Twelve out of twenty patients showed liver abscesses, three females and nine males. Seven had amebic dysentery and/or colitis, four females and three males. The last patient was asymptomatic. Five patients were tourists who visited endemic areas, three female and two males. Thirteen patients were immigrants from endemic regions, three females and nine males. Finally, three European patients did not show epidemiological risks, without history of travels to tropical and subtropical countries, one female and two males. Regarding the last two patients they had maintained sexual intercourse with immigrants from endemic areas. The analysis of SREHP and STRs confirmed the presence of several genotypes of E. histolytica.

CONCLUSION i) Amebiasis is an emergent parasitosis in Spain, as a consequence of the increased number of immigrants from endemic areas as well as the increase of travellers to the endemic regions.ii) Genetic diversity was confirmed among the E. histolytica clinical strains examined.

PA 23 Amebic and pyogenic liver abscess: importance of differential diagnosis in endemic areas of amebiasis
P. Moran1, A. Gomez2, A. Valadez3, F. Ramos1, E. Gonzalez4, G. Garcia1, A. Limon1, O. Valenzuela1, M. Ramiro5, H. Hidalgo1, E. Melendro1, and C. Ximenes1
1Faculty of Medicine, Autonomous University of Mexico, Experimental Medicine, Mexico, D.F., Mexico; 2Centro Medico Nacional Siglo XXI, IMSS, Hospital de Pediatría, Mexico, D.F., Mexico; 3University of Sonora, Chemical and Biological Science Department, Hermosillo, Sonora, Mexico; 4Clínica Lomas Altas, Mexico, D.F., Mexico; 5Hospital General de México de la SS, Servicio de Infectología, Mexico, D.F., Mexico

OBJECTIVES The aim of the present work was to analyze clinical data and laboratory indicators relevant to the differential diagnosis of liver abscesses of amebic or pyogenic origin in one of the major concentration hospital in Mexico City.

METHODS Clinical and laboratory data of adult patients admitted in Hospital General de Mexico, SS in Mexico City, with a presumptive diagnosis of a hepatic abscess was studied. Serum samples were obtained for anti-E. histolytica antibodies (IgG) using an ELISA system. The test was validated through the estimation of sensitivity, specificity and predictive values. However, the statistical analysis that best characterize the clinical utility of a given test that we also estimate was the likelihood ratios.

RESULTS The estimation of both specificity and sensitivity of the test were 81.6% and 97.1%, respectively, as assessed for diagnosis
of amebic liver abscess. The statistical analysis of differences in anti-amebic antibody levels, performed through the chi squared test between ALA, pyogenic liver abscess (PLA) and non-parasitized healthy individual groups show that these difference were statistically significant (P < 0.01 respectively). Even though, the estimation of predictive positive (70%) value was more than modest, the analysis of the likelihood ratio of the ELISA test allow us to conclude that this test have extremely low probability (0.04) to display a positive result in patient with an invasive amebic disease.

CONCLUSION The establishment of differential diagnosis of amebic liver abscess in endemic countries remains a challenge for both diagnosis and the establishment of specific therapeutic treatment. The likelihood ratio is the statistic that best characterize the clinical utility of a given test result under the two hypothesis to be considered —i.e., presence versus absence of disease.

ACKNOWLEDGMENTS The present work was partially supported by the Grants number: IN-206405-3, IN-226806-3 and IN-227006-2 from PAPIIT; PE-200105 from PAPIME and 52424-Q from CONACYT.

PA 25
Cloning and expression of Entamoeba histolytica calreticulin gene
E. Gonzalez1, N. Villeda2, R. Bonilla3, G. Garcia4, G. Mendizabal5, F. Ramos1, P. Moran1, A. Valadez6, A. Limon7, E. Melendro7, and C. Ximenez7
1Faculty of Medicine, Autonomous University of Mexico, Experimental Medicine, Mexico, D.F., Mexico; 2CINVESTAV, IPN, Molecular Biomedicine, Mexico, D.F., Mexico; 3Faculty of Medicine, Autonomous University of Mexico, Biochemistry, Mexico, D.F., Mexico

OBJECTIVES The aim of the present work was to clone and express the crt gene of E. histolytica parasite.

METHODS: We use the PCR technique to amplify the crt gene using specific oligonucleotides and nuclear genomic DNA of E. histolytica. Comparative analysis of the sequences with those registered in the data base of E. histolytica genome project (www.tigr.org/db/e2k/eha1) and the Gene Bank (NBRC) was performed. PCR products were cloned in plasmid K5 using E. coli XL1Blue strain. For the expression of CRT, the plasmids were sub-cloned in ProEx-HT-b and E. coli BL21 strain. The recombinant protein EhCRT was sequenced by tandem mass spectrometry (LC/ESI-MS/MS).

RESULTS: We obtain a 1200 bp PCR product that correspond to the complete crt gene, and two small amplification products of 650 and 550 bp that encodes the C-terminal and N-terminal end of CRT respectively. These fragments shown an identity of 100% with the gene EAL49835 which encodes for a probable CRT reported in 2005. The protein was in the insoluble fraction of bacteria lysate from where this purified. The protein has a predicted weight for the entire CRT around 49 kDa. The N-terminal and C-terminal ends of the protein were around 23.5 and 27.6 kDa respectively. The nine peptides obtained in LC/ESI-MS/MS were sequenced and all corresponded to CRT. The recombinant peptides were characterized with three anti-CRT heterologous antibodies.

CONCLUSION The expression of EhCRT recombinant protein encourages further investigation on the location and functions of this protein in both E. histolytica and E. dispar, particularly in the host-parasite relationship in human infection.

ACKNOWLEDGMENTS The present work was partially supported by the Grants number: DGAPA IN-206405, PAPIPE PE-200105, PAPIIT IN 226806-3, PAPIIT IN227006-2, CONACYT 52424-Q.

PA 26
Antisense inhibition of P-glycoprotein (EhPgp) enhances programmed cell death in Entamoeba histolytica
O. Medel1, V. Sanchez2, J. D. A. Villalba3, C. Gomez4, and D. G. Perez5
1Instituto Politecnico, Biologia Molecular, Mexico, Mexico; 2Laboratorio Multidisciplinario de Investigacion, Escuela Militar de Graduados de Sanidad Universidad del Ejercito y Fuerza Aerea, Mexico, Mexico

OBJECTIVES The present work was done to evaluate the effect of blocking the P-glycoprotein’s encoded by the EhPgps genes in the PCD mechanism.

METHODS PCR.RT/PCR, measurements pH, Cytoplasmic free Ca, pH, Reactive oxygen species.

RESULTS: We cloned the EhPgp5 ORF and the anti-Pgp5 antisense sequence to construct the pNeoPgp5 and pNeoanti-Pgp5 plasmids. Both plasmids were used to transfect sensitive trophozoites. RT/PCR assays showed that transfected trophozoites were able to efficiently overexpress the Pgp5 and anti-Pgp5 transcripts. While trophozoites transfected with the EhPgp5 gene were able to growth in the presence of G418 and showed an increment of cellular volume; the inhibition of EhPgp5 gene with antisense construct, produced the trophozoite death after G418 treatment. These trophozoites showed morphological characteristics of PCD, such as cell shrinkage, a reduction in the cellular volume and DNA fragmentation. Biochemically, we also observed, the overproduction of intracellular reactive oxygen species (ROS), a decrement in intracellular K+, an increment in cytosolic calcium, and the decreased in intracellular pH levels. These results showed that PGP could protect parasites against PCD, due the inhibition of PGP synthesis, strongly promotes PCD.

CONCLUSION We hypothesized additional mechanism whereby PGP overexpression may promote the survival of parasite in the context of host-parasite relationship.

PA 27
Differential gene expression during the induction of cell death in Entamoeba histolytica
V. Sanchez1, J. D. Villalba-Magdaleno2, M. O. Medel-Flores3, C. Gomez-Garcia3, and D. G. Perez Ishiwara4
1Laboratorio de Biomedicina Molecular I, Programa Institucional de Bio medicina Molecular, Escuela Nacional de Medicina y Homeopatia, IPN, Laboratorio Multidisciplinario de Investigacion, Escuela Militar de Graduados de Sanidad, Universidad del Ejercito y Fuerza Aerea, Mexico Distrito Federal, Mexico; 2Laboratorio de Biomedicina Molecular I, Programa Institucional de Biomedicina Molecular, Escuela Nacional de Medicina y Homeopatia, IPN, Mexico Distrito Federal, Mexico

OBJECTIVES Studying a death in Entamoeba histolytica for identifying genes that could participate in the control of cell death.

METHODS DNA-AFLP and Real Time RT/PCR.

RESULTS The results showed overexpression of five genes during PCD process (SIR-2, gramine 2, 40S ribosomal protein, saposin-like, and glutaminyl- tRNA synthase) The identified genes have been associated with ageing, calcium regulation, protein synthesis, lipid regulation, and importantly with apoptosis.

CONCLUSION The elucidation of molecular mechanisms and pathways of PCD would not only help to define the in vivo role of PCD in the host-parasite relationship but may also be useful to identify new target molecules for chemotherapeutic drug development.
Abstracts of the 5th European Congress on Tropical Medicine and International Health

PA 29
Diagnostic differentiation of Entamoeba histolytica from E. dispar by PCR technique in Iran
M. Rezeian1, and H. Hooshyar2
1Tehran University of Medical Sciences, Tehran, Iran; 2Islamic Republic of Iran

Entamoeba histolytica is a pathogenic protozoan parasite, which causes amoebic colitis, dysentery and liver abscesses in humans. The causative agent of amoebiasis is currently attributed to two distinct species (E. histolytica and E. dispar). National health programmers should provide a practical tool for the specific diagnosis of E. histolytica in humans and for investigating its epidemiology. The aim of this study was to differentiate these species by PCR in stool samples. After Malaria and Schistosomiasis, amoebiasis with up to 100,000 human deaths annually is the third causative of human harmful parasitic infections.

OBJECTIVES According to WHO suggestion the main objectives of present study was determine the ratio between E. histolytica and E. dispar occurrence in the country.

METHODS This study was carried out from Aug 1999 to Feb 2002, in order to determine the ratio of E. histolytica and E. dispar in some regions in Iran by PCR-RFLP Method. A total of 16,592 stool samples were randomly collected from different ages groups from rural and urban areas of Iran. From these, 226 stool samples were preliminary diagnosed as E. histolytica/E. dispers. The samples were examined by direct and formalin-ether concentration method. About 101 isolates were cultured successfully in HSr+S and Robinson media. These isolates were identified by 2 set of oligonucleotide primers and HinI1 endonuclease by PCR-RFLP technique.

RESULTS The study showed that 92.1% of isolates were E. dispers and 7.9% were E. histolytica or mix infection. The ratio of infection with two species in different areas were as follow: Central region E.d. 93%, E.h. 3.5% Mix 3.5%; Northern region E.d. 94.1%, E.h. 5.9% Mix; Southern region E.d. 88.9% E.h. 7.4% Mix 3.7%.

CONCLUSION As we are continuously observing plenty of patients claimed to be infected with E. histolytica while they do not exhibit any remarkable clinical sign and symptoms, our new findings however is supporting the fact that the frequency of real infection must be much lower than what we are receiving from the local laboratories. 44 isolates in Tehran, 92.2% were E. dispers, E. histolytica and 2.3% were mix infection. Meanwhile this study showed that there is no difference between main titer of specific antibody in E. dispers infected person and healthy ones.

Anaeemia in Early Childhood

PA 30
Preliminary data on the detection of human herpesvirus-8 (HHV-8) DNA from human saliva and seroprevalence in Cameroun: testing the potential role of promoter-arthropods transmission
R. Romano1, G. Russo1, S. Parenti1, B. Matteoi2, G.M. Paganotti1, F. Tabacchi1, L. Ceccherini-Nelli1, A. Angeloni1, and M. Coluzzi1
1University of Rome La Sapienza, Department of Tropical and Infectious Diseases, Rome, Italy; 2University of Pisa, Pisa, Italy

OBJECTIVES Human Herpesvirus-8 (HHV-8) infection is frequent in Africa in paediatric age: this suggests the existence of an alternative way of transmission beside the sexual intercourse. At high density of biting arthropods, presence of HHV-8 in saliva of seropositive mothers used to heal itching and scratching on the bite site of children, might represent the source of infection. We investigated the HHV-8 seroprevalence and HHV-8 DNA in human saliva in two groups of 50 mothers from Cameroun, the first collected in March and the second collected in December 2006.

METHODS The mothers were tested with a questionnaire about the habit to use saliva on the skin of children after arthropod’s bite. The serum samples were collected from 100 mothers from the town of Dschang and two villages nearby.

RESULTS The HHV8 seroprevalence was 84% in the first group and 58% in the second one; the HHV-8 DNA saliva positive samples was 12.2% and 10%, respectively. There was correspondence between saliva-DNA positivity and the presence of HHV-8 lytic antibodies. We didn’t find any statistic correlation between the use of herbs and saliva and the positivity to HHV-8 neither in sera and/or in saliva, but we found a relationship between the use of saliva and herbs (P < 0.001).

CONCLUSION Our findings led us to improve research on this topics through surveys on mother-children sera and saliva analysis to verify the promoter-arthropod hypothesis. This could be an attempt to control HHV-8 transmission addressed to a cohort of HHV-8 seropositive mothers (or relatives or caregivers) to make them aware on the risks of the use of saliva to relieve insect bites, and on the far safer habit to protect children against arthropod bites with insecticide treated nets (ITNs), repellents or anti-histaminic products to relieve the itching.

Anti Retroviral Treatment (ART) and Resistance

PA 31
Anti-retroviral treatment to patients in Pernambuco state, Brazil
M. Chiquillo
Universidad El Salvador, Posgrado de Salud Publica, San Salvador, El Salvador

OBJECTIVES To describe the result to the treatment of anti-retroviral in patients with AIDS.

METHODS Case series study with a population of patients >13 years diagnosed with AIDS (based on the Brazilian definition of cases of AIDS in adults of the Ministry of Health).

RESULTS Most of the studied patients were male 41 (59.4%), with age measured between 30 and 39 years old 28 (40.6%). It winds and seven patient (39.1%) he/she had from 4 to 7 years of study, 62% of the patients were heterosexual, the time of medium attendance was of 12 months, and 82.6% were bearers of AIDS in agreement with the criteria of CDC. A marked reduction of the viral load was observed starting from the 4th month of therapy the (400 copies/ml and at the end of the 12 months of treatment anti-retroviral most had the 69 accompanied patients CD4+ (200 cells/mm³ 48 (69.6%) they presented good answer to the treatment and 14 (20.4%) were the percentile of therapeutic flaw.

CONCLUSION HAART was effective in the 69%.
PA 32
Adherence to HAART among adults in four ARV sites in Botswana
J. Kgatlane1, R. Ogenni2, C. Ezieke1, H. Madasi3, S. Moyo4 and T. M. Moroka5
1Ministry of Health, Clinical Services, Gaborone, Botswana; 2Ministry of Health, Clinical Services, Mahalapye Hospital, Mahalapye, Botswana; 3Botswana Harvard Partnership Program, Gaborone, Botswana; 4Ministry of Health, Clinical Services, Molopoole, Botswana; 5Botswana-Harvard School of Public Health, AIDS Initiative Partnership, Gaborone, Botswana

OBJECTIVES To determine Adherence levels to Antiretroviral therapy and to identify factors that influence adherence

METHODS A cross section of 514 patients was interviewed using a structured questionnaire. Adherence rates were measured using self report methods (two-day patient recall, one month recall using a 10 cm visual analogue line) and one month pharmacy pill count. Adherence was measured as proportion of those who took their medication ≥95% of the time. Levels ≥95% was considered optimal and those below considered sub-optimal. A composite adherence measure was also calculated as an arithmetic mean of the three measures used.

RESULTS The mean adherence rates were 95% (n = 322) for the pill count, 92% (n = 496) for the one month self report and 98% (n = 508) for two-day recall. The optimal adherence rates were 75% (95% CI 70.3–79.7) for pill counts, 60% (95% CI 55.7–64.3) for visual analogue and 96% (95% CI 94.3–97.7) for two-day recall. The composite mean of the optimal adherence was estimated at 77% (95% CI 73.1–80.9). The main reasons cited for missing medication were: forgetfulness, logistics, work and home duties, stigma, lack of social support, food and alcohol use. A total of 58% reported having experienced drug side effects and 8% of these had skipped medication due to side effect. There was significant association between employment status and adherence (F = 5.116; P = 0.024).

CONCLUSION The adherence rates found in this study are encouraging and comparable to other studies in developing countries but are lower than optimum. Policies and structure to carry out longitudinal monitoring is needed as well as strategies to improve and sustain high adherence in order to ensure a successful HAART program.

PA 33
Adherence to antiretroviral therapy among pediatric patients in Mahalapye district hospital in Botswana
R. Ogenni
Ministry of Health, Clinical Services, Mahalapye, Botswana

OBJECTIVES To determine the adherence levels among pediatric patients on HARRT and to identify predictors of low adherence as well as assess the relative importance of different predictor of low adherence to antiretroviral therapy among pediatric patients taking HAART in the ART clinic in the hospital.

METHODS A quantitative, cross-sectional survey of caregivers of children under 12 years on ART was conducted using pre-tested questionnaire and a data collection form at Mahalapye District Hospital. Three methods were used to measure adherence, two self report methods (two-day patient recall, one month recall using a 10 cm visual analogue line and one month pharmacy pill count. Adherence was measured as proportion of those who took their medication ≥95% of the time. Levels ≥95% was considered optimal and those below considered sub-optimal.

RESULTS In total 140 caregivers agreed to be enrolled in the study. Their characteristics are as follows: 95% female, 79.3% with high school education or less, 84.3% unemployed, 60% under 40 years old, 76.4% single. Children were 55% male, 66% under 5 years old, and they were cared for respectively by their mothers in 42.9% of cases and 22.9% by their grandparents. Forty five percent of caregivers reported that their children had missed at least one dose during the last three days, and that only 20.8% achieved optimal adherence level of ≥95% by pill count versus 76.3% by visual analogue assessment. Only the child’s school standard was significantly associated with lower adherence, while two variables predicted optimal adherence: being cared for by the mother or and grandmother, and the unemployment status of the caregiver.

CONCLUSIONS Adherence level to antiretroviral therapy among the Pediatric population studied is low, and is a cause for concern. Group specific targeted interventions are needed to improve adherence.

PA 34
NNRTI-resistance mutations in HIV-1 DNA from peripheral blood mononuclear cells after single dose nevirapine for prevention of mother-to-child HIV transmission in Burkina Faso
L. R. Tomasoni1, B. Pedruazzi1, J. Simpore2, V. Del Punta3, S. Bigoni3, V. Pietra3, S. Pigatelli1, L. Manno3, G. Punzi4, A. Angarano5 and F. Castelli5
1University of Brescia, Institute of Infectious Diseases, Brescia, Italy; 2Centre de Recherche Biomolecule Pietro Annigoni, Ouagado- dougou, Burkina Faso; 3Centre Medical San Camille, Ouagadougou, Burkina Faso; 4University of Bari, Institute of Infectious Diseases, Bari, Italy; 5University of Poggia, Institute of Infectious Diseases, Poggia, Italy

OBJECTIVES Emergence of Nevirapine resistance (NVP) after single-dose (Sd-NVP) prevention of mother to child HIV transmission (PMTCT) is widely demonstrated in plasma viral RNA during first weeks after exposure but only few studies have investigated the risk of their filing into proviral DNA. Such event could cause failure of future antiretroviral treatment (TARV) or prophylaxis. The aim of this study was to determine the presence of mutations conferring resistance to NNRTIs archived in HIV-1 DNA in peripheral blood mononuclear cells (PBMCs) in women who received Sd-NVP in a program for PMTCT in Burkina Faso.

MATERIALS AND METHODS In the cohort of women who entered the PMTCT program at the S. Camille Medical Center in Ouagadougou in the period may 2002 to may 2006 and treated with Sd-NVP at delivery, entire blood spots (50 ml) were collected on filter papers at variable time after exposure, after informed consent. HIV-1 DNA, extracted from PBMCs by commercial kit QIAGEN, was amplified and sequenced pol region by BigDye dye terminator cycle sequencing kit with home-made protocol. For genotype analyses HIV-1 subtype B was used as wild type and single mutations were interpreted using Stanford database. At the same time CD4 lymphocytes count (FACScount), clinical assessment (WHO ‘03) and ongoing antiretroviral treatment were checked.

RESULTS Twenty nine treatment naïve women were investigated. K103N was present in 20% (1/5) of women tested in the first six months after exposure but not in those checked later (P = 0.18). One G190E was demonstrated at 24 months. Other polymorphisms on 103 codon was present in one patient out of nine (11%) tested beyond 24 months (at 38 months after delivery). No statistically significant correlation emerged between mutation risk and CD4+ lymphocytes count at Sd-NVP exposure (P = 0.64).

CONCLUSIONS The study demonstrates moderate risk of PBMC archived NNRTI resistance mutation until more than two years from Sd-NVP.
Antibiotic Resistance

PA 35
Antibiotic resistance and molecular detection of Tet(O) mediated tetracycline resistance in clinical and chicken Campylobacter jejuni

W. Pizzì1, M. Yousef2, A. Al Mahmeed3, K. Bindayana4, A. Senoki5 and G. Botta2

1Children Hospital, Ministry of Health, Microbiology, Jeddah, Saudi Arabia; 2Arabian Gulf University, Microbiology, Manama, Bahrain

OBJECTIVES Campylobacteriosis is a self-limited gastrointestinal infection. Erythromycin, ciprofloxacin and tetracycline are used in both veterinary and human medicines and increasing resistance has been reported worldwide.

METHODS One hundred chicken and clinical C. jejuni isolates were collected during two periods (2002–2003 and 2005–2006) to assess the pattern of susceptibility, plasmid profiles and to detect tet(O) gene by PCR. Disc diffusion and agar dilution methods were used to test the susceptibility and MICs of erythromycin, ciprofloxacin and tetracycline. Plasmid DNA extraction was performed using QIAprep Miniprep kit. Tet(O) gene was detected by PCR.

RESULTS Erythromycin resistance rates were low in both chicken and clinical C. jejuni isolates. Ciprofloxacin resistance rates were high in both periods but increased even more in both source of isolates during 2005–2006. Tetracycline resistance was higher in chicken (80.9%) compared to clinical (41.3%) isolates (P < 0.01). Although of tetracycline in humans is currently reduced, tetracycline resistance rates in human isolates increased up to 60.5% during the second period with no significant difference being observed among chicken isolates (P < 0.1). Most of isolates harbored two plasmids (23- and 35-kb). A significant correlation of tetracycline-resistance with plasmid carriage was found in chicken isolates.

CONCLUSION Abuse or misuse of antibiotic is likely to be associated with increasing resistance, but the ability of the organism to transfer resistance gene(s) to other strains by means of extra-chromosomal elements could be play a role of antibiotic resistance. As a consequence resistance originated and selected in poultry might be transferred to human strains and cause increased resistance in human even without their previous to the selected antibiotic.

PA 36
Frequency and susceptibility profile of pathogens causing urinary tract infections (UTI) in patients admitted to Fasa Educational Hospital during 2003–2006

F. Ghaffarpasand1, M. Ebrahim1, A. A. Karimi1, N. Abbas1, A. Amiri2 and T. Jamali3
1Fasa University of Medical Sciences, Internal Medicine, Shiraz, Iran, Islamic Republic of Iran; 2Fasa University of Medical Sciences, Internal Medicine, Fasa, Iran, Islamic Republic of Iran; 3Shiraz University of Medical Sciences, Medical Document, Shiraz, Iran, Islamic Republic of Iran

OBJECTIVES The aim of this study was to investigate the sensitivity pattern of pathogens causing urinary tract infection in Iranian patients.

METHODS During 2003–2006, a total of 3415 urine samples were collected from patients being admitted in Fasa educational hospital due to UTI. Urine was collected classically, i.e. by taking the second clean stream into a sterile test tube or by UrI cult test. The samples were cultured on blood plates and endo-agar. Identification was done by standard bacteriologic methods. Bacterium sensitivity to sixteen antibiotics (Amikacin, Ampicillin, Ceftriaxone, Cephalxin, Cephalosporin, Chloramphenicol, Ciprofloxacin, Co-trimoxazole, Erythromycin, Gentamicin, Imipenem, Nalidixic acid, Nitrofurantoin, Norfloxicin, Penicillin, and Tetracycline) was assessed with disc diffuse method on Muller-Hinton agars. The data was analyzed with SPSS software version 13.5.

RESULTS From 3415 collected urine samples, 983 were positive. Among the patients were 401 male (40.8%) and 382 female (59.2%). The mean age of the patients was 27.1 years (0.1–95 years). The most frequently isolated microorganism was Escherichia coli (54.3%) followed by Klebsiella spp (10.6%), Enterococcus spp (7.4%), Staphylococcus spp (7.3%), Streptococcus spp (6%) and Pseudomonas spp (5.6%). The sensitivity was high to Norfloxicin (76.1%), Ceftriaxone (75.3%), Imipenem (75%), Ciprofloxacin (68%) and Amikacin (59.6%). But sensitivity was very low to Ampicillin (8.9%), Cephalxin (21.4%), Tetracycline (22%), Penicillin (24%) and Co-trimoxazole (28%). Escherichia coli was found to be most susceptible to Norfloxicin (88.2%), Ceftriaxone (85.6%), Imipenem (80%) and Ciprofloxa- cin (73.9%). Klebsiella showed much more resistance and was found most susceptible to Amikacin (70.8%), Ciprofloxacin (68.3%) and Ceftriaxone (64.7%).

CONCLUSION E-coli is the most common causative agent of UTI. Thus the treatments should first focus on this microorganism. The antibiotics commonly used in UTI treatment are less effective. More powerful antibiotics should be used in UTI treatment. It is recommended that antibiotic prescription be done on the basis of antibiotic resistance tests. Since the present study was a cross-sectional study, regular monitoring is required to establish reliable information about resistance pattern of urinary pathogens.

PA 37
In vitro studies on susceptibility/resistance of Trichomonas hominis to metronidazole

L. Chomicz, M. Padyż, J. Plewarczyk and P. Zawadzki
1Medical University of Warsaw, Department of Medical Biology, Warsaw, Poland; 2Medical University of Warsaw, 2nd Department of Maxillofacial Surgery, Warsaw, Poland

OBJECTIVES Trichomonas hominis (Pentatrichomonas hominis), the worldwide flagellate parasitizing human large intestine, is often identified in human diarrheic stools. It is most common in warm climate, with prevalence up to 30%. Because of fecal-oral transmission rout, infection with the trichomonad is more often reported in children than in adults. At present, no optimal treatment is defined. Aim of our studies was to examine an influence of different concentrations and doses of metronidazole (the accept drug used in treatment of infection caused by related species -Trichomonas vaginalis) on number of surviving trophozoites of Trichomonas hominis.

METHODS One-day cultures of T. hominis grown on Pahm medium at 37 degrees Celsius were used. Metronidazole in different concentrations: 4, 8 or 12 μg/ml, in single dose or three-times repeated doses was added to the cultures and incubated 24 h, 48 h or/and 72 h. Number of moving trichomonads was determined microscopically after above mentioned time of incubation with the tested agent, then compared with this of control cultures and analyzed statistically (TStudent P < 0.05).

RESULTS In all experiments in which single dose of metronidazole has been applied, we observed clear resistance of T. hominis to different concentrations of the agent tested, i.e. number of the moving protozoans was significantly higher, up to 260% at concentration 8 μg/ml, in comparison to control cultures (100%) and up to 468% at 12 μg/ml concentration of the agent. In contrast, some antitrichomonad effect appeared if the repeated doses of metronidazole were used. Particularly, no moving
Protozoans were observed, when third dose of the agent in concentration 8 µg/ml and second dose in 12 µg/ml concentration were applied.

CONCLUSION Although trichomonads showed clear resistance to single doses of metronidazole, the reduction of amount of surviving flagellates appeared when two- or three-times doses of the chemotherapeutic were applied in short time intervals. It has revealed that susceptibility of T. hominis to repeated doses of metronidazole depended on concentration of the agent as well as time and frequency of exposition of trichomonad pathogens to the chemotherapeutic. The results of our in vitro studies, in which both, a resistance and susceptibility of T. hominis to metronidazole were revealed, confirm the importance of a mode of application of the prospective drug against the pathogens. Further search of protozoans were observed, when third dose of the agent in concentration 8 µg/ml and second dose in 12 µg/ml concentration were applied.

PA 39
Prevalence of Staphylococcus aureus carriage in patients on hemodialysis and the pattern of antibacterial resistance
R. Ghasemian and N. Najafi
Mazandaran University of Medical Science, Infectious Disease, Sari, Iran, Islamic Republic of Iran

OBJECTIVES Staphylococcus aureus is a virulent pathogen that is currently the most common cause of infection in hospitalized patients. These days, increment in antimicrobial resistance coupled with increasing prevalence of the agent as a nosocomial infection makes the situation even more complex. Patients on hemodialysis are at increased risk due to their immunocompromised state. The present study was designed to determine the prevalence of Staphylococcus aureus nasal carriage in a group of Iranian patients on hemodialysis.

METHODS For this descriptive study, sterile-cotton-tripped swabs were rotated into anterior nares of 84 patients on hemodialysis, and then cultured on blood-agar medium. Having grown the colony, gram stain, catalase, manitol, DNAase and coagulase tests were all performed and the pattern of antibacterial sensitivity was determined by using disc diffusion method. Also agar dilution method was performed to determine minimal inhibitory concentration of oxacillin and vancomycin.

RESULTS Of 84 patients on hemodialysis, 26 (31%) were nasal carrier of S. aureus. All isolated S. aureus were resistant to methicillin (MRSA). A total of 64% (12) were resistant to vancomycin, while 6.81% to clindamycin, 6.81% to ciprofloxacin; however, all microorganisms were sensitive to rifampicin.

CONCLUSION Patients on hemodialysis are at increased risk of S. aureus contamination, thus, screening these susceptible patients should be served as a health priority. Meanwhile, antibiogram should be ordered for all cases to optimize treatment options.
METHODS This cross sectional study was performed on 1067 patients who referred due to urinary symptoms to Inghelab laboratory in Rafsanjan (2004) Urine analysis and cultures with (Blood agar, Eosin metyle blue, Hinton Agar), were done. Catalase and coagulase assay were done.

RESULTS Coagulase negative staphylococci were isolated from 6% of cultures. Prevalence of this infection had no difference between female & male and also between different groups of ages. Sensitivity of this bacteria to ciprofloxacin was 95% to vancomycin; 65% and to the other antimicrobial agents were less that 5%. 

CONCLUSION Prevalence of urinary infection due to Coagulase negative staphylococci is considerable in Rafsanjan (%) and recognition of its antimicrobial resistance pattern is very important especially because misdiagnosis of this infection leads to wrong treatment.

Keywords Coagulase negative staphylococci, urinary infection, Rafsanjan, antimicrobial resistance

PA 41
Prevalence of urinary tract pathogens and antimicrobial susceptibility patterns in children at hospitals in Iran

E. Kalantar, M. Motlagh and H. Lornejad

1 Kurdistan University of Medical Science, Department of Microbiology, School of medicine, Sanandaj, Iran, Islamic Republic of Iran; 2 Ministry of Health and Medical Education, Family Health and Population, Tehran, Iran, Islamic Republic of Iran

OBJECTIVES To find out the bacteria causing UTI among children (0–5 years old) and to determine the antimicrobial pattern of the causative organisms.

METHODS During the one month period (July to August 2006) 55 hospitals from 12 states in Iran, representing different geographical areas participated in this study. A total of 1696 children with UTI aged 0 to 5 years referred to these hospitals were included in this study. Urine cultures were carried out and the isolates were identified by Gram staining and conventional biochemical methods. Antimicrobial susceptibility testing was done by disk diffusion method according to the current National Committee for Clinical Laboratory Standards (NCCLS) guidelines.

RESULTS Between July to August 2006, 438 urine isolates were obtained from 1696 children. E. coli was the most frequently occurring pathogen (54.80%), followed by Klebsiella pneumoniae (16.0%), Coagulase negative Staphylococci (11.2%), Enterobacter spp. (9.6%), Proteus spp 1.4% and P. aeruginosa (1.4%). Percent resistance rates of the isolates to different antibiotic tested were as follows: E. coli isolates: Co-trimoxazole- 85.9%; Penicillin- 80.0%; Ampicillin- 77.0%; Chloramphenicol- 68.0%; Ciprofloxacin- (12.9%); ceftriaxone- (12.9%); cephalotin- (12.9%); and amikacin- (14.0%). K. pneumoniae isolates were 18.5%, 20.0%, 24.0% and 29.0% resistant to Cephalothin, Ceftriaxone, Amikacin and Gentamicin respectively, while Penicillin (88.5%), co - trimoxazole (74.2%), and ampicillin (68.5%) were the least effective drugs.

CONCLUSION High prevalence of drug-resistant urinary tract pathogens, particularly for ampicillin and co-trimoxazole among Iranian children suggest cautious use of antibiotic therapy for treatment. Regular monitoring of developing antibiotic resistance pattern in urinary tract pathogens is necessary for optimal empirical therapy of patients with UTIs. Finally, we suggest that empirical antibiotic selection should be based on knowledge of the local prevalence of bacterial organisms and antibiotic sensitivities rather than on universal guidelines.

PA 42
Comparison of royal jelly effects with gentamicin and ceftriaxone on the growth of Escherichia coli, Bacillus cereus, Pseudomonas aeruginosa, Staphylococcus aureus, in a laboratory environment

H. Shirzad, N. Shahinfard, M. R. Naficy and M. Karami

Shahrekord University of Medical Sciences, Microbiology and Immunology, Shahrekord, Iran, Islamic Republic of Iran

OBJECTIVES Royal jelly is a product of honey bee which has great food qualities and contains water, protein, lipid and minerals. Despite the vast studies done on royal jelly, some of its characteristics such as antimicrobial properties still is not clearly understood, and there are controversial reports about it. It is believed that these characteristics refer to the enhancement of the immune system and existence of some antibacterial elements in the product. Due to increasing resistance of microbes to different antibiotics, the need for other alternatives such as royal jelly is considered. In this study the antibacterial effect of royal jelly and two antibiotics (Gentamicin & Ceftriaxone) is compared.

METHODS Escherichia coli, Bacillus cereus, Pseudomonas aeruginosa, Staphylococcus aureus were provided by microbiology reference laboratory, Tehran, Iran. Three set of 6 tubs were selected and 3 mils of culture media were added to each tubes. Two tubes of each set were used as positive and negative controls for. Four tubes of each set were selected and to each set of tubes Escherichia coli, Bacillus cereus, Pseudomonas aeruginosa, Staphylococcus aureus were added. To each above mentioned sets of tubs Gentamicin and Ceftriaxone with 50, 100, 200 & 300 microgram/ml doses and royal jelly 50, 100, 200, 300 mg/ml doses were separately added. After 24 hours incubation period the growth of bacteria were estimated by cloudy appearance of the culture media in tubes. To confirm the accuracy of the test, the bacteria were also cultured in BA and EMP culture media and their MIC were measured afterwards.

RESULTS Our experiment results showed that doses of 50 mg/ml and 100 mg/ml of royal jelly had no effect on the growth of cultured bacteria, but no bacteria growth was seen with 200 mg/ml and 300 mg/ml of royal jelly. The MIC for Ceftriaxone on, Pseudomonas aeruginosa, Bacillus Cereus, Escherichia coli and Staphylococcus aureus were 200, 50, 50 & 200 mg/ml and for Gentamicin were 300, 50, 50 & 300 respectively.

CONCLUSION Royal jelly has equal and even more antibacterial effect on Pseudomonas aeruginosa and Staphylococcus aureus compared to Gentamicin and Ceftriaxone. Although Gentamicin and Ceftriaxone have lower MIC on Escherichia coli compared to royal jelly but since today most bacteria are considered to be resistant to vastly used old and new antibiotics with many side effects, the use of royal jelly and other immune enhancers materials with no side effects could be more useful, but needs to be studied much more.

PA 43
Enterococcus species as a blood-culture isolate-antimicrobial sensitivity

T. Toscic, B. Stossovic, M. Jovanovic, L. Lavdovic and M. Pelemis

Institute for Infectious and Tropical Diseases, Belgrade, Serbia and Montenegro

OBJECTIVES Traditionally regarded as avirulent gastro-intestinal tract commensals, enterococci now can cause severe invasive infections like bacteremia, endocarditis, meningitis and wound and urinary tract infections. Over the last decade their resistance has increased.
METHODS We analysed antimicrobial susceptibility of 17 enterococcal strains isolated from blood cultures. The strains were collected over the 4-year period (2002–2005), and have been isolated mostly from the patients residing at the Institute for Infectious and Tropical Diseases. Only the non-duplicate isolates, from more than one blood culture, aerobic and anaerobic bottle have been considered.

RESULTS Our isolates were: Enterococcus faecalis (n = 13), Enterococcus faecium (n = 3) and Enterococcus durans (n = 1). Sensitivity to ampicillin was in 15 isolates (88.23%), amoxicillin-clavulanic acid 16 (92.12%), imipenem 15 (88.23%), tetracycline 3 (17.65%), ciprofloxacin 5 (29.41%), vancomycin 17 (100%), chloramphenicol 11 (64.71%), and rifampicin 11 (64.71%). Synergistic activity of penicillins or glycopeptides and aminoglycosides (gentamycin and streptomycin) was in 6 (35.29%) and 5 (29.41%) respectively. All E. faecium strains were multiresistant, as well as 6 (35.29%) E. faecalis.

CONCLUSION Our results indicate that ampicillin is still efficacious for serious enterococcal infections, since all E. faecalis and E. durans were sensitive to it. E. faecium was more resistant (one of three isolates sensitive to ampicillin). The sensitivity to imipenem was identical, while vancomycin-resistant enterococci were not isolated.

ART Pharmacology and Interactions

PA 44
Artemisinin increases CYP2A6 activity in healthy subjects
S. Asimus, T. N. Hai, N. V. Huong and M. Ashton
1 Gothenburg University, Pharmacology, Gothenburg, Sweden; 2 NIMPE, Hanoi, Vietnam

OBJECTIVE To investigate if artemisinin affects CYP2A6 activity in healthy subjects. Secondly, to compare the utility of coumarin and nicotine as in vivo probe compounds for CYP2A6.

METHODS Twelve healthy male Vietnamese subjects were given coumarin and nicotine as probes, both before and after five days of repeated oral administration of artemisinin in two different treatment periods, separated by a wash-out period of one month. Sequential blood samples were drawn at baseline seven days before and on the first and fifth day of artemisinin treatment in both treatment periods. Plasma concentrations of 7-hydroxycoumarin glucuronide (7-OHCG), nicotine, cotinine and artemisinin were analysed by HPLC and coumarin and 7-hydroxycoumarin (7-OHC) by LC-MS/MS. Urine, collected in two time intervals on the days of coumarin intake, was treated with glucuronidase and analysed for 7-OHC amounts.

RESULTS Artemisinin AU0−∞ values decreased significantly to 23% (95% confidence interval [CI], 18%–28%) on the fifth day of artemisinin administration compared to the first dose. No significant difference was found in artemisinin AU0−∞ values between the two treatment periods. The sum of renally excreted 7-OHC and 7-OHCG was increased by 1.2-fold (1.0–1.4) in the 0–8 h collection interval and by 1.7-fold (1.3–2.2) in the 3–8 h interval compared to baseline seven days before. The 7-OHCG/7-OHC AU0−∞ ratio increased by 1.9-fold (1.2–2.7) following five days of artemisinin intake. There was no significant change in the cotinine/nicotine AU0–11 h ratio between study days.

CONCLUSION Artemisinin increases CYP2A6 activity as indicated by a significant increase in the total amount of 7-OHC excreted in urine. A significant increase in the 7-OHCG to 7-OHC AU ratio suggests artemisinin to be an inducer of also glucuronidation. Since this may imply a risk for drug-drug interactions between ACTs and ARVs further investigation is needed.
of H5N1 infection were compiled and geocoded at the village/township level in the digital map from the Chinese Ministry of Agriculture and the World Health Organization. Geographic information systems techniques combined with a scan statistical technique were used to analyze the distribution patterns and spatiotemporal clusters of reported cases. Furthermore, we examined the relationship between the outbreaks of HPAI H5N1 in poultry and wild birds and some environmental factors by using a case control study design. Proximities to railways, freeways, national highways, major routes of migratory birds, major reservoirs, lakes and rivers; and land and atmospheric properties derived from remotely sensed data including land surface temperature and water vapor contents were considered in our analysis.

RESULTS We found that four spatiotemporal clusters of HPAI H5N1 in poultry and wild birds existed in mainland China, and spatial shifts on HPAI H5N1 distribution had taken place from peri-urban areas of metropolis to rural areas on epidemic areas from 2004 to 2006. The spatio-temporal distribution of H5N1 avian influenza epidemics was strongly associated with three environmental factors by a logistic regression analysis: national highway system, the migration routes of wild birds, and water body distribution.

CONCLUSION Our findings suggest that stronger control should be executed around poultry trade market places, and areas with major water bodies should be closely monitored to prevent cross usage of the same habitat between domestic poultry and wild birds in mainland China.

Clinical AIDS

PA 47
Molecular characterization of Cryptosporidium parvum isolates in the HIV/AIDS patients by using of 18s rRNA PCR-RFLP technique
M. Zavvar1, J. Sadraei2, H. Emadi3 and M. Pirestani4
1Tarbiat Modares University, College of Medicine & Tehran National University, College of Medicine, Parasitology & Clinical Microbiology and Tropical Medicine, Tehran, Iran, Islamic Republic of Iran; 2Tarbiat Modares University, Parasitology, Tehran, Iran, Islamic Republic of Iran; 3Department of Tropical Medicine and Research Microbial Disease at Tehran National Medical University, Tehran, Iran, Islamic Republic of Iran; 4Department of Parasitology at Tarbiat Modares University, Tehran, Iran, Islamic Republic of Iran

OBJECTIVES Cryptosporidium parvum is usually considered the agent of human Cryptosporidiosis. However, only in the last few years, molecular biology-based have allowed the identification of Cryptosporidium species and genotypes, and only a few data are available in Iran.

METHODS In the present work, we focused on identifying genotypes of Cryptosporidium prevalent among HIV infected patient. For this result we selected 164 of 492 inpatient files (1/3) were randomly reviewed and in the second 117 of 234 (1/2). Malaria cases confirmed by blood smear (n = 50 in February and n = 9 in August, reflecting the local seasonal variation) were excluded from analysis. Between the 2 surveys, clinical suspicion of HIV by PHT physicians (compared with ITMA experts) increased from 57% to 81% (P = 0.02) and cotrimoxazole coverage from 68% to 85% (P = 0.02). The median delay between admission and HIV test request decreased from 7 to 2 days (P < 0.001) and between test request and execution from 4 to 2 days (P = 0.02). In February, 42 of 114 non-malaria inpatients (37%) were diagnosed with HIV infection versus 58 of 108 (54%) in August (P = 0.01). In August, antiviral therapy was initiated during hospitalization in 15% of the patients newly diagnosed with HIV infection (versus nobody before), and 30/36 files (83%) of surviving HIV patients contained reference documents for ambulatory care (versus none previously). Also, the rate of erroneous ‘clinical malaria’ reported in the files as discharge diagnosis decreased from 17% to 3% between the 2 periods.

CONCLUSION Through simple measures debated with the medical staff, HIV care improved in the PHT, as reflected by the higher appropriate treatment. It is probably still possible to further reduce the missed opportunities of diagnosing HIV in hospitalized patients in this highly endemic setting.

PA 48
Improvement of HIV care in the medical wards of the provincial hospital of Tete, Mozambique, through enhancement of clinical awareness and strengthening of HIV testing capacity
M. Ponne1, E. Bottei2, T. Ngove3, B. Afficy4, R. Monanho5, M. Biec6, V. Hayat7 and L. Lynen1
1Institute of Tropical Medicine, Clinical Sciences, Antwerp, Belgium; 2Provincial Hospital (PHT), Tete, Mozambique; 3Médecins sans Frontières, Luxembourg, Luxembourg

OBJECTIVE To assess the quality of HIV care in the medical wards of the Provincial Hospital of Tete (PHT) before and after a multi-faceted intervention involving the Mozambican health staff and 2 foreign institutions providing an integrated technical assistance.

METHODS In March 2006, 2 ITMA experts reviewed the files of patients discharged in the previous month from the medical wards of the PHT in order to assess the morbidity profile and HIV management. Survey results were debated with, and appropriated by, the hospital staff. Consequently, clinical indexes of HIV suspicion and treatment recommendations were reminded during clinical meetings, and a hospital team of counselors was created to increase the HIV testing capacity. In September 2006, a similar cross-sectional survey was conducted.

RESULTS In the first survey, 164 of 492 inpatient files (1/3) were randomly reviewed and in the second 117 of 234 (1/2). Malaria cases confirmed by blood smear (n = 50 in February and n = 9 in August, reflecting the local seasonal variation) were excluded from analysis. Between the 2 surveys, clinical suspicion of HIV by PHT physicians (compared with ITMA experts) increased from 57% to 81% (P = 0.02) and cotrimoxazole coverage from 68% to 85% (P = 0.02). The median delay between admission and HIV test request decreased from 7 to 2 days (P < 0.001) and between test request and execution from 4 to 2 days (P = 0.02). In February, 42 of 114 non-malaria inpatients (37%) were diagnosed with HIV infection versus 58 of 108 (54%) in August (P = 0.01). In August, antiviral therapy was initiated during hospitalization in 15% of the patients newly diagnosed with HIV infection (versus nobody before), and 30/36 files (83%) of surviving HIV patients contained reference documents for ambulatory care (versus none previously). Also, the rate of erroneous ‘clinical malaria’ reported in the files as discharge diagnosis decreased from 17% to 3% between the 2 periods.

CONCLUSION Through simple measures debated with the medical staff, HIV care improved in the PHT, as reflected by the higher and faster detection of HIV infection and the reduced delay for appropriate treatment. It is probably still possible to further reduce the missed opportunities of diagnosing HIV in hospitalized patients in this highly endemic setting.
Current evidence suggests that such co-infections could accelerate both diseases. As highly active anti-retroviral therapy is unrolled additional concerns exist. Currently, in Malawi, the HAART regimen is a fixed combination of 3 drugs; Triomune®. It contains nevirapine, (associated with hepatotoxicity), lamivudine, which can treat chronic hepatitis B, but may also cause 'hepatic flares' with poor adherence. High prevalence of HBV or HCV co-infection with HIV may suggest HBV/HCV testing before commencing Triomune®, universal HBV vaccination and re-assessment of 'Triomune' usage.

METHODS A prospective study of consenting adults was undertaken over 3 months. Consecutive admissions were recruited one day each week. Rapid ELISA tests for HIV, HBV and HCV provided real-time results. Confirmation of point of care (POC) tests was undertaken in Liverpool. Overall prevalence, co-infection rates and stigmata of liver disease were recorded. If stigmata or HBV, HCV positive abdominal ultrasound was undertaken.

RESULTS A total of 226 patients (39% male) were enrolled, median age 35 years (range 14–80). HIV-1 prevalence was 76%. POC rapid antibody tests revealed HBsAg in 37% and HCV antibody in 4%. Co-infection with HIV-1 and HBsAg was found in 32%, HIV-1 and HCV co-infection occurred in 2%. HBV and HCV co-infection was noted in 2%, while triple infection was found in 1% of patients. Confirmatory testing found HBVsAg prevalence of 17%, co-infection with HIV 14%. HCV prevalence was 5%, co-infection with HIV 5%, and coinfection with HBV and triple infection 1%. Sensitivity for POC HBV was 60%, specificity 70%. POC sensitivity for HCV 11%, specificity 96%, 38 (17%) patients were noted to have liver disease stigmata; of these, 20 (53%) were HBsAg positive and 3 (8%) HCV positive. Of 53 HBsAg positive patients, 10 (19%) had evidence for parenchymal disease.

CONCLUSION The HIV prevalence is consistent with previous studies. POC testing urgently need further evaluation. High HBV/ HCV co-infection rates suggest that studies to assess side-effects and safety of Triomune® should be considered.

Control and Epidemiology

PA 50  
Economical and epidemiological impact of accurate parasitological diagnosis vs current situation of overestimation by malaria misdiagnosis in Africa

P. Besnard, Soname, OCEAC, IRD
Soname, Villedrom, France

In malaria endemic areas treating every fever episode as a malaria onset would result in overdiagnosis with a margin of error varying in function of epidemiological factors. When further compounded by overestimations related to errors in parasitologic diagnosis, clinical misdiagnosis leads to unwarranted hospitalisations and inappropriate treatment. In a company setting this would mean unnecessary treatments and loss of employee work time. False positive diagnosis causes overestimation of chemoresistance, overconsumption of malarial drugs and underestimation of other infectious diseases. Judging from these high costs, it can be assumed that improving the reliability of parasitological diagnosis would have a positive impact on the quality of clinical management, efficiency of antimalarial use and accuracy of epidemiological surveys. This assumption was confirmed by analysis of data following start up of a parasitologic laboratory for malaria diagnosis in the health care clinic at soname’s fabrication yard in Lobito, Angola. Laboratory personnel receives expert training, and audit findings demonstrate consistently reliable diagnosis. Simultaneously lost time and costs linked with malaria decreased a lot, as expected. This experience underscore the need for reliable parasitologic diagnosis as a prerequisite for any large-scale malaria control program.

PA 51  
Using molecular and genetic epidemiology against Plasmodium

A. Saha
R D Gardi Medical College, Community Medicine, Ujjain, India

OBJECTIVES What are the current options available to control malaria transmission using molecular genetics of vector-parasite interactions.

METHODS A narrative literature review.

RESULTS There are wide gaps between understanding of the vector - parasite interactions.

CONCLUSION A detailed analysis of the spatial and temporal expression of the effector molecules mediating the interactions between the mosquito and the parasite will provide an integrated picture of this fascinating and complex journey. Each of these critical steps is a potential target to interfere with malaria transmission to humans.

PA 52  
Current trends of HIV/AIDS epidemic in one of the largest areas in Russia

E. Vedenskaya, G. Moshkovich and L. Bykova
Regional AIDS Centre, Nizhny Novgorod, Russian Federation

OBJECTIVES The aim of the research was a detailed study and analysis of current state and trends of HIV/AIDS epidemiology in one of largest areas in Central Russia in order to show the growing need in treatment and palliative care for people living with HIV/ AIDS in the region.

METHODS We studied the official demographical data and the HIV/AIDS epidemiology data of the regional AIDS centre within the entire period of epidemics and compared it with the official federal statistics.

RESULTS As of January 2006, a cumulative number of people living with HIV/AIDS is 4330. The actual number of HIV cases is increasing and faster than registered in the last year or two. It is likely that there are 17 000–22 000 people living with HIV/AIDS in the region. Young people ages 15 to 29 account for 85.5% of all the registered HIV cases. HIV infection was attributed to injection drug use in 73.5% of all registered cases. Since 2002, experts have identified an increase in the sexual transmission. In 2003, 32.4% of all registered cases were attributed to sexual contact. Far more of the HIV-positive individuals are men (57.8%). The most recent and negative trend—the proportion of women infected increase. In 2005, the proportion of women among the overall number of people living with HIV in the area was 42.2%. As a result, there is an increase in the potential for the growing mother-to-child HIV transmission. Statistics refute the myth of an easing up of the HIV epidemic in the country. The problem is becoming worse as HIV spreads more widely from vulnerable groups into the general population.

CONCLUSION The results of our study show the major trends in HIV/AIDS epidemic progression and are used for making estimated and help policy makers to determine the impact of specific programs in the region.
PA 53
Sexual transmission versus unsafe medical care paradigms of HIV infection: assessing how health zones structurally and operationally address these two sides of HIV prevention in the eastern Kasai province, Democratic republic of the Congo
N. Bukonda1, T. Diasishi2 and M. Kabeya3
1Northern Illinois University, College of Health and Human Sciences, Public Health and Health Education Programs, Dekalb, USA; 2Université de Mbuji Mayi, Faculte de Medecine, Mbuji Mayi, Congo, Democratic Republic of.

OBJECTIVES While there is an ongoing debate on the respective impact of sexual activity and unsafe medical care in the transmission of HIV/AIDS in Sub-Saharan Africa, little is known regarding the actual implementation of the key organizational and operational features - such as establishment and operation of an HIV mitigation structure, appointment and performance of infection control managers, satisfaction with amount of allocated resources - of either of these paradigms within African health care systems. This study uses data from four health zones in the Eastern Kasai province to empirically assess the extent to which adherence to the key features of the sexual infection paradigm significantly outweighs adherence to the key attributes of the unsafe medical care paradigm.

METHODS We surveyed 279 health care workers working in 4 health zones in this province in 2005 and collected demographic data and other information on availability and operation of programs to control nosocomial and sexual HIV infection. Respondents indicated on their degree of satisfaction with the involvement of their facilities (scale of 1–4), the level of performance of existing organizational structure (scale of 1–4), the level of performance of the appointee in charge of such programs (scale of 1–4), the amount of allocated resources (scale of 1–4), and the provision of continuing education (scale of 1–4). We used SPSS to explore the correlation and differences on each of these five tenets of the two paradigms.

RESULTS About 57% of the respondents were aware of an organizational structure set up to address nosocomial infection issues against 45% for a structure set up for sexual infection. With the exception for organizational involvement in NHIC and SHIC activities where no difference was noted, there was a significant difference on each of the four other tenets of the two paradigms with SHIC dimensions receiving more favorable scores than their NHIC counterparts.

CONCLUSION There is a significant emphasis on activities related to sexual HIV infection control among health care organizations in the Eastern Kasai province.

DISCUSSION Because reputable health organizations, such as the WHO and UNAIDS, consider sexual activity as the major route of HIV infection in Africa, issues of unclean medical care are more likely to continue to receive relatively less publicity and less resources in sub-Saharan African health care systems in comparison to sexual activity related issues.

PA 54
Malaria in highlands of Yemen and its complications
A. Thabet1, M. Al-Dholae2
1Faculty of Medicine, Thamar University, Community Medicine, Hamar, Yemen; 2Faculty of Medicine, Thamar University, Internal Medicine, Thamar, Yemen

BACKGROUND It has long been known that malaria in highland areas (>2000 m) is hindered by low temperature, which limits the development of the parasites in the mosquito 3, 4.

OBJECTIVES To determine the extent of the disease in the high lands areas, to describe the most common complications of malaria and to formulate recommendations.

PATIENTS AND METHODS All cases of malaria admitted to the infectious diseases unit in the Medical Ward, Al-Gumhori Educational Hospital in Sana’a, from June 2002 to May 2003 and only cases in which the diagnosis was confirmed by a positive blood film were studied, and only those patients lives in highland lands (>2000 m) and were never been in the lowlands areas (<1500 m) were undertook to this descriptive clinical study. SPSS for windows statistical package was used for the statistical analysis.

RESULTS Eighty-four cases of malaria were clinically studied; of these (60%) were male and 40% were female, with an average of age 31.09 years. The majority of the patients referred to the hospital were living in Sana’a government (2377 m). Plasmodium falciparum is more common than other types of Plasmodium. The history of fever was universally present (89%). Jaundice (56%), and splenomegaly (34.5%) were the most common physical signs. Anaemia & thrombocytopenia are also the most complications. Five patients died from falciparum malaria. The average hospital stay was 699 + 299 days.

DISCUSSION AND CONCLUSION We report in this study cases of clinical malaria, which occurred in the high altitude of Yemen: Sana’a (2377 m), Thamar (2425 m) and Al-Mahweet (2300 m). These areas until then had been considered malaria risk free 3. This study demonstrates that areas endemic in malaria and populations at risk are more widespread than previously recognized, and more research work is needed to be done to evaluate the factors that increase the malaria transmission in highlands of Yemen.

Keywords: malaria, highland, clinical descriptive study, Yemen.

PA 55
Knowledge, attitudes and beliefs about HIV/AIDS among students in Thamar University, Yemen
A. Thabet1, A. Thamer2 and S. Audhaly2
1Faculty of Medicine, Thamar University, Community Medicine, Hamar, Yemen; 2Faculty of Medicine, Community Medicine, Thamar, Yemen

INTRODUCTION HIV/AIDS is considered to be important health problems world-wide. The purpose of this study was to determine the critical elements in knowledge, attitudes and beliefs towards HIV/AIDS among students of faculty of medicine and health science in Thamar University, Yemen, in order to design appropriate programme to fight the spread of HIV infection.

METHODS Cross-sectional type questionnaire survey was carried out at all branches of faculty of medicine and health science in Thamar University, between March and June 2006. The questionnaires were given to all students (1167) and 1005 (86%) of them answered the questionnaires. Knowledge, attitudes and beliefs regarding HIV/AIDS were asked.

RESULTS Overall knowledge about AIDS was remarkably good. Television and Radio were the predominant sources of information (30.6%). There was a common attitude among students that AIDS patients need to be isolated (66.5%) and about 70.4% believed that condom use should be encouraged.

CONCLUSIONS Findings of this study suggest that the students had satisfactory levels of knowledge on transmission and prevention of HIV/AIDS, although more than two thirds of them were not a ware of the symptomatic stage of HIV infection. Therefore, preventive strategy for HIV/AIDS for students in the University a
especially for the first year should be directed to an information, education and communication programme. As the possible risk behaviors of student are unknown, a behavior survey is recommended for designing an effective intervention to prevent HIV/AIDS.

PA 56  
Malaria transmission in Dakar: myth or reality
F. Pages, G. Texier, B. Pradin, L. Gadiaga, K. Penhoat and C. Sokhna
1IMTSSA le Pharo, Medical Entomology Unit, Marseille, France; 2IMTSSA le Pharo, Public Health Department, Marseille Armées, France; 3IMTSSA le Pharo, URBEP, Marseille, France; 4IRD Dakar, Unité de Paludologie, Dakar, Senegal

OBJECTIVES In Dakar, there was some evidence of local transmission from reports of malaria among permanent residents. But according to previous negative entomological studies, most of people didn’t believe to the reality of a malaria transmission in this town. The objective of this study was to assess the malaria transmission level in Dakar, Senegal.

METHODS An entomological evaluation has been conducted from May 2005 to May 2006 in two districts of Dakar (Ouakam, Bel air). Sampling of malaria vectors was carried out both indoors and outdoors by human landing catches. After morphological identification, members of the An. gambiae complex were identified to species and molecular form. Enzyme-linked immunosorbent assay was used to measure P. falciparum infection rate. Molecular assessment of pyrethroid knock down resistance (kdr) and insensitive acetylcholinesterase resistance (ACE1) has been done.

RESULTS During the study, 3600 An. gambiae s.l have been caught. The numbers of An. gambiae s.l bites reached from 37 per person per night in Ouakam to 180 per person per night in Bel air during the wintering period. Malaria transmission occurred only during this period from September to November in both areas. The entomological inoculation rate was then estimated to one infective bite per week. In Ouakam, An. arabiensis was the only member of the An. gambiae complex. In Bel air, An. arabiensis, An. melas and An. gambiae s.s, molecular form M accounted respectively for 97.8%, 2% and 0.2% of the An. gambiae complex. The kdr mutation frequency in the An. gambiae s.l population was 0.08. Ace1 mutation has not been identified in both members of the An. gambiae complex.

CONCLUSION Malaria transmission is a reality in Dakar. During the wintering, malaria level transmission can be very high and malaria control measures have to be strengthened. We present here the first detection of An. melas in Dakar.

PA 57  
Risk behaviour and motivation of hepatitis B cases in blood donors during 2005
L. Kasraian and A. Torab
Ibto Research Center, Shiraz, Iran, Islamic Republic of Iran

OBJECTIVES Hepatitis B infection is one of the most significant blood borne pathogens that threaten safe blood supply. It is essential to know the risk factor of getting HBV in HBV cases and their motivation of HBV cases for blood donation.

METHODS This is a cross sectional retrospective study that was done on HBV positive cases that were done their blood in Shiraz BTO in 2005 then we called them and fill out a questionnaire that was contained about epidemiological status, risk factor of getting infection and motivation of them for blood donation.

RESULTS In this study we called to 400 HBV cases and invited them to refer to BTS and fill out questionnaire for them. In this sample the mean age of HBV+ cases was 40.38 ± 10.57 and 80.6% was male and 92.8% was married and 58.4% was first time blood donor. Motivation of them for blood donation was 25.8% altruistic reason, 41.9% positive effect on their health, 16.1% health check up and 3.2% without any motivation and 3.2% curiosity about blood donation. Risk factor of getting HBS was 19.4% sexual contact, 6.5% history of blood transfusion, 22.6% history of hepatitis in their family and in 51.6% don’t have any risk factor.

CONCLUSION In this survey 17.6(%) of people donate blood for HIV check up and this can be dangerous for blood safety. The most risk factor that reported was sexual contact for safe blood supply we have to educate people in order to not donate blood for health check up and discussing population about residual risk of HIV transmission through blood and importance of blood donor for blood safety.

PA 58  
Surveillance of imported malaria in Belgrade
J. Poluga, M. Pelemis, Z. Dakic, G. Stevanovic, L. Lavadinovic, I. Oforici, B. Milosovic, S. Miskic and M. Pavlovic
1Institute for Infectious and Tropical Diseases, Department for Tropical Diseases, Belgrade, Serbia and Montenegro; 2Institute for Infectious and Tropical Diseases, Parasitological Laboratory, Belgrade, Serbia and Montenegro; 3Institute for Infectious and Tropical Diseases, Intensive Care Unit, Belgrade, Serbia and Montenegro

OBJECTIVES Since the 1960s only imported malaria presented a problem in Serbia. Most were treated in Belgrade, at the Institute for Infectious and Tropical Diseases.

METHODS Retrospective study of the pattern of imported malaria at the Institute for Infectious and Tropical Diseases, Belgrade from 2001 to 2006. Diagnoses of malaria were based on microscopic examination of peripheral blood smears. A rapid antigenic test has been in use since 2004.

RESULTS In this period at our Institute were examined 2853 samples of peripheral blood smears from 2297 travelers, 22% of them were with febrile episodes. A total of 65 imported cases of malaria (13% of travelers with febrile episodes) were treated in our hospital, annually from 6 to 16. Malaria was imported through the movement of the population abroad (89%), mostly. Most cases occurred in males above 40 years of age. Ten patients (15%) took prophylactic treatment. The most cases were imported from Africa (96%). The vast majority of malaria infections in our patients were due to P. falciparum (73%), alone or in the mixed infections. Smaller fractions were due to P. vivax and, P. malariae. In 11% of all cases the species of Plasmodium was not known. Generally, falciparum malaria was manifested within 14 days, and vivax malaria within 2–3 months after entering Serbia. The time to diagnosis in our hospital was 3 h and specific treatment immediately started according to the instructions of the WHO and our own experience. Average duration of parasitaemia was 2 days. The course of the disease was severe in 8 patients with falciparum malaria, with one fatal case. Two relapses with vivax and one recrudescence with falciparum malaria were noted.

CONCLUSION Malaria must be considered in all travelers with fever, without delay. A rapid antigenic test can help for prompt diagnosis of imported malaria.
Vulnerability for malaria in Belgrade area, Serbia

Z. Dakic1, M. Pelenis2, Z. Kulisec3, N. Stajkovic4, M. Bobalic5, J. Ofori-Belic1, G. Stavenovic2, J. Poluga3, L. Lavadinovic3, S. Mlici5 and M. Pavlovic1

1Institute for Infectious and Tropical Diseases, Parasitological Laboratory, Belgrade, Serbia and Montenegro; 2Institute for Infectious and Tropical Diseases, Department for tropical Diseases, Belgrade, Serbia and Montenegro; 3Faculty of Veterinary Medicine, Parasitology Department, Belgrade, Serbia and Montenegro; 4Military Medical Academy, Epidemiology Department, Belgrade, Serbia and Montenegro; 5Institute for Infectious and Tropical Diseases, Intensive Care Unit, Belgrade, Serbia and Montenegro

OBJECTIVES Since the early 1960s, only imported malaria have presented in Serbia. Most of these patients are treated in Belgrade. Global warming, presence of potential vectors and sporadic cases of autochthonous malaria in the neighboring countries is a warning that cases of autochthonous malaria might appear in Serbia, too. We examined the level of Belgrade’s vulnerability for malaria.

METHODS All individuals returning from endemic areas were screened for sexual parasites and gametocytes, in Belgrade from 1994 to 2005. Patients with estimated malaria were followed up for four weeks or longer.

RESULTS From 1994 to 2005, a total of 166 imported cases of malaria were treated in Belgrade: 159 (96%) at Institute for Infectious and Tropical Diseases, and others in Military Medical Academy. Malaria was mostly imported through the movement of the population abroad (94%). As in the past, dominant causative agent was P. falciparum alone or in mixed infections (67%), originally from tropical Africa. Historically, supposition is that local, potential vectors are refractory to infection by tropical P. falciparum. Prompt treatment of malaria cases was performed, mostly by artemisinin derivate. Of the 166 patients with imported malaria 60 (36%) had gametocytemia: 37 P. falciparum, 23 P. vivax. Gametocyte prevalence was 32.7% in P. falciparum and 41.8% in P. vivax infections. Most cases were imported from Africa (Ethiopia, Congo, E. Guinea, Nigeria), only 1 from Asia. The average presence of gametocyte in P. falciparum carriers was 12 days and in P. vivax 2 days. Of the 63 imported cases which were detected during potential malaria season (June-September) in Belgrade, only 18 were gametocyte carriers. They represented 10.8% of all malaria cases treated in Belgrade during the follow-up period and 30% of all gametocyte carriers. Of these 18 gametocyte carriers, 12 (67%) were of P. falciparum, and 6 (33%) of P. vivax.

CONCLUSION Belgrade’s vulnerability is low because of the low presence of gametocyte carriers during the season climatically favorable to transmission. The length of potential exposure of gametocyte carriers to mosquitoes was low. All patients are treated in two hospitals in the center of Belgrade and that limits mosquito-human contact. Simultaneous, mostly patients were treated by artemisinin derivate which reduced the transmission potential of falciparum malaria. Although Belgrade, Serbia has a well developed system of infectious disease surveillance and prevention, they should not be disregarded completely because the vectors are still present. harbour the heaviest infections and are most likely to suffer from associated morbidity especially when co-infections exist. We assessed the prevalence of fever, Plasmodium falciparum specific IgG and IgE antibodies, malaria parasitaemia and intestinal helminth infections and its impact on the incidence of anaemia in resident apparently healthy school children from a malaria endemic region of South Western Cameroon.

METHODS A cross sectional survey of 263 school children aged 4–12 years was conducted in Buea District. Fever status was determined at enrolment using a digital thermometer. Venous blood was collected for malaria parasite detection by microscopy. Indirect ELISA was used to measure plasma levels of total IgE, Plasmodium falciparum specific IgG, glycosylphosphatidylinositol (GPI) and IgE antibodies. Stool samples were analysed for helminth ova by the Kato-Katz technique. Area of residence, age and gender of each child was recorded at enrolment.

RESULTS The mean (± SD) age of the children was 7.56 ± 1.82 years. The prevalence of malaria parasitaemia was 59.3% (156/263) with a geometric mean parasite load of 56.5. There was an association between malaria parasite rates and febrile status (P = 0.042). Children at lower altitude had higher malaria parasite densities (PD) (P < 0.01). At lower altitude, public school children had higher PD compared to their mission counterparts (P = 0.010). Thirty-one (11.9%) anaemic cases were recorded; a majority (70.1%) of these were mild cases. A significant negative correlation (r = 0.224, P = 0.005) was observed between haemoglobin levels and PD. Infection with Plasmodium reduced red cell levels (P = 0.045), a condition that was further exacerbated by co-infection with helminths (P = 0.035). Plasma levels of IgE was higher in children with helminthiasis while IgG was higher in those with low grade parasitaemia. Anti-GPI antibodies increased with age and was higher in children at lower altitude and in those free of malaria parasites.

CONCLUSION Asymptomatic malaria parasitaemia co-exists with helminth infections in school children and stresses the importance of fever, altitude and school type. We also confirm that IgE may play a role in immune protection against helminthiasis while anti-GPI antibodies may be important in the development of immunity in these children. These findings reinforce the need for control programmes to consider reducing the prevalence of intestinal helminthes and malaria parasite infection which reduce anaemia incidence.

PA 61

Risk for tuberculosis among Lao children in resource-limited settings

H. Barennes, T. T. Nguyen, B. Martinez Aussel, V. Keolouangkhot and M. Strobel

Institut Francoophone de Medecine Tropicale, Vientiane, Lao People’s Democratic Republic of

OBJECTIVES There is a dramatic need to improve new test to diagnose the tuberculosis risk for children, particularly in countries lacking health facilities. In Laos, a country with high tuberculosis prevalence and mortality (318 et 25/100 000, respectively), there is a startling age gap in detecting tuberculosis in children. Tuberculin skin test is not currently available in the field. Only 5 (2.9%) children were detected through the National Tuberculosis Program (2003–2005) in southern Laos compared to an expected rate of 15 to 20%.

METHODS We evaluate the risk for infection (IR) among children living with tuberculosis patients in remote Northern Laos. Index patients were randomised among 208 tuberculosis treated patients in 30 villages. We visited 72 patients’ households, including 148 children < 15 years and 114 adults. The parents were interviewed by using a standardized questionnaire concerning medical history,
degree of contact, and characteristics of the household, distance to health Centre, presence of BCG scars. Nutritional status, clinical signs of tuberculosis and tuberculin skin test were evaluated. Three days sputum were collected. Index patients had completed their treatment (17/72, 23.6%), gave up (25/72, 34.7%) with a mean duration of 198.8 days, C.I95%: 62–235) or were under treatment (30, 41.6%). All but one was sputum negative by the time of interview. Three adults contacts were positive. One child had tuberculosis nod. Among children IR was 17/63 (26.9%, IC95% 15.7–38.2) vs 29/85 (34.1%, IC 95% 23.8–44.4) according to presence or absence of BCG scar, respectively (P = 0.3). IR trends increased with age without reaching significance. Multivariate analysis showed the following risk factors in children: current patient positive sputum, positive sputum prior treatment, and ethnicity (minorities). Other factors such as duration and degree of contact were not associated.

CONCLUSION New tools for TB diagnosis in children, improved active household case detection and follow up, and chemoprophylaxis are highly recommended.

PA 62
AIDS in Kosova: stigma persists
N. Ramadani1, L. Gashi2, A. Kalaveshi and S. Gashi-Naka3
1 Kosova National Institute of Public Health, Department of Epidemiology, Pristina, Albania; 2 Medical Faculty, Forensic Institute, Pristina, Albania

OBJECTIVES Epidemiological characteristics of AIDS in Kosova, analysis cases, morbidity, mortality and letality, risk factors.

METHODS Epidemiological surveillance data and retrospective method.

RESULTS From 1986 until December 2006 we have analysed cases using retrospective method. During this period of time 67 persons have been affected while 25 of them died. The highest number of cases was registered in 2001 with 12 cases or 5.7 cases in 100 000 inhabitants. The highest number of deaths was registered in the years 1987, 1992 and 1996 (5 cases and Lt 100%). While the lowest number of cases was registered in 1991, 1993, 2000 and 2003 (1 case). In 1988, 1989, 1990, 1998, 2001 and 2002 no case was reported. During the period that we analysed the highest number of cases were register in Pristina municipality 7, Peja municipality 6 and Ferizaj 4. Overall, 65% were males and 35% females. The most affected age groups were 30–39 (37.7%), 20–29 (26.4%) and 40–49 (18.8%). According to the present data we could say that epidemiological situation in Kosova is not so alarming compared to other countries. Problem is not knowing the number of HIV carriers. Kosova is still among countries with low prevalence of HIV/AIDS.

CONCLUSION Since there are many foreign citizens coming to Kosova as well as many Kosovars returning from foreign countries, the situation is expected to be worsen. So, the frequency of AIDS in Kosova is strongly associated with individual risk factors.

PA 63
Tuberculosis: epidemiological situation and surveillance system in Kosova
A. Kalaveshi1, N. Ramadani1, L. Gashi1, B. Tigan2 and G. Mullig3
1 Kosova National Institute of Public Health, Department of Epidemiology, Pristina, Albania; 2 Ministry of Health, Global Fund, Pristina, Albania; 3 Kosova National Institute of Public Health, Department of Microbiology, Pristina, Albania

OBJECTIVES Aim of this study is to present epidemiological characteristics of TBC in Kosova and strategic plan against this disease until 2008.

METHODS Surveillance data, epidemiological assessment, descriptive method, has been used for the study, based on the retrospective and prospective research.

RESULTS During the period 1990–2006 in Kosova were registered in total 16 113 new TB cases with 116 fatality cases. According to the data available for the past three years, the TB burden is increasing. The incidence rate of notified TB cases in Kosovo is still 2–3 folds higher than that of its neighboring countries, and significantly higher than Western European incidence rates.

CONCLUSION Kosova has one of the highest TB case rates in the Europe. The National TB program strengthening includes scaling up of the laboratory component. A second five year plan, (2005–2009) was produced in 2003 by the TTC, DOW and international consultants, to consolidate the results achieved so far and to build up the basis for program strengthening through Global Fund resources.

PA 64
Prevalence of HIV in Georgian risk groups
P. G. Gabunia and N. Bolokadze
Georgian Infectious Diseases, AIDS and Clinical Immunology Research Center, Inpatient Department, Tbilisi, Georgia

OBJECTIVES Prevalence of HIV in 6075 Georgian risk-groups (data per 2003 year): IDU-s, commercial sex workers (CSW), homosexuals (HS), patients with HBV, HCV, TB and STD-s has been investigated.

METHODS Screening for anti-HIV antibodies was done using the following test systems: Vironostiva HIV UniForm II plus O (Organon-Tecnika, Netherlands) and HIV 1 + 2 HUMAN ELISA (human, Germany). HIV Western Blot (HIV BLOT 2.2 Western Blot ASSAY, Genelabs Diagnostics, Singapore) was used for confirmation. Data were entered into FoxPro database and analyzed using SPSS version 8.0.

RESULTS Of the 6075 risk-groups 1660 (27.3%) were IDU-s, 1330 (21.9%) –CSW-s, 89 (1.5%) –HS-s, 1221 (21.1%)–patients with STD, 1125 (18.5%)–patients infected with HBV and HCV, 650 (10.7%) were TB patients. Of the 6075 risk-groups 5091 (83.8%) were male and 984 (16.2%) female. The majority of the samples were young, with 10.6, 19.9, 34.5 and 35% being 18–24, 25–30, 31–40, and over 40 years of age, respectively. Of the 1660 IDU-s screened 43 (2.6%) had anti-HIV . Prevalence of HIV between CSW-s was 0.15% (2), HS-s–0.8% (9). Prevalence of HIV between male patients was 1.3% (66), females–0.2% (2). Prevalence of HIV between investigated risk-groups per 2003 year in Georgia was 1.045%.

CONCLUSION Prevalence of HIV in Georgian risk-groups is higher between IDU-s. Prevalence of HIV in Georgian risk-groups is lower than national prevalence estimates of HIV in neighboring countries.

PA 65
Prevalence of Plasmodium sp. infection in children of Kuanza Sul province, Angola
C. Mendes, F. Dias, V. E. do Rosário, L. Varandas and A. P. Arez
Instituto de Higiene e Medicina Tropical, Centro de Malária e outras Doenças Tropicais, Lisboa, Portugal

Two first authors equally contributed to this work.

OBJECTIVES Malaria remains one of the main public health problems in the world, including in Angola where 30 years of civil war hampered the coverage by health facilities and accuracy of
reporting systems. According RBM/WHO, malaria is presently the first cause of morbidity and mortality in this country, changing from hypendemic to a mesoendemic level in Luanda and moving from 6th to 1st place in the ranking of causes of children mortality. The main objective of this study is to assess the real prevalence of malaria infection and distribution of the different Plasmodium species over the country since accurate information is still scarce. This is an on-going study and we present here the first results obtained in the Kuanza Sul province.

METHODS A total of 870 peripheral blood samples were collected from asymptomatic 2 months to 8 years old children, in four villages (Gabela, Porto Amboin, S. Kissala and S. Praia). DNA was obtained from all samples by phenol/phenol-chloroform extraction and ethanol precipitation and the Plasmodium species detection and identification was performed by nested-PCR.

RESULTS Overall, 28% of the children analysed were infected with, at least, one of the four species of Plasmodium sp. Gabela shows the higher prevalence of infection (52.9%), whereas in the other three villages (Porto Amboin, S. Kissala and S. Praia) the prevalence was 28.0%, 9.8% and 18.3%, respectively. Plasmodium falciparum predominated, occurring in 98% of the infected samples, Plasmodium malariae in 12.2%, Plasmodium ovale in 4.9% and Plasmodium vivax in 2.4%, both in single and mixed infections. Even if the overall prevalence of infection had been high in the two age groups considered (≤ 1 and ≥ 1 year-old), infants less than 1 year-old had shown a lower prevalence of infection (19.8% vs 34%).

CONCLUSION Although still preliminary, the results seem to point to a different, generally higher, prevalence of each Plasmodium species from the one previously reported.

PA 66

Occurrence of imported malaria in Parma, Northern Italy, during the period 2000–2006 by comparing microscopy and molecular methods

A. Calderaro, S. Peruzzi, C. Gorrini, G. Piccolo, G. Dettori and C. Chezzi

University of Parma, Department of Pathology and Laboratory Medicine, Section of Microbiology, Parma, Italy

OBJECTIVES Malaria is the most common imported infection in Italy because of increasing of population movements from endemic countries (Romi et al., 2002). Our study aimed to describe the occurrence of imported malaria in Parma, Northern Italy, during the period 2000–2006 comparing the data obtained with microscopic observation and molecular methods (Nested-PCR and Real-time PCR).

METHODS Blood samples were collected on admission from 639 patients presenting to Parma University Hospital with symptoms consistent between January 2000 and December 2006. Samples were submitted to immunochromatographic rapid assay, microscopy (orange acridine and Giemsa stain) and 6 different PCR assays (NP-1993, NP-2002, NP-2004, NP-3005, RT-2004P and RT-2004R) (Sounou et al., 1993-2002; Ndou et al., 2004; Calderaro et al., 2007; Perandin et al., 2004; Rougemont et al., 2004).

RESULTS One hundred forty-two cases of malaria were diagnosed by microscopy (118 P. falciparum, 7 P. ovale, 10 P. vivax, 5 P. sp., 1 P/FP, spp. and 6 mixed infections) and 147 by PCRs (118 P. falciparum, 14 P. ovale, 6 P. vivax, 3 P. malariae and 6 mixed infections). One hundred thirty-four patients were foreigners or tourists coming from Africa, 2 from Indonesia and 10 patients were from unknown country of origin or visit. Most of patients had no chemoprophylaxis and presented relevant specific clinical symptoms and signs for malaria (such as fever, headache).

CONCLUSION Our data confirm that the most prevalent malaria cases in Italy were imported from Africa and were due to P. falciparum (80.2% of cases). PCRs revealed a major number of P. ovale and mixed infections respect to microscopy, followed by P. vivax and P. malariae infections. Despite microscopy remains the first diagnostic method, we observed that in some cases molecular assays are the only ones allowing a diagnosis, in particular to detect species other than P. falciparum and mixed infections.

PA 67

Molecular epidemiology: some host genetics factors related to malaria in Santiago, Cabo Verde islands

J. Alves1, P. Machado1, N. Gonçalves1, J. Silva1, L. Gama1, C. Alves2, L. Manco3, V. E. dos Rosários1, A. Amorim4 and A. P. Arez1

1Instituto de Higiene e Medicina Tropical/UL, Centro de Malária e Outras Doenças Tropicais, Lisboa, Portugal; 2Instituto de Patologia e Imunologia Molecular da Universidade do Porto, Porto, Portugal; 3Universidade de Coimbra, Centro de Investigação em Antropologia, Coimbra, Portugal; 4Instituto de Patologia e Imunologia Molecular da Universidade do Porto; Faculdade de Ciências/UP, Porto, Portugal

OBJECTIVES Malaria in Santiago (Cabo Verde) is unstable with great variation in morbidity. Although the presumably weak immunity of the population, previous studies had disclosed the presence of asymptomatic infections and moderate clinical symptoms. To verify if this moderate morbidity could be a consequence of human genetics determinants, we analysed the HbB (β-globin gene), g6pd and the pklr gene (recently associated to malaria protection, and 1456C > T, pklr gene (recently associated to malaria protection in a rodent model).

METHODS We studied these three genes in DNA samples from 1050 individuals involved in previous epidemiological research. Of these, a sub-sample of 265, Infected and Not-Infected unrelated individuals, were recruited for the present study. Detection of CD6A > T mutation in the HbB gene and mutations in the g6pd gene was carried out by Multiplex PCR and PCR-RFLP. In the pklr gene, the presence of two mutations, 2691T > A, identified in mice as strongly associated to malaria protection, and 1456C > T, common in Portugal and some Sub-Saharan regions, was investigated; some newly described microsatellite regions (STRs), inside and down the gene, were also examined. The amplified fragments were analysed and their sequence determined (ABI 310 system, software GeneScan 3.1.2. and Sequencing Analysis 3.7.) to obtain the number of repeats. Statistic analysis of the results was carried out with Arlequin 3.1.

RESULTS From the 87 samples fully analysed for the HbB gene, 63% presented the HbAA, 29% the HbAS and 8% the HbSS genotypes. These results point to an allelic frequency of HbS of 22%. Regarding the g6up gene, from the 126 samples fully analysed, 83% presented the B, 17% the A and 0.8% the A- genotypes. These results point to allelic frequencies of B, A, A- alleles of 69.5%, 29.5% and 1%, respectively. So far, none of the previously described mutations in the pklr gene were found in the Santiago isolates. The new STRs investigated revealed to be highly polymorphic and three new STRs, one in the gene and two downstream, the gene, were also examined. The amplified fragments were analysed and their sequence determined (ABI 310 system, software GeneScan 3.1.2. and Sequencing Analysis 3.7.) to obtain the number of repeats. Statistic analysis of the results was carried out with Arlequin 3.1.

CONCLUSION HbB allelic frequency is in accordance with the described frequencies for the Sub-Saharan African population. Until the moment, no differences were found between Infected and Not-Infected groups and no haplotype was found to be associated with presence of malaria infection. However, this study is presently on going and results are still preliminary; thus we cannot exclude yet this association in the human population.
PA 68
Comparing access to TB diagnosis between rural-to-urban migrants and urban-residents in Chongqing, China

Q. Long
Chongqing University of Medical Sciences, School of Public Health, Chongqing, China

OBJECTIVES To understand the health seeking behavior of rural-to-urban migrants in Chongqing in response to chronic cough, in order to identify the factors influencing delays in receiving TB diagnosis.

METHODS A prospective cohort study of adult suspect TB patients (>3 weeks cough and/or hemoptysis) was undertaken in two districts representing a relative developed and a less developed area of Chongqing. The patient survey was conducted in 23 selected tertiary, secondary and primary health facilities and respondents were interviewed again by home visit after 3 months. Two standard questionnaires were used to collect general demographic and socio-economic information of the subjects and their pathway to seeking health care.

RESULTS Of the 1003 people recruited (776 urban-residents and 229 rural-to-urban migrants), 67.7% of migrants experienced a patient delay ≥2 weeks (median 23 days), compared to 54.0% of urban-residents (median 18 days) (P < 0.01). Non-coverage by health insurance, low education level, less TB related knowledge, self-treatment, female sex (P < 0.01); unemployed and without spouse are all independently associated with longer patient delay (P < 0.05). About 37.1% of migrant patients chose private clinics or institutions for their first contact with service providers, which were 1.5 times more than urban-residents. 61.0% of respondents were sent for X-ray and 19.1% for sputum smear test; less than 10% were referred to TB center. There are not significant difference between migrants and residents (P > 0.05). A total of 680 interviewees (67.7%) (528 urban-residents and 152 rural-to-urban migrants) were successfully followed up, of which 426 people still had cough symptoms. But only 238 (55.9%) sought professional care and migrants were less likely to seek care (39.1%) than urban-residents (58.8%) (P < 0.05). About 18 cases (13 urban-residents and 5 rural-to-urban migrants) were diagnosed as TB at end of the survey.

CONCLUSION Patient delay in seeking TB related care was more serious among the rural-to-urban migrant than urban-resident, but there was not significant difference on system delay between two groups. Socio-economic factors do affect access to health care in general and to TB related services in migrant group. Doctors in general hospitals prefer X-ray as diagnosis tool than sputum smear test to identify TB case. Poor referral practices resulting from doctors fear of losing patient fee lead to loss of TB suspect case and also low case detection. The policies and regulation related to TB control have not been well disseminated to the general hospital, the public and especially the migrants, which to some extent affected the effectiveness of TB control.

PA 69
Long-lasting insecticidal hammock nets (LLIHN) for controlling forest malaria in Vietnam

T. Ngo1, A. Erhart2, H. Le3, M. Coosemans1 and U. D’Alessandro1
1Prince Leopold Institute of Tropical Medicine, Antwerp, Belgium; 2National Institute for Malariaology, Parasitology and Entomology, Hanoi, Vietnam

OBJECTIVES To evaluate the effectiveness of LLIHN as a new strategy for malaria control in forested areas of central Vietnam.

METHODS A community based, clustered randomised trial on LLIHN was carried out in Central Vietnam. Twenty clusters (about 1000 inhabitants each) situated in a forested area in Ninh Thuan province were identified. During the year before the intervention a census of the study population was done. Passive detection of clinical cases was started and continued until the end of the study. In addition, two malariometric surveys (one at the beginning and one at the end of the transmission season) were conducted yearly before and after the intervention. After the distribution of LLIHN in 10 clusters, the population was followed for 2 additional years. We present here the results of the baseline year, before the distribution of LLIHN.

RESULTS The population comprised 18 646 people, median age was 19 years and the main ethnic group Raglai (88.5%), traditionally nomadic tribes living in the forest. Educational level as well as socio-economic status was generally low. The main activity was forest work (94% of the active population). In 2004, the malaria incidence rate was 69/1000/year. People sleeping in the forest had a significantly higher risk of clinical malaria (OR = 1.7; P < 0.01). Gender, age, occupation, ethnicity, education and socioeconomic status were also risk factors for malaria. Parasite prevalence varied between 14.2% in April and 17.8% in December. P. falciparum and P. vivax were the main parasite species, equally represented. However, 80% of clinical cases detected by passive surveillance were P. falciparum. While 86% of the population used to sleep under ITNs in the village, this proportion dropped to 12.5% among people sleeping in the forest.

CONCLUSION Considering that forest work is a significant risk factor for malaria, LLIHN could have a protective effect against malaria infection.

PA 70
Prevention, control and treatment of HIV/AIDS among intravenous drug users in Indonesia

L. Pinxten1, J. Mose1, G. Nugraha Irawan1, R. van Crevel1 and B. Alisjahbana1
IMPACT Integrated Management for Prevention And Control and Treatment of HIV - Bandung 1Padjadjaran University, Bandung, Indonesia; 2Radboud UMC Nijmegen, Nijmegen, Netherlands

BACKGROUND HIV/AIDS has a low prevalence in the general population in Indonesia, but HIV-transmission through needle sharing has shown a dramatic increase in recent years, and more than 80% of new HIV-infections are now due to intravenous drug use (IDU). Current interventions targeted at prevention and care of HIV/AIDS in IDUs in Indonesia are fragmentary, small-scale and difficult to access for IDUs.

METHODS A 5-year program was designed to improve prevention and care of HIV/AIDS in Bandung, West Java, by targeting the main risk factor, intravenous drug use (IDU). Its comprehensive approach combines the following main activities: health promotion about HIV-related risk behaviour in adolescents; scaling-up voluntary counselling and testing and improving its accessibility to IDUs in the community, prison and hospital; harm reduction strategies, including methadone maintenance; scaling-up care for HIV/AIDS, including antiretroviral treatment; capacity building and transfer of knowledge about IDU and HIV/AIDS.

RESULTS Since its start in December 2006, significant progress had been made. Among other things, an effective methadone-program has been established, an assessment of occupational risk for blood-borne infections has been made, infrastructure for providing harm reduction and HIV care have been prepared in prison, and a number of research projects covering all aspects of the program have been started.
CONCLUSION These activities-locally embedded and in line with accepted policy-will lead to evidence-based and comprehensive HIV-prevention and care in the context of IDU in Indonesia, with the potential for scaling up and replication in other settings.

PA 71 Malaria in pregnancy before and after the implementation of a national IPTP program in Gabon

M. Ramharter1, K. Schuster1, M. K. Bouyou-Atokè2, A. A. Adégnika1, K. Schmitt1, G. Mombo-Ngoma1, S. T. Aognadi1, J. Nemeth1, S. N. Afene1, S. Issifu1, I. Ndiamondi Omus1, S. Bélard1 and P. G. Kremanser1

OBJECTIVES Intermittent preventive treatment in pregnancy (IPTP) with sulfadoxine-pyrimethamine has recently been adopted by many African countries to reduce maternal and neonatal morbidity and mortality associated with malaria in pregnancy. We assessed the impact of a newly established national IPTP program on maternal and neonatal health in Gabon.

METHODS Data on prevalence of maternal Plasmodium falciparum infection, anemia, premature birth and birth weight were collected in cross sectional surveys in urban and rural regions of Gabon before and after the implementation of IPTP in a total of 1403 women and their offspring. A subgroup analysis, restricted to primi- and secundigravid women, was additionally performed.

RESULTS Following the introduction of IPTP the prevalence of maternal P. falciparum infection at delivery decreased dramatically from 10.5% to 1.7% (risk ratio 0.16, P < 0.001). Whereas an only modest effect on the rate of anemia in pregnant women was observed (30.3% vs 49.8%), there was a marked benefit on the prevalence of low and very low birth weight (11.7% vs 10.3%, 0.8% vs 0.3%, respectively) and premature birth (23.9% vs 20.1%) for women adhering to national recommendations. These effects were most pronounced in primi- and secundigravid women where IPTP was associated with a significantly reduced rate of premature births (22.2% vs 17.3%), an increase in mean gestational age at delivery (38.4 vs 39.0 weeks; P = 0.005) and significantly elevated maternal hemoglobin levels and birth weight (10.4 g/dl vs 10.9 g/dl; P = 0.004 and 3029 g vs 3112 g; P = 0.029, respectively).

CONCLUSION These data show that a strategy for preventing malaria burden in pregnancy has successfully been translated into national policy and program implementation. Implementation of a national IPTP program paralleled by operational advances in the distribution of impregnated bed nets may therefore be an effective approach for the prevention of malaria in pregnancy.

PA 72 Prevalence of head lice and related factors in primary school students in Sanandaj, Iran

B. Davari1, R. Yaghmaie2 and G. Zamin1

1Kurdistan University of Medical Science, Parasitology & Entomology, Sanandaj, Iran, Islamic Republic of Iran; 2Kurdistan University of Medical Science, Dermatology, Sanandaj, Iran, Islamic Republic of Iran

OBJECTIVES Pediculosus is one of the most important health problems among students in Sanandaj city. Close physical contact among students provides favorable conditions for transmission of this parasite to other students. Pediculosus is a health problem, and has adverse psychological and social effects. This research was carried out to study the prevalence of head lice and to determine the related factors with this problem.

METHODS This research was a descriptive- analytical one. After calculating sample volume, the stratified sampling method was used to select a boys and girls school in every region randomly. Cases were selected based on the required sample by using the school list of students name. The required information was obtained by questionnaire and interview.

RESULTS In this study 1195 student from 18 primary schools were examined. Results showed that contamination rate is 19.7%. There was a significant relation between contamination by louse and every of the following factors including sex, interval of bathing, using common personal tools, previous louse contamination, personal hygiene, family help in doing personal hygiene, educational degree of parents, parents job, number of family members and presence of a bath room at home, while no significant relation was found between this contamination and hair style. The maximum contamination rate (57%) was among the students of the second and third grade of the primary school.

CONCLUSION The results showed the variable including contamination of females, bathing interval, using other persons personal tools, history of previous louse contamination, family help in doing personal health affairs, educational degree of parents, fathers job, number of family member and presence of a
bathroom at home are compatible with other investigations. However the results regarding hair style contradict the observations from other investigations. It seems that cultural differences influence the results of our study rending it to be either compatible or incompatible with other research works.

PA 74
Tolerance and therapeutic efficacy of amodiaquine, sulfadoxine-pyrimethamine and their combination for treatment of uncomplicated Plasmodium falciparum malaria in Bobo-Dioulasso, Burkina Faso: a randomised clinical trial

F. Assogba, H. Zigani, I. Zongo, N. Rouamba and J. E. Ouedraogo
Institut de Recherche en Science de La Sante, Clinical Research, Ouagadougou, Burkina Faso

BACKGROUND Increasing Plasmodium falciparum resistance to chloroquine in Sub-Saharan African impose urgently using of alternative antimalarial drugs. Efficient alternative treatments include Sulfadoxine-Pyrimethamine and Amodiaquine combinai-

can increase therapeutic efficacy and delay emergence of drug resistance. This study compares the efficacy and the tolerance of Sulfadoxine-Pyrimethamine, Amodiaquine and their combination for the treatment of uncomplicated malaria in children from Bobo-Dioulasso (Burkina Faso).

METHODS We randomly allocated 6 months and older patients in three groups of treatment (Amodiaquine, Sulfadoxine-Pyri-

methamine and their combination). Patients were followed-up for 28 days according to WHO 2003 protocol, and PCR genotyping were used to distinguish recrudescence and new infections. Per protocol and intention to treat analysis were used.

FINDING Of the enrolled patients, 88% (829/944) successfully completed the follow-up. The results have shown that the AQ + SP combination was significantly more effective than SP and AQ alone among children under 3 years [recrudescence rates were 1.3% (AQ + SP); 7.5% (SP); 8.8% (AQ), P < 0.05]. But, for the older patients, the recrudescence rates were similar [3% (AQ + SP); 4.5% [SP]; 6.6% (AQ), P > 0.05]. The fever clearance time was significantly shorter in AQ + SP (98%), and AQ (97%) than in SP group (P < 0.05). Similarly, the parasite clearance was better with AQ + SP than with SP (7%) or AQ (10%). Clearance of gametocytes was slower in SP (19%) than in AQ (8%) and AQ + SP (8%). We obtained similar results with the intention to treat analysis. No severe adverse events were observed with none of the drugs. The results have also shown that the three regimens are effective for the haematological recovery.

INTERPRETATION This study has shown that the AQ + SP combination remains effective, and could be a low-cost alternative to ACTs.

PA 75
Clinical and microbiological aspects of pulmonary tuberculosis in a rural hospital in Cameroon

D. Caudri1, S. F. van den Heuvel1 and J. Nouwen2
1Erasmus MC, Rotterdam, Netherlands; 2Erasmus MC, Medical Microbiology and Infectious Diseases, Rotterdam, Netherlands

OBJECTIVES This study aimed to assess clinical and microbiologi-

cal aspects of mycobacterial infection in patients presenting at the Presbyterian Medical Institutions Manyemen, Cameroon.

METHODS All adult patients suspected for pneumonia were included. They were seen by local medical staff, who ordered for routine diagnostic tests according to hospital guidelines. Parallel, all included patients were interviewed and had a standard full physical, laboratory and microbiological examination performed by two investigators. Subspecies of the isolated mycobacteria and drug resistance of all Mycobacterium tuberculosis strains were determined. A diagnostic rule was derived using clinical charac-

teristics and compared with local guidelines using ROC-curves.

RESULTS A total of 183 patients were enrolled, of which 83 were HIV-infected. 88 (48%) patients had a mycobacterial infection, of whom 71 had pulmonary tuberculosis. Using local guidelines and available resources, the Manyemen medical staff identified 58 (66%) cases of mycobacterial infection. 30 cases were not detected, 17 (49%) in the HIV-infected and 13 (25%) in the HIV-negative group. In one third of the missed cases direct sputum ZN smears were not performed because mycobacterial disease was not suspec-
ted clinically. In the remaining two thirds sputum ZN smears were performed but remained negative. Considering patients with pulmonary tuberculosis exclusively, the direct smear performed by the local staff missed only 14 cases, 6 (26%) in the HIV-infected and 8 (17%) in the HIV-negative group. The derived prediction rule for HIV-positive patients had a diagnostic yield comparable with the direct sputum ZN smear. Of the 73 isolated Mycobacterium Tuberculosis strains 4 (8%) were resistant to Isoniazid and 2 (3%) were resistant to both Rifampicin and Isoniazid.

CONCLUSION Prevalence of HIV in patients presenting with pulmonary complaints in the Presbyterian Medical Institutions of Manyemen is 45%. The prevalence of mycobacterial infection is 48% and of pulmonary tuberculosis 39%. Due to limited resources and due to a specific clinical presentation, one third of all mycobacterial infections and one fifth of pulmonary tuberculosis cases goes undetected. The use of a diagnostic rule based on clinical characteristics may be useful to diagnose pulmonary tuberculosis in HIV-positive patients. 3% of the isolated Myco-

bacterium tuberculosis strains is multi-drug resistant.

PA 76
Redefining 'high-risk' sex - the condom gap and HIV transmission among married couples in Kenya

J. Papa1 and E. Baus2
1Department of Public Health and Primary Health Care, University of Oxford, Oxford, UK; 2Kenya Medical Research Institute, Kilifi, Kenya

OBJECTIVES Using data from the 2003 Kenya Demographic and Health Survey, estimate the number of new HIV infections arising from unprotected sexual intercourse among married couples over the course of one year.

METHODS The number of new infections among married indi-

viduals aged 15-49 over a one-year period was calculated as follows: number of men and women 15-49 years old * % population currently married * % couples who are HIV discordant * % population not tested for HIV * % married couples not using condoms * probability of HIV transmission per coital act * sexual acts per year. The following values were used: In the absence of data specific to Kenya, the values for HIV transmission per coital act and frequency of sex are based on a study among monogamous heterosexual discordant couples in Rakai, Uganda (Lancet 2001).

% population currently married 52.2%
% couples who are HIV discordant 7.4%
% population not tested for HIV 84.5%
% married couples not using condoms 98.8%
Probability of HIV transmission per coital act 0.0011
Frequency of sexual intercourse per year 106.8 acts

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RESULTS Given a population of 15,381,966 individuals between 15–49 years old (2004 projection, 1999 Kenya Population and Housing Census), the estimated number of new infections among married couples is 58,276 cases. These cases represent 0.73% of married individuals and 9.81% of individuals in discordant relationships; out of the total number of new infections, these cases represent 64.75% of new infections, estimated at 90,000 for the year 2004 (Kenya National AIDS Control Council, 2005).

CONCLUSION These results highlight the heavy burden of HIV transmission among married couples in settings with high HIV prevalence. Condom promotion efforts have focused on high-risk groups and ‘high-risk’ sex, defined as sex with a non-marital and non-cohabiting partner. This overlooks men and women in steady partnerships engaging in regular unprotected sexual activity with a potentially infected partner. Given the generalised nature of the HIV epidemic in Kenya, in the sub-Saharan African countries, there is an urgent need for increased testing among couples, and for a new wave of condom promotion efforts aimed at men and women in steady yet discordant partnerships.

PA 77
The impact of increasing resistance to sulfadoxine-pyrimethamine on the efficacy of intermittent preventive therapy for the control of malaria in pregnancy: a systematic review of trials
F. O. ter Kuile1, A. M. van Eijk2 and S. J. Filler3
1Liverpool School of Tropical Medicine, Child and Reproductive Health Group, Liverpool, UK; 2Department of Infectious Diseases, Tropical Medicine & Aids, Academic Medical Center, University of Amsterdam, Amsterdam, Netherlands; 3Centers for Disease Control and Prevention (CDC), Malaria Branch, Division of Parasitic Diseases, Atlanta, GA, USA

OBJECTIVE To determine the impact of increasing resistance of Plasmodium falciparum to sulfadoxine-pyrimethamine (SP) on the efficacy of intermittent preventive therapy in pregnancy with SP (IPTp-SP) for the control of malaria in pregnant women in Africa.

METHODS We searched PubMed to identify IPTp-SP trials in Africa conducted from 1966 to Dec 2006. Each study was matched with a treatment efficacy study involving symptomatic children by location, and study year. Unpublished data were also solicited from individual research groups. Data was extracted data on the protective efficacy (PE) of IPTp-SP on placental and peripheral malaria, birthweight/low birth weight (LBW) and 3rd trimester anaemia, with a treatment efficacy study involving symptomatic children by location, and study year. Unpublished data were also solicited from individual research groups. Data was extracted data on the protective efficacy (PE) of IPTp-SP on placental and peripheral malaria, birthweight/low birth weight (LBW) and 3rd trimester anaemia.

RESULTS Nine IPTp-SP trials were identified. Six trials among primi/secundi-gravidae compared IPTp-SP to case-management/placebo (n = 4) or chloroquine prophylaxis (n = 2); the matched efficacy in children studies showed that the corresponding degree of SP resistance by day 14 ranged from 3 to 30%. The protective efficacy against placental malaria, LBW, and anaemia was 42% (95% CI 33–51), 26% (12–38), and 15% (11–19) and did not decline significantly with increasing SP resistance. Three trials compared 2-dose with monthly IPTp-SP (range SP-resistance 8–39%). In HIV-infected primi/secundi-gravidae, monthly IPTp-SP was more efficacious at all levels of SP resistance. We also compared the proportional reduction in parasite density at delivery versus 3rd trimester in eight trials. Among HIV-uninfected women the reduction in parasite density remained constant at >60% across the range of SP-resistance (3–39%) with 2-dose IPTp-SP. However, among HIV-infected women, the reduction with 2-dose IPTp-SP dropped to 21% in the single trial conducted at 39% SP resistance, but was >80% with monthly dosing.

CONCLUSIONS The 2-dose IPTp-SP regimen continues to provide substantial benefit to HIV-uninfected semi-immune pregnant women in areas with up to 30% SP treatment failure in children by day 14. However, more frequent dosing is required in HIV-infected women. More data is required about the efficacy of IPTp-SP in areas with higher SP resistance and about the effect of concomitant use of insecticide treated nets. The identification of alternative antimalarials for malaria in pregnancy is a research priority.

PA 78
Seasonal patterns of malaria in adolescent girls in a high transmission area of Malawi
G. K. Chapotera and B. Brabin
Child and Reproductive Health, Liverpool School of Tropical Medicine, Liverpool, UK

BACKGROUND Malaria infection among adolescents (10–19 years old) is thought to be infrequent in highly endemic areas, is usually asymptomatic and therefore can remain undetected and untreated. There is uncertainty about its true frequency and there is limited or no data on seasonal patterns of clinical and parasitological malaria in adolescent girls.

OBJECTIVE To describe the point prevalence of malaria parasitaemia and symptomatic malaria in adolescent girls during the dry and wet seasons.

METHODS Two community-based cross-sectional surveys of adolescent girls were completed during the dry (Sept to Dec 2005) and the wet (Jan to June 2006) seasons in Chikwawa, rural Malawi. Single-stage random cluster sampling was used. Demographic and health characteristics were obtained. Paracheck rapid test on finger prick blood was used for determining malaria parasitaemia. Symptomatic malaria was defined as malaria parasitaemia in the presence of measured fever (≥37.5 °C).

RESULTS Mean age for each survey was 13.9 years. Asymptomatic malaria prevalence was significantly higher in the wet than dry season (17.9% vs 12.5%; P = 0.011). Symptomatic malaria prevalence was higher in the wet than dry season but this difference was not significant (7.2% vs 6.1%; P = 0.415). Anaemia (Hb <12 g/dl) was highly prevalent in the wet (54.9%) than in the dry season (71.2%); P < 0.0001. Severe anaemia (Hb <8 g/dl) was less prevalent during the wet (3.2%) than during the dry season (8.4%); P < 0.001.

CONCLUSION The prevalence of asymptomatic malaria was twice that of symptomatic malaria amongst adolescent girls and their anaemia prevalence was highest following the wet season. The risk of malaria in these adolescent girls is substantial and increased efforts to prevent these episodes are required.

PA 79
Level of knowledge about HIV/AIDS in a cohort of Sub-Saharan African immigrants living in Madrid, Spain
M. Navarro, A. Guionnet, B. R. Navaza, G. Biosca, P. Zamarron and R. Lopez-Velaz
Tropical Medicine, Ramón y Cajal Hospital, Madrid, Spain

OBJECTIVES To determine the level of knowledge of HIV/AIDS in a cohort of Sub-Saharan immigrants living in Madrid, Spain.

METHODS A survey was carried out in some NGOs devoted to immigrants in Madrid, Spain, during the winter of 2006. A KAP (Knowledge, Attitude and Practice) questionnaire was administered to a cohort of 138 Sub-Saharan African immigrants. After
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PA 80
Does community involvement into the case management systems lead to meeting the expectations of tuberculosis patients? Literature review
M. Drabo1, H. Ouedraogo2, R. Zerbo2, A. Frank1, J. B. Ouedraogo1, B. Dujardin2 and J. Macq2
1Institut de Recherche en Sciences de la Sante, Sante Publique, Ouagadougou, Burkina Faso; 2Université Libre de Bruxelles, ESP-Politiques et Systèmes de Santé, Bruxelles, Belgium

OBJECTIVES The tuberculosis burden is growing in many Sub-Saharan Africa, when the formal care supply systems face geographical, and sometimes cultural access problems for the served populations. This situation reinforced the interest for community involvement in tuberculosis control. This paper aims at reviewing the community participation experiences in the tuberculosis case management process in developing countries, the outcomes and the inadequacies in relation with tuberculosis patients’ expectations.

METHODS It is a review of the published literature, using a) a specialised search engine (Pubmed), b) the abstract book of the 37th Conference on Respiratory Health held in Paris and c) direct requests from authors through the web.

RESULTS Fifteen studies have been registered from African, Asian and South American countries. The participation of the community was implemented for similar reasons for the most of the sites, including the better access to care and/or the increasing in the cases detection, the compliance to treatment and cure rates. Usually, the participation approach is organized by health professionals, and standardized according to the level of the intervention. The published results show more the outcomes in terms of screening and treatment to the detriment of the quality of the process and the patient’s satisfaction. Still, screening and drug administration concern one side of the patients’ expectations, but also the solving of psychological and financial issues. So, it becomes interesting to understand the reason why an interest for the medical aspect of the tuberculosis to the detriment of its psychological aspect.

CONCLUSION Taking into account TB patients’ expectations, involves not only the reforms on the management of cares supply, but also behavioural changes at the level of care providers, and a larger material and psychological contribution from the people around the patient. Keywords: Tuberculosis; community involvement; patient expectations; health care delivery system; developing countries.

PA 81
Intra-household mosquito net use in Ethiopia, Ghana, Mali, Nigeria, Senegal, and Zambia: are nets being used? Who in the household uses them?
C. A. Baume1 and C. Mars2

OBJECTIVES In recent years there has been tremendous expansion in mosquito net ownership in Africa; however, expansion in net ownership will have an impact on malaria only if the nets are used and the most vulnerable household members are given priority for use. The purpose of the study is to examine intra-household net use: the percent of nets owned that are used, the percent of different household members sleeping under a net, the mean number of people under a net, what the sleeping group patterns are, whether there is childhood gender bias in net use, and the effect of baby net ownership on the use of hanging nets. Knowing the extent to which nets are used and who is using them is important for crafting more effective malaria control programs.

METHODS The data are from household surveys conducted in 2003/2004 in Ethiopia, Ghana, Mali, Nigeria, Senegal, and Zambia. In Nigeria, Senegal, and Zambia, the same survey was conducted in 2000, and comparisons are made to look at change over time. Respondents were women of reproductive age who were responsible for a child under five. The same sampling approach and instrument was used in each country, and where data was collected at two points in time, it was collected at the same time of year to control for seasonal effects.

RESULTS Across countries, priority is given to the most vulnerable; nets are most often used to cover children under five (especially those under two), and the mother. Adult males and children 5–14 are least likely to be under the net. Male and female under-fives are equally likely to be under a net. Nets cover 2–3 people in all countries except Nigeria, where they cover 1–2 people. In all countries, the mean number of people under a net is greater in rural than urban households. When a household owns a baby net, fewer people are likely to use the hanging net. A pregnant woman is now more likely to use the household net than she was in 2000. However, in all countries except Senegal, a sizeable minority of nets that are owned are not being used.

CONCLUSION In the countries surveyed, little effort needs to be expended on education regarding vulnerable groups. However, programs need to find out why people do not use the nets they own and devise ways to increase nightly use.
PA 82  
Screening for HIV and HCV infections among antenatal clinic attendees in Central Brazil  
Z. Costa¹, G. Machado¹, M. Avelino², C. Gomes Filho³, J. V. Macedo⁴,  
A. L. Minuzzi⁵, M. Turchi⁶ and C. Martelli⁷  
¹Institute of Tropical Medicine and Public Health/Federal University of Goiás – Brazil, Public Health Department, Goiânia, Brazil; ²Medical School, Federal University of Goiás, Goiânia, Brazil; ³Health State Secretariat of Goiás, Goiânia, Brazil; ⁴Associação de Pais e Amigos dos Excepcionais de Goiânia - APAE, Goiânia, Brazil  

OBJECTIVES To assess prevalence of HIV, HCV infections among women attending antenatal clinic (ANC) and risk factors associated with seropositivity.  

METHODS Screening for HIV and hepatitis C virus (HCV) infections is offered free of charge to pregnant women attending antenatal clinic (ANC) in the public health system in a large urban area in Central Brazil (≈1.7 million inhabitants) comprising the city of Goiânia and two surrounding municipalities, from 2003 through 2005. First screening was performed in dried blood spot onto filter paper (ELISA tests); HIV infection was confirmed by serology (ELISA) or Westernblot/Nested PCR; HCV infection detected by PCR technique. HIV and HCV prevalence were calculated. Prevalence ratio for HIV and HCV infections associated with ethnicity, gestational factors were evaluated by uni and multivariate analysis. Number needed to screen to prevent a vertical transmission was estimated taking into the account the parameters published by Agency for Healthcare Research and Quality (2005).  

RESULTS About 28 576 pregnant women attending public pre-natal care were screened; only 13 refused HIV testing. 95% participants were screened before 27 weeks gestation. Participants mean age was 23.9 years (SD = 5.6). 45.6% were first time pregnancy and 55% had normal delivery. The overall prevalence of antibodies anti-HIV was 0.13% with nine confirmed HIV infections per 10 000 screened. Black participants had 4.8% (IC 95% 1.4–16.7) fold risk of HIV infection compared to white/mixed race. The number needed to screen for one HIV vertical transmission ranged from 2 161 to 16 734. Prevalence of HCV infection was 0.15%, with increasing infection among women older than 30 years of age (P < 0.01). HCV genotype 1 was predominant.  

CONCLUSION The coverage and acceptability of the antenatal screening program for HIV infection was high in Central Brazil. Overall prevalence of HIV infection was similar than prevalence of HCV infection among ANC attendees. 5–14 HIV vertical transmissions per year could be prevented by this antenatal screening program. Financial support: Programa de Proteção a Gestante do Estado de Goiás/Secretaria de Estado de Saúde e APAE.  

PA 83  
Community involvement to reduce the malaria burden in pregnancy in Burkina Faso  
S. Gies¹, S. O. Coulibaly², K. Peeters³ and U. D’Alessandro⁴  
¹Parasitology, Prince Leopold Institute of Tropical Medicine, Antwerp, Antwerp, Belgium; ²ULB Sciences de la Santé, Université de Ouagadougou, Ouagadougou, Burkina Faso; ³Partners for Applied Social Sciences, PASS International, Tessenderlo, Belgium  

OBJECTIVES To evaluate the effectiveness of a health promotion campaign for intermittent preventive treatment with sulfadoxine-pyrimethamine (IPT/SP) targeted to pregnant women.  

METHODS In a rural health district in Burkina Faso, 12 health centres were randomly assigned to one of three study arms: IPT/SP with a community-based promotion campaign, IPT/SP alone or weekly chloroquine (standard national policy in 2003). Health messages and communication strategies were defined according to local knowledge and attitudes. Between April 2004 and February 2006, all primi- and secundigravidae were identified and followed until delivery. Yearly cross-sectional surveys on pregnant women (all parities) were conducted at the end of each rainy season. An anthropological study to evaluate the acceptance of IPT/SP and the perception of the promotional campaign was conducted in 2006.  

RESULTS Within the cohort of 2288 primi- and secundigravidae, the coverage of at least 3 antenatal clinic (ANC) visits was 62.3% in the IPT/SP arm with promotion, 42.3% in the IPT/SP alone and 45.8% in the weekly chloroquine arm (P < 0.001). Uptake of at least 2 SP doses was 69.6% in the IPT/SP arm with promotion against 48.2% in the SP alone arm (P < 0.001). The simpler intake of IPT/SP when compared to weekly CQ was perceived as an important advantage by both pregnant women and the health staff. Administration of the 2 doses of SP at the right time may be difficult because of the irregularity of ANC visits by the women and the inaccurate estimation of gestational age by the health staff. On busy days, observation of SP intake can be too demanding. Some women refuse directly observed intake of SP during Ramadan because of fear of vomiting and fatigue.  

CONCLUSION It is possible to increase the coverage of IPT/SP with a promotional campaign targeted to pregnant women. This would also increase ANC attendance.
PA 85
HIV-1 molecular epidemiology in São Tomé e Príncipe
I. Bonfim1, A. P. Carvalho2, A. V. Carvalho2, B. Sousa3, C. Palm4, J. Cabana3, A. Rosário5, P. Gomes5, J. Nina5, V. Rosário5 and R. Camacho1
1Instituto de Higiene e Medecina Tropical de Lisboa, Centro de Malária e outras Doencas Tropicais, Lisboa, Portugal; 2Hospital Egas Moniz, Laboratório de Virologia, Rua da Junqueira, Portugal; 3Ministério da Saúde, Gabinete do Ministro, Caixa Postal, São Tomé e Príncipe; 4Ministério da Saúde, PNLS, São Tomé, São Tomé e Príncipe; 5Instituto de Higiene e Medicina Tropical de Lisboa/Hospital Egas Moniz, Centro de Malária e outras Doencas Tropicais/Serviço de Medicina Tropical, Lisboa, Portugal

INTRODUCTION HIV-1 group M has a high genetic variability, with 9 Subtypes, 34 Circulant Recombinant Forms (CRFs) and numerous Unique Recombinant Forms (URFs) described so far. An impact on natural history, rates of vertical transmission, efficacy of diagnostic tests, therapy response and on the efficacy of a possible future vaccine, is a concern. São Tomé e Príncipe (STP) is a small archipelago country at the West Central African coast, with a moderate HIV endemicity. There is political will to address the HIV crisis, however there is also lack of comprehensive data on the large HIV diversity already found on preliminary studies (I Bonfim, B Sousa et al. (2006) Resistance to Antiretrovirals in Drug-Non HIV-1 Infected Patients in São Tomé e Príncipe (Abstract)). Rev Antivaral Therap 2,32; I Bonfim, A Rosário et al. (2006) HIV-1 Genetic Diversity in São Tomé e Príncipe (Abstract). Acta Parasitol Port 13, 108.

OBJECTIVES To study HIV-1 molecular epidemiology in patients from STP.

METHODS A total of 83 HIV-1 infected samples were collected from 2004 to 2006 at STP Health Centres. The entire protease, and codons 1–335 from reverse transcriptase were genotyped, using ViroSeq HIV-1 Genotyping Kit ver 2.0 (Abbott) and an automated sequencer (ABI 3100). Subtype was performed using the REGA subtyping tool; when the tool reported an unassigned subtype, sequences were edited and aligned with group M reference sequences available at Los Alamos database, using Bioedit and Clustal W, and then subtyped using Simplot and the PHYLIP package as described elsewhere.

RESULTS From the 83 sequences obtained, 36 were classified as CRF02_AG (43%), 12 as subtype A (11%) (4.4%), 3 as subtype C (4%), 4 as D (5%), 7 as F (sub-subtype F1) (8.4%), 3 as subtype H (4%), 7 as G (8.4%), 4 as CRF06_cpx (5%), 2 A/U (2.4%), 1 G/U (1%), 2 J (2.4%) and 2 CRF02_AG/U (2.4%).

CONCLUSION A high genetic variability was found in HIV-1 strains circulating in STP, probably reflecting several introductions of the virus in the country. This high variability must be taken in consideration when selecting diagnostic assays or drug therapy protocols, and may have a negative impact on the future use of a possible vaccine.

PA 86
Imported malaria in immigrants and travellers living in Valencia, Spain: a five-year study
A. Gil-Brusola1, E. Calabuig2, M. Narvaez3, J. Peman1, M. Salvest2, M. Gobernado4 and J. Lopez-Aldeguer2

1Department of Microbiology, University Hospital La Fe, Valencia, Spain; 2Infectious Diseases Unit, University Hospital La Fe, Valencia, Spain

OBJECTIVES Immigrants from endemic zones who live in Europe have the greatest risk of acquiring malaria during trips to their home countries, since they usually travel for longer periods of time and without prophylaxis. The number of Spanish travellers visiting malaria endemic areas, and the number of immigrants from endemic countries arriving in Valencia (Spain) are continuously increasing. However, little information about imported cases in Valencia is available. The aim of this study was to determine the demographic and clinical characteristics of malaria in our hospital.

METHODS An observational and descriptive study was performed between January 2002 and December 2006, collecting all patients that were diagnosed of malaria at a referral teaching hospital in Valencia, Spain. All patients with clinical symptoms coming from endemic areas were studied. A thin blood smear was examined in all of them. An antigen test was performed in samples collected from 2004 onwards. Demographic, clinical and outcome data were collected.

RESULTS Over the period studied, 63 episodes of malaria were diagnosed in 62 patients, median age 29 years (range 1–62 years). 59.7% were male. Most patients were African immigrants (71%) who had recently left their countries of origin or immigrants residing in Spain who had travelled to Africa for a short visit. 16.1% were Spanish travellers. The distribution of cases by species was: Plasmodium falciparum 76.2%; mixed infection by P. falciparum and P. vivax, 20.6%; mixed infection by P. falciparum and P. malariae, 1.6%; and one episode of P. vivax (1.6%). Clinical data were non-specific in the majority of episodes and the percentage of severe complications was low (3.2%). One death was reported in an Spanish woman.

CONCLUSION Our series shows that P. falciparum is the most frequently diagnosed species, followed by mixed infection with P. vivax. Africa is the continent from which most cases are imported and immigrants contribute 71% of all cases. Access to information on prevention and chemophylaxis should be available to all travellers, particularly immigrants visiting their countries of origin.

PA 87
Prevalence of Plasmodium falciparum pfmrd1 gene polymorphisms associated with chloroquine resistance in isolates from Iran

Medical Parasitology and Mycology, Tehran University of Medical Sciences, Tehran, Islamic Republic of Iran

At present drug-resistant malaria represents a major health care concern in countries where malaria is endemic. In these countries, therapy policies requires current data on resistance. The limitations of available in vivo and in vitro methods for monitoring resistance, molecular markers are used in many studies focusing on malaria drug resistance. In Iran Plasmodium falciparum resistance to chloroquine (CQ) has been documented in 1983 and has since gradually increased but little information exists on resistance-associated gene frequencies. In this study we describe the prevalence of single nucleotide polymorphisms (SNP) associated with chloroquine resistance in multidrug resistance, the gene that encoding the P-glycoprotein homologue 1 (Pgh1) protein of Plasmodium falciparum parasite. Pre-treatment blood from patients with uncomplicated but symptomatic P. falciparum infection was analyzed. Polymorphisms at codons N86Y, Y184F, S1034C,N1042D and D1246Y of the pfmdr1 gene were determined by polymerase chain reaction/restriction fragment length polymorphisms method. The result of this study showed that chloroquine-resistant Plasmodium falciparum needs to be monitored in the field for surveillance and effective malaria control strategies.
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PA 88
Anti-mosquito control measures available in Kinshasa, DR Congo
T. Bobanga and M. P. Mulumba
Service de Parasitologie, Université de Kinshasa, Kinshasa, Congo

The spread of *P. falciparum* to antimalarial drugs on the one hand, and that of insecticides resistance *Anopheles*, on the other, makes it difficult to control malaria in areas of perennial transmission. The insecticide Treated Net (ITN) occupies a central place in Roll Back Malaria Strategy. However, many people, cultural the acceptability, accessibility (in of cost) and lack of information about correct use of ITNs create major impediment to successful implementation of the strategy, without forgetting the effectiveness of selected insecticides, explain all the complexity of the malaria control problems.

OBJECTIVE To determine how most common anti-mosquito control measures available in Kinshasa.

METHODS A KAP survey (knowledge-attitude-practical) was carried out near a sample of 2.335 households of Kinshasa (1 household of 340). The most significant interactions between the apprehended factors were identified by use of the log-linear analysis, and the respective odds ratios were calculated.

RESULTS Insecticides were the most common anti-mosquito methods mentioned (50.8%), followed by the mosquito net (32.9%). In this economy, the ITN represented only 6.8%. Four factors showed a significant associated with ITN use. The geographic location (city center vs periphery), number of persons in the household, the knowledge of ITNs and the number of children<5 years old. Bed net usage was proportional to the degree of the mosquito nuisance, which was higher toward the center rather than at periphery where the malaria transmission is greatest.

CONCLUSION There is a role for ITN in the National Malaria Control Program. However, they remain under utilized in areas of highest transmission. Possible alternatives could be the insecticide treated curtain and indoor residual spraying which have no compliance issue.

PA 89
Peer health education for promoting knowledge and practice of malaria prevention among school children and their families
B. Muss Joo², A. Dawson², A. Palmer³, A. Dibba¹, S. Yehuenou¹, B. Devaney¹, C. Ocran¹, Y. B. Cheung¹, Y. Kasse⁵ and P. Milligan⁷
¹Centre for Innovation Against Malaria, Banjul, Gambia; ²Liverpool School of Tropical Medicine, Liverpool, UK; ³Nova Scotia Gambia Association, Banjul, Gambia; ⁴Medical Research Council Laboratories, Banjul, Gambia; ⁵London School of Hygiene and Tropical Medicine, Epidemiology and Population Health, London, UK

OBJECTIVES Health promotion in schools aims to improve the health and well being of students by empowering them with the knowledge, skills and confidence to take responsibility for their own health. We incorporated a malaria component into an established peer health education programme in schools in The Gambia, and evaluated its impact on knowledge attitudes and practice (KAP) of school students and their families using a cluster randomized design.

METHODS Students were encouraged to explain what they learned to their families, and we sought to evaluate whether the malaria messages were taken up by mothers of young children living in the same compound as the students. Evaluation endpoints were KAP among students, and among women, and the proportion of children under 5 years in the compound sleeping under a bednet. 12 school communities were randomized to receive the PHE programme immediately or after a delay of 6 months.

RESULTS Knowledge scores were high in women and school students in both intervention and control communities. After 10 weeks of intervention, practice scores among women, and bednet coverage, were higher in intervention communities ($P = 0.028$). The programme was introduced into some control schools before the 6 month evaluation period was completed. By 6 months, scores and net coverage in the control communities had increased and were similar to the intervention communities. Among students, practice scores were significantly higher in intervention communities after 6 months, but the difference was not significant at 10 weeks.

CONCLUSION School-based peer education programmes combined with outreach activities can improve practice of appropriate prevention and treatment seeking in the community. Education programmes in health promotion should be more widely evaluated.

Cysticercosis

PA 90
Establishing and implementing a Global Campaign to Combat Cysticercosis
A. L. Willingham and Bellagio ‘Global Campaign for Combating Cysticercosis’ Conference Groups
WHO/FAO Collaborating Center for Parasitic Zoonoses, Department of Veterinary Pathobiology, University of Copenhagen, Frederiksberg, Denmark

Conferences were held at the Rockefeller Foundation’s International Conference Center in Bellagio, Italy on ‘Establishing a Global Program for Combating Cysticercosis’ and ‘Implementing a Global Program for Combating Cysticercosis’ in September 2004 and September 2006, respectively. The conferences built on outcomes of the International Action Planning Workshop on Cysticercosis-Taeniosis held in Arusha, Tanzania in August 2002 which emphasized the need and instigated the international initiative for establishing a global-level ‘driving force’ for combating cysticercosis.

OBJECTIVES The overall objective of convening the conferences was to improve human health and well-being, smallholder pig production, the domestic food supply and export opportunities for pork in endemic countries by further facilitating organization of a global campaign for combating the burden of cysticercosis.

METHODS The conferences were organised by the WHO/FAO Collaborating Center for Research and Training on Parasitic Zoonoses and DBL – Institute for Health Research and Development with the Rockefeller Foundation providing the venue for both meetings. Due to Bellagio Conference Center restrictions a maximum of 23 people were invited to participate in each meeting. Participants were selected with regard to equitable representation of different geographical regions, genders and professional backgrounds. The involvement of persons from different sectors (e.g. health, agriculture, industry, etc.) with various areas of expertise and experience promoted an integrated approach to the issue.

Emphasis of the meetings was on inclusion of participants involved in conducting research and/or control activities on cysticercosis/taeniosis in endemic countries. As the conferences were not intended as technical meetings emphasis was not placed on specific tools for surveillance, prevention and control of cysticercosis but rather on general needs and utilization of such tools. Several international organizations (e.g. WHO, FAO, ILRI, GALVmed) were represented at the conferences.
RESULTS An international consensus was reached for establishing and implementing a global campaign for combating the burden of cysticercosis and a Global Action Plan (GAP) for implementing and monitoring such a campaign.

CONCLUSIONS The Global Campaign should serve as a platform for advocacy and networking efforts with high priority on establishing and supporting regional cysticercosis working groups. These regional working groups would then be responsible for planning, implementing, monitoring and evaluating activities regarding research, training, surveillance, prevention and control based on regional needs and priorities. Establishment/strengthening of cysticercosis working groups for the endemic regions (i.e. The Americas, Eastern and Southern Africa, Western and Central Africa, South and Southeast Asia) was deemed essential for accomplishing the campaign’s long term goals.

PA 91
Cysticercosis in Portugal: is there a probability for re-emergence?
M. Vilhena1, J. Torgal2 and S. Dias3
1Instituto de Ciências Agrárias Mediterrâneas, Évora, Portugal; 2Instituto de Higiene e Medicina Tropical, Lisboa, Portugal; 3Faculdade de Ciências Médicas, Lisboa, Portugal

INTRODUCTION Cysticercosis is the result of infection with the larval, metacestode stage of the zoonotic pork tapeworm Taenia solium. Cysticercosis is transmitted to humans via ingestion of T. solium eggs from a human tapeworm carrier directly through the faecal-oral route or by contaminated food or water. The availability of new serological and imaging diagnostic techniques has revealed the existence of new cases including in countries such as Portugal where the disease was considered eliminated and it has not been mandatory to report cases for surveillance and control. In Portugal these new cases have hitherto been assumed to be imported cases.

OBJECTIVES To determine the prevalence and origin of Portuguese cases of human cysticercosis in order to establish the geographic distribution of the disease in the country and assess whether the cases detected are imported or autochthonous.

METHODS We analysed the information received from all public Portuguese hospitals through the Ministry of Health’s data base ‘Grupos de Diagnóstico Homogéneos’, concerning the reasons for inpatient hospitalisation.

RESULTS Between 1993 and 2004, there were 1120 diagnostics of cysticercosis (586 belonging men and 354 belonging women) in the Portuguese hospitals. Of these 14.7% (165) were <24 years of age. While there are indications that many of these diagnoses in the larger cities were immigrants there is evidence indicating autochthonous cases in the northern part of the country. This northern area of concern (Trás os Montes) as well the Alentejo area rear pigs/pork under familiar and free-ranging conditions and are famous for their pork- butcher’s shop, which could provide the factors to enable the complete life cycle of T. solium to establish resulting in an endemic situation.

CONCLUSION Although there are a significant number of imported/travel-related cysticercosis cases, Portugal may also have an endemic focus of the disease which needs to be further investigated. We provide information concerning the geographic distribution of the diagnosed cysticercosis cases.

PA 92
Role of the cytokines and chemokines in the regulation of innate immunity in dengue virus infection
B. Sierra1, K. Vogt2, A. B. Perez1, G. Garcia3, S. Kathrin4, E. Aguirre5, F. Kern2, M. Alvarez6, V. Hans-Dieter7 and M. G. Guzman8
1Tropical Medicine Institute Pedro Kouri, Virology, Havana, Cuba; 4Institute for Medical Immunology, Berlin, Germany

INTRODUCTION In contrast to other countries, characterized by the co-circulation of several serotypes, Cuba represents a unique scenario, with known clinically and serological dengue markers, to perform studies that help to clarify the role of various cytokines and chemokines in the pathogenesis of DHF.

OBJECTIVES The aim of this study was to analyze the levels of IL-8, RANTES, MIP-1 alfa, MCP-1 y CCR-1, IL-12p40, TNF alfa, IL-6, IL-1 alfa and IL-1 beta in the course of a 24 hours ex vivoinfection of peripheral blood mononuclear cells (PBMC) from dengue non-immune individuals.

METHODS PBMC were isolated and ex vivo stimulated by dengue infectious virus particles for 24 h. Supernatant were collected for ELISA analysis of IL6, IL-8; and RNA was prepared from cells for real-time RT-PCR expression of IL-1 beta, MIP-1 alfa, CCR1, MCP-1 and Rantes.

RESULTS In this study we demonstrated the strong inflammatory cell activation induced in peripheral blood mononuclear cell after 24 culture with dengue virus.

CONCLUSION Given the fact that intensity of DV replication during the early times of infection could determine clinical outcomes, which ranges from febrile illness (DF) to life-threatening disease (DHF), our results give insights about the impact of DV infection on innate immunity, the earliest defence against microbial infection, that also profoundly regulates the adaptive T-B immune responses.

PA 93
Gene polymorphisms of cytokines involved in the pathogenesis of dengue virus infection
A. B. Perez1, B. Sierra1, N. Babel2, G. Garcia3, E. Aguirre1, G. Andrade1, Y. Medina1, H.-D. Volk1 and M. G. Guzman2
1Tropical Medicine Institute Pedro Kouri, Virology, Havana, Cuba; 2Institute for Medical Immunology, Berlin, Germany; 3Tropical Medicine Institute, Virology, Havana, Cuba

INTRODUCTION Host genetic factors may be relevant and predispose some individuals to the severe dengue disease. The unique history of dengue outbreaks in Cuba is extremely advantageous for genetic studies of dengue disease resistance or susceptibility.

OBJECTIVES To study the -1082IL-10, -819IL10, -592IL-10 and -308TNF-alpha gene single nucleotide polymorphisms (SNP) in individuals who suffered different clinical pictures or subclinical form of dengue virus infection.

METHODS The -1082IL-10, -819IL10, -592IL-10 and -308TNF-alpha gene single nucleotide polymorphisms (SNP) were studied by polymerase chain reaction-sequence specific primer (PCR-SSP).

RESULTS Significant association of the tumor necrosis factor-alpha (-308) GG genotype was found when comparing asymptomatic and dengue haemorrhagic fever cases. No associations of interleukin-10 polymorphisms with any studied groups were detected. We failed to observe significant differences in cytokine genotype distribution between dengue fever and dengue haemorrhagic fever patients.
CONCLUSION Our study give insights about the predictive value of cytokine genotype for the development of clinical output of dengue infection.

PA 94
Contribution of endothelial cell transcriptional analysis to the understanding of endothelial dysfunction occurring in dengue infection
P. Coumont-Paris1, C. Sapet1, C. Peyrefitte1, S. Devignot1, D. Puthier2, F. Joly3, C. Nguyen3, H. Puggelli4 and H. Tolou1
1Institut de Médecine Tropicale du Service de Santé des Armées, Unité de Virologie Tropicale, Marseille Armées, France; 2TAGC-ERM206, Marseille, France

Dengue shock syndrome (DSS) resulting from massive but transient vascular leakage, is the major life-threatening clinical form in severe dengue infections. Improving the knowledge of pathophysiologic mechanisms leading to vascular leakage, is a key to identify predictive markers of severe dengue or in the development of therapeutic approaches to prevent those clinical forms. Moreover, dengue is not only an arboviral infection of major importance in the world, but is also a model of interest to investigate the molecular and the cellular mechanisms underlying the vascular dysfunction associated to several viral hemorrhagic fevers. In the absence of relevant animal models, we attempted to investigate the dysfunction occurring in human endothelial cells in response to dengue infection, using an in vitro model based on microvascular human cell lines from different vascular beds. Previous studies by our group showed that direct infection of such microvascular cells by unadapted DEN-2 virus, induces some phenotypic and functional changes. Such an approach was completed by analysing the transcriptional profile of those cells in response to infection. This study allowed us to identify a cluster of genes of which expression levels were specifically modulated in the course of DEN-2 infection. Quantitative RT-PCR experiments confirmed the results obtained in the transcribed gene clustering analysis, identifying not only genes involved in innate cell defense mechanisms but also genes related to other functions currently under investigation. The interest of such approaches to analyse the host cell response to pathogens is discussed.

PA 95
Immunocomplex fraction of sera from dengue fever and dengue hemorrhagic fever patients mediates cellular citotoxicity
V Garcia, B. Sierra, A. Perez, Y. Medina, E. Aguirre, L. Morier and M. Guzman
Institute for tropical Medicine Pedro Kouri, Virology, Havana, Cuba

OBJECTIVES In our work we have measured the capacity of dengue antibody present in secondarily infected D2 individual with different clinical pictures (DF or DHF) of mediating ADCC by testing the releasing of IFN gamma as other cytotoxic function of NK cells.

METHODS PBMC from non immune dengue donors, used as source of NK cells, were cultured in presence of D2 and D1 infected C636 cells, used as target cells, and of the immunocomplex fraction or the free IgGs of sera of D2 infected individuals, collected in two moments of the acute dengue disease (1 and 7 days after symptoms debut).

RESULTS ADCC activity was detected in the immunocomplex fraction of sera. Free IgGs not showed ADCC activity. Immunocomplex fraction of sera of DHF patients showed an increasing index of ADCC activity from day 1 until day 7 against D1 and D2 infected C636 cells. On the contrary, DF cases described a decreasing index of ADCC.

CONCLUSION The declining detection of ADCC mediating antibodies in DF cases in vitro could suggest and expression of its possible in vivo consumption leading to their depletion in the serum. Considering this, ADCC function could be associated to a protective capacity against the development of DHF.

PA 96
Cost of a large scale vertical control programme to control Aedes aegypti and prevent dengue
A. Baly1, K. Rodriguez3, M. E. Toledo1, J. R. Benitez2, M. Rodriguez3, V. Vanlerbergh2, M. Boelaert2 and P. Van der Stuyf2
1Institute of Tropical Medicine Pedro Kouri, Ciudad de La Habana, Cuba; 2Unidad Provincial de Vigilancia y Lucha Antivectorial, Guantanamo, Cuba; 3Institute of Tropical Medicine Antwerpen, Antwerpen, Belgium

OBJECTIVES Information on the cost of large scale vertical control programmes to control Aedes aegypti is limited. We conducted an economic appraisal of such programme with high level of coverage (>95%) which has achieved very low vector infestation levels in a setting with low prevalence of Dengue.

METHODS Costs of the programme were calculated monthly for the year 2006 year for covering whole city of Guantanamo, Cuba. We collected cost and entomological data using interviews, direct observations and documentary revisions including health information system.

RESULTS The programme is labor intensive. The most important cost are fixed ones in a form of salaries which varies from 30% to 80% of the total cost depending on the level of the health services organization. These costs can have small rise in presence of dengue cases for a short periods of time. The rest of the costs are variables in a form of insecticides, fuel and lubricants. These can rise sharply in a presence of dengue cases. The total cost per inhabitant to keep the house index below 1% was in average between 10 USD and 23 USD depending on the exchange rate we used. This figure can be reduced to 8 USD (20 USD), for example, if the revision of houses reduces from two to one time in a month.

CONCLUSION Because the high coverage, the information on the volume of resource use, breakdown and estimation of the costs can be useful for the health decision making in terms of the resource allocation for the vector control programmes of the other countries.

PA 97
Getting research into practice: facilitators and effectiveness of vector control program for dengue prevention in Cuba
M. E. Toledo1, V. Vanlerbergh2, D. Perez1, J. R. Benitez2, M. Rodriguez3, D. Gomez1, A. Baly1 and P. Van der Stuyf2
1Institute of Tropical Medicine Pedro Kouri, Ciudad de La Habana, Cuba; 2Institute of Tropical Medicine Antwerpen, Antwerpen, Belgium; 3Unidad Provincial de Vigilancia y Lucha Antivectorial, Guantanamo, Cuba; 4Centro Provincial de Higiene y Epidemiologia, Guantanamo, Cuba

OBJECTIVES Acceleration of the use of research’s evidence in policy development, practice and community action is a key challenge in order to strengthen the health systems in the fight against emerging and re emerging diseases. We show the main results of the process of research translation of the community based vector control strategy into practice of the vector control program for dengue prevention in Guantanamo municipality.

METHODS The research findings of two case studies (quasi experimental and randomized control trials) conducted in two provinces of Cuba are synthesized into evidence and inserting in the routine practice of the vector control program at municipality level. We evaluated the compliance of the main component of the
community based control strategy with routine practice one year after the implementation. We identified the facilitators of this process, changes in entomological indicators and community behaviours using qualitative and quantitative techniques.

RESULTS The main components of the new practice are: community organizing, institutionalization of community surveillance of environmental risk and febrile syndromes, intersectoral coordination and social communication guided to achieve behavioural changes. The facilitators of this process are: the relative advantage, the compatibility with vertical control program, the observably and credibility of the results and the leadership of policy makers. House indices were reduced from 0.5 to 0.02. The breeding sites located inside the houses decreased from 70% to 30%.

The percentage of Aedes aegypti loci detected by quality control, decreased from 40% to 5%. The satisfaction of vector control workers and the community acceptability was verified.

CONCLUSIONS This study demonstrated that research can help to produce better decision on practice design and implementation. The recognition of the facilitators and barriers are key elements for reducing the time of translation the research to and the strengthening of the health practice.

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PA 98

Imported dengue hemorrhagic fever case presenting as acalculous cholecystitis

A. Wroczynska, 1 A. Kuna, 2 W. Nahorski 1 and I. Felczak-Korzybska 2

Department of Tropical Parasitology, Interfaculty Institute of Maritime and Tropical Medicine, Clinic of Tropical and Parasitic Diseases, Gdynia, Poland; 1Academic Centre of Maritime and Tropical Medicine, Clinic of Tropical and Parasitic Diseases, Gdynia, Poland; 2Interfaculty Institute of Maritime and Tropical Medicine, Clinic of Tropical and Parasitic Diseases, Gdynia, Poland

Dengue fever (DF) is a mosquito-borne viral disease, endemic in large areas of tropical countries, including South America. Typically it presents as a mild febrile illness or as a hemorrhagic fever with or without shock, but unusual clinical manifestations can occasionally occur. Abdominal complications of DF include fulminant hepatitis and acute pancreatitis. Acalculus cholecystitis, however, has been rarely reported in course of DF so far. The aim of this presentation is to describe the case of acalculous cholecystitis in febrile adult patient admitted to the Clinic of Tropical and Parasitic Diseases after return from Brasil. Dengue haemorrhagic fever (DHF) was suspected basing on patient’s history, low platelet count, presence of petechiae and nausea with abnormalities in laboratory liver function tests. This diagnosis was confirmed first by rapid immunochromatographic test and later with the use of enzyme-linked immunosorbent assay. Ultrasound revealed the presence of a thickened gall-bladder wall up to 8 mm with minor ascites. Due to recrudescence fever and progression of abdominal symptoms, surgical treatment was introduced. Intraoperative findings, however, revealed abdominal lymphadenopathy, but normal gallbladder. Thus, no cholecystectomy was performed. Postoperative period remained uncomplicated and the patient recovered with no recurrence of symptoms. Acalculus cholecystitis has never been extensively investigated in DF patients. Nevertheless, some studies have recently reported gall bladder involvement in up to 7.6–52% of DF cases. Pathology of this complication of DF is unknown. Conventional treatment for acalculous cholecystitis of other etiology is surgical removal of the gallbladder. In DHF, a risk of postoperative bleeding should be always regarded.

Treatment options for acalculous cholecystitis in DF are discussed in this study.

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PA 99

Molecular characterization of dengue viruses in 2006 outbreak in Delhi, India

H. S. Chahar, P. Bharaj, L. Dar and S. Broor

All India Institute of Medical Sciences, Microbiology, New Delhi, India

OBJECTIVES Dengue virus infection is an acute viral disease that has recently taken endemic proportion in India caused by any of the four virus serotypes (DEN-1, DEN-2, DEN-3, and DEN-4). There was a major dengue outbreak in northern India in and around Delhi in June–November 2006 after a number of sporadic cases in 2004 and 2005. We report the molecular and epidemiological findings of this outbreak by RT-PCR.

METHODS A total of 69 acute phase serum samples were deposited on ice to the virology laboratory for virus detection and characterization by RT-PCR. The presence of dengue virus RNA was done by a published multiplex RT-PCR (Lanciotti et al. 1992.) assay.

RESULTS The molecular analysis of 69 suspected serum samples revealed 69.5% positivity. Although all four serotypes were found to be circulating during this outbreak, DEN-3 serotype dominated the outbreak followed by DEN-1. The analysis also revealed that the outbreak had maximum number of cases occurring during rainy months and subsided with onset of winter months. More males than females were affected and the positive cases were concentrated in the 20–30 year age group. We have closely monitored dengue outbreaks in and around Delhi for the past 9 years and observed that different serotypes pre-dominated different outbreaks. The trend has shifted from DEN-2 dominating in 1996 to DEN-3 in 2003 and 2006 with both DEN-1 and DEN-3 co-circulating in sporadic cases of 2004 and 2005.

CONCLUSION The 69.5% positivity and increasing trend of co-circulation of all four dengue virus serotypes suggests that Delhi is becoming a hyperendemic state from an endemic one. Co-circulation of different dengue virus serotypes is being reported for the first time as detected by RT-PCR from one outbreak. The factors that influence spread of dengue virus infection need to be monitored carefully as this will help to undertake effective control and management strategies at the earliest.

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PA 100

High efficacy of a pediculicide based on dimeticone in a population with a high intensity of infestation: a randomized controlled trial

J. Heukelbach 1, D. Pilger 2, F. Araujo Sales de Oliveira 3, A. Khakban 4, L. Ariza 5 and H. Feldmeier 6

1School of Medicine, Federal University of Ceará, Department of Community Health, Fortaleza, Brazil; 2Charité – University of Medicine, Campus Benjamin Franklin, Institute for Microbiology and Hygiene, Berlin, Germany; 3Federal University of Ceará, Doutorado em Ciências Médicas, Fortaleza, Brazil; 4Mandacaru Foundation, Fortaleza, Brazil

OBJECTIVES To assess the efficacy of a product based on the silicon oil dimeticone against head lice infestation, as compared to permethrin.

METHODS We conducted a randomized, controlled, observer blinded clinical trial in children (5–15 years) from a resource-poor community in Fortaleza, Brazil. A dimeticone-based product identical to NVDA® l.w. was compared to a product containing 1% permethrin (Kwell®). To minimize reinfestation during the trial, study participants were transferred to a resort outside the endemic area where treatment and monitoring occurred. The participants were treated topically on days 1 and 8. Visual inspection was done to detect head lice before treatment, and wet combing were
performed on days 2 and 9. Clinical inspection included the presence of erythema, papules, excoriations, eczema, secondary infection and of enlarged cervical or retro-aural lymph nodes. Degree of itching was assessed daily based on an ordinal visual analogue scale, and cosmetic acceptability was assessed using an ordinal scale (including smell, irritation of scalp, cosmetic changes of hair and changes in combing). Major outcome measures were the presence of viable head lice on days 2 and 9, and the reduction of clinical morbidity.

RESULTS In total, 145 individuals (73 in the dimeticone group; 72 in the permethrin group) were included in data analysis. Sex and age distribution, intensity of infestation before treatment and length of hair did not differ between both groups. Overall cure rates (defined as the complete absence of active lice and lice with major vital signs) were: day 2 – dimeticone 94.5% and permethrin 66.7% (P < 0.0001); day 9 – dimeticone 97.2% and permethrin 67.6% (P < 0.0001). Itching was reduced similarly in both groups. At day 9, cosmetic acceptability was significantly better in the dimeticone group as compared to the permethrin group (P = 0.01). Only one possibly related adverse event occurred, in the permethrin group.

CONCLUSION NYDA 1 L is a safe and highly efficacious pediculicide in a population with a high intensity of infestation. Due to its probable mode of action (inhibition of oxygen and water exchange in the spiracles of the lice), the development of resistance is unlikely.

PA 101
A rapid assessment method for estimating the prevalence and severity of tungiasis in endemic communities in Brazil
L. Ariza 1, J. Heukelbach 1, A. Jackson 1, T. Wilcke 1, M. Gomide 1, and H. Feldmeier 1
1 Federal University of Ceara, Doutorado em Ciências Médicas, Fortaleza, Brazil; 2 School of Medicine, Federal University of Ceara, Department of Community Health, Fortaleza, Brazil; 3 Charité – University of Medicine, Campus Benjamin Franklin, Institute for Microbiology and Hygiene, Berlin, Germany; 4 Federal University of Rio de Janeiro, Instituto de Estudos em Saúde Coletiva, Rio de Janeiro, Brazil

OBJECTIVES To develop a rapid and accurate method for the estimation of the prevalence and severity of tungiasis (sand flea disease) in affected communities.

METHODS We analyzed data from eight surveys realized between 2001 and 2003 in three distinct communities in northeast Brazil: a fishing community and an urban slum in Ceará State, and a rural community in Alagoas State. In all surveys, representative samples of the populations were examined clinically for the presence of tungiasis. Lesions were counted, staged, and the exact topographic localizations were documented. The elaboration of a rapid assessment method (RAM) was based on the prevalence of tungiasis on six specific topographic localizations on the feet, as compared to the overall prevalence. Prevalence of tungiasis and severe tungiasis was estimated using linear regression analysis. The R^2 values and relative errors were calculated to identify the most accurate RAM.

RESULTS Prevalence of tungiasis varied between 21.1% and 54.4% in the eight surveys. The presence of tungiasis on periungueal sites of the toes was the topographic localization resulting in the most accurate estimation of the prevalence (R^2 = 97%; P < 0.0001, Figure). The equation: (estimated overall prevalence) = 1.17 × (prevalence on periungueal sites) + 3.7 very accurately predicted the true tungiasis prevalence (relative errors all <11.3%). Moderate and severe tungiasis defined as the presence of >10 or >20 sand flea lesions was also predicted accurately using the respective equations (R^2 = 75% and P = 0.006; R^2 = 68% and P = 0.01, respectively).

CONCLUSION The identification of periungueal lesions on the toes can be used to estimate accurately the true prevalence of tungiasis in a community, as well as the prevalence of severe tungiasis. As morbidity is positively associated with the intensity of infestation, the RAM can also be applied to appraise the severity of disease in a community. In a few seconds, both toes of an individual can be inspected by paramedics for the mere presence of any tungiasis lesions, with minimally disturbing the affected individuals. The RAM will help to plan and monitor control measures aiming at the reduction of tungiasis in affected communities.

PA 102
Tropical pathology in the field: statistics of dermatological consultation in the tropic
J. R. Gómez Echevarria 1 and F. Moll 2
1 Fontilles Association, Vall de Lagoa (Alicante), Spain; 2 Fontilles, Alicante, Spain

OBJECTIVES The communication tries to enumerate the different tropical dermatological diseases diagnosed during the development of an active leprosy detection campaign placed in 25 settlements of 3 Districts of Equatorial Guinea.

METHODS In a place adapted with a good visibility, 975 individuals were evaluated (47% men, 53% women, aged from 0–4: 23%, 5–14: 19%, 15–24: 25%, 25–64: 31% and >65 years: 2%). The evaluation was carried out in a clinical manner for everyone who voluntarily reported to the consultation. The entire body surface was examined in all cases. The final aim of the campaign was to corroborate the results obtained in the daily work of the National Program Leprosy Control.

RESULTS - Only 20% of the population who was evaluated did not present dermatological pathology. The more frequently observed diseases were: scabies (72%), pediculosis (80%), pityriasis versicolor (23%), tinea capitis (15%), candidiasis (4%), dermatosis viral (1%), pyodermas and folliculitis (3%), pityriasis alba (6%), vitiligo (1%), keloids (9%) and tropical ulcers (2%).

CONCLUSION The tropical dermatological diseases constitute an important percentage of the daily consultations evaluated on the area. The infectious-contagious dermatological illness are extremely frequent in these communities. Since the work was done as part of an active campaign searching for newly diagnosed leprosy cases, we can conclude that this disease does not constitute an important public health problem in Equatorial Guinea and the information that we obtained correlated with the information presented in the work from the National Program.
Diagnostics

PA 103 Fine-needle aspiration of enlarged lymph nodes, in the absence of TB culture facilities adds specificity and sensitivity to standard methods in detecting lymph node tuberculosis in Ethiopia

R. Iwnetu1 and J. van den Hombergh2
1AHRI, Addis Ababa, Ethiopia; 2KIT, Development Policy and Practice, Amsterdam, Netherlands

OBJECTIVES In Ethiopia, with 120 000 detected TB patients in 2005 and an HIV prevalence of 4.4% among adults, the proportion of extrapulmonary TB among all TB patients detected and treated is more than one third, of whom the majority are diagnosed as Lymph Node Tuberculosis (LNTB). Given these data and the high prevalence of M. bovis among cattle in Ethiopia, a study was carried out to establish the comparative and combined sensitivity of various diagnostic tools for LNTB against a standard of mycobacterial culture among patients clinically diagnosed with LNTB.

METHODS Four health facilities were selected and 150 consecutive patients 5–65 years old, presenting with enlarged lymphnodes and being registered for treatment of LNTB following the national diagnostic algorithm were enrolled. A questionnaire was completed. Fine Needle Aspiration (FNA) and full excision biopsy was carried out, examined macro- and microscopically, stained for ZN smear and transported for LJ culture and PCR.

RESULTS Out of 150 patients, 117 (78%) were confirmed LNTB. PCR identified M. tuberculosis in all culture-positive specimens (100% sensitivity, 83% specificity). M. bovis was not identified in any. Of all patients 21% were HIV-positive, vs 24% of 117 culture proven LNTB patients. Ziehl-Neelsen (ZN) staining of the 117 FNA and biopsy specimens detected acid fast bacilli (AFB) in 32% and 27% respectively. FNA cytology (FNAC) and histopathology detected 88 (75%) and 105 (97%) of the 117 culture proven LNTB patients respectively. Macroscopic cæsation was found in 79 (68%) of excised nodes and 78 (67%) of the fine needle aspirates. The presence of cæsation was associated with LNTB (P = 0.002). The association between HIV and urban residence (P = 0.002), as well as female gender (P = 0.006) in proven LNTB patients was significant. The combination of macroscopic examination, cytology and ZN-staining of FNA materials detected 112 (96%) of the proven LNTB patients.

<table>
<thead>
<tr>
<th>Laboratory methods</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ziehl-Neelsen FNA</td>
<td>34</td>
<td>91</td>
<td>93</td>
<td>29</td>
</tr>
<tr>
<td>Ziehl-Neelsen Biopsy</td>
<td>29</td>
<td>86</td>
<td>86</td>
<td>27</td>
</tr>
<tr>
<td>Macroscopic</td>
<td>67</td>
<td>64</td>
<td>88</td>
<td>34</td>
</tr>
<tr>
<td>Examination of FNA</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Macroscopic</td>
<td>68</td>
<td>63</td>
<td>88</td>
<td>34</td>
</tr>
<tr>
<td>Examination of Biopsy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FNAC</td>
<td>76</td>
<td>88</td>
<td>96</td>
<td>52</td>
</tr>
<tr>
<td>Histopathology</td>
<td>92</td>
<td>88</td>
<td>97</td>
<td>71</td>
</tr>
</tbody>
</table>

CONCLUSION The specificity of this algorithm for LNTB in field conditions was 78% and may contribute to unnecessary TB treatment for a substantial number of patients. M. bovis does not appear to be the underlying cause of lymphnode enlargement. Adding macro- and microscopic examination of FNA to the current algorithm will increase its specificity.

PA 104 Symptoms indicative of gynecological S. haematobium - implications for syndromic protocols? A study in rural Zimbabwean women

E. Kjetland1, E. N. Kurewa2, P. D. Ndulug1, E. Goma1, T. Mdulula1, N. Mdz2, L. Gwanzura3, P. R. Mason4, L. Sandvik5, H. Friis6 and S. G. Gundersen7
1Center for Imported and Tropical Diseases, Ullevaal University Hospital, University of Oslo, Oslo, Norway; 2National Institute for Health Research - Blair Research Institute, Harare, Zimbabwe; 3College of Health Sciences, University of Zimbabwe, Harare, Zimbabwe; 4Biomedical Research and Training Institute, Harare, Zimbabwe; 5Center for Clinical Research, Ulleval University Hospital, Oslo, Norway; 6Department of Human Nutrition, University of Copenhagen, Copenhagen, Denmark; 7Research Unit, Sorlandet Hospital, and Agder University College, Kristiansand, Norway

Schistosomiasis affects 1 in 30 people worldwide, most of whom are in Africa. In adults genital schistosomiasis is at least as common as urinary schistosomiasis. The populations do not completely overlap. As has been reported by us previously gynaecological S. haematobium ova was the most important predictor for mucosal sandy patches and mucosal bleeding in an area in rural Zimbabwe. Genital schistosomiasis may be the most common mucosal lesion in certain parts of Africa. However the diagnostic methods are either invasive and cannot be used routinely, or too high-tech and/or costly for most endemic areas. There is increasing evidence that STDs may provide points of entry for HIV transmission. Moreover we have previously shown a 3-fold higher HIV-prevalence in women with gynaecological schistosomiasis.

OBJECTIVES This study sought to divulge if subjective symptoms and low-resource investigations can be used to determine if women have genital schistosomiasis.

METHODS A cross-sectional study was performed on permanently resident women between the ages of 20 and 49 in rural Zimbabwe, assessing history, clinical, and laboratory investigations for S. haematobium and STDs.

RESULTS Current regular use of the river, and childhood water body contact were significantly associated with the presence of sandy patches. Women with sandy patches described their discharge as smelly (P = 0.025), yellow (P = 0.003), and they had genital itch (P = 0.048). However urinary schistosomiasis alone was not associated with genital tract symptoms.

CONCLUSION Abnormal discharge is an unspecific symptom and may hence be indicative but not conclusive of gynaecological schistosomiasis. Some schisto-endemic areas are using a syndromic protocol for the management of vaginal discharge. We suggest the addition of praziquantel into the protocol should be considered. Praziquantel may be a possible intervention against HIV-transmission.

PA 105 Validation of the lacrimal specific secretory anti-T. gondii IgA test in patient with active uveitis presumably due to Toxoplasma gondii

M. I. Lynch1, L. F. Lynch1, E. Malagueño2, S. Ferreira3 and F. Orféu3
1Universidade Federal de Pernambuco, Ophthalmology, Recife, Brazil; 2Universidad Federal de Minas Gerais, Ophthalmology, Belo Horizonte, Brazil

OBJECTIVES To verify the validation of Lacrimal Specific Secretory anti-T.gondii IgA Test in Patient with Active Uveitis Presumably Due to Toxoplasma gondii.
METHODS A total of 156 patients with active posterior uveitis were analysed, 82 with active uveitis presumably due to Toxoplasma gondii (with clinical gold standard pattern) and 74 with others uveitis rather than toxoplastic etiology. All were tested to lacrimal specific secretary anti-T.gondii IgA with ELISA method. The study was double-blind.

RESULTS Where the two groups were analysed the IgA anti-T.gondii test show a sensibility of 63.9% (IC 95%: 54.5–75.4), specificity of 71.6% (IC 95%: 59.8–81.2), positive predictive value of 72% (IC 95%: 60.3–81.5), negative predictive value of 65.4% (IC 95%: 54–75.4), positive likelihood ratio of 2.33 and negative likelihood ratio of 0.49. The reactivity rate of IgA test was higher in the toxoplastic uveitis. \( P = 0.004 \).

CONCLUSION The results show that the studied test is valid for the differential diagnosis of uveitis due to Toxoplasma gondii.

Diarrhoea

PA 106

Occurrence of Aeromonas bacterium and heterotrophic bacteria in Isfahan's drinking water distribution system in summer

S. Dobaradaran, B. Bina and B. N. Isfahania
Boushehr University of Medical Sciences, Tehran University of Medical Sciences, Environmental Health Engineering, Tehran, Iran, Islamic Republic of Iran

OBJECTIVES Aeromonas is one of the gram-negative, non spore-forming, rod-shaped, facultative anaerobic and opportunistic bacteria that can cause systematic infections, lesion and diarrhoea in human. Fairly high bacterial population in distribution system in not only considerable in respect of affecting consumer health but also it makes difficult to find coliform bacterium indicator. So, the relationship between Aeromonas and heterotrophic bacteria growth with pH, temperature, turbidity, free residual chlorine and Do was measured in this study.

METHODS ADA- V media was used in presumptive stage to count Aeromonas bacteria for the first time in Iran on the basis of 1605 E. coli (2001) method and used oxidase tests, trehalose fermentation and indol test in confirmative stage. R2A media was used to count HPC bacteria and other factors measured on the basis of standards.

RESULTS The results showed that positive cases of Aeromonas bacteria and HPC increase in higher temperature and turbidity and lower pH. In contrast, positive cases of Aeromonas bacteria and HPC decrease while free residual chlorine and Do increase.

CONCLUSION It was not seen any positive case of Aeromonas in higher than 0.2 mg/l concentration of free residual chlorine.

PA 107

Persistent diarrhoea in Iranian children 2006–07

N. Arjmand1, B. Noorinayer1, F. Jafari1, E. Nazemalhoseini1, F. Mola2, M. A. Pourhoseingholi1 and M. R. Zali1
1Research Center for Gastroenterology and Liver Diseases, Shabedeh Behesti University of Medical Science, The National Research Department of Foodborne Diseases, Tehran, Iran, Islamic Republic of Iran; 2Mofid Hospital, Gastroenterology Ward, Tehran, Iran, Islamic Republic of Iran

OBJECTIVES To identify microbial etiology and some characteristics of Persistent Diarrhoea (PD) in a sample of Iranian children.

METHODS From June 2006 to January 2007, 256 children aged less than 12 years old hospitalized with acute diarrhoea in a referral pediatric hospital in Tehran, Iran were followed prospectively until resolution of diarrhoeal symptoms. Stool samples were examined by standard parasitological methods for protozoa and PCR for bacterial causes. The frequency of parasitological and bacterial etiologies found, were compared between acute and persistent cases. Fisher exact test was used for statistical analysis.

RESULTS A total of 40 (15.6%) had diarrhoea lasting at least 14 days or more (PD). The mean age in acute and persistent group was 28.25 ± 28.25 and 16.29 ± 19.11 months, respectively \( P = 0.001 \). In PD group, 47.5% of the patients were male and 52.5% were female compared to 57.4% and 42.6% in acute cases, respectively. We found at least one potential pathogen in 14 (35%) of PD cases. Salmonella and EAEC were detected more in PD group compared to acute cases, although these differences did not reach to statistical significance (2.5% vs. 0%; \( P = 0.156 \) for Salmonella and 22.5% vs. 19.4%; \( P = 0.399 \) for EAEC). Shigella was identified in 1.4% of acute and 5.0% of persistent diarrhoea episodes \( P = 0.175 \). In comparison to the acute group, other protozoa and bacteria were detected approximately with a similar or lower rate in the PD group (Table). The mean duration of acute and persistent diarrhoea episodes was 5.85 (SD = 2.7) and 30.50(SD = 24.0) days, respectively. No deaths were associated with PD.

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Acute No.(%)</th>
<th>Persistent No.(%)</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cryptosporidium parvum</td>
<td>3(1.4)</td>
<td>0</td>
<td>0.60</td>
</tr>
<tr>
<td>Giardia lambia</td>
<td>7(3.2)</td>
<td>0</td>
<td>0.30</td>
</tr>
<tr>
<td>Entamoeba histolytica</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Blastosistis hominis</td>
<td>9(4.2)</td>
<td>0</td>
<td>0.21</td>
</tr>
<tr>
<td>STEC</td>
<td>15(6.9)</td>
<td>3(7.5)</td>
<td>0.56</td>
</tr>
<tr>
<td>ETEC</td>
<td>9(4.2)</td>
<td>0</td>
<td>0.21</td>
</tr>
<tr>
<td>EPEC</td>
<td>16(7.4)</td>
<td>2(5.0)</td>
<td>0.45</td>
</tr>
</tbody>
</table>

CONCLUSION Like studies from other regions of the world, we found that PD occurs mostly in younger children. In most cases an infectious agent could not be found. Although it was not statistically significant, EAEC was the most frequently found organism in PD group.

PA 108

Prevalence of gastrointestinal symptoms in the population of Tehran, Iran

A. Zarghi1, M. A. Pourhoseingholi1, M. Habibi1, M. Rostami Nejad1, A. Ramazankhani1 and M. R. Zali1
1Research Center for Gastroenterology and Liver Diseases, Shabedeh Behesti University of Medical Science, HSR Department, Tehran, Iran, Islamic Republic of Iran; 2The head of Research Center of Gastroenterology and Liver Diseases, Shabedeh Behesti University of Medical Science, Tehran, Iran, Islamic Republic of Iran

OBJECTIVES Baseline information on frequency of gastrointestinal diseases and symptoms, their relation with selected demographic, socioeconomic, cultural, and psychologic factors and viewpoints of patients about their disease and provision of preventive and medical care services and use and costs of these services provide a solid basis for better provision of healthcare services, our aim is estimate the prevalence of gastrointestinal symptoms and liver diseases in population of Tehran.

METHODS In this cross-sectional study a valid and reliable questionnaire was performed during May and December 2006, on cluster sampling of 1306 people from Damavand and Firozkoh cities of Tehran province. At least one physician was consulted for symptoms in respondents.
RESULTS Overall, 100,000 of Iranian population (48.7% men and 51.3% women). Mean age of the responders was 34.8 ± 16.6 years (range 12–70). Prevalence of gastrointestinal symptoms included: abdominal pain was 10.1%, constipation 6.2%, diarrhoea 11.1%, abdominal bloating 10% dyspepsia 11.3% proctalgia 1.5%, nausea and vomiting 1.2%, incontinence 0.5%, GI bleeding 0.7%, weight loss 0.9% and dysphagia 0.6%.

CONCLUSION Dyspepsia is the most common (male and female 11.3%). Constipation (F = 7.6% and M = 4.7%) and abdominal pain (F = 2.1% and M = 0.8%) are common in female (P < 0.05), and other symptoms are statistically equal in both female and male.

PA 109 Prevalence of Dientamoeba fragilis genotypes in different Danish populations as assessed by PCR and SNP genotyping

C. R. Stensvold1, C. Jepsen-Sorensen2, K. Dinesen3, K. Møller1 and H. V. Nielsen1
1 Statens Serum Institut, Dept. of Bacteriology, Mycology and Parasitology, Copenhagen, Denmark; 2 Statens Serum Institut, Dept. of Biochemistry, Copenhagen, Denmark; 3 Technical University of Denmark, Kgs. Lyngby, Denmark; 4 Statens Serum Institut, Department of Epidemiology, Copenhagen, Denmark

OBJECTIVES Dientamoeba fragilis is an intestinal protozoan parasite commonly hosted by patients suspected of an intestinal parasitosis. Although the pathogenetic properties of D.fragilis are not clear, several studies indicate that the parasite is capable of inducing intestinal symptoms as for instance diarrhoea and abdominal pain. Two genotypes of D.fragilis have been described, but due to limited data, the prevalence of the two genotypes (I/I) have only been sporadically reported. The genetic characterisation of isolates might reveal a genotype-related variation in the pathogenicity of D.fragilis, and thereby explain the difference in the presence/absence of gastrointestinal symptoms in D.fragilis positive individuals.

METHODS Panels of genomic DNA extracted from symptomatic and asymptomatic individuals were screened for D.fragilis using PCR and isolates were genotyped using dideoxynucleotidsequencing and a newly developed SNP-genotyping method based on pyrosequencing. DNA from 50 patient specimens positive for Giardia intestinalis, 50 positive for Cryptosporidium, 100 specimens positive for Blastocystis, and 150 samples from healthy individuals were screened by PCR. Amplicons were SNP-genotyped using a pyrosequencing assay targeting a SNP (T/A) in position 420 of the small subunit rRNA gene of D.fragilis.

RESULTS The study is ongoing and results will include information on the prevalence and distribution of D.fragilis genotypes in different study populations based on an easy, inexpensive and high-throughput met hod for SNP-genotyping D.fragilis.

CONCLUSION As the study is ongoing, conclusions cannot yet be inferred.

PA 110 Enteropathogenic Escherichia coli in traveller's diarrhoea

A. Gonzalez1, E. Mendes1, J. Ruiz1, S. Ramon1, J. Muñoz1, J. Vilà2 and J. Gascon1
1 Centre de Salut Internacional. IDIBAPS. Hospital Clinico de Barcelona, Secció de Medicina Tropical, Barcelona, Spain; 2 IDIBAPS. Hospital Clinic de Barcelona, Serveis de Microbiologia, Barcelona, Spain

BACKGROUND Enteropathogenic Escherichia coli (EIEC) is increasingly recognized as a cause of acute and persistent diarrhoea in different populations.

OBJECTIVES To describe the clinical and epidemiologic characteristics of traveller’s diarrhoea (TD) associated with EAEC in people attending our Tropical Medicine Department between January 2005 and December 2006.

METHODS We collected and analyzed epidemiologic and clinical data from people with TD associated with EAEC identified from stool cultures by PCR technique.

RESULTS EAEC was isolated from 64 people with TD 72% of whom were women, with a median age of 29 years (ICR 24–37 years). Most were Spanish (86%), the rest came from other European countries (8%), Africa (3%) and Central America (3%). Thirty-four percent had travelled to the Indian Subcontinent (91% to India), 20% to West Africa (54% to Senegal), and 11% to Central America. At the time of their visit 33.1% were still experiencing acute diarrhoea whereas 28.1% had persistent (>15 days) disturbances, 83.3% reported intermittent symptoms, and 18.8% no longer had enteric symptoms. Eleven people had already taken ciprofloxacin, 4 metronidazol and 3 other antibiotics. Stools were watery (65%) or loose (35%), 81% presented abdominal pain, mainly abdominal cramps (66%), 40% had nausea or vomiting, 32% reported fever and 5% blood in stools. Forty-three percent received an antibiotic during follow up (76% improved after treatment). Globally, 51% people improved spontaneously, 38% after specific treatment and in 11% symptoms persisted despite treatment (although none had EAEC isolated again). Other enteropathogens were identified in 30% of patients, the most common were Giardia lambia (6 subjects), ETEC ST (4), Shigella flexneri (2) and Entamoeba hystolotica dispers (2).

CONCLUSION Presently, EAEC is one of the main causes of traveller’s diarrhoea in our setting. Although half of the patients improved spontaneously, 28% had symptoms lasting for more than 2 weeks and 53% received specific treatment. Efforts should be made to improve knowledge about the different presentations and evolution of this infection.

PA 111 Application of RAPD-PCR for differentiation of Shigella and Salmonella spp

Islamic Azad University, Tehran, Iran, Islamic Republic of Iran

OBJECTIVES Shigella and Salmonella spp. are important agents of gastrointestinal diseases. Typing methods are useful tools for performing epidemiological surveys of pathogenic bacteria. The efficiency, rapidity and flexibility of the RAPD-PCR method make it a useful tool for typing of bacteria in subspecies level. The aim of this study was to compare homology rate of Shigella and Salmonella isolates and also to determine genetic diversity of isolated strains by RAPD-PCR.

METHODS Thirty three Shigella and twenty one Salmonella isolates from different clinical centers of Tehran were studied. They were cultured on XLD and MacConkey agar. Biochemical and Serological tests were done. After chromosomal DNA extraction by phenol-chloroform method RAPD-PCR by two primers (1283 and 1254) was done. PCR products were observed by gel-electrophoresis. Data were analysed by NTSYSpc-2.02e software.

RESULTS Between these two primers 1283 for Shigella and 1254 for Salmonella was shown to have more divergence than the other one. Minimal similarity of observed homology for Salmonella and Shigella isolates were 61% and 45% respectively. Maximum
homologies in Shigella spp. was seen in Shigella sonnei (93%) and in Salmonella belong to Salmonella typhi (95%).

CONCLUSION Results declared that RAPD-PCR by 1254 primer is a useful tool for study of Salmonella isolates polymorphisms. Whereas 1283 primer was useful for differentiation of Shigella sonnei from other Shigella species, but it was not useful for study the polymorphisms inside of Shigella sonnei isolates.

Disease Surveillance

PA 112
Response capacity to epidemic emergencies: a challenge of the new millennium
A. Gala González
Institute of Tropical Medicine 'Pedro Kouri', Epidemiology, La Lisa, Cuba

The infectious diseases that have emerged in the last years have demonstrated their great dissemination capacity and potential to saturate national resources causing emergencies of great span. The most recent epidemics demonstrated that only strengthened systems of health along with a strong capacity to respond to events of this nature will be able to control future occurrences. All over the world countries have recognized the necessity to promote the initiative of strengthening national capacities for surveillance, prevention and control of the emergencies caused by epidemics. In this work main elements are identified that allow guiding the efforts of the governments with the support of international organizations toward the achievement of a common objective: National Systems of Alert and Competent Effective Response to situations of epidemic emergency. The most important aspects are presented, with emphasis in the syndromic management of diseases for constructing surveillance systems with great sensibility for the detection of any early signs of an event that suppose a danger of becoming an epidemic of serious consequences for public health.

PA 113
The use of Cercariae infection the Bulinus truncatus snail as a model for evaluation of schistosomiasis control program in Khuzestan province, south western Iran
A. Farahnak, I. Moebedi and M. R. Eshraghian
School of Public Health, Tehran University of Medical Sciences, Dept. of Parasitology and Mycology, Tehran, Iran, Islamic Republic of Iran

OBJECTIVES Infection with urinary schistosomiasis, which was widely distributed and prevalent in parts of Khuzestan Province, southwest, Iran has been successfully controlled and almost eliminated. Because of the limited number of infected cases (if any), assessment of transmission status by finding infected cases is difficult and costly. Therefore, based on the decision of the national health authorities, a new approach for evaluating the transmission status of S. haematobium by finding cercariae of the parasite among local B.truncatus, the intermediate host snail, was tried.

METHODS A total of 2400 Bulinus snails collected from Dezful areas during years 2004–2006 were examined for cercariae using shedding and crushing methods.

RESULTS From the total number of Bulinus snails which examined for cercariae, 52 snails were found to be infected with Amphistome cercaria and 13 snails with Strigea cercariae, however, S. haematobium cercariae was not found in samples.

CONCLUSION Lack of S. haematobium cercariae in our samples in this region revealed that snails are free from this parasite and support this theory that transmission of schistosomes cecaria does not occur in the districts and therefore this disease is still under control and this is good news for inhabitants of the region as well as for local health authorities.

PA 114
Epidemiological surveillance: a growing role in humanitarian emergencies
F. Riccardo 1, L. E. Pacifici 2, A. G. De Rosa 2, E. Scaroni 2, L. Nardi 2, G. Russo 1 and V. Vullo 2
1University of Rome 'La Sapienza', Infectious and Tropical Diseases, Rome, Italy; 2Italian Red Cross, International Health Cooperation for Development office, Rome, Italy

OBJECTIVES Epidemiology is assuming an important role in a multi-sector approach to humanitarian aid. This presentation examines the rationale and application of communicable diseases epidemiological surveillance in humanitarian emergencies.

METHODS The partnership model involved developing (Sri Lanka District health authorities) and industrialized countries (Italian Red Cross - ItRC in collaboration with infectious disease physicians of the University of Rome ‘La Sapienza’) with a unilateral donor (IrRC). The policy innovation consisted in the introduction of a programme of systematic communicable diseases epidemiological surveillance within a health assistance project in the Eastern Province of Sri Lanka. This area was not only wracked by a tsunami of unprecedented violence in 2004 but is also politically unstable since 1983. Since the beginning of the programme, passing from a late-emergency phase to a post-emergency phase, there has been a priority shift to development and a slow replacement of IDP (internally displaced people) camps by villages even if the persisting political instability does not allow the population to settle definitively.

RESULTS Clusters of scabies and acute hepatitis were identified and interventions made on both local and district levels. Medical teams were deployed in the affected IDP camps acting on treatment/isolation of cases and prevention campaigns; cases were notified according to local laws, coordination meetings were held at district level with health authorities and NGOs; ‘community health’ trainings were organised for local volunteers in IDP camps. Achievement of cooperation and coordination with all organisations present in the assessed area, value attribution to existing public health plans and capacity building in epidemiological surveillance applied to public health were some of the major outcomes. No epidemics followed the containment interventions on the clusters identified in the IDP camps. The added value of the partnership can be found locally since a connection was made between clinical assistance and public health programmes in areas from which information is not available in official statistics. This allowed rapid containment strategies avoiding the spread of communicable diseases in poor hygiene settings. Moreover coordination achieved with the divisional health authorities and NGOs that increased accountability and strengthened the relationship with the host country. The IrRC is the only currently accepted humanitarian organisation offering health assistance in the area.

CONCLUSION Comprehensive knowledge, respect of existing systems (e.g. notification) in the host country, consequent adaptation and the choice of capacity building strategies are applicable with good results in humanitarian emergency management.
PA 115
The prevalence of intestinal parasites in the province of Izmir, Turkey
1 Ege University School of Medicine, Parasitology, Izmir, Turkey; 2 Ege University School Of Medicine, Parasitology, Izmir, Turkey

OBJECTIVES Turkey is located in the subtropical climate zone and the prevalence of intestinal parasites varies between the regions. The province of Izmir is in western Turkey, with a population of almost 3.5 million. The aim of this first local and second nationwide population-based study was to investigate both the prevalence of intestinal parasites in Izmir province, together with related personal and environmental risk factors.

METHODS A total of 2047 local people were chosen by cluster sampling. Stool samples were obtained from each individual, after an inquiry form was completed in house visits. They were examined by wet mount, formalin ethyl acetate concentration and trichrome staining methods. The data were analyzed with SPSS 11.0® by t-test and chi-square tests. Geographical mapping showing the density and variation of the species of intestinal parasites in Izmir was done, after all maps were scaled and the coordinates were determined with GeoMedia5.0®.

RESULTS The prevalence of the intestinal parasites was found to be 25.6%. There was a prevalence variation between the districts of the province (P = 0.000). Blastocystis hominis was the leading parasite and the parasites were more common in children, with no significant difference. There was also no significant difference between the parasite prevalence and sex, marital status, education, income, frequent eating outside and habitual eating raw meat. Significant differences were found between the parasite prevalence and crowded families (P = 0.001), early immigrants (P = 0.002), individuals with no social security (P = 0.004) and people who had close contact with their livestock (P = 0.03). The parasites were found to be less common among individuals who drank bottled water (P = 0.018) and lived in a house with a sewage system (P = 0.03).

CONCLUSION The results revealed a correlation between the intestinal parasites and living conditions in our study group. We further plan to expand the study group to cover all regions of Turkey.

PA 116
Eradication of poliomyelitis in Kosova: is it possible?
L. Gashi, N. Ramadani, A. Kalaveshi and S. Gashi-Noke
1 Kosova National Institute of Public Health, Department of Epidemiology, Prishtina, Albania; 2 Medical Faculty, Forensic Institute, Prishtina, Albania

OBJECTIVES Epidemiological characteristics of poliomyelitis situation in Kosova, the success of active AFP surveillance, possibilities for stopping circulation of polio virus until the year 2003 and eradication of the disease by the year 2007.

METHODS Surveillance data, epidemiological assessment by using descriptive component, the retrospective observation of the phenomenon by time, reporting data from active AFP surveillance, communicable disease surveillance and immunization coverage reported in the Department of Epidemiology.

RESULTS Since 1991 through 2006, 54 suspected cases of poliomyelitis have been registered in the territory of Kosova with two lethal cases. The highest number of cases was noticed during 1996 (25), with morbidity 1.16 and lethality 4.0. Last ten years no cases of poliomyelitis have been registered. Type I, II, III of ‘wild virus’ of polio was isolated in 12 cases. 9 cases were negative and other three were not typed. Last four years no case of poliomyelitis was recorded. During sub-NID in Kosova, imple-mented in 6 rounds in the year 1996 in the age-group 0–5 years with polio immunization were covered 97% of the children, in 1997 (93%) and 1998 (80%). During this period 80% of the children’s have been completely covered with immunization.

CONCLUSION Thanks high immunization coverage against poliomyelitis no cases of poliomyelitis have been registered within last ten years, it is foreseen that by the end of year 2003 the transmission of wild polio virus can be interrupted and the goal set for the eradication of the disease by the year 2007, the goal set up by health authorities in Kosova. To accomplish it, an active surveillance of polio has been undertaken as well as a vaccination targets established for the next years. It is expected that the percentage of the population to be vaccinated will be 95% in 2005, 2006 and 2007.

PA 117
Excess mortality associated to a large chikungunya outbreak in Reunion Island
1 Institut de veille Sanitaire, Saint-Maurice, France; 2 CIRE Réunion-Mayotte, Saint-Denis de la Réunion, France

Reunion Island (population 770 000), a French Indian Ocean’s territory was affected in 2005–2006 by a large chikungunya outbreak responsible for 266 000 cases (attack rate 38%). Most cases occurred during the first 6 months of 2006. Over this period, physicians in La Réunion reported 240 chikungunya-related deaths, most of them in people aged 70 and over.

OBJECTIVES To assess the impact of the outbreak of chikungunya on mortality in La Réunion.

METHODS We compared the crude death rate (CDR) observed during the outbreak with an expected CDR computed from historical data. Monthly number of deaths was obtained from communes registries. The study covered the 2-year period 2005–2006.

RESULTS Over the year 2005, observed monthly CDR remained within the range of statistical variation when compared to expected values. From January to April 2006, monthly CDR were respectively 7.1%, 34.4%, 25.2% and 10.1% higher than expected (P < 0.01 for February and March). This represented an excess 232 death during the 4 month period corresponding to the peak of the outbreak. From June 2006 on, observed monthly CDR was systematically below expected values. Overall, 3715 deaths were observed in La Réunion in 2006 while 3751 were expected.

CONCLUSION This chikungunya outbreak was the first described in a developed country’s environment with exhaustive death registration. The 2006 crude mortality pattern in La Réunion is compatible with a ‘harvest’ effect caused by the outbreak. This hypothesis is consistent with the median age of chikungunya-related deaths as reported by physicians. Chikungunya was, until recently, considered a self limiting disease associated to universal recovery. Our study suggests that a large outbreak of chikungunya impacts on mortality in the most vulnerable sub-groups.

PA 118
Clinico-epidemiological comparison between travellers and VFRs to Sub-Saharan Africa
1 Tropical Medicine, Ramón y Cajal Hospital, Madrid, Spain

OBJECTIVES To compare clinical and epidemiological features of a group of Spanish travellers with a group of migrant travellers (VFRs: Visiting Friends and Relatives) to Sub-Saharan Africa.

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METHODS Descriptive retrospective study of a cohort of Spanish travellers and another of VFRs attended at a referral Tropical Medicine Unit in the period 1990–2006. All of them travelled to Sub-Saharan Africa, and the trip lasted >3 months. Statistical analyses were made using the chi-square test and when expected frequencies were <5 with Fisher’s exact test. \( P > 0.05 \) was considered statistically non-significant (ns).

RESULTS A total of 433 patients 326 (75.3%) travellers and 107 (24.7%) VFRs. Average time from arrival till first visit at the Unit: 2.8 months in travellers and 4.8 months in VFR. Average age: 35.1 years in travellers and 33.2 years in VFRs. Average trip duration: 1.3 months in travellers and 1.2 months in VFR. Most common symptoms were: fever in 152 (46.6%) travellers and 67 VFRs (62.6%) \( (P = 0.004) \); diarrhoea in 77 (23.6%) travellers and 14 (13.1%) VFRs \( (P = 0.02) \); skin disorders in 82 (25.2%) travellers and 26 (24.3%) VFRs (ns); respiratory symptoms in 28 (8.6%) travellers and 7 (6.5%) VFRs (ns); urgenital symptoms in 33 (10.1%) travellers and 8 (7.5%) VFRs (ns). Diagnoses: malaria in 66 (20.2%) travellers and 46 (43%) VFRs \( (P = 0.000) \); intestinal parasites in 36 (10.3%) travellers and 2 (1.9%) VFRs \( (P = 0.004) \); gastrointestinal infections in 34 (10.4%) travellers and 11 (10.3%) VFRs (ns); extra-intestinal parasitosis in 16 (4.9%) travellers and 16 (15%) VFRs \( (P = 0.001) \); skin infections in 25 (7.7%) travellers and 4 (3.7%) VFRs (ns); viral infections (mainly post hepatitis B infection) in 16 (4.9%) travellers and 41 (38.3%) VFRs \( (P = 0.000) \); respiratory infections in 11 (3.4%) travellers and 4 (3.7%) VFRs (ns); sexually transmitted diseases (STDs) in 3 (0.9%) travellers and 9 (8.4%) VFRs \( (P = 0.000) \); urinary infections in 4 (1.2%) travellers and 4 (3.7%) VFRs (ns).

CONCLUSION Fever was more common in VFRs, while diarrhoea was more common in travellers. There were not significant differences between travellers and VFRs in respiratory, cutaneous and urogenital syndromes. VFRs suffered more frequently from malaria, extra-intestinal parasitosis and STDs. Intestinal parasites were more common in travellers. There were not significant differences comparing diagnoses of gastrointestinal, skin, respiratory and urinary infections.

PA 119 Clinical and epidemiological differences between short term and long term travellers to Central/Caribe and South America

Ramón y Cajal Hospital, Tropical Medicine, Infectious Diseases, Madrid, Spain

OBJECTIVES Compare clinical and epidemiological features between two groups of returned travellers from America: short term and long term travellers.

METHODS Descriptive study of two retrospective cohorts, Short term (ST) and long term (LT). Spanish travellers returned from Central and South America and attended at a referral Tropical Medicine Unit from 1990 to 2006. Short term traveller’s trip lasted >3 months and long term traveller’s trip lasted >3 months. Statistical analysis was made by chi-square test and when expected frequencies were <5 with Fisher’s exact test \( (P > 0.005 \) was considered non-significant, ns).

RESULTS A total of 1037 patients 777 (74.93%) ST and 260 (20.07%) LT. Mean time from arrival until consultation was 5.01 months in ST and 4 months in LT. Average age: 34.06 years in ST and 33.33 years in LT. Average trip duration: 0.96 months in ST and 34 months in LT. Most common symptoms were: Fever: 261 (33.6%) ST and 46 (17.7%) LT \( (P = 0.000) \); Diarrhoea: 304 (39.1%) ST and 102 (39.23%) LT (ns), cutaneous lesions: 301 (38.7%) ST and 46 (17.7%) LT \( (P = 0.000) \); respiratory symptoms: 67 (8.6%) ST and 23 (8.8%) LT (ns), urogenital symptoms: 43 (5.5%) ST and 27 (10.4%) LT \( (P = 0.007) \). Diagnoses obtained were: Malaria: 30 (3.9%) ST and 5 (1.9%) LT (ns), intestinal parasites 105 (13.5%) ST and 51 (19.6%) LT \( (P = 0.017) \), gastrointestinal infections: 161 (20.7%) ST and 27 (10.4%) LT \( (P = 0.000) \), extra intestinal parasitosis: 10 (1.3%) ST and 7 (2.7%) LT (ns), skin infections: 100 (12.9%) ST and 21 (8.1%) LT \( P = 0.037 \), viral infections: 28 (3.6%) ST and 8 (3.1%) LT (ns), respiratory infections: 36 (4.6%) ST and 9 (3.5%) LT (ns), STD: 6 (0.8%) ST and 3 (1.2%) LT (ns), urinary infections: 16 (2.1%) ST and 4 (1.5%) LT (ns), Mycobacterium tuberculosis infection 41 (5.3%) ST and 26 (10%) LT \( (P = 0.007) \), viral hepatitis 25 (3.2%) ST and 12 (4.6%) LT (ns), and HIV infection 7 (0.9%) ST and 3 (1.2) LT (ns).

CONCLUSION Fever and skin symptoms were more frequent among ST travellers; in other hand urogenital symptoms were more frequent among LT travellers. Intestinal parasites and Mycobacterium tuberculosis infections were more common diagnoses among LT travellers, other way skin infections were more common among ST travellers. It is important to know what the most frequent symptoms and diagnoses among each traveller group are, because it changes the diagnosis orientation of the health provider.

PA 120 Study on sero-epidemiological relationship between Epstein–Barr virus (EBV) infection and multiple sclerosis (MS) disease in Iran

A. Mirjalili and R. Taherkhani
Razi Vaccine and Serum Research Institute, Biotechnology, Karaj, Iran, Islamic Republic of Iran

OBJECTIVES Many studies were performed in an effort to link MS with a microbial cause. EBV was suggested as a causal agent of MS disease in the early 1980s due to the increased titers of EBV antibodies to MS patients and the similarity between the epidemiology of MS and that of infectious mononucleosis, frequently caused by EBV. This study conducted toward finding any relationships between MS disease and EBV antibody titer for the first time in Iran.

METHODS Sera were collected from 21 definitive MS cases (5 males mean age 40 years and 16 females mean age 39 years) with disease duration of 2.8–26 years as the test group and 105 healthy individuals (match in sex and age with test group) without previous history of MS disease, neurological disorders, systemic disease, etc as control group. To test the sera, three laboratory techniques including: indirect immunofluorescence test, a commercial and an in-house ELISA kit both detecting anti-VCA were used.

RESULTS Our results displayed all MS patients had a positive response against EBV and antibody titer was higher in MS patients than control group.

CONCLUSION This research also showed similar results with other studies on relationships between MS disease and EBV infection and it’s the first report from Iran indicating high titer of EBV antibody in MS patients.
Abstracts of the 5th European Congress on Tropical Medicine and International Health

Echinococcosis

PA 121 Evaluation of a coproantigen enzyme linked immunosorbent assay for the diagnosis of canine echinococcosis in Iran

M. Saeedi
Pastor Institute of Iran, Parasitology, Tehran, Iran, Islamic Republic of Iran

OBJECTIVES Cystic echinococcosis has been recognized as a major public health problem in sheep-rising regions of the world. Different studies in Iran have shown that echinococcosis is a main problem among human and domestic livestock in several provinces of the country. Due to this fact that providing a reliable diagnostic method for detection of this infection in definitive host is a critical pre requirement for establishment of appropriate control programs in our country, we designed this project for evaluation of coproantigen ELISA (CA-ELISA).

METHODS For performing the study, one hundred and sixteen carnivores including 80 stray dogs, 27 jackals, 8 foxes and one wolf were collected from rural areas of Hamadan, Azarbaijan and Tehran provinces. All the specimens were examined by direct microscopic examination of intestinal contents and CA-ELISA using a standard commercial kit (Echinostest®, Dr. Bommeli Diagnostics, Switzerland).

RESULTS The overall prevalence of canine echinococcosis using CA-ELISA was 43.1% (50/116) in comparison with microscopic method that showed 37% (43/116). The specificity and sensitivity of the CA-ELISA as referenced by necropsy findings was 72.1% and 74% respectively.

CONCLUSION So far we found this assay to be a suitable and advantageous method for surveillance of canine population especially in regions with endemic echinococcosis.

PA 122 Prevalence in patients infected with hydatid cyst who were referred to three hospitals in Khoram-Abad during 2002–06

M. Rostami Nejad1, N. Hosein Khan1, E. Abdinia2 and K. Cheraghipour3
1Research Center of Gastroenterology and Liver Diseases, Shahed Beheshti University of Medical Science, Department of Foodborne and Diarrheal Disease, Tehran, Iran, Islamic Republic of Iran; 2Razi University of Kermanshah, Kermanshah, Iran, Islamic Republic of Iran; 3Medical Science University of Hamadan, Hamadan, Iran, Islamic Republic of Iran

OBJECTIVES Echinococcosis or hydatid cyst (H.C) is considered as one of the major parasitic infections in Iran that causes many health problems and economic losses in communities. The aim of this study was to determine the prevalence of H.C in patients referred to surgery wards of three hospitals in Khoram-Abad Lorestan-Iran from 2002 to 2006, where High prevalence of H.C has been reported.

METHODS In this study 64 513 medical records of patients referred to surgery wards of Shohadaye ashayer, Tohid and Taamine ejtemaee hospitals in Khoram-Abad Lorestan were studied. These patients had gone under surgical operations for different reasons during 2002–2006.

RESULTS Among these medical records, 43.7% belong to Shohadaye ashayer, 8.2% to Tohid and 18.1% to Taamine ejtemaee hospital. Cysts were found in liver and lung in 61.5% and 20.5% of cases respectively. Also cysts were found in brain, muscle, kidney eye and pretoein in the remaining 18% of cases.

CONCLUSION A very low level of knowledge about hydatid disease was found in the community. This is the first epidemiological study of H.C in Khoram-Abad hospitals. We conducted this study on patients referred to three hospitals in Khoram-Abad. The incidence rate of H.C in all surgeries was 39 cases. In a similar study that was performed by using data on children referred to Tehran’s Taleghani hospital between 1988 and 2000, 32 cases of H.C were reported. In this studied community, the mean age of patient was 40.2 years and the highest rate of infection with H.C was observed in women. Further studies are required to find the etiologic factors of H.C in Khoram Abad Lorestan-Iran.

Education in International Health

PA 123 An innovative way to teach international health

P.-M. Roy1, C. Valois2, F. Couturier2 and R. Williams2
1Université de Sherbrooke, Family Medicine, Sherbrooke, Canada; 2Université de Sherbrooke, Family Medicine, Longueil, Canada

The Université de Sherbrooke Faculty of Medicine and Health Sciences recently endorsed a short program in International Health given by the Continuous Education Centre. This initiative follows the development of a curriculum by family physicians involved in international health in Mali for a number of years. This short program consists of course of lectures and workshops that can be followed by a clinical internship in Mali. The 90 h of theory cover tropical diseases, primary health care, public health interventions, and the socio-political and economic aspects of international health. Most of the course is given by family physicians, supported by medical specialists as needed. The course is given at the Université de Sherbrooke’s Longueil Campus and simultaneously videoconferenced to students (n = 54) in 4 other distant cities. At each session, students present ‘clinical capsules’ related to the lecture material. In addition, all the students are invited to make presentations at the one-and-a-half day annual meeting. Guest Malian physicians are involved in this annual meeting. Following the International Health short program, students can complete their training with a clinical internship in Mali. It gives students the opportunity to apply their knowledge by doing medical consultations in 3 medical clinics in Mali located in urban and rural environments. The internship program is now in his tenth year and is mature and well established. A Canadian physician supervises 2 Canadian residents and a Malian student, who also acts as an interpreter. Family medicine values form the core of the medical interventions. Teaching methods include direct supervision and case studies. There is also a ‘grand round’ each week. In parallel with the courses and internship, the physicians who coordinate the program, along with some Malian physicians, are studying the impact of the intervention.

PA 124 Malaria knowledge and prevention in a group of travellers to endemic countries

R. Teódósio and J. Atouguia
Institute of Hygiene and Tropical Medicine, Tropical Medicine Unit, Lisboa, Portugal

OBJECTIVES To investigate malaria knowledge and prevention used by travellers residents in the Lisbon area, travelling to Portuguese Speaking African countries (Cape Verde, Guinea-Bissau, Sao Tome and Principe, Angola and Mozambique).

METHODS A cross-sectional survey was undertaken at the Lisbon International Airport. Passengers were invited to participate in the study according to their position in the queue at check-in. Only passengers aged at least 15 participated. The interviews were...
conducted during July–August 2001. Data were analyzed using the SPSS package. The statistical tests used were chi-square test and Mann–Whitney test.

RESULTS A total of 1188 travellers agreed to participate in the study. 53.1% were male and 46.9% female. The average age was 34.61 years (SD = 13.12 years). 35.2% travelled to Cape Verde, 24.1% to Angola, 16.4% to Mozambique, 14.5% to Sao Tome and Principe and 9.8% to Guinea-Bissau. Only 568 individuals (47.8%) had pre-travel advice. 77.4% knew that mosquitoes bite can transmit malaria, but only three quarters of this group knew that mosquitoes bite can transmit malaria. Travellers travelling to Cape Verde didn’t usually know malaria transmission (P < 0.001). From the group who travelled to Guinea-Bissau, Angola, Sao Tome and Principe and Mozambique, those who knew malaria transmission had a higher educational level and previous stays in the tropics (P < 0.001 and P = 0.009, respectively) and only 472/770 travellers took chemoprophylaxis against malaria (43% took mefloquine and 33.7% chloroquine); 26.0% (200/769) took chemoprophylaxis against malaria and intended to use repellent during the journey. From the group who travelled to Guinea-Bissau and Sao Tome and Principe, those who took chemoprophylaxis were older (P < 0.001), travelled to Guinea-Bissau and Sao Tome and Principe (P < 0.001), didn’t have previous stays in the tropics (P < 0.001), and had some advice before travelling (P < 0.001).

CONCLUSION Travellers’ knowledge about malaria and preventive measures against this disease must be improved. Travellers residents in the Lisbon area need advice before departure.

PA 125
Educational essentials for a career in international health: medical students’ perspective
A. L. Goldstein
Medical School for International Health and Medicine at Ben-Gurion University of the Negev, Be’er Sheva, Israel

OBJECTIVES The purpose of this study was to gain insight into the perspective of medical students enrolled in the Medical School for International Health and Medicine at Ben-Gurion University, a unique school specializing in International Health (IH), on what educational objectives are essential in order to best prepare them for a career in IH.

METHODS A questionnaire was emailed and distributed to the student body (n = 141) asking the question: ‘In your opinion, what are the top five essential educational objectives that a medical school should provide in order to well prepare students for a career in International Health?’ 10 general themes emerged, each with more specific sub-themes, and a content analysis of the qualitative data was conducted.

RESULTS Fifty-one students replied with a total of 283 educational objectives. 97.2% of the objectives were categorized into one of 10 recurrent themes. The most frequent number of objectives pertained to cultural issues with the largest sub-theme being education about different cultures. This was followed by the themes (and largest sub-theme): working with limited resources (lab techniques), education (the core medical curriculum), contact with organizations and workers in the field (understanding how international and bilateral agencies work), public health (epidemiology), clinical skills (diagnostic ability), communication (between different cultures), hands-on (field experience), tropical medicine (infectious disease), and monetary factors (health economics).

CONCLUSION This study summarizes within 10 themes what medical students, who chose to attend a medical school specialized in IH, view as essential elements of their medical education. Further research should compare this data to the responses of an experienced faculty and professionals in IH to a similar questionnaire, as well as an assessment of the realistic needs of the field, in order to create comprehensive, reality-based objectives around which to build an International Health medical curriculum.

PA 126
General practitioners and pharmacists: travel advice against yellow fever
R. Teodósio and J. Atougua
Institute of Hygiene and Tropical Medicine, Tropical Medicine Unit, Lisboa, Portugal

OBJECTIVES To identify the advice given about transmission and prevention of yellow fever.

METHODS A cross-sectional survey was undertaken. A self-administered questionnaire was given to general practitioners/family doctors (n = 1315) and to pharmacists (n = 628) in the Lisbon area, during the period of November 2001–March 2002.

RESULTS A total of 430 general practitioners/family doctors agreed to participate in the study (32.69% and 39.96% of responses, respectively). General practitioners/family doctors: 37.9% were male; the average age was 47.5 years (SD = 5.35 years); 91.4% did not have any training in travel medicine; 66.3% have lived (short or long stays) in tropical countries; 50.9% (112/220) informed about transmission by mosquito bite but 16.4% did not know yellow fever transmission; 29/254 (11.4%) didn’t indicate yellow fever vaccine to protect against this disease; only 21.2% (48/226) indicated correctly all Portuguese Speaking Countries with and without the need of yellow fever vaccine (Sao Tome and Principe, Guinea Bissau, Angola and Brazil, and Cape Verde, Mozambique and Timor, respectively). Pharmacists: 20.1% were male; the average age was 43.55 years (SD = 13.75 years); 93.2% didn’t have any training in travel medicine; 68.8% have lived (short or long stays) in tropical countries; 57.9% (77/133) informed about transmission by mosquito bite but 9.0% did not know yellow fever transmission; 22/104 (21.2%) did not indicate yellow fever vaccine to protect against this disease; only 8.8% (6/69) indicated correctly all Portuguese Speaking Countries with and without the need of yellow fever vaccine.

CONCLUSION Studied general practitioners/family doctors and pharmacists need training in travel medicine. Their advice about yellow fever is incomplete and/or incorrect and must be improved.

Equity and Health Services
PA 127
Inequity of maternal health in Guatemala
W. Flores
CEDIM, Guatemala City, Guatemala

OBJECTIVES To analyze the gaps in maternal health between indigenous and non-indigenous women in Guatemala.

METHODS The ‘Reproductive Age Mortality Survey’ (RAMOS) year 2000, was the source of data for maternal mortality rates (MMR). The maternal and child health survey (DHS), year 2002, was the source of data for information on access to obstetric care and other maternal health care services. Quantitative analysis (descriptive statistics) was used to carry-out the analysis.
RESULTS MMR in indigenous women is three times higher than MMR in non-indigenous women. Although 48% of all deliveries occur in indigenous women, they make up 78% of all maternal deaths. Incidence of cesarean sections as an indicator of access to quality of care showed that Only 5% of indigenous women had a delivery by cesarean section where this number was 16% for non indigenous. More than 50% of indigenous women deliver at home without the assistance of qualified provider whereas up to 85% of non-indigenous women deliver in a hospital.

CONCLUSION There are serious inequities of maternal health outcomes (MMR) and access to obstetric care and other services between indigenous and non-indigenous women in Guatemala.

Ethical Issues in International Health

PA 128

Relationships of volunteers’ comprehension and research assistants’ attitude toward informed consent process

N. Kaewponsiri1, W. Okanurs1, D. Kriaysorn2, J. Kaewkungwai2, S. Thameree4 and S. Vijaykadga4

1Mahidol University, Faculty of Tropical Medicine, Social and Environmental Medicine, Bangkok, Thailand; 2Bumrungrad International Hospital, Bumrungrad Clinical Research Center, Bangkok, Thailand; 3Department of Tropical Hygiene, Mahidol University, Faculty of Tropical Medicine, Bangkok, Thailand; 4Department of Pharmacology, Chulalongkorn University, Faculty of Medicine, Bangkok, Thailand; 5Department of Disease Control, Ministry of Public Health, Nonthaburi, Thailand

OBJECTIVES To measure volunteers’ comprehension concerning a clinical trail that they participated and to find out association between volunteer’ comprehension and research assistants’ attitude concerning informed consent process.

METHODS This study was a cross-sectional study. Volunteers who participated in a malaria clinical trial three days after being recruited into the trial were interviewed concerning their comprehension about the trial and informing method during December 2004–December 2005. Research assistants were interviewed about their understanding about the trial and their attitude regarding informed consent process.

RESULTS Eighty-one volunteers and eight research assistants were recruited into the study. It was revealed that comprehension mean score among volunteers equal to 11.5 or 66.6% of the total score. About 30% of volunteers believed that they could not withdraw from the trial. The results of this study indicated that method of informing the volunteers about the trial affected their comprehension level. It was also found that the level of volunteers’ comprehension level associated with research assistants’ attitude toward informed consent process. Six research assistants had positive attitude toward informed consent process but five of them had negative attitude toward clinical trial. Volunteers who were informed by positive attitude research assistants were more likely to have higher comprehension score than those who informed by research assistants who had negative attitude.

CONCLUSION The volunteers were not truly informed. Some research participants did not understand disclosed information. Research assistants’ attitude toward the trial and informed consent were associated with volunteer comprehension. Resulted of the study demonstrated that there is need to improve the informed consent process and training for research assistants. The data from the research could serve as a base-line information for improving informed consent process.

PA 129

Abuse of ‘cosmetics’ in sub-Saharan Africa

E. J. Masenga

Regional Dermatology Training Centre (RDTC), Moshi, United Republic of Tanzania

Cosmetics include a range of articles that are used to enhance or protect the appearance or odor of the human body. They may be used inforn of creams, powders lotions perfumes, lipsticks, nail polishers, eye/facial make up, permanent waves, hair colors baby products, bath substances etc. The intended effects of cosmetics such as attractiveness, beautification and cleansing are not supposed to alter the anatomy or physiology of the body. This Western civilization is getting into the Developing World at very fast speed especially with the female population. Majority of cosmetic users in Sub Saharan Africa are now getting access to over-the-counter ‘Cosmetics’ many of which contain fairly harmful ingredients. Unfortunately, these majorities of cosmetics users are not even aware of the dangers of cosmetics let alone the means of protection. The commonest range of substances applied as cosmetics in Sub-Saharan Africa are described including the related side effects.

Fever, Syndromic Approach

PA 130

Diagnosis of bacteremia using universal PCR in febrile ill children

S. Afsharpaiman1 and S. Mamish2

1Baghhatallah University of Medical Sciences., Pediatric, Tehran, Islamic Republic of Iran; 2Tehran University of Medical Sciences, Department of Pediatric Infectious diseases, Tehran, Islamic Republic of Iran

OBJECTIVES Early diagnosis of bacteremia and its complications is the most important part of care and management of the patients. However, a major population of patients who appear to be clinically septic have negative blood culture. The use of polymerase chain reaction (PCR) techniques has allowed identifying the pathogenic organisms rapidly and accurately. The objective of this study is to investigate the prevalence of bacteremia in febrile pediatric patients, comparing universal PCR and conventional blood culture.

METHODS One hundred consecutive febrile children (45 males and 55 females) admitted to the Pediatric Medical Center for suspected septicemia were evaluated. A total of 100 paired blood samples were collected from children to analyze for bacterial detection using universal PCR and culture.

RESULTS The PCR were positive in 19 patients. The comparison revealed sensitively, specificity and accuracy of 91.67, 90.91 and 91%, respectively, for PCR.

CONCLUSION The present study shows that the use of PCR is more sensitive than the use of conventional blood techniques for the detection of bacteria pathogens based on patients’ clinical context.

PA 131

First molecular detection of relapsing Borrelia fever in Morocco


Research, Institut Pasteur, Casablanca, Morocco

OBJECTIVES Relapsing fever (RF), due to Borrelia spp., is an endemic disease in some African countries. A soft tick (Ornithodoros) is the known vector of these bacteria. Our aim was to
estimate the incidence of RF in Kenitra region (Northwest of Morocco) and to characterize the Borrelia spp. strains responsible for the disease.

METHODS A total of 129 febrile patients suspected of RF borreliosis were included in the study. Blood from these patients was extracted by using the Qiagen kit. Three targets were used to amplify Borrelia DNA from patient’s blood: the 16S rRNA, the flagellin (fla) gene and the large intergenic spacer (IGS) between the rrs-rfl genes of Borrelia spp. PCR products were sequenced. A phylogenetic study of sequences allowed to us to assess the genetic diversity of Borrelia strains responsible for RF in Morocco.

RESULTS From 2005 to 2006 we investigated 129 suspected patients. Specific sequences of relapsing fever Borrelia were detected in 30 patients (23%). All positive patients were from rural areas. All the cases were diagnosed at the spring and the beginning of autumn with more than half cases in June (21/30 (70%). The clinical signs were: fever (100%); pain (62%); gastrointestinal disorders (54%). The male/female ratio (M/F) was 0.76 (13/17). All the cases were treated with cyclines for 7 days and they had a favourable evolution, without complication nor death. Sequence determination of isolated Borrelia from positive patients allowed to identify them as belonging to Borrelia hispanica. fla gene and IGS sequences provided the larger diversity.

CONCLUSION This study describes the first molecular assay for the diagnosis of relapsing fever caused by Borrelia spp. in Morocco. Our results emphasize that RF are endemic in Morocco and mainly caused by B. hispanica.

PA 132
Differential patterns of endothelial activation in ‘typhus-like’ illness
D. H. Paris1, K. Jenjaroen2, S. D. Blacksell1, P. Rattanaphone2, P. N. Newton1, G. D. Turner4 and N. P. Day1
1Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; 2Mahosot Hospital, Vientiane, Lao People’s Democratic Republic; 3Department of Microbiology, Mahosot Hospital, Vientiane, Lao People’s Democratic Republic; 4Department of Clinical Pathology, University of Oxford, Oxford, UK

OBJECTIVES Tropical infectious diseases with similar clinical presentations but different aetiologies pose a challenge for establishing guidelines for empirical chemotherapy. ‘Typhus-like’ illness is a clinical entity commonly seen in Southeast Asia involving fever and skin rash, often coupled with neurological symptoms, ranging from mild confusion to delirium and deep coma. Rickettsia spp target host leukocytes and endothelium, but data for Scrub Typhus (O. tsutsugamushi) is incomplete. We hypothesised that high levels of endothelial activation would accompany endothelial cell tropism and analysed levels of circulating soluble cellular adhesion molecules (sCAM) in a wide disease spectrum of patients presenting with ‘typhus-like’ illness.

METHODS A total of 242 admission serum samples of patients presenting with ‘typhus-like’ illness were analysed, including Scrub typhus (n=66), murine typhus (n=62), leptospirosis (n=24), dengue fever (n=17), dengue hemorrhagic fever (n=16), Salmonella typhi (n=22), uncomplicated malaria (n=25) and negative control healthy blood donors (n=10). We performed quantitative ELISA measurement of endothelial and leukocyte expressed sCAM, including E-selectin, sL-selectin, sICAM-1, sVCAM-1 and endoglin as a constitutive endothelial cell (EC) marker, to assess and compare the extent of systemic endothelial activation in these patients.

RESULTS During the acute phase of infection, increased serum levels of both sL-selectin and sE-selectin were noted in Scrub typhus, leptospirosis, malaria and typhoid when compared to other diseases. sE-selectin levels in dengue and dengue hemorrhagic fever patients were comparatively low. sL-selectin in scrub typhus patients were significantly higher than any other typhus-like illnesses.

CONCLUSION Different patterns of markers of EC and mononuclear activation can be distinguished in a spectrum of typhus-like illness. Mononuclear cell activation, as judged by sL-selectin release, appears to be an early characteristic of Scrub typhus. This data may indicate O. tsutsugamushi tropism to mononuclear cells during the early dissemination phase, or local immune activation during initial local replication within the eschar. Correlation with clinical severity will be discussed.

Fungal Diseases
PA 133
A study on causative agents of cutaneous fungal infections in Yasuj, Southwest of Iran in 2005
M. Moradi1, B. Sarkari2 and K. Paikash3
1Department of Microbiology and Immunology, Faculty of Medicine, Yasuj University of Medical Sciences, Yasuj, Islamic Republic of Iran; 2Department of Immunology, Yasuj University of Medical Sciences, Yasuj, Islamic Republic of Iran; 3Department of Parasitology and Mycology, Shiraz University of Medical Sciences, Shiraz, Islamic Republic of Iran

OBJECTIVES Dermatophytes are one of the main health problems all over the world including Iran. The aim of this study was to find out the situation of cutaneous fungal disease and their causative agents in Yasuj.

MATERIAL AND METHODS Samples were collected from 117 cases suspected of cutaneous fungal infection who referred to laboratories in Yasuj city. Collected samples were examined microscopically and also by culturing using Sabouraud dextrose agar medium with different antibiotics. Fungal agents were detected using common mycological methods such as slide culture and clandoconidium medium.

RESULTS Results of this study showed that from 117 suspected cases of cutaneous fungal infection, only 25 samples had positive culture and 60% of them were belonged to women. The most frequent type of disease was tinea manum (24%) followed by tinea pedis (20%), tinea cruris (20%), tinea capitis (16%), tinea corporis (16%) and tinea unguium (4%). The most common fungal agent was T. verrucosus (28%), Candida albicans (24%), E. floccosum (20%), T. mentagrophytes (8%), Rhodotorulla (8%), T. violaceum (4%), T. tonsurans (4%) and Candida albicans (4%). Results of this study showed that 4.27% of cases were positive only by culture and 37% only by direct microscopic observation.

CONCLUSION Considering the high prevalence of disease in women, it seems that sex is a risk factor for acquiring fungal infection in this area. Results also showed that fungal agents in our study are usually zoophilic, therefore control of animals contacts could be an effective method for prevention.

KEYWORDS dermatophyte, fungal infection, Yasuj, Iran

PA 134
Anti – fungal effects of nystatin, clotrimazol, and miconazol against Candida species isolated from patients
S. Farahy, M. Palahati, M. Mahmoodian, M. H. A. Roodaki and M. J. Sharati
Department of Parasitology and Mycology, Iran University of Medical Sciences and Health Services, Tehran, Islamic Republic of Iran

OBJECTIVES Candida genus consists of diverse species of yeast and yeast-like fungi. A part of natural flora in the body is formed
by some kinds of Candida, particularly, Candida albicans. Candida is an opportunistic pathogen, causing infections in predisposed individuals. There are limited numbers of effective drugs against them in the markets; this may have led to the initiation of fungi resistance to the drugs.

METHODS This current experimental study was designed to evaluate the anti-fungal effects of Nystatin, Clotrimazole, and Miconazole drugs in both broth and agar media against Candida species. These drugs were applied in vitro. The MIC values of the drugs were determined against a number of Candida species (n = 60), isolated from the patients. Of these numbers, were C. albicans (n = 30) and C. non–albicans (n = 30), and a number of standard sensitive and resistant species.

RESULTS The results indicated that C. albicans had higher sensitivity to Clostrimazol and Nystatin in comparison to Miconazol (P < 0.1); whereas C. non-albicans had high sensitivity to the three used drugs.

CONCLUSION In addition, the study demonstrated that compared to C. albicans, C. non-albicans, had a greater sensitivity to these drugs (P < 0.1). There were no significant differences between obtained MICs, using either Sabouraud dextrose agar or Sabouraud dextrose broth macro dilution methods. Mean MICs for Nystatin, Clotrimazol, and Miconazol against C. albicans and C. non-albicans species were 2.2, 2.6, 18 and 0.81, 0.56 , 1.2, respectively. The entity showed the importance of identifying the kinds of species and performing the strain–drug susceptibility test before any treatment.

PA 135
Antifungal and interactive effects of NO donor complexes and common antifungal drugs on Candida species and Cryptococcus neoformans
Medical Parasitology and Mycology, Iran University of Medical Sciences, Tehran, Islamic Republic of Iran

OBJECTIVES Nitric oxide (NO) is a molecule with expanded and numerous roles in biologic system of the body. It shows antitumor and antimicrobial activities. Stimulation of macrophages by different microorganisms leads to the production of a large amount of NO with toxic property that causes the death of microorganisms. Mechanisms related to NO perform an important role in host’s defense against fungal infections. In candidial an infection NO is regarded as the most important factor in killing Candida albicans by polimorphonuclear cells.

METHODS This experimental study was designed to investigate antifungal potential of two NO donor complexes namely DPTA/NO (Dipropyleneaminetritre oxide) and DEA/NO (Diethyleneamine nitric oxide) per se and in combination with antifungal drugs such as ketoconazole and Amphotericin B against Candida albicans, Candida parapsilosis, Candida tropicalis, Candida glabrata, and Cryptococcus neoformans. In order to do so, we determined MIC (minimum inhibitory concentration) and MFC (minimum fungidal concentration) of the above – mentioned complexes as per NCCLS (National Committee of Clinical Laboratory Standards) using microdilution broth method.

RESULTS The obtained findings showed that DPTA/NO complex per se exerted antifungal effects. In addition, this complex revealed synergetic effects on C. tropicalis, C. glabrata II (resistant to Ketoconazole), and Cryptococcus neoformans (FIX < 0.5) and additive effects on C. albicans, C. glabrata I (sensitive to Ketoconazole) and C. parapsilosis (0.5 < FIX < 1) in combination.

CONCLUSION NO donor complexes indicated anticanidial and anticytococcal effects and interacted with antifungal drugs differently, depending on the species of the fungi involved. Accordingly, they can be used as therapeutic agents in the treatment of fungal infections.

PA 136
Design and synthesis of 1,2,3-benzotriazole derivatives as antifungal agents
Z. Rezaei, S. Khobaradideh and F. Amiri
Shiraz University of Medical Sciences, Medicinal Chemistry, Shiraz, Iran, Islamic Republic of Iran

OBJECTIVES Invasive fungal infections are major problems in immune-compromised patients. The recent expansion of antifungal drug research has occurred because there is a critical need for new antifungal agents to treat these life-threatening invasive infections.

METHODS In pervious report we described the preparation of some imidazole derivatives with biological interest. In this study a series of 1,2,3-benzotriazole derivatives were synthesized using alkylation on the N1-position of 1,2,3-benzotriazole with trityl substitution and alkyl alkyl chains in the presence of potassium carbonate, sodium hydroxide and tetraethylammonium iodide. The cytochrome P450 sterol 14-demethylase enzyme (CYP51) is the target of azoles antifungal. These compounds also docked into the active site of MT-CYP51 (PDB code, 1EA1) using Autodock program and compared with clotrimazole and fluconazole.

RESULTS The structures of all the new compounds were confirmed by 1H-NMR and Mass spectroscopy. In docking study these compounds showed a good affinity for the enzyme like fluconazole and clotrimazole.

CONCLUSION Therefore, these compounds may be effective like fluconazole and clotrimazole.

PA 137
Design and synthesis of 1–2-4-triazole derivatives as antifungal agents
S. Khobaradideh, Z. Rezaei and H. Hosseini
Medical Chemistry, Shiraz University of Medical Sciences, Shiraz, Islamic Republic of Iran

OBJECTIVES During the past two decades, a number of different classes of antifungal agents have been discovered. Although since the discovery of amphotericin B, there has been much progress in this field, there is still a critical need for new antifungal agents to treat life-threatening invasive mycoses. In our pervious study we synthesized several new derivatives of clotrimazole and also some 1-alkylimidazole analogous as potent antifungal agents.

METHODS In this study different series of Imidazole, benzimidazole and triazole derivatives were docked in the active site of the 14-α-demethylase enzyme using Auto Dock program and compared with clotrimazole and fluconazole. From the above derivatives five triazole compounds (three with trityl and two with alkyl chain substitution on the N1-position of the triazole ring) with the best binding energy were chosed for synthesis.

RESULTS The reactions proceeded in a high yield and the structures of all the new compounds were confirmed by 1H-NMR and mass spectroscopy.

CONCLUSION All of the compounds had better binding energy than the clotrimazole on the active site of the 14-α-demethylase enzyme and may be better than clotrimazole in antifungal studies.
Gender and Health

PA 138
Sociological trend to investigate the forms of gender based violence, its frequency and inherent vulnerability (consequences) among women and children in Nigeria

K. Adedayo
SDCE, RH, Port Harcourt, Nigeria

ISSUES/OBJECTIVES Violence towards women and children takes many forms – physical, sexual, psychological, restricted freedoms, coercion and threats which cuts across the segment of the society – the family institution, schools, the poor and the rich. The study aims to establish forms of gender based violence among women and children, its frequency, inherent vulnerability among the populace and attendant effects on the society.

METHODS/DESCRIPTION The survey investigated the forms of gender based violence, its frequency and devastating consequences such as life long emotional distress mental health problems, poor reproductive health and STI/STD/HIV/AIDS infections among 500 women and children victims in four locations in Nigeria – Port Harcourt, Lagos, Abuja and Kaduna.

RESULTS The survey revealed that gender based violence was more rampant in homes, schools, tertiary institutions and the types of violence included rape, child abuse, abduction, abduction, torture, molestation, sexual harassment, sexual exploitation, dating violence, battering, verbal abuses and intimidation. The study revealed that abusers were under psychological, emotional and physical states – results of substance abuse, anger, poverty and transferred aggression.

CONCLUSION/RECOMMENDATIONS Civil society, institutions, government should build and sustain strong multi-sectoral prevention strategies with systematic and sustained actions coordinated across the segment of the society; and urgent concrete measures/laws to secure gender equality and protect women’s human rights should be established and sustained in Nigeria.

Good Governance in the Health System

PA 139
Health services and decentralised institutions

J. Kumpatla
National Institute of Rural Development, Centre for Panchayati Raj, Hyderabad, India

OBJECTIVES India the largest democracy had enacted the 73rd Constitutional Amendment in 1992 to strengthen and empower local institutions (Panchayat Raj Institutions- PRIs) with a firm belief that ‘Local Problems have local solutions’, promoting Good Governance. PRIs with people’s representatives can both identify and cater to several basic needs, enabling collective decision making. The study identified Health delivery services by PRIs- as they are visualized as the best available alternatives to reflect on grassroots level operational issues and timely interventions. Uttarakhand is one of the states which has oldest institutions viz., Van Panchayats (Forest) and Nyaya Panchayats (dispense justice at the village level). These community based institutions authenticate that social mobilisation is not new to the Himalayan state. A best combination of these community based facilitating units need to accelerate accountability, transparency and responsiveness among Health functionaries and improve services. The state was forging ahead with public private partnership to enhance Health service delivery.

METHODS In Uttarakhand, field based investigations were taken up in two districts of Bhageshwar and Udham Singh Nagar of Kumaon Region. The study includes both primary and secondary data, discussions with stakeholders viz., health officials, elected representatives, community based organisations and people. Structured schedules, checklists and focus group discussions were organised.

RESULTS India ranks 53 position among the 102 developing countries and the Human Poverty Index-1 measures severe deprivation in health. (UNDP, HDR, 2006). At 0.9% of GDP, public expenditure on health in India is also the lowest among South Asia. The National Health Policy, 2002, the 2004 Common Minimum Programme of the Government of India, and the National Rural Health Mission, 2005, endorsed the need to increase health expenditure to about 2–3 percent of GDP by 2010. Uttarakhand requires additional central transfers to provide basic health services.

CONCLUSION The state has pretty poor indicators viz., lowest sex ratio, couple protection rate, crude birth rate, crude death rate, maternal mortality rate, infant mortality rate, institutional deliveries, Safe delivery, unmet need of family planning, women with three and above children, Reproductive track Infections(RTI) among women, and complete immunization. The state has a high risk of Tuberculosis. Community volunteers-women are appointed from the village level to address the issues related to these indicators. Efforts are made to enhance their capacities through skill development and training. The community based institutions and the PRIs interact with the community in the Gram Sabha - Village Assembly and formulate perspective plan and provide better quality of life.

Haemorrhagic Fever

PA 140
Crimean Congo haemorrhagic fever in Kosova

N. Ramadani, L. Gashi and A. Kalaveshi
Kosova National Institute of Public Health, Department of Epidemiology, Prishtina, Albania

OBJECTIVES Epidemiological characteristics of haemorrhagic fever in Kosova, the success of active surveillance, possibilities for stopping circulation of CCHF virus epidemiological analysis of outbreaks in Kosova.

METHODS Descriptive – retrospective analysis of the data taken from official surveillance system of the Kosova National Institute of Public Health, Department of Epidemiology in Prishtina.

RESULTS The first case of CCHF in Kosova was registered in the village of Nishor of Suhareka municipality in 1954. 1995 – 2006 year was the period when 352 confirmed cases where registered with 31 death cases resulting with fatality rate 8.8%. CCHF occurred as outbreak during the year 1995 with 65 cases or incidence 3.07/100.000 and seven death cases with fatality rate 10.7%; during the year 1996 with 23 cases, or incidence 1.06/100.000 and five death cases with 21.7% fatality rate. After quiet period for 4 years with few sporadic cases in year 2001 this disease appeared again in epidemic form with 31 cases or incidence 1.44/100.000 and seven death cases with fatality rate 22.5% in 2006 are registered 80 cases. Of 352 cases of disease in this period, in 234 or 66.5% the mode of transmission was tick bite, in 79 cases or 22.4% contact between people was the mode of transmission and the way of contracting the virus is unknown in 39 cases or 11.1%. The largest number of the confirmed 352 cases in this period is in the frame of the age group 15 – 45 years with 214 cases or 61.2%. During the time period 1995 – 2001, 60.8% of the cases were male and 39.2% were female. The largest number of cases as anticipated in all time periods was in the group of farmers 154 cases or 43.75%, housewives 87 or 27.53%.
CONCLUSION The territory of Kosova, dating from year 1954, when first cases were registered is endemic zone for this disease. Taking into consideration that Kosova is an endemic – epidemic and epizootic area with CCHF, also with enormous population of Hyalomia Plumbeum ticks, permanent surveillance of disease and appropriate prophylactic and epidemic prevention measures were taken. Despite that we can conclude that epidemiological situation in Kosova is uncertain and in the future we can expect new cases of disease or outbreaks.

Health Financing

PA 141
Presentation of mechanisms to control hospital costs in Iran
A. Khayatzadeh Mahani
Manchester Business School, Manchester University, Manchester, UK

INTRODUCTION Scarcity of resources in health sector is the main reason of considering productivity and efficient utilization of resources in this sector. Among different parts of health system, hospitals constitute the most costly part needing specific consideration.

OBJECTIVES The main objective of this study was presenting some applicable mechanisms for controlling hospital costs in Iran to be applied by hospital managers.

METHODS This study drew on a range of literature, information and participants. The literature was searched via Internet and reviewed. The possible mechanisms were evaluated. Experts in the field of Hospital Administration; Health Services Management; and Health Economics were contacted about their knowledge of existing mechanisms of controlling hospital costs. To present mechanisms applicable and suited to the situation of Iran, Delphi Technique was used and possibility of each mechanism was studied and analyzed. Also some qualitative methods such as expert consultation, key informant interviews and group discussion were applied.

RESULTS AND CONCLUSION Controlling hospital cost must be performed well since it helps make additional resources to use in other economic sectors which in turn would improve welfare of the mass. To reach the aim of controlling hospital costs the following instructions must be taken into account: To be familiar with hospital costs. To recognize factors influencing hospital costs volume. To present mechanisms for controlling hospital costs. To apply proposed mechanisms in hospitals.

PA 142
Impact of transport refunds on research participants commitment to study
M. Chaponda
Tropical Diseases Research Centre, Clinical Sciences, Ndola, Zambia

OBJECTIVES To compare the effect of transport refunds on the commitment of participants coming for scheduled visits in two clinical trials performed in Ndola, Zambia.

METHODS The participants of one study were given an equivalent of a dollar each as transport refund for every scheduled visit made to the site. The other group of participants was receiving an equivalent of five dollars each for every scheduled visit made.

RESULTS It was observed that the study whose participants were refunded a dollar equivalent recorded thirty-three (33%) scheduled visit absentee compared to the study that refunded its participants an equivalent of five dollars for transport which recorded 3.4% absences.

CONCLUSION On average a two-way taxi in Ndola, Zambia costs about four dollars. The participants who were refunded five dollars for transport could thus afford to book a taxi to and from the research centre for their scheduled visits. The group which was refunded a dollar for transport could only afford a bus to and from the research centre for their scheduled visits. Easy accessibility to the Research centre increased the turnout of participants for the scheduled visits. Reasonable resources must be allocated to the welfare of research participants especially when it involves visiting the centre from time to time. However, these transport refunds must not compromise good clinical practice.

PA 143
Performance based health financing, a comparison of system development and outcomes in three continents
G. Leerink1, F. Griffiths2, M. Naseem3, J. P. Kashala4 and E. Klinkenberg1
1HealthNet TPO, Amsterdam, Netherlands; 2HealthNet TPO, Phnom Pen, Cambodia; 3HealthNet TPO, Jalalabad, Afghanistan; 4HealthNet TPO, Kananga, Congo

OBJECTIVES Free health care is not sustainable and not affordable in the long term. HealthNet TPO collaborates with local partners to develop health financing systems that are culturally accepted, economically viable and possible to implement on a large scale. The systems are adopted to best fit local circumstances but lessons can be learned for scaling up and development in other countries. We undertook a review of the research that has been conducted to evaluate performance based health financing (PBHF) projects in three countries to investigate the impact of the program and make recommendations for development of future programs.

METHODS The programs in Afghanistan, Cambodia and Congo all have been running for several years and were compared in terms of: impact on household health expenditures, usage of the public health system and population health indicators. Although each of the three projects has a locally developed and adapted system, there are important similarities: all make use of user fees for cost-recovery of health expenses whereby patients pay a certain percentage of the actual expenses. Targets are set for different services. Income realised from user fees and subsidies from HealthNet TPO are used for providing staff incentives and running costs of the health facilities. The health unit manages all or part of their expenses in order to maximize resources where they need them most.

RESULTS The program in Cambodia is implementing a contracting in system since 1999 and is the longest running. Results from household surveys in 2001 showed that despite introduction of user fees, there was increased use of public services and a decrease on household expenditure of about 40%. The project in Afghanistan so far only introduced user fees and partial cost recovery and set delivery targets. A follow up survey is just completed and the data are being analysed at the moment to compare the impact of the program over the last 2 years. In Kasai, Congo, the program started in 2004 and contracts have been made with the different health centres. Results show increased use of services and improvement of health indicators. We are at present undertaking a comparison between the three systems and their impact on health indicators for which results will be available during the conference.

CONCLUSION Data are still being analysed but the analysis will indicate the impact of improved health financing mechanisms in the three programs and will highlight important lessons learned.
Health in Emergency Situations

PA 144
Feasibility of solar energy in disinfection of drinking water in disasters in Iran
A. Mahvi
School of Public Health, Center for Environmental Engineering, Tehran University of Medical Sciences, Environmental Health Engineering, Tehran, Islamic Republic of Iran

OBJECTIVES The main objective of this study was to determine the efficiency of locally available bottles (not transparent to UVS and semi-transparent to UVA) for use in solar disinfection of water in non-urban areas of Iran. For this purpose PET bottles were used and the solar disinfection efficiency was investigated in terms of fecal coliform reduction of contaminated surface water samples.

METHODS Two types of locally available PET bottles with UV transmittance value of 0.1% and 0.8% were selected as possible containers, and used in disinfection process of samples of surface polluted water according to WHO guidelines about SODIS. Examinations of microbiological quality of all water samples have been performed by determination of fecal coliform group (five tube fermentation technique) according to the procedure outlined in standard methods. Water sampling had been accomplished in the winter 2006.

RESULTS Results indicate that SODIS is also possible if available plastic bottles with less transparency are used instead of standard bottles. According to the results, about 99.9% disinfection of water (up to three log reduction in fecal coliform) is possible in 39.6 °C. Also it should be noted that by substituting bottle with less UVT with more transparent bottle, the required contact time for 3-log reduction of pathogens indicator can be decreased from 8 to 6 h.

CONCLUSION Results of this study clearly indicate that use of both locally available bottles as the possible containers may have enough justification for SODIS process in non-urban areas and communities of Iran with warm climates and in warm seasons.

PA 145
Viral infection of hepatitis C and B in intravenous drug users
L. Garotic-Ilic1, V. Vlaskovic-Ilic’ and V. Babic-Dunjic2
1Institute of Public Health of Belgrade, Center for Prevention and Control Diseases, Belgrade, Serbia and Montenegro; 2Institute of Public Health of Belgrade, Center of Microbiology, Belgrade, Serbia and Montenegro

AIM Intravenous drug users are highly susceptible for viral hepatitis C and B. The aim of our paper is to show the risk of those infections in the above group by determining the prevalence of HCV and HBV markers.

METHODS Our research covered 116 IVDUs in Belgrade, aged 17–50. Serology of HCV infection was made using IV generation ELISA and confirmative Western Blot. Serology of HBV infection was made using III generation ELISA for the presence of HBV markers.

RESULTS Of 116 tested IVDUs in Belgrade, (December 2005 – June 2006) we detected markers of HCV infection in 55 (47.4%). In 20 (17.2%) we detected only certain markers of HBV infection. Of 55 IVDUs with HCV infection, we found only markers of HCV infection in 38 (69.1%). In 17 (30.9%), we detected both HCV and some HBV markers: HBsAg in 4 (7.3%) and anti-HBs antibodies in 13 (23.6%). In 3 (12.3%) we confirmed the presence of only anti-HBs antibodies. Greatest number of infected persons, 22 or 60%, was in the 20–30 age group. There were 11 persons (20%) younger than 25. Anti-HCV prevalence ranged from 11.0% (6) in IVDUs who have been using drugs for less than 3 years to 38.2% (21) in IVDUs who have been using drugs for 6–10 years. Among our cases, 80% were males.

CONCLUSIONS Anti-HCV positive status is present in younger IVDUs, correlating with the length of drug abuse. HCV is more readily transmitted than HBV. Correlation of HCV infection and carrier state of HBs in IVDUs is low and is better correlated with old HBV infection.

Health Systems and Communities

PA 146
Health needs of the urban poor: findings from 22 low-income settlements in Surat, India
A. Acharya
CSS, Surat, India

Although, urbanisation has led to increased productivity and economic diversifications, it has also resulted into pockets of poverty, deprivation and marginalisation. Urban poor constitutes nearly third of India’s urban population and is growing at three times the national population growth rate. Health status, access as well as utilisation of health services in these low income population groups remain quite low and is in no way better than deprived rural areas. The paper analyses the data generated by the survey of 544 households living in 22 low income settlements in Surat. Surat is one of the fastest growing cities of the world and it also has greater proportion of slums compared to other important cities of Gujarat. The research investigated ranged of aspects like socio economic status (access to water, toilets, electricity, assets, education etc.), morality, morbidity requiring inpatient care as well as outpatient care, burden of health care expenditure, provider preference, disease awareness, infant and maternal mortality, antenatal care as well as immunisation levels. Socio-economic variables are found to be closely related with health and can determine health care seeking behaviour to a significant extent. There is a considerable preference for private providers for common illness episodes but public providers are preferred in case of antenatal care and immunisation services. More than half of all births take place at home through a Dai (midwife). Direct and indirect costs associated with hospitalisation episodes are quite high even in case of public provider and poses a great burden of the households. Almost all hospitalisation episodes have been financed through either borrowing or selling household assets. Protection from this catastrophic cost is required to improve the access and utilisation of health services. Most women have found to be using irreversible contraception techniques like tubectomy and therefore awareness about other reversible techniques and male participation needs to be emphasised.

PA 147
Community health partnerships – getting it done
D. George1 and J. Eby2
1Human Services Center Corporation, McKeesport Collaborative, McKeesport, USA; 2Mon Yough Community Services, Outpatient/Prevention/Student Assistance, McKeesport, United States of America

OBJECTIVES By the end of the presentation attendees will be able to create effective grassroots partnerships, recognize the importance of conducting community needs assessments and impact studies, develop logic models identified by assessments for key areas of community needs and discuss ways to create collaborative, far-reaching health initiatives beyond individual communities as a means to strengthen effectiveness.
METHODS The purpose of this presentation is to educate participants in a community health partnership that has been proven effective and has tripled in size as its inception. Through lecture, group discussion, and participation, attendees will learn that by partnering with a local foundation their community partnership can become a catalyst to attract outside funding and to direct such funding to areas of greatest community need. Attendees will appreciate the importance of having key leaders develop logic models for emerging needs that are identified through community assessments and impact studies. It will be understood that the philosophy to centralize research-based programming and outcomes data collections, and to decentralize the dissemination of health care information motivating health change at the community level is a proven best practice.

RESULTS Those in attendance will obtain practical and applicable information that can be duplicated in their community to create, strengthen or expand a health partnership in their neighborhood.

CONCLUSION Through lecture and small group discussion, each attendee will leave this session with specific information and resources that can be applied in their own communities. This session will also provide information on innovative ways to fund community partnerships focusing on health initiatives.

Health Systems Research

PA 149
Removal of cadmium from aqueous solution by Platanus orientalis leaves
F. Gholami Boroujeni1, A. H. Mahvi2, J. Nouri3 and S. Dobaradaran4
1Environmental Health Engineering, Tehran University Medical School, Tehran, Islamic Republic of Iran; 2Tehran University Medical School, Tehran, Islamic Republic of Iran; 3Boushehr University Medical School, Boushehr, Islamic Republic of Iran

OBJECTIVES Removal of cadmium (II) from aqueous solution was studied, using Platanus orientalis leaves (POL) and their ash in 2006 in Iran.

METHODS Bach adsorption experiments were performed as a function of solute concentration, contact time, pH and ionic strength for the experiment. The effect of Ca2+, Mg2+, Na and K+ on adsorption was then studied.

RESULTS The effect of this adsorbent on COD in aqueous solution showed that 1 g/l of adsorbent caused increase of 120 and 95 mg/l COD in dionized water in 120 min for POL and its ash. The maximum removal took place in the pH range of 7 contact time 120 min and initial concentration 20 mg/l.

CONCLUSION The cadmium sorption obeyed both the longmuir and fraunlich isotherms. The study showed POL ash was more favorable than living ones as well as the in removing cadmium from the aqueous solution.

PA 148
The epidemiologic study of animal bites in Rafsanjan, southeast Iran, from 2003 to 2005
N. Zia Sheikholeslami1, M. Rezaeian2, Z. Salem3 and 1542 cases due to animal bites referred to Rafsanjan Health Center, South-East of Iran 2003–2005
1Rafsanjan Medical University of Medical Sciences, Infectious and tropical medicine, Rafsanjan, Islamic Republic of Iran; 2Rafsanjan Medical School, Social Medicine, Rafsanjan, Iran, Islamic Republic of Iran; 3Medical University of Rafsanjan, Social Medicine, Rafsanjan, Islamic Republic of Iran

OBJECTIVES Babies is one of the most common viral causes of mortality in the developing world. Exposure to the virus has significant medical and economic implications in all over the world. Approximately 4 million people receive post exposure treatment (PET) annually. Annually, rabies is the cause of approximately 100 000 deaths throughout the world. The incidence of animal bites in Iran has been increased and it has been raised from 35.1 per 100 000 in 1987 to 151 per 100 000 in 2001. Studies from different parts of Iran revealed the increased incidence rates of animal bites. This study presents epidemiological aspects of animal bite and offers some suggestions about the control of this problem.

METHODS This study was descriptive and over the 3 years period i.e. 2003–2005, a total of 1542 cases were studied. Anyone who was bitten in any part of the region and referred to Rafsanjan Health Centre was subject of this study. A Questionnaire was completed by expert healthcare workers for each case. Data were analyzed using SPSS software version 14 applying Chi-square and t student tests.

RESULTS This study was descriptive and over the 3 years period i.e. 2003–2005, a total of 1542 cases were studied. Anyone who was bitten in any part of the region and referred to Rafsanjan Health Centre was subject of this study. A Questionnaire was completed by expert healthcare workers for each case. Data were analyzed using SPSS software version 14 applying Chi-square and t student tests.

CONCLUSION To consider the increased incidence rate of animal bite in Rafsanjan, we studied the epidemiological aspects of animal bite and offered some suggestions about the control of this problem on educational, health and social solutions.

PA 150
A qualitative study into disease concepts, patterns of health seeking behaviour and sources of health information in two villages in Bauphal sub-district, Bangladesh
M. Yink
Alumni MPH Royal Tropical Institute Amsterdam; MOA (Medische Opsvang Asielzoekers), Nieuw Vennep, Netherlands

OBJECTIVES To describe disease concepts for health problems, ranked as ‘most frequent’ by the local population.To describe patterns of health seeking behaviour for these health problems.To describe sources of health information.To identify potential community stakeholders and strategies for health promotion activities.

METHODS Qualitative exploratory study in two randomly chosen villages in Bauphal sub-district, Bangladesh. Methods used in this study were Focus Group Discussions with groups of nine participants, divided by sex and age group, and semi-structured interviews. Group sessions involved discussion topics and participatory methods (health facility mapping, Venn diagrams). In each village interviews were performed with local health care providers (traditional healers, ‘village doctors’, private practitioners and TBAs) and with village leaders, teachers and imams. Government health care practitioners and NGO representatives in the area were also interviewed. The study was performed in November 2003 by a group of four researchers, of whom three speak Bangla.

RESULTS Results of this study are based on 16 Focus Group Discussions (8 in each village), 14 interviews with local health care providers, village leaders, teachers and imams and 10 general interviews. Research data show that many local people hold traditional beliefs related to disease concepts and disease causation. Mentioned causes frequently relate to types of food (not) eaten, hard work and climatic circumstances. Local disease definitions can differ considerably from medical definitions. Gynaecological problems (mostly due to unsafe deliveries) seem
Prevalence of enteric parasitic infections in eastern cities of Tehran Province, Iran

M. Rostami Nejad1, E. Nazemalhosseini1, A. Haghighi2 and M. R. Zali1
1Department of Foodborne and Diarrheal Disease, Research Center of Gastroenterology and Liver Diseases, Shahed Beheshti University of Medical Science, Tehran, Islamic Republic of Iran; 2Department of Parasitology and Mycology, Shahed Beheshti University of Medical Science and Health Service, Tehran, Islamic Republic of Iran

OBJECTIVES Intestinal parasitic infection is a major health problem in many developing countries. By increasing Standards of health and controlling the carriers or intermediate hosts, most industrialized countries have successfully decreased the rates of infestation. Geographical conditions and poor nutritional and Socioeconomic status contributes to making Iran a favorable area for parasitic infections. The aim of this study is to investigate the prevalence of intestinal parasitic infection in East cities of Tehran province (Firoozkoh and Damavand).

METHODS From September to December 2006, three hundred and fifty fecal samples by cluster sampling were examined for intestinal parasites. We used microscopic and staining method to examine the stool samples for presence of trophozoites, ova, cysts, larvae and oocysts of intestinal parasites by standard technique.

RESULTS Of 350 fecal samples (64.2% female and 35.8% male), with mean age of 41.66 years, 126 isolates (36%) including pathogen and non-pathogen parasites were positive. The frequency rate of E. coli, Endolimax nana, Giardia lamblia, Blastcystsis hominis, Iodomoeba butcheli, Chilomastix mesenelli, Entamoeba histolytica/Entamoeba dispar complex, Ascaris lumbricoides, and Enterobius vermicularis were 44 (34.9%), 42 (33.3%), 12 (9.5%), 8 (6.5%), 6 (6.5%), 5 (4%), 4 (3%), 2 (1.5%), 1 (0.8%) respectively.

CONCLUSION In this study G. lamblia showed the most prevalent rate in the infections and E. coli was higher among the non-pathogenic protozoa. Based on the result of present study, stool examination should be taken for high-risk populations in the low level hygiene to increase knowledge of people about personal and community health and hygiene.

KEYWORD prevalence, enteric parasite, Iran

PA 151

An integrated model system for improving the quality of malaria parasites microscopy and AFB microscopy in Kano State of Nigeria

F. Sarkinfada, I. Bates and C. Chavasse
Liverpool School of Tropical Medicine, Disease Control Strategy Group, Liverpool, UK

OBJECTIVES Kano state in Nigeria has begun to establish a state-wide quality checking process for TB microscopy but does not have any system for quality checking malaria microscopy. We aim to test the feasibility of designing, implementing and evaluating an integrated model system for improving the quality of malaria parasites and Acid Fast Bacilli (AFB) microscopy in Kano State of Nigeria. A pilot study showed that while 92–97% of AFB microscopy results were correct, only 70–75% of malaria readings were correct.

METHODS Five district hospital laboratories in which both malaria parasites and AFB microscopy were conducted were selected for the project. A team of five quality assurance officers comprising the state AFB quality control officer and two quality control officers each for AFB and malaria parasite microscopy were recruited and trained to assist with project implementation at state level. Community tuberculosis control supervisors in the five selected centres were trained to incorporate supervision and sampling for quality checking of malaria slides into the existing TB system. A model system based on blinded re-checking of sampled malaria parasites and AFB slides with on-site training and supervision at three monthly intervals was instigated in March 2006.

RESULTS By January 2007 the model had been fully implemented in 1/5 centres with 100% sensitivity and specificity for the presence of AFB and malaria parasites on microscopy. The model had been partially implemented in 3/5 centres and not implemented in one centre. Implementation of evaluation is still ongoing but factors that promoted successful implementation included adequate support from the hospital administration, proper supervision and motivation from the microscopists.

CONCLUSION It could be feasible to design, implement and expand an integrated model system for quality assessment of malaria parasites and AFB microscopy in a low-resource country.

Health Technology Assessment

PA 153

Visual exploration of spatio-temporal patterns in epidemiological data

B. K. Masaka
National Institute for Medical Research, Health Statistics and IT, Dar Es Salaam, United Republic of Tanzania

Physicians in health services (e.g., hospitals, clinics and dispensaries) collect huge amount of health data describing diseases of patients on a daily basis. Such data are used in epidemiological studies, where by one is interested in the spread of the disease in space and time. In particular, one is interested in the direction and speed of spread of diseases as well as in the factors influencing this. Most of health data collected is recorded, stored and presented in tabular format. Presenting data in this format may not allow a rapid insight into the spatial or spatial/temporal aspect of the data such as a skillful interaction with the data, the genesis of new research hypotheses and the drawing of relevant conclusions. A solution to this problem is the application of visualization methods that will allow the exploration and analysis of spatio-temporal data. Most of epidemiologists are
not familiar with visualization, so they prefer to use statistical methods. Statistical methods are unable to show/answer 'where and when' the disease is (direction and speed of spread). This study aims to investigate how visualization environment can support the statistical methods in analyzing spatial, temporal and spatio-temporal patterns in epidemiological data. The study is illustrated with data on malaria reported cases in Njombe district, Tanzania collected from 2000 to 2004. Temporal animation and PCP (linked to a map) are visualization techniques selected to discover patterns in this study. The techniques are incorporated in the visualization environment, which was designed based on the functionalities of two existing software packages: GeoVISTA for PCP and ArcGIS 9.2 which support the temporal animations. An evaluation test was conducted to assess how well the functions of the visualization environments can support epidemiologists to identify and describe patterns. Given the results obtained from the tasks carried out in this research, it can be seen that by using visualization it is possible to identify and describe spatial, temporal, and spatio-temporal patterns, the user has the advantage that he/she can see where the clusters are, how the clusters change with time. Where as statistical methods did not reveal spatial and spatio-temporal patterns, but could be used to verify and determine the significance of patterns found visually. In order to identify, describe and confirm that a patterns exists; then both methods should complement each other. Visualization is a good technique to start with as it will provide a clue of the patterns, particularly the spatial and spatio-temporal ones, such as areas with high values of malaria, and or months showing similar patterns. Then, statistics is needed to confirm what has already been observed in visualization.

**Keywords** epidemiology, visualization, statistics, spatial and temporal patterns, parallel coordinate plot, animation

### Human Resources in Health

**PA 155**

An action-research network for epilepsy care in rural Mali, West Africa

G. Farnarière,
P. Genton,
K. Nimaga,
O. Dourouma,
D. Desplets

**University De La Mediterranee, Neurophysiologie Clinique, Marseille cedex, France**

**Centre Saint Paul-Hôpital Henri Gastaud, EPILEPSIOLOGIE, Marseille cedex, France**

**Association des Medecins de Campagne du Mali, Bamako, Mali**

**Faculte de Medecine, Epidemiologie des Affections Parasitaires, Bamako, Mali**

**Sante Sud, Marseille cedex, France**

**OBJECTIVES** The treatment gap in epilepsy is very important in rural Africa. Two conditions need to be fulfilled to try and fill this gap: (i) a good knowledge on epidemiology and cultural aspects of epilepsy in the African setting and (ii) the presence of competent medical staff, with tools for diagnosis, pharmacological treatment and follow-up.

**METHODS** After preliminary on-the-ground ethnological and epidemiological studies in rural Mali, six volunteer general practitioners were selected among the ‘country doctors’ installed by Sante Sud, a NGO with funding from the EU. Each covers a health area of 10 000 inhabitants. This group was trained in epilepsy in order to diagnose the different types of seizures and syndromes, and to control practical aspects, including the delivery of anticonvulsants. The organization of drug supply was improved thanks to the support of Sanofi-Aventis. All patients with epilepsy were included in a prospective database with follow-up at 4-month intervals over the first 3 years of management, the protocol included an initial file with 93 items and many follow-up files with 63 items. This database is now used as a source of information on epidemiological, clinical and therapeutic aspects of epilepsy in rural Africa.

**RESULTS** After 3 years, 1200 patients of all ages have been included in the database. A very good compliance is noted and more than two third of the patients had no more seizure and a clear physical, psychic and social improvement.

**CONCLUSION** A practical, step by step and rational approach to the many problems posed by epilepsy may help reduce the treatment gap in rural Africa. Efficient managing of epilepsy is possible founded on the training of local medical resources. Access to medication requires a specific organization. Such a protocol accompanied by an “action-research” program is a method to obtain many important clinical and therapeutic data.

**PA 156**

Migration of health personnel from Africa to Switzerland

I. A. Dia

**Department of Sociology, University of Geneva, Geneva, Switzerland**

**OBJECTIVES** The objective of this joint IOM-University of Geneva research financed by the Geneva International Academic Network was to analyze: (i) the causes, trends and statistical data of the Migration of Health Personals from Democratic Republic of Congo, Cameroon, and Senegal to Switzerland; (ii) the impact of Migration of Health Personals in the countries of origin and country of residence; (iii) the links between migration of health personals and the development of country of origin; and (iv) and identify local and international good practices.

**METHODS** This study used the following methodology: (i) literature review; (ii) selection of Cameroon, DRC and Senegal using Swiss official statistics; sampling strategy (50 health personals) using the snowball effect methodology; (iii) test of qualitative and quantitative methods; (iv) qualitative and quantitative interviews with health personals and students from selected countries; (v) focus group with migrants, diasporas associations, policymakers and employers in the health sector; (vii) data analysis; and (viii) findings of the study during a roundtable.

**RESULTS** A great potential of development and initiatives (remittances transfer, knowledge transfer, access to drugs and health facilities, construction of health centers, etc) for the country of origin; (i) however, lack of state support and many constraints that hinder developmental contribution; lack of collective and institutional initiatives: migrants and diasporas initiatives often individual and informal; (ii) negative perceptions of the country of origin’s health system and poor outcome of migration for the health system; (iii) family as main beneficiary of the transfer of resources by migrants and diasporas; (iv) the way migrants and diasporas are integrated in the health system and in the country of residence and the political, economic and social situation of the country of origin impact on their developmental contribution; and (v) many constraints both in country of origin and country of residence that hinder return to the country of origin. Need for political support and dialogue, including migrants, Diasporas and policymakers.

**CONCLUSION** This research analyzed the contribution of African migrants in the health sector in Switzerland to their country of origin; the impact of migration on their living and working conditions. One of the main recommendations is the need for policy dialogue and state support to strengthen migrants and Diasporas initiatives and mobilize them for the benefit of the country of origin.
Immigrant Health

PA 157
Blinding trachoma epidemiology in internal displaced persons camps in Sudan
D. I. Sankara
Rollins School of Public Health, Global Health, Emory University, Atlanta, USA

OBJECTIVES The participants will be able: (i) to understand the methodology and approach to conducting a baseline evaluation of blinding trachoma; (ii) to review the results of the baseline evaluation; and (iii) to demonstrate the use of a community participatory approach in population based surveys.

METHODS We used a cross sectional survey which involved 2 stage random sampling, with selection of camp’s sections using probability proportional to size in the first stage, and compact segment sampling within each section in the second stage. Verbal consent was obtained from the camp leaders, all individuals and parents of young children. The Institutional Review Board of Emory University approved the protocol, and permission to conduct the surveys was obtained from the state ministries of health. Participants were screened using the WHO simplified trachoma grading system, and a member of each household completed a questionnaire. Data were double entered and validated using Epi Info version 6.04. Confidence intervals and descriptive statistics were generated using the SUDAAN.

RESULTS Prevalence of active trachoma (TF and/or TI) in children aged 1–9 was 3.06% (95% CI 0.32–5.80) regardless of gender; within this age group, active trachoma prevalence for females was 2.86% and 3.29% for males. In people aged 10 and above, the prevalence was higher 9.63% (95% CIs 7.68–11.58%). Females did not have more active trachoma than men. Prevalence of Trichiasis (TT) in people aged 15 and over was 1.13% for females and 1.12% for males, with an overall prevalence of 1.13% (95% CIs 0.29–1.96). Regarding the estimated trachoma burden in this camp about 386 persons need immediate trichiasis surgery, and about 3025 persons are suffering from active trachoma. 24% of the households claimed to wash children’s face more than twice a day.

CONCLUSION Consistent with three other studies previously conducted in Sudan, persons aged 10 and above in these populations are more likely to have active trachoma. Trichiasis surgery, face washing, and environment improvement strategies will be implemented to control the disease in the camps. This study was conducted as a partnership of The Jimmy Carter Center Atlanta, the State and Federal government of Sudan and community leaders in the IDP camps. The same partners are the implementing partners for the trachoma SAFE implementation strategy.

PA 158
Hemoglobinopathies and congenital hemolytic anemias in immigrant population in Almeria, Southern Spain
M. A. Molina1, J. A. García1, R. Pérez1, M. J. Jiménez2, M. T. Gallego1, M. T. Cabezás1, M. I. Cabezás1, A. M. Jiménez1, J. Salas1, A. B. Lozano3, C. Aviravan4 and Tropical Medicine Unit 1, Microbiology and Clinical Parasitology, Hospital de Poniente, El Ejido, Almería, Spain; 2Transfusion Center, Almería, Spain; 3Hematology and Hemotherapy, Hospital de Poniente, El Ejido, Almería, Spain; 4Biotechnology Area, Hospital de Poniente, El Ejido, Almería, Spain; 5Hospital de Poniente, Internal Medicine, El Ejido, Almeria, Spain

OBJECTIVES To describe the cases of congenital hemolytic anemias occurring in the immigrant population in our area, mostly coming from the Maghreb and sub-Saharan Africa, compared to those detected in our autochthonous population.

METHODS Anemia work-up protocols from January 1997 to December 2005 have been reviewed. From October 2002 we have used the Hi-AUTO A1c 8160 (Menarini-R) high-pressure liquid chromatography (HPLC) system, which allows the detection of abnormal variants of hemoglobin; its final characterisation was made by acidified medium electrophoresis.

RESULTS Of the 2672 anemia protocols reviewed, 364 corresponded to immigrant patients (13.6%). We detected 62 cases of hemoglobinopathy (17%), 10 cases of GP6DH deficiency (2.7%) and seven cases of hereditary spherocytosis (1.9%). Among hemoglobinopathies, we found: 14 Hemoglobin (Hb) AS; 14 beta-thalassemia minor; 11 Hb AC: six homozygous HbS (Hb SS); four intermediate beta-thalassemia; four double heterozygous Hb SC; 3 Hb CC; three heterozygous alpha-thalassemia; 1 Hb SS + alpha-thalassemia; and one Hb SS + beta-thalassemia. Since we used the HPLC abnormal hemoglobin band detection system: 45 Hb AS; 10 Hb AC; four beta-thalassemia minor; one Hb CC and one persistence of fetal hemoglobin (HPPH) have been added. Considering autochthonous population, 2308 anemia protocols were carried out, detecting: 119 hemoglobinopathies (5.16%), 50 cases of hereditary spherocytosis (2.17%) and seven cases of GP6DH deficiency (0.3%). Among hemoglobinopathies: 63 beta-thalassemia minor; 22 intermediate beta-thalassemia; 20 alpha-thalassemia; 11 delta-beta thalassemia; 1 Hb AC; 1 HPPH and 1 Hb AS or Hb AD that we were unable to characterise. Using the HPLC system, we added: 6 Hb AD; 3 Hb AS; 3 Hb AC; 2 delta-beta thalassemia; 2 Hb AS/AD; 1 intermediate beta-thalassemia; 1 beta-thalassemia minor; 1 PHFH and 1 Hb C/E.

CONCLUSIONS Of the anemia investigation protocols carried out, 13.6% were on the immigrant population, which is similar to the percentage of stimated immigrant population living in our area overall. In this population, we have found hemoglobinopathies, even without anemia, that are unusual in local patients, and should not be underdiagnosed. HPLC, an abnormal hemoglobin band detection system, is of great usefulness in the screening of structural hemoglobinopathies. Hereditary Spherocytosis, the most prevalent hemolytic anemia in white people, should not be ignored when investigating anemia in immigrants. Beta and alpha-thalassemias are more frequent in our autochthonous population, but also Hb S carriers can be found.

PA 159
Malaria chemoprophylaxis in VFRs: a study with the Delphi method
G. Calleri1, F. Gobb1, R. H. Behrens2, Z. Bisoofi3, A. Bjorkman4, F. Castelli5, J. Gascon6, M. P. Grobusch7, T. Jelínek8, M. L. Schmidt9, M. Niero10, P. Caramello11 and TropNetEurop1
1Amedeo di Savoia Hospital, Infectious Diseases, Torino, Italy; 2London School of Hygiene and Tropical Medicine, Infectious and Tropical Diseases, London, UK; 3Sacro Cuore Hospital, Tropical Diseases, Negrar, Italy; 4Karolinska Institute, Medicine, Stockholm, Sweden; 5Infectious and Tropical Diseases, University of Brescia, Brescia, Italy; 6Hospital Clinic, International Health Centre, Barcelona, Spain; 7Division of Clinical Microbiology and Infectious Diseases, University of Wittenberand, Johannesburg, South Africa; 8Berlin Centre for Travel and Tropical Medicine, Berlin, Germany; 9Department of Infection and Tropical Medicine, Newcastle General Hospital, Newcastle upon Tyne, UK; 10Educational Sciences, University of Verona, Verona, Italy

OBJECTIVES The Delphi method is a consensus development technique, useful where no unanimity of opinion exists owing to lack of scientific evidence. Essential requisite of the method are anonymity, controlled feedback, and statistical group response.
Aim of this study was to investigate the opinion and practice of major European experts based in different countries, about complex situations and debatable areas of malaria prophylaxis prescription in VFRs; secondly to try and create a consensus or at least to make practice in referral centres and indications to periphery, more homogeneous.

METHODS Questionnaires were administered to site managers of TropNetEurop, a network for imported diseases surveillance, including 47 sites in 16 countries. Part 1 asked experts to give data about their experience (work with VFRs, area of origin, different approach to VFRs or children) and respond to questions (problematic situations in prescribing malaria prophylaxis, factors to be considered, relevance of drugs’ characteristics, importance of insect bite prevention) with a score on a visual scale. Part 2 described 16 chemoprophylaxis scenarios: possible responses were prophylaxis yes/no/uncertain.

RESULTS Around 25/47 questionnaires were returned (53%). Evidences from part 1: Risk perception of malaria and accessibility of travel clinics is lower in VFRs than in other travellers, but very variable, due to cost and cultural problems. VFRs are about 10% of travel clinics visitors, and most are from West Africa. Experts tend to modify their prescription in VFRs, mostly to reduce cost of travel, itinerary and underlying pathologies must be considered, but no consensus exist on the importance of likely compliance, cultural level of the traveller and duration of travel. Important characteristics of drugs are efficacy and, to a lesser extent, tolerability and convenience. Cost and causal activity are relevant only for a subset of experts, but more than in non-VFRs. Part 2 showed a consensus in 12 scenarios: it was very poor in four cases focusing on repeated travels, India, long stay and multi-resistant area. In these cases the judgement distribution was influenced by the practice area of experts, with maximum willingness to give prophylaxis in Northern Europe, and minimum in Central Europe.

CONCLUSIONS The variability in experts opinion deserves a profound discussion at referral centres level and improved data on safety and efficacy of chemoprophylaxis.

RESULTS Among 91 patients studied, 75 (82.4%) presented serologic markers for HBV infection; 24 (26.4%) were chronic carriers (HBsAg+), 24 (26.4%) presented the anti-HBe alone profile. Anti-HBs (+) and anti-HBc (+) profile was present in 27 patients (29.6%). There was not a significant difference in serologic HBV profile between different countries. DNA-PCR was determined in 14 VHB chronic carriers. Six patients (43%) presented DNA-PCR positive and eight patients (57%) presented DNA-PCR negative. HVC antibodies were found in five patients (5.5%), 1 HVC-HBV co infection, two without HBV markers and two with markers of prior HBV exposure.

CONCLUSION We found a real high prevalence of HBV infection in sub-Saharan Africa immigrants patients referred to the Tropical Medicine Unit in Hospital de Poniente (Spain). More than 25% are HBsAg chronic carriers. HBV carriage in black Africans is less established in early childhood, and induces diseases, especially hepatocellular carcinoma and cirrhosis. It is necessary to closely follow these patients to prevent the development of these significant illnesses. We think that HBV and HVC markers must be requested in all patients coming from sub-Saharan Africa countries.

PA 161
Microbiological diagnoses in the patients referred to the Tropical Medicine Unit of the Hospital de Poniente

J. Salas Coronas, J. Vázquez Villegas, T. Cabezas Fernández, I. Cabezas Barrera, A. B. Lozano Serrano, M. A. Molina Arrebola, M. C. Rogado García, M. L. Sánchez Benítez de Soto and Unidad de Medicina Tropical de Hospital de Poniente, El Ejido, Spain

OBJECTIVES To analyze the microbiological diagnoses made in the patients sent to the Tropical Medicine Unit (TMU) of the ‘Hospital de Poniente’.

METHODS Of the 107 patients attended until October 2006 in the TMU, 83 (78%) came from Sub-Sahara Africa, 11 (10%) from the Maghreb, 9 (8%) from South America and 4 (4%) from other locations. 42 patients (40%) had been living in Spain for 1–2 years, 48 (46%) between 3–5 years, and 8 (7.6%) <1 year. 17% are women, and the mean age 30.3 years (6–66). 65% of the patients were derived from Primary Attention, the rest from other hospital specialities. The reason for consultation was in 36% of the cases abdominal pain, 18% eosinophilia, 12% hematuria, 7.5% lymphadenopathy, 6.5% cutaneous lesions.

RESULTS In 80% of the patients a microbiological diagnosis was reached. In the case of patients with parasitisms, in 31 (57%) a single isolation was observed, in 13 (24%) 2 isolations and in 10 (19%) 3 or more organisms were found. Among the isolated parasites there were Schistosoma haematobium (16), hookworms (14), Entamoeba coli (14), Blastocystis hominis (10), Strongyloides stercoralis (6), Giardia (6), Dicrocoelium dendriticum (6), Schistosoma mansoni (5), Endolimax nana (3), Trichuris trichuria (2), Ascaris (2), tapeworms (2), P. falciparum (1), E. hystolitica (1), Hymenolepis (1). Three patients were diagnosed with Chagas’ disease and 11 of tuberculosis.

CONCLUSION In 80% of the patients derived to the TMU of the ‘Hospital de Poniente’ a microbiological diagnosis has been made. The parasitic isolations predominate between sub-Saharan patients, being the most frequent diagnoses the parasitism by Schistosoma (haematobium and mansoni) and hookworms. Multi-parasitism is a frequent fact. It is important to emphasize the high number of parasitic isolations in spite of the long stays of these patients in Spain.
PA 162
The risk of a missed or delayed diagnosis in a changing epidemiological context
M. Boscolo, S. Marocco, A. Angheben, G. Monteiro, M. Anselmi, A. Rossanese and Z. Bisoffi
S. Caure Hospital, Centre for Tropical Diseases, Negrar (Verona), Italy

BACKGROUND The increasing population mobility between different epidemiological environments represents a challenge for the management of infectious diseases (Gushulak BD, Globalization of infectious diseases: the impact of migration, CID, 2004). In this changing epidemiological context, a missed and delayed diagnosis may become an important threat to patient safety in non-endemic diseases with long latency period. We report three cases: 1. A 30-year-old from Ghana. After 6 months fever, severe weight loss and abdominal pain, a total-body tomography shows multiple retroperitoneal adenopathies and ascites. Admitted to an Oncologic Department, only after 11 months a correct diagnosis (peritoneal tuberculosis) is made. Case 2: a 28-year-old from Rumania. During a short stay in home country, she complains of fever, diarrhoea, periorbital oedema and rash for a few days. After 2 weeks, fever, myalgia, generalized oedema, severe hypoalbuminemia, and hyperesinophilia (Eo 7700/ul) develop. Only after 20 days hospitalisation she is referred to our Centre for trichinosis. She recovers after 40 more days. Case 3: a male, 38-year-old, from Ghana. After 2 months of gastrointestinal symptoms, he develops fever, myalgia, hypereosinophilia, and hypereosinophilic (Eo 7700/ul) develop. Only after 20 days hospitalisation she is referred to our Centre for trichosisis. She recovers after 40 more days.

OBJECTIVES To illustrate through recent clinical examples the risks involved in missed/delayed medical diagnosis with immigrant patients.

METHOD Case reports. Case 1: male, 30-year-old, from Ghana. After 6 months fever, severe weight loss and abdominal pain, a total-body tomography shows multiple retroperitoneal adenopathies and ascites. Admitted to an Oncologic Department, only after 11 months a correct diagnosis (peritoneal tuberculosis) is made. Case 2: female, 28-year-old, from Rumania. During a short stay in home country, she complains of fever, diarrhoea, periorbital oedema and rash for a few days. After 2 weeks, fever, myalgia, generalized oedema, severe hypoalbuminemia, and hyperesinophilic (Eo 7700/ul) develop. Only after 20 days hospitalisation she is referred to our Centre for trichinosis. She recovers after 40 more days. Case 3: male, 38-year-old, from Ghana. After 2 months of gastrointestinal symptoms, he develops fever, myalgia, hypereosinophilia, and hypereosinophilic (Eo 7700/ul) develop. Only after 20 days hospitalisation she is referred to our Centre for trichinosis. She recovers after 40 more days.

CONCLUSION Cognitive errors, reflecting misdiagnosis from faulty data collection or incomplete knowledge, can never be eradicated, because of the intrinsic limitations of human mental process. (Grabber M, Reducing diagnostic errors in medicine: what’s the goal? Acad Med, 2002). However, categorizing process errors and studying their relations could help efforts to prioritize strategies to prevent the most common and life-threatening ones. Elder NC. Classification of medical errors and preventable adverse events in primary care: a synthesis of the literature, 2002). In particular, the basic and fundamental error concerning immigrants is an incomplete process of hypothesis triggering due to limited (if any) knowledge of different epidemiological contexts. A particular focus on non endemic diseases is mandatory in clinical training of Western professionals.

Immunology

PA 163
Isolated tuberculous liver and spleen microabscesses in Down syndrome
S. Ahtrarpaiman1 and P. Tabatabaei2
1Pediatrics Disease, Baghiatallah University of Medical Sciences, Tehran, Islamic Republic of Iran; 2Pediatrics, Tehran University of Medical Sciences, Tehran, Islamic Republic of Iran

Isolated tuberculous liver and spleen abscesses have documented in the literature rarely. This report describes the challenging diagnosis of primary liver and spleen TB. We report a 10-year-old girl who had fever and chills, anorexia and intermittent vomiting. The ultrasound and computed tomography revealed multiple abscess-like lesions in the liver and spleen. To our knowledge, this is the first reported case of primary TB of the liver and spleen without evidence of involvement elsewhere in Down’s syndrome. The thought of tuberculous should be considered in patients with hepatic and splenic abscesses who have possible immunodeficiency such as Down’s syndrome.

PA 164
Different parameters to evaluate infection progress and therapy response in mice infected with Mycobacterium tuberculosis and their relevance to clinical practice
J. de Steenwinkel1, M. ten Kate1, G. de Knecht2, A. van Belkum3, J. Nouwen2, H. Verbrugh1, R. Schiffelers3, D. van Soolingen3, R. Hernandez-Pando3, I. Bakker-Woudenberg3
1Department of Medical Microbiology and Infectious Diseases, Erasmus University Medical Centre Rotterdam, Rotterdam, Netherlands; 2Department of Internal Medicine, Section Infectious Diseases, Erasmus University Medical Centre Rotterdam, Rotterdam, Netherlands; 3Department of Pharmacometrics, Utrecht Institute for Pharmaceutical Sciences, Utrecht University, Utrecht, Netherlands; 4National Reference Laboratory for Mycobacteriology, National Institute of Public Health and the Environment, Bilthoven, Netherlands; 5Department of Pathology, Section of Experimental Immunology, National Institute of Medical Sciences and Nutrition Salvador Zubiran, Mexico City, Mexico

OBJECTIVES The use of different parameters in the characterization of an animal model of tuberculosis (TB) is of great value for the interpretation of experimental results and their translation to clinical medicine. To that aim, we attempted to characterize our mouse TB model. Different parameters to measure infection progress and therapy response included: microbiology, histopathology, immune response and Mycobacterium tuberculosis gene-expression. In view of the clinical relevance, we investigate whether the cytokine profile in serum, can be indicative of the progressive infection and therapy response in TB patients. We established the value of the cytoketic bead array (CBA) in this respect.

METHODS Mycobacterium tuberculosis strain H37Rv was used to infected female Balb/c mice via the respiratory route. The anti-tuberculosis treatment applied was isoniazid (INH), rifampicin (RIF) and pyrazinamid (PZA) for the first 2 months, followed by 4 months with INH and RIF. This treatment simulates clinical therapy, and is human pharmacokinetic-equivalent in terms of dosage and duration. The infection progress and therapy response was followed at different intervals by means of: quantitative cultures of lung, spleen, liver and blood, histopathological examination of infected organs, immunohisto-chemical-staining of lung sections to assess immune response in situ and determination of cytokine profile in serum, lung- and spleen homogenates by PCR and by CBA. In order to
achieve a broad evaluation of the immune response we focused on both Th-1 and Th-2 derived cytokines: INF-γ, TNF-α, IL-2, IL-4, IL-6, IL-10 and IL-12 p70.

RESULTS The acute and chronic phase of the infection was characterized by granuloma formation and presence of pneumonia, respectively. The mycobacterial load in the infected organs increased during the acute phase and stabilized in the chronic phase. Therapy resulted in a substantial reduction of mycobacteria. Some of the serum cytokines levels, established with the CBA, correlated with the cytokine expression in situ in the lung.

CONCLUSION Our mouse TB model is mimicking human TB and is as such helpful in future research at therapy modification and improvement. The CBA-technique may be of value to establish the cytokine levels in serum of TB patients and in this way helpful to monitor infection progress and therapy efficacy.

PA 165 Interferon gamma response in diabetic lung tuberculosis patients
E. Nelwan1, J. Stalenhoef1, O. Maryantoro2, Z. Amin3, H. Pohan2 and B. Alispahana2
1Department of Internal Medicine, Tuberculosis Working Group, Jakarta, Indonesia; 2Department of Internal Medicine, University of Indonesia, Jakarta, Indonesia; 3Department of Internal Medicine, University of Padjuaran, Bandung, Indonesia

OBJECTIVES To obtain the response of IFN-γ between diabetic lung TB patients compare to non diabetic lung TB and healthy controls To determine the influence of controlled blood glucose level to IFN-γ response.

METHODS Among new cases of lung TB patients with positive AFB, cross sectional we perform screening of diabetes mellitus and include 23 TB-diabetic patients, thirty four lung TB patients and 37 healthy controls matched age and sex. We perform clinical and laboratories examinations. To identify IFN-γ response of diabetic lung TB patients, TB and healthy controls, we draw morning blood and stimulated in vitro with sonicated M. tuberculosis (MTB), lipopolysaccharide (LPS) and phytohaemagglutinin (PHA). After incubation at 37°C for 22–24 h, we centrifuged and IFN-γ response was evaluated from the supernatant with ELISA.

RESULTS Clinical characteristic of TB-diabetic patients and TB patients was similar. Lung TB infection among diabetics were less severe compare to non diabetic ones. Lung TB patients have the lowest IFN-γ response after MTB stimulation compare to diabetic lung TB and healthy controls (not statistically significant), after PHA stimulation, diabetic lung TB patients have the lowest response compare to other groups (significant between all groups, P < 0.01). On diabetic lung TB patients, there is no difference in IFN-g response between good and poor control blood glucose.

CONCLUSION Diabetic lung TB patients have higher IFN-γ response than non diabetic TB patients, this might due to difference of disease severity among TB infection of diabetics and non diabetic ones. This difference statistically not significant and co-morbidity of diabetes mellitus among moderately ill TB patients has shown similar response of advance ill TB patients. Among diabetics lung TB patients with uncontrolled blood glucose, IFN-γ response was lower compare to controlled ones, and this might be due to almost all diabetics lung TB patients has uncontrolled blood glucose concentration.

Immunology and Biology of Malaria
PB 1 Genetic polymorphism of the P126 Plasmodium falciparum protein have no influence in the development of specific immune response
L. Pratt-Riccio1, S. Sallenave-Sales1, B. Silva1, M. Zaila2, J. Oliveira-Ferreira1, F. Santos1, M. D. F. Ferreira-da-Cruz1, D. Canas1, C. Daniel-Ribeiro1 and D. Banic1
1FIOCRUZ, Immunology, Rio de Janeiro, Brazil; 2UFRJ, Rio de Janeiro, Brazil; 3LCEN, Porto Velho, Brazil; 4Institut Pasteur de Lille, Lille, France

INTRODUCTION AND OBJECTIVES The amino-terminal portion of the P126 protein, containing 6-octamer repeats, has been shown to be involved in the induction of protection against P. falciparum. However, a polymorphism present in some isolates that contained 5- instead of 6-octamer repeats was observed. In this study we evaluated the genetic polymorphism of N-terminal region of the P126 in P. falciparum isolates and its possible role in development of specific immune response in individuals living in Brazilian endemic areas.

METHODS The frequency of polymorphism was verified in 83 isolates from Porto-Velho (RO) and 92 isolates from Peixoto-de-Azevedo (MT) by SSCP-PCR and DNA between fragments with same size and only one SSCP pattern was observed for each fragment identified. Sequence analysis of the two alleles identified in our study showed a high conservation in amino acid sequences of P126 in both areas studied: I (199 pb) and II (175 pb). In Porto-Velho, the allele I was detected in a higher frequency (92%) than allele II (8%). In Peixoto-de-Azevedo the alleles I and II were observed in similar frequencies, 59% and 41%, respectively. Analysis by SSCP did not reveal microheterogeneities of sequences between fragments with same size and only one SSCP pattern was observed for each fragment identified. Sequence analysis of the two alleles identified in our study showed a high conservation in amino acid sequences of P126 in Porto-Velho and Peixoto-de-Azevedo. The two alleles presented sequences very similar, differing one each other only by the insertion of the repetitive motif TVGDQAGN in the third unit position of allele I. No association was observed between allelic fragments and the humoral immune response against Nt47.

CONCLUSIONS The data presented here show that the limited genetic polymorphism of the P126 observed in isolates from Porto-Velho and Peixoto-de-Azevedo does not seem to influence the development of specific humoral immune response in infected individuals.

PB 2 Partial purification and characterization of DNA polymerase from Plasmodium falciparum and its role on base excision repair
P. Chavalitswinkoon-Petnir1, P. Nuntawarasinp1 and S. Petnir1
1Faculty of Tropical Medicine, Mahidol University, Department of Protozoology, Bangkok, Thailand; 2Faculty of Tropical Medicine, Mahidol University, Department of Tropical Nutrition and Food Science, Bangkok, Thailand

OBJECTIVES This study aims to purify and characterize Plasmodium falciparum DNA polymerase β including its role on base excision repair. The result will lead to exploitation of the development of drugs that specifically target this enzyme.

METHODS Plasmodium falciparum parasites were cultivated by a large scale cultivation method. Partial purification of P. falciparum DNA polymerase β was performed using fast protein liquid chromatography. Crude extract was loaded onto Resource Q, Hitrap Heparin, Hitrap Blue HP and ssDNA columns. In a presence
of aphidicolin and N-ethylmaleimide (NEM) DNA polymerase β activity could be monitored during purification step. Molecular weight of the partially purified enzymes was determined by SDS-PAGE. Partial purified DNA polymerase β from P. falciparum was tested with some inhibitors such as aphidicolin, NEM and 2′,3′-dideoxythymidine-5′-triphosphate (ddTTP). Poly(dT)200. oligo (dA)12–18 was used as template/primer to investigate the enzyme processivity. Repair activity of P. falciparum DNA poly β was identified by detecting repaired products using a 28-mer with a UG mismatch located in the middle of the sequence.

RESULTS In this study, DNA polymerase β, the major enzyme operating during base excision repair in eukaryote, was detected in crude extracts of P. falciparum trophozoites and partial purification of enzyme showed a yield of 2.8% and 825-fold. Approximately six dense bands including 15, 17, 27, 37, 52 and 64 kDa of partially purified P. falciparum DNA polymerase β were observed on SDS-PAGE. P. falciparum DNA polymerase β was highly resistant to aphidicolin and N-ethylmaleimide, as seen in other eukaryotic enzymes, but was resistant to 2′,3′-dideoxythymidine-5′-triphosphate and to other synthetic nucleoside analogs. The parasite enzyme showed low processivity. P. falciparum DNA polymerase β was able to repair a patch size of 3–5 nucleotides.

CONCLUSION This study has shown the existence of P. falciparum DNA polymerase β. It differs from human enzyme in its resistance to ddTTP. Differences in sensitivity of the parasite enzyme to known inhibitor of mammalian enzymes/should allow exploitation of the development of drugs that specifically target P. falciparum DNA polymerase β. Moreover, the parasite enzyme indicates its roles in a long patch repair pathway, the first evidence of such a property in malaria parasite DNA.

PB 3

Responses to TLR ligands in neonates born to P. falciparum infected mothers
A. A. Adégna1, S. Olu1, S. T. Agradiami, L. Labuda1, D. Schonkeren1, E. Weerdenburg2, C. Koehler2, S. Issifou1, A. J. F. Luty3, P. G. Kremsner1 and M. Yazdanbakhsh4
1Albert Schweitzer Hospital, Lambarene, Gabon; 2Leiden University Medical Center, Leiden, Netherlands; 3University of Tubingen, Tubingen, Germany

OBJECTIVES The immune system of neonates born to mothers infected with falciparum malaria during pregnancy may be altered due to exposure to the infection or antigens thereof, in utero.

METHODS To assess how innate immune responses are affected in neonates born to infected mothers, we measured cytokine (IFN-g, IL-5, IL-10 and TNF-a) production to toll like receptor ligands (poly I:C and LPS) by cord blood mononuclear cells (CBMC) of neonates born to mothers with different Plasmodium falciparum infection history during pregnancy.

RESULTS The CBMC of neonates born to mothers with a recent P.falciparum infection, showed significantly higher IFN-g production in response to TLR ligands (poly I:C 139 pg/ml, 11–580; and LPS 272 pg/ml, 5–1036) compared to those free of P. falciparum infection (poly I:C 5 pg/ml, 5–15.2; P < 0.001; and LPS 5 pg/ml, 5–5.1; P < 0.0001) during the second and third trimester of pregnancy or those who were infected but successfully treated (poly I:C 7 pg/ml, 5–31; P = 0.018, LPS 5 pg/ml, 5–9; P = 0.003). In contrast, the TNF-a responses to the TLR ligands showed the exact opposite pattern. Lower production was found in cord blood of neonates born to mothers with recent malarial infection (poly I:C 40 pg/ml, 10–281; LPS 141 pg/ml, 10–699) compared to those free of infection (poly I:C 474 pg/ml, 204–971; P = 0.006, LPS 980 pg/ml, 421–2035; P = 0.001) or those successfully treated during pregnancy (poly I:C 493 pg/ml, 169–937; P = 0.007, LPS 954 pg/ml, 433–2039; P = 0.002).

CONCLUSION These findings indicate that maternal P. falciparum infections history affects the innate immune responses of their newborns.

PB 4

Host genetics-related evolution of the antibody responses to P. falciparum MSP2 during the transmission season in Senegal
D. Courtin1, G. Berdin2, J. Milet2, J. B. Sarr1, P. Deloron1, A. Garcia4, F. Mignot-Nabias1 and M. Vafa5
1RCMD / Radboud University, Medical Parasitology, Nijmegen, Netherlands; 2Institut de Recherche pour le Developpement (IRD), UR010, Paris, France; 3Université Cheikh Anta Diop, Biologie Animale, Dakar, Senegal; 4IRD, UR010, Cotonou, Benin; 5Stockholm University, Wenner Gren Institute, Immunology, Stockholm, Sweden

OBJECTIVES We determined the evolution of the antibody levels directed to Plasmodium falciparum Merozoite Surface Protein 2 (MSP2) during the annual malaria transmission season in Senegal, and examined its relationships to clinical and parasitoligical data as well as host (sickle-cell trait and G6PD A-deficient variant) and parasite genetic polymorphisms (based on msp2 genotyping).

METHODS A systematic parasitological assessment (5 measures of the asymptomatic parasite densities) combined to a twice-a-week active clinical survey were performed among 413 children aged from 2 to 10 years and living in the rural area of Niakhar in Senegal, during the 8 months circumscribing the malaria transmission season. An individual mean parasite density was calculated using a linear mixed model analysis, which took into account the measured individual and environmental risk factors. IgG, IgG1 and IgG3 directed to both MSP2/3D7 and MSP2/FC27 recombinant proteins were determined on plasma samples collected before and after the transmission season. Associations were tested using a multivariate logistic regression.

RESULTS They showed that 1) the occurrence of an uncomplicated malaria attack during the transmission season was related to a higher increase of IgG and IgG3 to both MSP2 proteins, 2) the carriage of either sickle-cell trait or G6PD A- variant was related to a lower increase of IgG1 and/or IgG3 to MSP2/FPC27 and3) this last observation was independent of the multiplicity of the plasmodial infections.

CONCLUSION We hypothesized that there was a qualitative and quantitative redistribution of malarial antigens, at reduced doses, within sickle-cell trait and G6PD A- carriers, originating a lower stimulation of the antibody responses. Other ways of the specific immune response, such as cellular mediated immunity, could explain the clinical protection afforded by these genetic traits in our study.

PB 5

Anopheles albimanus immune response to single and mixed infections with Plasmodium falciparum and Plasmodium vivax
L. F. Lopes1, F. Zamora2, L. Rocha2, P. X. Marques1, C. Mendes1, J. Martinez-Barnetche, M. J. Leandro3, S. Herrera4, V. E. do Rosario5, A. P. Arez1 and H. Sivieira1
1Instituto de Higiene e Medicina Tropical, Universidade Nova de Lisboa, Centro de Malária e Outras Doenças Tropicais, Lisboa, Portugal; 2Instituto de Immunologia del Valle, Cali, Colombia; 3Instituto Nacional de Salud Pública, Centro de Investigaciones sobre Enfermedades Infecciosas, Mexico, Mexico

AIMS Mixed infections are common in malaria endemic areas but the information about the effect of parasite interaction on...
transmission is very scarce. Our aim is to study the immune response of the mosquito Anopheles albimanus to single and mixed infections with *Plasmodium falciparum* and *Plasmodium vivax*.

**METHODS** Experimental mixed-infections of *Plasmodium falciparum* and *Plasmodium vivax* in Anopheles albimanus mosquitoes were carried out in Buenaventura, Colombia. These mixtures were analyzed in order to assess reciprocal interactions of these species during the sporogonic development. Parameters such as composition of parasites in the bloodstream, infection rates, overall ookysts and sporozoite numbers in midguts or salivary glands were assessed. Vector-parasite interactions were studied through the identification and transcription analysis of the mosquito genes involved in immune response to each parasite and to parasites mixed.

**RESULTS** The transcription profiles of PGRP-LB, defensin, cecropin 3, attacin and gambiacl were analyzed. The 7 ribosomal protein was used as a housekeeping gene. In general, a higher expression of these genes was observed in the fat body, at day 8 post-infection, in all infected groups, but these observations were not statistically significant due to high variability between experiments.

**CONCLUSION** So far, we have analysed in this study five genes of the mosquito immune system; the gene PGRP-LB that codes for a recognition protein, from the family of peptidogelan recognition proteins (PGRPs), and four genes coding for four antimicrobial peptides (defensin, cecropin 3, attacin and gambiacl). We have observed different expression patterns in different experiments, which are probably due to high variability of infection rates and parasite densities, analysed through oocyst counts. A trend to a higher expression of these genes in the fat body probably reflects an higher activity of these genes in the hemolymph. This could mean that the action of these genes could be enhanced when sporozoites are released from the oocysts. These studies could gather some insights into how the development of one species can affect the development of another and how the mosquito immune system reacts to each species together or separately.

**PB 6**

**The role of Rab5 proteins in endocytosis in Plasmodium falciparum**

L. I. Ochoa, 1 S. A. Ward 2 and M. L. Chance 2

1 KEMRI/Wellcome Trust Programme, Nairobi, Kenya; 2 Liverpool School of Tropical Medicine, Liverpool, UK

**OBJECTIVES** The ingestion of haemoglobin by *Plasmodium falciparum* during the erythrocytic cycle is an important pathway targeted by chloroquine. The Rab5 protein regulates early endocytic vesicular events in higher eukaryotic cells. Endocytosis in the parasite was characterised using its orthologue PrRab5, endocytic fluid phase markers and endocytic inhibitors.

**METHODS** Three PrRab5 isoforms were identified from PlasmodB; PrRab5A, PrRab5B and PrRab5C. The analyses carried out on these 3 sequences were: nucleotide and amino acid sequence alignments, phylogeny, northern and Southern blots, indirect immunofluorescence assays (IFA), transfections using green fluorescent protein (GFP) tagged PrRab5 isoforms and endocytic assays.

**RESULTS** PrRab5A, PrRab5B and PrRab5C are present as single copy genes, their amino acid sequences share on average an identity of 35%, with PrRab5C being the most divergent protein. PrRab5A contained an insertion sequence within its guanine nucleotide binding domains and PrRab5B exhibited an amino-terminus myristoylation motif instead of the characteristic carboxy-terminus prenylation motif. The IFAs revealed that PrRab5A was most likely associated with small vesicular structures in the parasite cytoplasm, PrRab5B with discrete vesicular structures in the parasite and erythrocyte cytoplasm and on both plasma membranes and PrRab5C with small vesicles in the parasite cytoplasm and less discrete vesicular structures on the parasite and erythrocyte plasma membranes. The carboxy-terminally tagged GFP PrRab5B construct indicated similar vesicular-like associations. An endocytic dextran fluid phase assay confirmed that the greatest endocytic activity in the parasite occurs during the trophozoite stages. Additionally, this assay in combination with endocytic inhibitors suggested that endocytic activity may primarily be actin and microtubule dependent, indicating processes such as macropinocytosis or phagocytosis.

**CONCLUSION** *Plasmodium falciparum* has an intricate membrane structure that requires 3 PrRab5 isoforms, indicating a complex endocytic process. The characterisation of the PrRab5 proteins has provided information on the mechanism of control of endocytosis in *P. falciparum* that could be an invaluable subcellular tool.

**PB 7**

**The effect of Toxoplasma gondii antigens and BCG on fibrosarcoma tumor in Balb/C mice**

H. Yousof Darani, H. Shirzad and F. Manoussir

Cell and Molecular Research Center, Shahrekord University of Medical Sciences, Shahrekord, Iran, Islamic Republic of Iran

**INTRODUCTIONS** Previous investigation and available data demonstrating that there are different patterns of diseases distribution in developed and developing countries. While in developed countries one of the major causes of death is cancers, in developing countries one of the main cause of death is infectious diseases. Various factors may be responsible for different causes of death in two those countries. However there are raising scientific evidences that some infectious and parasitic organisms when enter the body may interfere with the tumor growth. In order to explore the above presumption, in this work the effect of *Toxoplasma gondii* antigens and BCG on fibrosarcoma tumor growth in mouse model has been investigated.

**MATERIAL AND METHODS** In this experimental study a group of inbred Balb/C mice were injected with *T. gondii* antigens in alum as the first case group. This group received two boosters of the same antigens fortnightly. Also another group of those mice were injected with BCG as the second case group. A group of mice were also injected with alum alone as control group. After one month all of the mice in case and control groups were challenged with fibrosarcoma cells. The size of growing solid tumors was measured in individual mice every 2 days up to 2 weeks. Tumor area was also calculated for every single mouse.

**RESULTS** Results of this work showed that the mean size of tumor in case groups was smaller than that of control group and the difference between the tumor size in case and control groups was statistically significant.

**DISCUSSION** Results of this investigation revealed that there was a significant difference between the tumor size in case and control mice. The immune system raised by parasite or BCG may nonspecifically interfere with the tumor growth.
PB 8
Anti-malarial immunity in migrants from endemic areas to Italy. An immunological study
F. Castelli1, F. Buelli1, E. Peduzzi2, N. Saleri1, S. Calgaris1, M. Tamborini3, S. Sirima1, I. Nebie2 and G. Pluschke1
1 University of Brescia, Institute for Infectious and Tropical Diseases, Brescia, Italy; 2 Swiss Tropical Institute, Basel, Switzerland; 3 Centre National de Recherche et Formation sur le Paludisme, Ouagadougou, Burkina Faso

INTRODUCTION Malaria still represents one of the most killing diseases in many areas of the world. The way to an effective vaccine is made difficult by the incomplete understanding of the immunological mechanisms conferring resistance to the disease. The observed decay of anti-malarial resistance in migrants from endemic areas to Europe provide an unique opportunity to study immunological determinants of resistance.

OBJECTIVE To study time-dependent decay of humoral immunity to specific P. falciparum antigens in long-term migrants from malaria endemic areas to malaria-free zones.

METHODS Adult migrants recently (less than 4 months) arrived to Italy from Burkina Faso, a western-Africa malaria hyperendemic country were asked to enter the study. After informed consent, haemocysopically parasite-free subjects at baseline were enrolled and prospectively followed at quarterly intervals for at least 15 months, provided that no travel to any malaria endemic country was performed in the meantime. The following P. falciparum antigens were serially tested by ELISA: MSP1 83/30, MSP1 38/42, MSP3, 090 (CD). Total lysates of in vitro grown P. falciparum K1 blood stage parasites were also used to assess by western blot potential changes in response patterns to malaria antigens.

RESULTS Five migrants were recruited and prospectively followed (range 6–30 months). Challenge with MSP-1 (merozoite surface protein 1) and MSP-3 lead to the strongest humoral reactivity. ELISA IgG titers (especially Ig-1 and Ig-3) against MSP-1 (merozoite surface protein 1) and MSP-3 slowly decreased over time in all patients. The measured decreases in IgG titres were remarkably slow. At western blood analysis, all study participants showed serum IgG responses cross-reactive with a range of P. falciparum blood stage parasite antigens. A striking stability of individual response patterns was observed.

CONCLUSIONS The decay of humoral reactivity can be monitored over time when P. falciparum stimulation is interrupted, as in the case of long-term migrants to malaria-free areas. Results indicate that acquired semi-immunity to malaria may be lost more quickly than IgG titres against a range of immunodominant malaria antigens.

ACKNOWLEDGEMENT This study was made possible by the Italian Ministry of University and Research (MIUR) (grant COFIN 2003/MIUR Italy prot. 2003062534_006).

PB 9
Association of pro- and anti-inflammatory cytokines and antibodies to heat shock proteins serum levels with clinical manifestations of malaria
A. Wroczynska1, A. Kuna2 and W. Nahorski1
1 Interfaculty Institute of Maritime and Tropical Medicine, Department of Tropical Parasitology, Gdynia, Poland; 2 Academic Centre of Maritime and Tropical Medicine, Clinic of Tropical and Parasitic Diseases, Gdynia, Poland; 3 Interfaculty Institute of Maritime and Tropical Medicine, Clinic of Tropical and Parasitic Diseases, Gdynia, Poland

OBJECTIVES Cytokines are supposed to be involved in malaria pathogenesis. Few studies, however, describe their relationship with manifestations of the disease, including both individuals with imported infection and those from malaria endemic areas. Heat shock proteins (HSP) play important roles in host-parasite interaction, while anti-HSP immune response has been rarely studied in malaria. The aim of this study was to evaluate the association between clinical course of malaria and the serum levels of selected cytokines as well as anti-HSP antibodies in patients with uncomplicated and severe disease, defined according to WHO criteria.

METHODS The study was performed at Interfaculty Institute of Maritime and Tropical Medicine in Gdynia, Poland and Sao Lucas Medical Center in Kifangondo, situated in malaria holoendemic region of Angola. So far, altogether 123 P. falciparum infected patients were included into the study, with 34 of them being residents of Angola. Serum concentrations of IL-18, IL-12, IL-6, IFN-γ, TNF, IL-10, IL-13 were determined on admission in malaria patients with the use of enzyme-linked immunosorbent assays. In 46 aseptic and asymptomatic patients measurements were repeated after the recovery. Moreover, in 29 adults with imported malaria serum levels of anti-HSP60 and HSP70 antibodies were determined and compared with the control group consisting of healthy individuals from Poland.

RESULTS Significant associations between a number of pro- and anti-inflammatory cytokines serum levels and severity of the disease were noted in both African and Polish groups of patients. Severe malaria in non-immune adults was associated with elevated level of IL-18 and relative deficiency of IL-12 mediated response in comparison to uncomplicated malaria cases. The latter finding was not seen in Angolan children, in which severe malarial anaemia was characterised by high IFN-γ expression. Moreover, significant differences were found in serum levels of both anti-HSP60 and HSP70 antibodies between adults with imported malaria and the control group. Elevated levels of these antibodies were associated with uncomplicated clinical pattern of malaria.

CONCLUSION These preliminary results support the hypothesis that effective resolution of P. falciparum infection along with uncomplicated course of the disease depend on regulation of pro- and antiinflammatory responses mediated by relevant cytokines. The excessive inflammatory response pattern demonstrated in the study by high IL-18 expression may be the common feature of severe malaria in non-immune adults as well as children from endemic regions. Further studies are planned on larger group of patients to determine their involvement in particular clinical manifestations of the infection.

PB 10
Murine cerebral malaria development is independent of toll-like receptor signalling
D. Togbe1, L. Schofield2, G. E. Grau1, B. Schneider3, V. Boissay1, S. Charron1, S. Rose1, B. Beutler4, V. F. J. Quensinoux1 and B. Ryffel1
1 Molecular Immunology and Embryology, CNRS and University of Orleans, Transgense Institute, Orleans, France; 2 The Walter and Eliza Hall Institute, Parkville, Victoria, Australia; 3 The University of Sydney, Department of Pathology, Camperdown, NSW, Australia; 4 Scripps Research Institute, La Jolla, USA

Malaria pigment hemozoin was reported to activate the innate immunity by Toll-Like Receptor (TLR) 9 engagement. However, the role of TLR activation for the development of cerebral malaria (CM), a lethal complication of malaria infection in humans, is unknown. Using Plasmodium berghei ANKA (PbA) infection in mice as a model of CM, we report here that TLR9 deficient mice are not protected from CM. To exclude the role of other members of the TLR family in PbA recognition we infected mice deficient for single TLR1, 2, 3, 4, 6, 7 or TLR9 and their adapter proteins MyD88, TIRAP and TRIF. In contrast to lymphotoxin α deficient
mice which are resistant to CM, all TLR deficient mice were as sensitive to fatal CM development as wild type control mice and developed typical microvascular damage with vascular leak, hemorrhage in the brain and lung, together with comparable parasitaemia, thrombocytopenia, neutrophilia and lymphopenia. In conclusion, the present data do not exclude the possibility that malarial molecular motifs may activate the innate immune system. However, TLR dependent activation of innate immunity unlikely contributes significantly to the proinflammatory response to PβA infection and the development of fatal cerebral malaria.

Integrated Approaches to the Social Determinants of Health

**PB 11**

*Development of HIV behavioural risk reduction intervention programmes for people living with HIV/AIDS in support groups*

N. Dwadwa-Henda, L. Simbayi, A. Strebel, A. Cloete and N. Lewa

*Human Sciences Research Council, Behavioural Social Aspects of HIV/AIDS & Health, Cape Town, South Africa*

**OBJECTIVES** To establish how effectively two culturally-adapted US-developed interventions which promote HIV status disclosure and behavioural risk-reduction strategies among people living with HIV/AIDS (viz., Healthy Relationships, and Options for Health) work in a mainly rural South African context with a high prevalence of HIV/AIDS.

**METHODS** Group-level interventions.

**RESULTS** Study in progress.

**CONCLUSION** Shared progress.

**PB 12**

*Global partnership for people’s health*

M.-L. Rodriguez1 and E. Espinoza2

1University of El Salvador, Rectoría, San Salvador, El Salvador; 2University of El Salvador, Observatorio de Políticas Publicas y Salud, San Salvador, El Salvador

**OBJECTIVES** The talk will focus on the role of international cooperation in health, understood as the solidary response to efforts that people around the world have been making since the 1978 Alma Ata meeting in the USSR.

**METHODS/RESULTS** 1. The Alma Ata Declaration sent a clear message of denounce and made an urgent call to all the world’s people to unite in seeking health for all and in promoting core principles of solidarity, equity and social participation. 2. In light of the failure to keep the promises of Alma Ata, we will analyze efforts that have arisen around the world in attempting to respond to the grave social and economic disparities that affect humankind. These efforts include the Millennium Development Goals adopted by the United Nations Member States, which, among other things, set forth a clear commitment to fostering a global partnership for development, which should be interpreted as giving support to the Health for All movement and its unmet demands 22 years later. 3. The movement is no longer limited to leaders; it now includes the Kel Tamasheq society’s social services needs and the main health inequities in the world. 4. We analyse the approaches and criteria that have developed in relation to people’s commitment to international health cooperation and the conceptions that have been used by the international community of nations in the international health field.

**CONCLUSION** These have led to the urgent need to bring a new perspective to international health, which requires breaking with the criteria used for paternalistic, dependency-creating aid that are not helping to developing the existing potential of developing countries, in order to create the conditions for building a better world that is healthy and safe for all.

**PB 13**

*The meaning and representation of illness, health and curing among the Kel Tamasheq in northern Mali*

A. Münch1, B. Diallo1, B. Bonfoh2, E. Ag Mohamed3, S. Doumbia4, S. T. Diop5, and J. Zinsstag6

1University of Bern, Institute for Islamic and Middle Eastern Studies, Bern, Switzerland; 2Institut du Sable, Bamako, Switzerland; 3Institut du Sable, Bamako, Mali; 4Université de Bamako, FMPOS, Bamako, Mali; 5Swiss Tropical Institute, Epidemiology and Public Health, Basel, Switzerland

At the mercy of the harsh ecological and economic environment, nomadic societies are repeatedly forced to migrate and relocate. Their mobility, their proximity and dependence on their livestock, a traditionally dairy-rich diet and arid habitat make pastoral societies exposed to a variety of health risks. This is reflected by one of the highest infant mortality rates in the world: in the Azawad-region of northern Mali up to 50% of children die before their fifth birthday.

**OBJECTIVES** Mali’s community based healthcare services are not geared towards the nomads’ mobile lifestyle. Women and children in particular, have virtually no access to external healthcare facilities, among others due to socio-cultural barriers. Very little research has been done on their internal networks, their perception of illness, the perceived causes and their ensuing behavior.

**METHODS** Kel Tamasheq society’s social services needs and the local risks they face can neither be identified by biomedical assessments alone, nor simply by taking a socio-cultural approach. For this reason, local health determinants in their area are ascertained and interpreted with the help of interdisciplinary research methods, combining clinical and epidemiological studies with their cultural and linguistic counterpart.

**CONCLUSION** The present interdisciplinary case study on nomad women’s general understanding of health issues as well as diseases and their epidemiology does not only serve to fill a knowledge gap. It is also fundamental to build up a socio-cultural awareness and to define local health strategies which could help concerned authorities and organizations to develop a reliable medical care system.

**Intestinal Helminths**

**PB 14**

*Screening and characterization of the epitopes of Ts87 protein from Trichinella spiralis with phage display peptide library*

Y. Gu1, X. Zhi1, J. Li1, J. Yang2, Q. Li2, Z. Liu1 and Y. Yang2

1School of Basic Medical Sciences, Capital Medical University, Department of Parasitology, Beijing, China; 2Beijing Centers for Disease Control and Prevention, Beijing, China

**OBJECTIVE** A novel gene named as Ts87 was obtained by screening the adult *Trichinella spiralis* cDNA library with sera from rabbits immunized with crude larval extracts of *T. spiralis* and sera from rabbits infected with *T. spiralis*. Compared with the control group, immunization of the Balb/C mice with the
prokaryotic expression product of Ts87 with Freund’s adjuvant via the subcutaneous route induced a significant muscle larvae burden reduction after T. spiralis challenge. This study was to obtain the specific epitopes of Ts87 protein which could induce protective immunity against T. spiralis infection.

METHODS Monoclonal antibody 5A3 against Ts87 recombinant protein (rTs87) was used to screen a phage display peptide library. Three rounds of bio-panning were carried out and twenty phage clones were selected randomly. After being further identified by ELISA and competitive ELISA, positive clones were sequenced and the deduced amino acid sequences were compared to that of Ts87 protein. Balb/C mice were immunized with individual positive phage clones via the subcutaneous route without additional adjuvant. The antibody responses stimulated were detected by Western blot, ELISA and Immunofluorescence assay. The mixture of two phage clones which could stimulate specific antibody responses was used to vaccinate the mice and the muscle larvae reduction was calculated after challenge experiment.

RESULTS Nine phage clones could be recognized by monoclonal antibody 5A3 and showed a high inhibition rate in competitive ELISA. Among them, one deduced amino acid sequence of the phage-displayed peptide showed the high homology with partial sequence of Ts87 protein. Two effective phage clones could elicit specific antibodies against rTs87 assessed by ELISA and Western blot. The antisera from the mice immunized with the two individual phage clones bound specifically to rTs87 and crude larval extract of T. spiralis by Western blot and showed positive reactivity with T. Spiralis larval tissue sections. Mice vaccinated with these two combined phage clones showed 28.7% worm burden reduction compared with controls (P < 0.01).

CONCLUSION The peptides displayed by two identified phage clones represented specific epitopes of Ts87 protein and induced partial immune protection. It suggested that these two phage-displayed peptides could be considered as potential vaccine Candidate epitopes for T. spiralis.

PB 15
Strongyloides hyperinfection syndrome
A. E. Pinilla and M. C. Lopez
1Universidad Nacional de Colombia, Internal Medicine, Bogota, Colombia; 2Universidad Nacional de Colombia, Public Health, Bogota, Colombia

OBJECTIVES 1. Study the eosinophilia etiology in patient with chronic obstructive lung disease. 2. Discard the parasites presence as cause of eosinophilia in a tropical country.

METHODS Study possible cause of eosinophilia in this clinic case through the analysis of sputum and stool smear examinations.

RESULTS An 81-year-old male, born in a rural zone of Colombia, who had worked as a farmer, as a coffee collector 50 years ago and as a gardener for 22 years, presented with abdominal pain in the epigastrium and mesogastrium, dyspnea and productive cough which started 10 days earlier. He had a history of chronic obstructive lung disease, cor pulmonale, had been a smoker of 25-20-cigarette boxes per year, and had received oral prednisone and inhaled beclometasone on several occasions, including his last hospital admission. The main findings on physical examination were undernourishment, tachycardia, tachypnea, crackles in the base of the right hemitorax; the abdomen was soft, with pain upon deep palpation in the epigastrium and right hypochondrium. He was admitted to the hospital with a diagnosis of systemic inflammatory response syndrome, characterized by tachycardia, tachypnea, leukocytosis, 37,600 leukocytes/μl, and persistent eosinophilia ranging from 52% to 60%. The laboratory showed: right pleural effusion, normal hepatic ultrasound and the endoscopic results evaluation showed gastritis and duodenitis, IgE concentration 180 IU/ml. Sputum and fecal sample examinations were carried out because of the persistent eosinophilia, showing rhabditiform Strongyloides stercoralis larvae (Graph 1,2). Ivermectine, 200 mg/kg weight/dose, was prescribed, with clinical and laboratory followup.

PB 16
How may gains in the control of soil-transmitted helminthiasis be sustained?
D. Crompton
University of Glasgow, Institute of Biomedical and Life Sciences, Glasgow, UK

Good progress has been made in recent years in controlling morbidity due to soil-transmitted helminthiasis and the efforts are
expanding. Control programmes have developed from (1) acceptance of the public health significance of S-TH infections, (2) application of mathematical techniques to study the population biology of S-THs, (3) use of GIS methods to elucidate the epidemiology of S-TH infections and (4) collaboration between diverse partners with the common objective of S-TH control. Most progress in reducing morbidity, however, has come from the availability of highly cost-effective anthelmintic drugs and an improved understanding of how to use the drugs in public health programmes. Sustaining this progress presents a major challenge in terms of planning and resources. Despite the low cost of drugs, can governments afford to purchase sufficient supplies to meet the need? Are procedures in place to detect and manage the emergence of drug resistance? The more widely the drugs are used, the greater the risk of resistance; new drugs are slow to develop. Are health awareness programmes keeping pace with the use of anthelmintic drugs? Are resources available to carry out operational research to improve the monitoring and evaluation of control measures? Do realistic plans exist to continue with S-TH control if and when partners and donors withdraw? Long-term sustainability depends on greater access to safe sanitation. How and when will this most important need be met?

**PB 17**

**Allergic diseases, eosinophilia and infestation of Enterobius vermicularis in rural children 1–6 years old of Kurdistan, Iran**

G. Zamini, M. B. Khadem Erfan, M. R. Rahmani and M. N. Karimi

1Faculty of Medicine Kurdistan Uni. of Med. Sci., Parasitology, Sanandaj, Iran; Islamic Republic of Iran; 2Faculty of Medicine Kurdistan Uni. of Med. Sci., Immunology, Sanandaj, Iran; Islamic Republic of Iran; 3Kurdistan University of Medical Science, Sanandaj, Iran; Islamic Republic of Iran

**OBJECTIVES** The effect of intestinal helminths on allergic diseases is inconsistent across different epidemiological studies. To explore the association between Enterobius vermicularis and allergic symptoms and eosinophilia, this study was conducted.

**METHODS** The prevalence of Enterobius vermicularis and eosinophilia were examined by perianal tape test and peripheral blood samples. Allergic symptoms and demographic data were assessed by questionnaire under supervision of a physician.

**RESULTS** A total of 137 (41.1%) cases had positive tape test for Enterobius vermicularis with less allergic symptoms, but there were no protective effects of Enterobius vermicularis infection against allergic symptoms. 22 cases had eosinophilia which 17 (77.3%) of them were positive for Enterobius vermicularis. ($P < 0.001$).

**CONCLUSION** Although less allergic symptoms were seen in positive individuals for Enterobius vermicularis, these data, however, do not allow any conclusion on the nature of the possible association between Enterobius vermicularis and allergic diseases.

**PB 18**

**Anti-inflammatory properties of N. brasiliensis and its excretory-secretory (ES) products**

M. Zhao, J. MacCallum, D. Brown and L. Proudfoot

School of Life Sciences, Napier University, Edinburgh, UK

**OBJECTIVES** N. brasiliensis is a rodent intestinal nematode. Its definitive host is the rat. Before migrating to the intestine, N. brasiliensis moult to L3 larvae in the lungs. This is an important stage for the maturity of N. brasiliensis and the development of host-parasite immune responses. Primary infection with N. brasiliensis in the rat results in lung damage. However, previous work showed that tumor necrosis factor-$\alpha$ (TNF-$\alpha$), which is a central pro-inflammatory cytokine, was not detected in the lung spaces and neutrophils were only moderately raised in numbers (although significantly) during the pulmonary migratory stage. The pathology of the lungs was minimal after the larvae had left and the cytokine profile was Th2 dominant in the lung stage. This has led to the investigation of anti-inflammatory properties of N. brasiliensis lung stage larvae (L3 larvae). Excretory-secretory (ES) products of helminths have been demonstrated to include a wide variety of immunomodulatory molecules and anti-inflammatory properties of N. brasiliensis L3 larvae ES products (L3 NES) are also examined in this study.

**METHODS** NR8383 is a rat alveolar macrophage cell line. NR8383 cells were stimulated by 25 ng/ml lipopolysaccharide (LPS). The effect of L3 larvae and L3 NES on the production of pro-inflammatory mediators, including nitric oxide (NO) and TNF-$\alpha$, were measured by enzyme linked immunosorbant assay (ELISA) and Griess assay. Gene expression level of iNOS and TNF-$\alpha$ were determined by RT-PCR. The protein profiles in L3 NES and L3 larvae lysate were analyzed by SDS-PAGE.

**RESULTS** Both L3 larvae and L3 NES were able to inhibit NO and TNF-$\alpha$ production and this was shown further by RT-PCR results. SDS-PAGE analysis provided evidence for the protein profile of the concentrated L3 NES and L3 larvae lysate.

**CONCLUSION** N. brasiliensis L3 larvae and L3 NES modify the inflammatory response in NR8383 cells via the inhibition of TNF-$\alpha$ and NO, and the anti-inflammatory properties were associated with the protein components.

**PB 19**

**Trends and prevalence of soil transmitted helminths in a rural area of Colombia, 1995–2005**


1Universidad Nacional de Colombia, Salud Publica, Bogotá D.C., Colombia; 2Universidad Nacional de Colombia, Microbiologia, Bogotá D.C., Colombia

**OBJECTIVES** To describe the prevalence trends of soil-transmitted helminthiasis in children aged under 15 years in the village of La Virgen, Cundinamarca Department.

**METHODS** Three non-random surveys were carried out in school children aged 0 to 15 years. In three cross-sectional studies, intestinal parasitism was determined by direct examination of fecal samples and by the modified Ritchie-Frick concentration method. The distribution of intestinal parasitism was analyzed and the trend during the 1995–2005 period is described.

**RESULTS** Prevalence of intestinal parasitism in children under 5 years of age increased from 62.5% in 1995 to 66.66% in 2001 and to 68.96% in 2005; prevalences of soil-transmitted helminthiasis in this age group were 37.5% in 1995, 23.61% in 2001 and 27.58% in 2005. For children aged over 5 years of age, the prevalence of intestinal parasitism increased from 86.16% in 1995 to 89.13% in 2005 and the prevalences of soil-transmitted helminthiasis were 62.94% in 1995, 39.81% in 2001 and 23.91% in 2005. The most frequently found nematodes were Ascaris lumbricoides and Trichuris trichiura and Giardia intestinalis and Entamoeba histolyticaEntamoeba dispar complex were the most frequently found pathogens protozoa. However the most prevalent parasite were no pathogens protozoa, this found would show the contamination of soil with human stools.

**CONCLUSION** Soil-transmitted helminthiasis are endemic and presented high prevalences during the study period. Effective control measures are needed to prevent intestinal parasitism in pre-
school and schoolchildren. Soil transmitted helminthes continue to be a public health problem in some areas in Colombia.

**PB 20**

**Diagnosis of Strongyloides stercoralis: diagnostic accuracy of ELISA compared with direct methods and indirect immunofluorescence test**

S. Gatti1, M. Boscolò2, C. Klersy3, M. Gobbo4, A. Bruno4, C. Cevini1, M. Degani2 and Z. Bisoffi2

1 Found.IRCCS San Matteo, Virology Service, Laboratory of Parasitology, Pavia, Italy; 2 Ca’ Foscari Hospital, Centre for Tropical Diseases, Negram (Verona), Italy; 3 Found.IRCCS San Matteo, Biometry and Clinical Epidemiology Service, Pavia, Italy; 4 Found.IRCCS San Matteo, Research Labs, Infectious Diseases Dept, Pavia, Italy

**BACKGROUND**

Strongyloides stercoralis infection is a very common albeit underestimated problem in the Tropical world. Some Mediterranean countries, including Italy, still have endemic cases, especially observed in the elderly population. This infection is largely underdiagnosed and deaths from disseminated strongyloidiasis are reported every year.

**OBJECTIVES**

1. To evaluate the diagnostic accuracy of a commercially available ELISA test for Strongyloides stercoralis (Ss) infection versus coproparasitological examination and agar culture and versus an indirect Immunofluorescence Antibody Test (IFAT); 2. to identify predictors of the infection.

**SUBJECTS AND METHODS**

A total of 383 subjects with suspected strongyloidiasis were examined (58% males). Diagnostic protocol included: coproparasitological examination of 3 to 5 formalin-fixed fecal samples and/or agar culture; serology with a commercially available ELISA (Strongyloides ELISA®, Diagnostic Automation Inc., Calabasas, CA); IFAT with whole filariform Ss larvae from cultured human faecal samples, developed at the Centre for Tropical Diseases, Negram (Boscolò, Clin Vaccine Immunol. 2007;14(2):129–33). The statistical analysis was made with STATA 9 Software Package (Stata Corporation, College Station, TX).

**RESULTS**

The mean age was 54 years (DS 21). Main risk factors were: history of farm work (159; 69%); international travel (137; 36%); immigration (83; 22%). Main symptoms were: itching (171; 45%); abdominal pain (118; 31%); diarrhoea (88, 39%); skin rash (99, 26%). Eosinophil count > 10% was found in 214 subjects (59%). 126/383 patients (39.9%) were found positive for Ss larvae with coproparasitology and/or agar-culture. Of these, 111/123 (90%) showed also ELISA O.D. values > 0.2 (cut-off of the kit) and 118/124 (95.2%) IFAT values > 1/20. Diagnostic accuracies were for ELISA ≥ 0.2: Kappa: 0.52 (SE 0.04), sensitivity 90.2 (95%CI: 83.6–94.9); for IFAT > 1/20: Kappa: 0.41 (SE 0.04), sensitivity 95.2 (95%CI: 89.8–98.2); for IFAT ≥ 1/80: Kappa: 0.53 (SE 0.04), sensitivity 75.0 (95%CI: 66.4–82.3). Specificity of both serologic methods could not be reliably determined in this group, due to lack of a gold standard for true negatives. The agreement between ELISA and IFAT tests was substantially comparable both for IFAT = 1/20 and ≥1/80 (Kappa 0.60 vs. 0.62).

**CONCLUSIONS**

The new, commercial ELISA is a sensitive test (almost comparable with IFAT at lower dilution) for S. stercoralis infection. Although specificity of indirect methods was not determined for the reason explained above, serology positive patients should be considered suspect cases and treated, even with negative direct tests. At multivariate analysis, age > 65 years and history of soil contact (farm working) were independent predictors of S. stercoralis infection.

**PB 21**

**Soil-transmitted helminths related perceptions among mothers and children in San Juan y Martínez, Cuba: implications for control**

A. Escobedo1, R. Junco2, L. Menocal3, K. Alfonso4, A. Escobedo5, A. Hernández1, M. Woerdemann2, K. Polman3, B. Gryseels5 and M. Bones3

1 Academic Paediatric Hospital ‘Pedro Borra’, Microbiology & Parasitology, La Habana, Cuba; 2National Institute of Hygiene, Epidemiology and Microbiology, Havana, Cuba; 3Prince Leopold Institute of Tropical Medicine, Antwerp, Belgium

**OBJECTIVES**

To gain insight into mothers and children’s knowledge, attitudes and practices with respect to soil-transmitted helminths (STH) in San Juan y Martínez, Cuba.

**METHODS**

A qualitative study was carried out in San Juan y Martínez, Cuba in 2004. Focus group discussions (FGDs) four with schoolchildren and four with mothers were conducted to explore and gather information about the awareness of STH, their symptoms and mode of transmission, the source of information about the disease, possible ways of prevention, treatment seeking behaviour, and barriers for not adopting preventative behaviours.

**RESULTS**

Mothers and children have knowledge of STH. Manifestations like diarrhoea, abdominal pain and loss of weight were cited; however, asymptomatic forms of these infections are hardly accepted in both groups. Attitudes towards the control of these infections were appropriate, but subsequent behaviour was not. Wearing shoes and washing hands and vegetables were mentioned among the principal ways of preventing these infections. The most commonly mentioned reasons for not adopting preventive behaviours included lack of time and low level of perception of severity among mothers and forgetting and lack of motivation among children. Treatment-seeking behaviour when STH are suspected mainly included visiting the nearby family doctor; however, visiting a traditional healer and using home remedies were also mentioned by some mothers, either prior or after visiting modern forms of health treatment.

**CONCLUSION**

There is a pressing need for accessible, available, culturally acceptable and sustainable STH interventions. Findings from this study will help tailor interventions for the control of STH infections through the preparation of prevention messages and other complementary support strategies designed to cross the bridge between knowledge with respect to STH and the consistent adoption of preventive hygienic behaviours in San Juan y Martínez.

**PB 22**

**Learning ability is associated with delayed psychomotor development in Cuban schoolchildren**

A. Collado1, R. Junco1, L. Menocal1, K. Alfonso1, A. Escobedo5, A. Hernández1, M. Woerdemann2, K. Polman3, B. Gryseels5 and M. Bones3

1 National Institute of Hygiene, Epidemiology and Microbiology, Havana, Cuba; 2 Academic Paediatric Hospital ‘Pedro Borra’, Microbiology & Parasitology, Havana, Cuba; 3 Prince Leopold Institute of Tropical Medicine, Antwerp, Belgium

**OBJECTIVES**

To assess the relation between learning abilities, intestinal parasitism and others variables in Cuban children from the municipality of San Juan y Martínez, Pinar del Rio.

**METHODS**

During December of 2003 and January of 2004, 399 children between 6–12 years old from five elementary schools, obtained by random selection after double stratification for municipality and area, were observed during a cross-sectional study. A parent or guardian of each child was
Abstracts of the 5th European Congress on Tropical Medicine and International Health

PB 23
Worm recovery of Clonorchis sinensis in humans by praziquantel treatment and purgation
M.-H. Choi1, J.-H. Kim1, J.-K. Lee1, C. Shen1, Y. M. Bae1, J.-K. Oh2, M. K. Lim2, H.-R. Shin2 and S.-T. Hong1
1Seoul National University, Parasitology and Tropical Medicine, Seoul, Korea, Republic of; 2National Cancer Center, Research Institute for National Cancer Control and Evaluation, Goyang, Korea, Republic of

OBJECTIVES Prevalence of Clonorchis sinensis infection was evaluated among inhabitants of an endemic area of clonorchiasis in Korea, and worm recovery was undertaken from infected persons by praziquantel treatment and purgation.

METHODS Stools of 969 individuals (408 men and 561 women, age range: 29–86 years) were screened for C. sinensis eggs using the Kato-Katz method and formalin-ether sedimentation technique. The egg positive rate of C. sinensis was 36.8%, with an EPG (eggs per gram of feces) range of 24–28 800, and egg positive persons were treated with three doses of 25 mg/kg praziquantel in a day.

RESULTS A total of 158 worms were recovered by praziquantel treatment and purgation from five of eight infected persons (1000s-EPG) who agreed to join the worm recovery. Worm recovery was 3–108 in each individual, and not correlated with EPG of each subject. Recovered worms were 10–20 mm × 2–3 mm in size, intact except for three impaired worms, and showed white, red, or brown-pigmented body color.

CONCLUSION It is suggested that adult worms of C. sinensis are paralyzed by praziquantel administration and discharged passively by peristaltic movement of the bowel.

PB 24
Serodiagnosis of active clonorchiasis with Clonorchis sinensis 7-kilodalton recombinant protein by ELISA
Seoul National University, Parasitology and Tropical Medicine, Seoul, Korea, Republic of

OBJECTIVES Human Clonorchis sinensis (Cs) infection is endemic in East Asian countries. The present study produced the recombinant 7 kDa molecule of C. sinensis (Cs7) and applied the recombinant protein as the ELISA diagnostic antigen instead of the crude antigen.

METHODS We produced a recombinant protein (rPCs7) encoding Cs7 by using EasySelectTM Pichia expression kit. The genes were cloned into pPICZaA and transformed into Pichia pastoris-KM71H. The rPCs7 was purified from the culture supernatant via Ni-NTA purification system. The rPCs7 was coated on 96-well ELISA plates and screened with reference and control sera.

RESULTS The positive reaction of IgG antibodies to the rPCs7 showed in 81.3% (87/107) of active clonorchiasis patients and in 23.1% (6/26) of cured clonorchiasis individuals. However, the positive rates were 7.0% (3/43) of controls, 10% (1/10) of paragonimiasis patients and 20% (2/10) of sparganosis patients, as a false-positive reaction. In absorbance data, mean absorbances of serum samples of the controls and active clonorchiasis for rPCs7 were 0.103 ± 0.077 and 0.352 ± 0.145. Cut-off value of absorbance to specific IgG antibodies of C. sinensis was 0.250.

CONCLUSION These data suggest that the rPCs7 should be useful for serodiagnosis of active clonorchiasis with reliable sensitivities and specificities.
CONCLUSION These results strongly suggest that the public health programme from the City of Belo Horizonte to control intestinal parasites at Cabana ghetto is being effective.

Leishmaniasis

PB 26 Susceptibility of Aedes aegypti (Diptera: Culicidae) cell line to the infection with Leishmania panamensis
A. C. Zapata1, A. R. Ramirez2 and F. J. Bello3
1Universidad De La Salle, Ciencias Basicas, Bogotá DC, Colombia; 2Universidad del Rosario, Ciencias Basicas, Bogotá DC, Colombia

OBJECTIVES The objective of the present work was to evaluate the infection in vitro of Leishmania panamensis in Aedes aegypti cell cultures.

METHODS The Grace/L-15 medium, supplemented with 10% of bovine fetal serum (SFB), was utilized for the maintenance of the cell cultures. The experimental conditions were: CO2 (0%, and 5%), pH (5.0, 5.5, 6.0, 6.8 and 7.2) and temperature (26, 32 and 37°C). The susceptibility was analyzed at 3, 6 and 9 days post-infection.

RESULTS The highest percentage (56%) and index (114.2) of infection were produced in presence of the following conditions: CO2 5%, 26°C and pH of 6.8, at 6 days post-infection.

CONCLUSION We demonstrated that the Aedes aegypti cell line permitted la internalization of the Leishmania panamensis parasites.

PB 27 Association between e-Selectin gene polymorphisms and soluble e-Selectin levels and their relation to visceral leishmaniasis
M. Fallah1, A. Bazrani2, A. Mzum3, M. Hajilui4 and H. Taherkhani5
1University of Medical Sciences, School of Medicine, Parasitology and Mycology, Hamadan, Iran, Islamic Republic of Iran; 2Drug Applied Research Center, Tabriz University of Medical Sciences, Tabriz, Iran, Islamic Republic of Iran; 3Hamadan University of Medical Sciences, Immunology, Hamadan, Iran, Islamic Republic of Iran; 4Tabriz University of Medical Sciences, Parasitology, Tabriz, Iran, Islamic Republic of Iran; 5University of Medical Sciences, Parasitology, Hamadan, Iran, Islamic Republic of Iran

OBJECTIVES Visceral leishmaniasis (VL) is a parasitic disease caused by protozoan parasite Leishmania sp. The parasite reside in reticulo-endothelial system, mainly in macrophages. Inflammation initiates after leishmanial infection and then leukocytes migrate to the site of infection. E-selectin is expressed on cytokine-induced endothelial cells and plays an important role in leukocyte-endothelium interactions and inflammatory cell recruitment. The aim of this study was measuring the soluble e-selectin and determining of e-selectin gene polymorphism between three groups of patients (VL), seropositive and seronegative healthy groups.

METHODS We measured serum soluble e-selectin levels as well as two polymorphisms of the e-selectin (Ser128Arg and Leu554Phe) in a cohort of patients with documented visceral leishmaniasis (n = 64), a healthy control group (n = 74) and a seropositive for VL but without any symptoms (n = 81) that determined in a large scale screening program. Circulation concentration of e-selectin levels measured in three studied groups by an enzyme-linked immunosorbent assay (ELISA) technique. We used the amplification refractory mutation system (ARMS)-PCR procedure for detecting Ser128Arg and Leu554Phe polymorphism.

RESULTS The mean of e-selectin levels significantly differed between three studied groups (P < 0.026) by ANOVA test, and e-selectin levels were increased in patients in comparison with other groups. Significance were most considerable between two groups of patients and healthy individuals (P < 0.008). E-selectin polymorphisms were associated with e-selectin levels and altogether explained 14.4%, 7.2%, and 8.7% in patients, Seropositive and seronegatives healthy groups respectively. Distribution of polymorphism of 128Ser/Arg and 554Leu/Pha among three groups was not different significantly, however, there was a considerable arrangement in distribution of 128Ser/Arg polymorphism and 128Arg allele in healthy group was more than two fold of patients (55% against 20%).

CONCLUSION In conclusion, this study revealed an association between soluble e-selectin levels and visceral leishmaniasis, which suggests that this molecule might have significant roles in the inflammatory process in some infectious disease such as visceral leishmaniasis. Moreover, frequency of 128Arg allele in healthy group was higher than patients one.

PB 28 Evaluation of direct agglutination test (DAT) based on freeze-dried antigen for sero-diagnosis of visceral leishmaniasis (VL) in human and canine reservoir in Iran
A. Jalil1, M. Mohebali2, G. h. Edrissan3 and M. Moghadampour4
1Social Security Organisation, Reference Laboratory, Tehran, Iran, Islamic Republic of Iran; 2School of Public Health and Institute of Public Health Research, Tehran University of Medical Sciences, Medical Parasitology and Mycology, Tehran, Iran, Islamic Republic of Iran; 3Razi Vaccine and Serum Research Institute, Karaj, Iran, Islamic Republic of Iran

OBJECTIVES In order to increase the application potential of Direct Agglutination Test (DAT) for detection of anti Leishmania antibodies in human and canine reservoir serum samples, specially in field condition, we developed a Freeze-Dried (FD) antigen based on stained Leishmania infantum promastigotes and compared the newly produced antigen with Aquous(AQ) antigen in the DAT.

METHODS DAT antigen was prepared as described previously by Harith et al. 1988. Part of the antigen was Freeze-Dried and sealed under vacuum. DAT was performed essentially as described by Harith et al. 1988. Prior to use FD antigen reconstitute in 3 ml of normal salin.

RESULTS The FD antigen remained fully active in the DAT over six months storage at room temperature, 20 days at 37 degree centigrade and for a week after reconstitution and storage at 4 degree centigrade. In 13.5 percent of human sampels and in 0.5 percent of canine sampels FD antigen gave a titer that was one dilution step lower than the titer obtained with AQ antigen. No cross-reactivity was observed with serum samples from patients suffering from malaria, toxoplasmosis, tuberculosis and amoebiasis. With a cutoff value 1:3200 for human samples and 1:640 for canine samples, the sensitivity of the DAT with FD antigen was 94.4 percent and 95 percent respectively. The Specificity of the DAT with FD antigen was 100 percent.

CONCLUSION The major advantages of the FD antigen are that the production of a large batch of this antigen allows reproducible results in the DAT over a long period of time and that the FD antigen can be store at ambient temperature which makes the test a valuable diagnostic tool for use in the field conditions.
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PB 29
Cutaneous leishmaniasis in patients referred to Pasteur Institute of Iran
M. Farahmand, M. Assmar and Z. Farzanehnejad
Pasteur Institute of Iran, Dept. of Parasitology, Tehran, Iran, Islamic Republic of Iran

OBJECTIVE Cutaneous Leishmaniasis (CL) is one of the most important diseases in the world and it is endemic in many parts of Iran. The non leishmanial skin lesions maybe misdiagnosed and mistreated. In the present analytical study the frequency of leishmanial and non leishmanial skin lesions were assessed.

MATERIAL AND METHODS Initial variable included age, sex, occupation, place of residence and number of lesions that were all recorded in an information data. Patients with ulcerative skin lesions were referring to the department of parasitology, Pasteur Institute of Iran were examined for CL by using direct and culture methods.

RESULTS Leishman body was observed in 43.4% out of 322 patients by direct smear and 43.34% by cultivation. In this study some cases of non healing and recidivans leishmaniasis were observed. Most of patients had traveled to Kashan that is one of the endemic area for CL in Iran.

DISCUSSION The results indicates that although CL is endemic in many parts of Iran, but the frequency of non leishmanial skin lesion is very high and diagnostic test should be used before to commence the treatment.

KEYWORDS Iran, cutaneous leishmaniasis, non leishmanial skin lesion

PB 30
Diagnosis and species identification of cutaneous leishmaniasis using prepared smears from clinical specimens by PCR-RFLP
E. Kazemi rad1, H. Hajjaran, M. Mohabali, S. Rezaei, S. Mamishi, H. Herfat and M. Karampoor
1Institute of Public Health Tehran University, Department of Parasitology & Mycology, Tehran, Iran, Islamic Republic of Iran

OBJECTIVES Cutaneous Leishmaniasis is an increasing public health problem in some parts of Iran. There is a concern that it is spreading with increased incidence, so the ability to distinguish among Leishmania species is crucial when proscribing treatment, as well as, in epidemiologic studies to determine possible control measures. However Leishmaniasis diagnosis in the regions where multiple species exist should identify each species directly in the clinical sample without parasite culturing. In this study we used ITS1 fragment PCR-RFLP technique for direct diagnosis of cutaneous Leishmaniasis and parasite identification on prepared smears.

METHODS Forty Giemsa-stained skin scarping smears had been isolated from lesions of cutaneous Leishmaniasis patients from some parts of Iran. All the smears were studied microscopically by light microscope (X 1000). The DNA extraction were performed on the samples and characterized them by PCR method. The ribosomal internal transcribed spacer 1 (ITS1) was amplified with specific primers and PCR products was digested with one restriction Enzyme (Hae III).

RESULTS The amplification of the ITS1 gave approximately a 328 bp fragment in size. Digestion of the PCR product with Hae III produce two distinct bands for Leishmania tropica (200 bp, 70 bp) and two distinct bands for Leishmania major (225 bp, 170 bp). Of the 40 microscopy-positive slides 37 (92.5%) of these were positive by PCR that 22 (59.5%) was L. tropica and 15 (40.5%) was L. major.

CONCLUSION ITS1 PCR-RFLP with the restriction Enzyme Hae III is a method of choice for species identification of cutaneous Leishmania sp. In smears that prepared from clinical specimens.

KEYWORDS Cutaneous leishmaniasis, human characterization, PCR-RFLP, Giemsa -stained smear

PB 31
Human and canine leishmaniasis in Misiones, Argentina: a new emerging focus?
1. Cruz1, M. N. Gutiérrez2, L. Acosta1, C. Nieto1, C. Cañavate1, J. Deschutter2 and F. J. Borrany3
1Centro Nacional de Microbiología, Instituto de Salud Carlos III, WHO Collaborating Center for Leishmaniasis, Servicio de Parasitología, Magadahonda, Madrid, Spain; 2Universidad Nacional de Misiones & Ministerio de Salud Pública de Misiones, Misiones, Argentina; 3Universidad Miguel Hernández, Elche, Alicante, Spain

OBJECTIVES Visceral Leishmaniasis (VL) has never been reported before in the province of Misiones (Argentina). In addition, only four specimens of Lutzomyia longipalpis, the sandfly vector for Leishmania chagasi, have been trapped in this area (years 1951 and 2000). Nevertheless, since June 2006 four human VL cases were detected in Posadas, Misiones. Encouraged for this finding a canine parasitological and serological survey was carried out in Posadas to ascertain the incrimination of the dog in this new focus.

METHODS Blood and lymph node samples were obtained from 97 domestic dogs. Seroprevalence analysis was performed by rk39 immunochromatography and IFAT. PCR analysis of blood and bone marrow was carried out targeting the SSUrRNA and the ITS-1 regions. On the other hand molecular characterization of the parasites was detected by kDNA minicircles fingerprint.

RESULTS Seroprevalence of the dogs in this area reached 37%, while parasite presence was detected in 30%. In all cases the incriminated specie was L. infantum/L. chagasi.

CONCLUSION In association with new cases of human VL the dogs studied in Posadas showed a high prevalence of Leishmania infection by both serological and parasitological methods. L. infantum/L. chagasi was the parasite found in all infected dogs as well as in the human cases. The results obtained point out the significance of the dog as a reservoir and highlight the need to undertake a control programme in order to prevent appearance of new human VL cases.

ACKNOWLEDGEMENTS Dirección General de Cooperación al Desarrollo, Generalitat Valenciana, Spain. & Control Strategies for Visceral Leishmaniasis (VL) and Mucocutaneous Leishmaniasis (MCL) in South America: applications of molecular epidemiology (LEISHEPINETS). European Commission Sixth Framework Programme.

PB 32
Leishmaniasis cutaneous tests: reliability in Tunisia
J. Bettaieb1, N. Ben Alaya Bouafia2, H. Louzie3, K. Dallagi4 and A. Ben Salah1
1Institut Pasteur Tunis, Medical Epidemiology, Tunis, Tunisia; 2Institut Pasteur Tunis, Immunology, Tunis, Tunisia

OBJECTIVE This work aimed to evaluate the effect of antigenic preparation (Leishmania infantum vs. Leishmania major) and dose of Leishmania antigens [5 × 10(6) vs. 2.5 × 10(6) parasites in the same volume] on the reproducibility of delayed type hypersensitivity Leishmania skin test.
METHODS A cross sectional study by door to door including healthy individuals was conducted in the governorate of Kairouan where coexist a visceral leishmaniasis endemic area situated in the district of Sbikha and a zoonotic cutaneous leishmaniasis endemic area in the district of Nasrallah.

RESULTS Results showed that among 34 individuals involved from visceral leishmaniasis endemic area, 26 (76.5%) had a positive Leishmania infantum LST (L-L. infantum) and 27 (79.4%) to Leishmania major LST (L-L. major). Mean size of cutaneous reaction was 5.94 ± 2.66 mm for L-L. infantum and 5.41 ± 3.23 mm for L-L. major, with a significant positive linear association (P < 0.05). Intra-class correlation coefficient was 0.80 [CI 95% = (0.64–0.93)] and concordance Kappa was 0.57 [CI 95% = (0.40–0.74)]. Among 135 individuals from zoonotic cutaneous leishmaniasis, 92.9% revealed a positive test for both types of leishmanin (L-L. major full dose vs. L-L. major half dose). Mean size of cutaneous reaction was 12.61 ± 4.65 mm for the reference test and 11.30 ± 3.95 mm for diluted one, with a positive linear association (P < 0.05). Intra-class correlation coefficient was 0.78 [CI 95% = (0.71–0.84)] and concordance Kappa (kappa) was 0.82 [CI 95% = (0.73–0.91)].

CONCLUSION These results demonstrate a limited effect of LST in diagnosis and antigenic variation and antigen dose on the reproducibility of delayed type hypersensitivity induced by the leishmanin test.

PB 33
Prevalence and risk factors of leishmanin-skin test positivity in the center of Tunisia
J. Bezaa1, N. Ben Aya Bouatif1, K. Dallal2, S. Chil3 and A. Ben salah1
1 Institut Pasteur Tunis, Medical Epidemiology, Tunis, Tunisia; 2 Institut Pasteur Tunis, Immunology, Tunis, Tunisia

OBJECTIVES The overall prevalence of leishmanin skin test positivity in Tunisia has been recently evaluated. It is about 54.7% in healthy individuals. This positivity is higher in visceral leishmaniosis patients (86%) and their family members (75%). Risk Factors associated with geographic extension and transmission of this disease are not identified. This work aims to estimate prevalence and evaluate risk factors of leishmanin-skin test positivity.

METHODS A cross-sectional leishmanin skin test study was carried out on a sample of 3180 healthy volunteers living in the governorates of Kairouan and Kasserine in Leishmania infantum transmission area in the center of Tunisia.

RESULTS Standardized age prevalence of leishmanin-skin test (LST) positivity was 45.9% [CI 95% = (43.9–47.9)] confirming the hyper endemicity of this region. The rate of leishmanin-skin test positivity ranged from 73.9% [CI 95% = (71.9–75.9)] in Zaghdou (Kairouan) to 63.5% [CI 95% = (53.7–51.1)] in Abdellahim (Kasserine). There is no significant difference between men and women supporting a similar exposure to infection by gender. In the districts of Zaghdou, Sidi Amor, El Hajej and chikha, age specific rates showed a rapid increasing prevalence with age reaching a proportion exceeding 80% after the age 15 years. However, the age specific prevalence from other districts showed a progressive increasing trend with age, with a low rate for younger children and a plateau of 75% after 45 years. Multivariate analysis of leishmanin-skin test positivity risk factors showed that only district and age are determinants of this infection.

CONCLUSION This investigation clearly demonstrates geographic variability of LST positivity related to heterogeneity in parasites contact with men due to environmental modification favorable to vector and reservoir proliferation.
The existence of these hybrids seems to increase endemic areas which reach Leishmania infantum. Although serological techniques showed high specificity, future work for improve their sensitivity should be done since serodiagnosis has the advantage of being a non-invasive procedure and very useful to both groups (immunocompromised and young children) of patients. This work was supported by funding from the EC research project no. INCO-CT2005-035407 and FCT grant SFRH/BD/12523/2003.

**PB 36**

**Validation of serodiagnosis for visceral leishmaniasis in paediatric and immunocompromised patients**

C. Maia, J. M. Crastoívo, J. Ramadas and L. Campino

*Instituto de Higene e Medicina Tropical, Leishmaniasis, Lisbon, Portugal*

**OBJECTIVES** Mediterranean visceral leishmaniasis (MVL) was traditionally more prevalent in infantile age than in adults. However, in the last two decades most of the cases are related to immunocompromised adults, the great majority HIV infected. The main objective of this study was to assess the efficacy of three serological techniques for the diagnosis of MVL in Leishmania-HIV co-infections and paediatric cases.

**METHODS** IFAT-Indirect Immunofluorescence Antibody Test, CIE-Counterimmunoelectrophoresis and rK39 immunochromatographic test were used for the diagnosis of MVL in two groups of patients: immunocompetent young children and immunocompromised adults, using bone marrow culture and/or polymerase chain reaction (PCR) as reference tests. In some of these cases sera before and after treatment were tested.

**RESULTS** CIE detected anti-Leishmania antibodies in more cases than IFAT or rK39. Sensitivity was 57% and 81% in young children and between 69% and 77% in immunocompromised patients who were confirmed to be infected by PCR or culture. The specificity of serological diagnostics was 100% in a group of sera from healthy individuals and immunocompromised patients with other opportunistic infections than leishmaniasis.

**CONCLUSION** Although serological techniques showed high specificity, future work for improve their sensitivity should be done since serodiagnosis has the advantage of being a non-invasive procedure and very useful to both groups (immunocompromised and young children) of patients. This work was supported by the EU/FEDER project POCTI/VT/56357/2004 from Fundação para a Ciência e Tecnologia (FCT), Ministério da Ciência, Tecnologia e Ensino Superior, Portugal. C. Maia (SFRH/BD/12523/2003) is a fellowship from FCT.

**PB 37**

**Diagnosis and molecular characterization of imported leishmaniasis in Spain**

I. Cruz, C. Chicharro, M. D. Flores and C. Cabañete

*Centro Nacional de Microbiología, Instituto de Salud Carlos III, WHO Collaborating Center for Leishmaniasis, Servicio de Parasitología, Majadahonda, Madrid, Spain*

**OBJECTIVES** Leishmania infantum is the causative agent of both cutaneous (CL) and visceral (VL) leishmaniasis in Spain. However, the increase in international travels, humanitarian cooperation and military interventions in areas where different *Leishmania* species are endemic occasionally makes the physicians to face imported leishmaniasis cases which prognosis can be different of that for *L. infantum*. In addition to this, there is an increase in immigrant population from different *Leishmania* endemic areas who reach the primary health centers with ‘imported’ pathologies. The Parasitology Department at Instituto de Salud Carlos III is a reference center for leishmaniasis diagnosis in Spain. A panel of molecular diagnosis techniques were optimized and now are routinely applied to identify the causative species of imported leishmaniasis thus providing the National Health System with a useful information for the management of cases.

**METHODS** Between years 2003–2006 biological samples obtained from patients with suspected imported leishmaniasis were analysed by both NNN culture and PCR (SSUrRNA, ITS-1 and T2B4).

**RESULTS** In the study period 19 cases of imported leishmaniasis were diagnosed, 17 CL and 2 VL. Ten cases were immigrants and nine Spanish professionals or tourists. The place of infection was Latin America in 16 cases, Africa in two and Middle East in one case. Fourteen cases were due to *L. braziliensis* complex, two to *L. amazonensis*, two to *L. infantum* and one to *L. major*. While all the cases were diagnosed and characterized by PCR, only 10 cases were positive by NNN culture.

**CONCLUSION** This work shows the usefulness of PCR with regard to NNN culture to diagnose and characterize *Leishmania* infection. Identification of imported leishmaniasis to the level of complex or species is necessary in order to prevent a virulent/complicated evolution and establish a correct treatment protocol, especially in countries as Spain where there is only one endemic *Leishmania* species.

**ACKNOWLEDGEMENTS** Control Strategies for Visceral Leishmaniasis (VL) and Mucocutaneous Leishmaniasis (MCL) in South America: applications of molecular epidemiology (LEISHEPINETS), European Commission Sixth Framework Programme (LEISHMANIA GENOTYPING), European Commission Fifth Framework Programme.

**PB 38**

**Visceral leishmaniasis in Senegal**

B. Faye1, J. L. Ndjayé, O. Konaté, O. Gaye1, A. A. Niang2, M. Senghor3, A. L. Banuls4, B. Bucheton5, M. Hide6, M. Clair6, M. M. Dione6 and I. Sy1

1Laboratory of Parasitology, Faculty of Medicine, Cheikh Anta Diop University, Dakar, Senegal; 2Institut Fondamental d’Afrique Noire (IFAN), Cheikh Anta Diop University (UCAD), Dakar, Senegal; 3Institut de Recherche pour le Développement (IRD), Montpellier, France; 4Ecole Inter Etats d’Etudes de Sciences et Médecine Vétérinaire (EIESMV), Cheikh Anta Diop University (UCAD), Dakar, Senegal

**OBJECTIVES** To understand the epidemiology of the visceral leishmaniasis in Senegal, we carried out in 2006, a parasitologic, serologic and molecular study in the human and the dog and an entomological study in the area of Thiès which is a hearth of leishmaniasis.

**METHODS** For the human patients suspect of visceral leishmaniasis and for subjects living in contact with the tank of parasite., we are take blood samples for a immunochromatographic test (IT-Leish) and Western Blot for the dogs, in addition to two tests immunochromatographic (IT-Leish and Speed Leish) for serology, we made an parasitologic examination and a parasite culture on ganglionics samples. A PCR was carried out starting from the total blood of all the examined dogs. In the various villages of study area, we made sandfly captures with oil-paper, CDC trap and intra domiciliary pulverization.

**RESULTS** A total of 133 patients were examined, 44 presented a positive Western blot. All the IT-leish tests were negative. On 40 examined suspect dogs, 14 presented a positive parasitologic
examination with amastigote forms. 14 cultures were positive. The species genotyping is on going in Montpellier. Serology by the two tests was positive for 17 dogs (42.5%). The PCR revealed the presence of the parasite in 15 dogs (37.5%). Concerning the entomological study, 3788 sandflies were captured including 45.4% of females. Two Phlebotomus species and seven Sergentomyia species were found.

CONCLUSION These results show the active character of the Thiès area. However, no case of visceral leishmaniasis was found.

PB 39
Cloning of Leishmania major p4 gene
M. Shaddel1, H. Oormazdi1, L. Akhlaghi1, B. Kazemi2, and M. Bandehpour3
1Iran University of Medical Sciences and Health Services - Army University of Medical Sciences, Parasitology and Mycology, Tehran, Iran, Islamic Republic of Iran; 2Shahid Beheshti University of Medical Sciences and Health Services - Molecular and Cellular Biology Search Center of Shahid Beheshti University of Medical Sciences and Health Services, Parasitology and Mycology, Tehran, Iran, Islamic Republic of Iran; 3Molecular and Cellular Biology Search Center of Shahid Beheshti University of Medical Sciences and Health Services, Parasitology and Mycology, Tehran, Iran, Islamic Republic of Iran

OBJECTIVES Leishmania major p4 gene is normally expressed during amastigote form of the parasite and can be good Candidate for producing an effective vaccine. In this study we cloned this gene in suitable vector for further vaccine studies.

METHODS Leishmania promastigote was grown in NNN medium and mass culture in RPMI 1640 cell culture medium. Total Leishmania genomic DNA was extracted by centrifugation of promastigote and lysed by lyses buffer followed by boiling method. PCR was carried out using p4 gene specific primers. PCR product was detected by agaros gel electrophoresis and cloned into pBluescript plasmid via T/A cloning method. Reaction was transformed into XL1-Blue competent cell and recombinant plasmid screened using agar plate contained X-gal and IPTG.

RESULTS Plasmid was extracted and cloned gene was released by restriction enzyme and subcloned into pPQE-30 expression vector.

CONCLUSION This construct is ready for protein expression in vitro.

PB 40
Isolation and identification of Leishmania isolates from different endemic foci of Iran
M. R. Razavi1, M. Asmar1, M. R. Shirzadi2, S. R. Naddaf1, H. Nekoie1, N. Hasan1 and B. Ghasinejad3
1Pasteur Institute of Iran, Parasitology, Tehran, Iran, Islamic Republic of Iran; 2Center for Diseases Management, Zoonosis, Tehran, Iran, Islamic Republic of Iran

OBJECTIVES The leishmaniases are a group of illnesses of skin, mucosa and the reticuloendothelium caused by protozoa of the genus Leishmania. Of these, the cutaneous form is the most widespread, affecting primarily rural and periurban populations. The cutaneous form is one of the main public health problems in the Middle East and about 20 000 cases of that have been recorded in different regions of Iran during 2006. Identification of the causative strains and the epidemiology of the disease is the most important mean for the control and prevention of leishmaniases.

METHODS During 2006, different isolates of Leishmania were isolated from human, sand fly and rodents. The samples were cultured on NNN medium and others enriched media. Then the parasites were harvested from medium, DNA were extracted by phenol-chloroform and isoamylalchle and precipitated by ethanol. The purified DNA was randomly amplified with different decamers.

RESULTS The comparison of the products pattern of isolates with standard strains by using of type specific bands, reviled that Leishmania major and Leishmania tropica are common species in different regions and there are different types of each species in some foci.

CONCLUSION The RAPD-PCR procedure can be used for identification and typing of different strains from different endemic area. The causative agents are not uniform and we need the exact epidemiological information for control the disease.
PB 42
Factors causing the high demand of leprosy patients in a reference centre in northeast Brazil
L. Cavalcanete Trindade, J. N. Pontes de Aquino, M. Maia Cantidão, M. da Silveira Mendes, D. Hinders and J. Heukelbach
1 Complexo Hospitalar Clementino Fraga, João Pessoa, Brazil; 2Programa de Saúde da Família Uniao, João Pessoa, Brazil; 3Leprosy Relief Association, Natal, Brazil; 4School of Medicine, Federal University of Ceará, Department of Community Health, Fortaleza, Brazil

OBJECTIVES To identify factors causing the high demand of leprosy patients in a reference centre in northeast Brazil, despite ongoing efforts to decentralize the National Leprosy Elimination Programme.

METHODS We undertook a study of the reference centre for leprosy in João Pessoa, capital of Paraíba State (northeast Brazil). All patients with leprosy treated during a period of three months were interviewed using pre-tested structured questionnaires.

RESULTS In total, 296 patients treated during 1161 consultations were included in the study. Of this total, 493 (42.5%) consultations were carried out by nurses, 458 (39.5%) by physicians, and 210 (18.0%) by physiotherapists. Eighty (27.0%) were new leprosy cases. The most common reason for consultations were: nurses-distribution of supervised multi-drug therapy (MDT) (95.7%) of consultations; physiotherapists-assessment of the disability grade (98.6%); and physicians-treatment of leprosy reactions (63.5%). Interestingly, the majority (94.8%) of consultations (excluding new cases) had been scheduled by the reference centre itself. On the other hand, 86% of the 296 patients had been transferred from Primary Health Care (PHC) network for confirmation of diagnosis. Ten percent of patients referred indicated that they did not want to be treated at a PHC clinic fearing stigma associated with leprosy.

CONCLUSION The high concentration of leprosy patients at the reference centre was inappropriate, reflected by the number of patients that did not need to be treated at the tertiary level (such as supervised distribution of MDT). This is caused mainly by the high number of new cases without complications or reactions being transferred from PHC network to the reference centre, and lack of counter-referral from the reference centre back to the PHC level. The efforts to improve decentralisation of the Leprosy Elimination Programme need to focus on these aspects, for example by improving communication between PHC units and reference levels.

PB 43
Paucibacillary leprosy and its differential diagnosis
J. R. Gómez Echevarría and F. Moll Cervera
Fontilles Association, Vall de Llaguart (Alicante), Spain

OBJECTIVES We try to present Paucibacillary Leprosy (PL) according to the Operational Classification of the WHO (1982), as well as to describe meticulously the clinic of the dermatological lesions of this type of leprosy. We also describe different cutaneous diseases that require differential diagnosis from PL.

METHODS The material for this presentation was collected from the work on leprosy diagnosis and control carried out by the Fontilles Association in collaboration with various Ministries of Health and their Programs of Fight against Leprosy, always following the guidelines recommended by the World Health Organization. Fontilles Association started its labour with leprosy patients in 1908 in Spain and it joined to the world campaigns of fighting against this disease through ILEP (International Federation of Anti-Leprosy Associations) in 1966. At present we are working in several countries: Brazil, India, Equatorial Guinea, China, Nepal, Angola, Nicaragua.

RESULTS Different types of dermatological manifestations in ML patients aiming at the diagnostic criteria for this disease are described: macule, patch, infiltration, nodule... Photographically different dermatological diseases are showed for the differential diagnosis of multibacillary leprosy (medicines reactions, chromomycosis, lobomycosis, neurofibromatosis, lipomatosis, ichthyosis...).

CONCLUSION -Diagnosis and treatment of the multibacillary patient is a specially important part of the Campaigns on Leprosy Control since they are an important source of transmission and propagation of new cases.-On the other hand, we should emphasize the simplicity of the diagnosis if leprosy is suspected, since it does not need any specialized set of instruments, and the efficiency of the Multi-Drug Treatment (MDT) recommended by the WHO.

PB 45
Importance of early diagnosis in leprosy. Indeterminate leprosy and its differential diagnosis
J. R. Gómez Echevarría1 and F. Moll Cervera2
1 Fontilles Association, Vall de Llaguart (Alicante), Spain; 2Fontilles Association, Vall de Llaguart, Spain

OBJECTIVES With this presentation we try to review the clinical cutaneous manifestations of indeterminate leprosy and to emphasize its diagnosis as a basic purpose in Leprosy Programs.
The material for this presentation is gathered from the Fontilles Association in collaboration with different Ministries of Health in the Programs of Fight against Leprosy, and always following the guidelines recommended by the World Health Organization. Fontilles Association started its labour with leprosy patients in 1908 in Spain and it joined to the world campaigns of fighting against this disease through ILEP (International Federation of Anti-Leprosy Associations) in 1966, and since then we are present in different countries such as Brazil, India, Equatorial Guinea, Xina, Nepal, Angola, Nicaragua...

RESULTS We describe in detail the dermatological manifestations of indeterminate leprosy, together with photographic material of this disease and other dermatological diseases that can be clinically confusing (pityriasis alba, pityriasis versicolor, vitiligo, nevus congenital, post-inflammatory dermatosis...).

CONCLUSION - Indeterminate leprosy affects the skin exclusively, with involving any stopping peripheral nervous trunk. The patient diagnosis in this phase will avoid, therefore, the appearance of later disabilities. - Indeterminate leprosy appears fundamentally in cohabitants of multibacillary patients. It is specially important to control them searching for indeterminate leprosy in order to treat new cases of leprosy.

PB 46

Erosive arthritis and tenosynovitis mimicking rheumatoid arthritis caused by leprosy. A case report

W. Van der Laan¹, W. Faber², N. De Vries³ and P. P. Tak¹

¹AMC, Clinical Immunology and Rheumatology, Amsterdam, Netherlands;
²AMC, Dermatology, Amsterdam, Netherlands

INTRODUCTION Leprosy is a chronic granulomatous disease caused by infection with Mycobacterium Leprae. It has a spectrum of manifestations, depending on the immunologic response of the host, varying from tuberculoid to lepromatous leprosy with the borderline form in between. Musculoskeletal symptoms are not uncommon in this disease and may be difficult to differentiate from other rheumatologic conditions.

CASE Here, we describe a case of a 65-year-old man from Suriname who presented with chronic tenosynovitis of the hand extensors as well as arthritis of the right wrist and several metacarpal joints. Laboratory tests showed elevated inflammatory parameters, but the rheumatoid factor and anti-CCP were not elevated. Imaging showed multiple erosions in the distal ulna of the right wrist, in the carpal and the metacarpal bones. The patient was diagnosed with rheumatoid factor negative, erosive rheumatoid arthritis and was treated with prednisone and methotrexate. The joint symptoms responded quickly. Three months after onset of therapy the prednisone was stopped. A couple of weeks thereafter he presented in the emergency room with acute-onset multiple erythematous plaques and periorbital edema. He also complained of sensory loss in the fingers. Skin biopsy showed epitheloid-cell granulomas with influx of lymphocytes and damaged of nerve fibres. Staining for mycobacteria was positive. Antibodies against PGL-1 were elevated.

CONCLUSION Erosive arthritis is a rare complication in borderline leprosy but is more common in lepromatous leprosy. In patients with joint disease combined with neurological symptoms who have stayed in endemic areas for leprosy, the diagnosis leprosy should be considered.

Leptospirosis

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Study on the incidence of leptospirosis in Rasht, Guilan, Iran, from 2003 to 2005

H. Honarmand¹, A. Heidarzadeh², R. Jaearshad³ and Z. Zareichian⁴

¹Guilan University of Medical Sciences, Cellular and Molecular Research Center, Labijan, Iran, Islamic Republic of Iran;
²Guilan University of Medical Sciences, Dep of Epidemiology, Faculty of Medicine, Rasht, Guilan, Iran, Islamic Republic of Iran;
³Guilan University of Medical Sciences, Gastrointestinal and Liver Research Center, Guilan, Iran, Islamic Republic of Iran;
⁴Center of Public Health, Labijan, Guilan, Iran, Islamic Republic of Iran

OBJECTIVES/BACKGROUND Leptospirosis is a major global zoonosis mainly representing as an occupational hazard. Large outbreaks have occurred in (sub)tropical regions. The flat area of Guilan province has climatologic, environmental and socioeconomic conditions that are highly favorable for leptospirosis, i.e. a subtropical and humid climate, abundance of rodents and wild animals and many surface waters. Rice farming is the main activity of villagers and keeping domestic animal (cattle, horses and dogs) is very common in rural regions. Rasht is the capital of Guilan province with lots of villages and high population. We performed IgM-ELISA and MAT for 788 patents with clinical symptoms of leptospirosis, from 2003 to 2005, to establish leptospirosis and to explore demographic and epidemiological features of the disease in the area.

METHODS A total of 788 blood samples were collected from patients attending Razi hospitals with clinical symptoms consistent with leptospirosis. IgM-ELISA was performed by using a commercial kit (quantitative, serion ELISA classic leptospira IgM, made in Germany) and MAT was performed by using six pathogenic strain (Icterohaemorrhagia, Grippotyphosa, Hardjo, Pomona, Canicola, Ballum). All sera with 160 at least one pathogenic strain in MAT and with titer ≥ 160 in IgM-ELISA were scored positive.

RESULTS Leptospirosis was confirmed in a total of 327 cases (41.5%), 71.4% of the cases were male and 28.6% were female. About 67.0% of patients were aged between 20 to 60 years. 97.0% of cases had a history of working in rice field and 78.0 of them were farmer, 11.5% of patients were housekeeper village who had high activity in rice fields and other cases were urban resident people but all of them had history of contact with surface waters and most of them worked in a rice field for a short time. 1.2% of positive cases had a history of swimming in loca river. Icterohaemorrhagia, Grippotyphosa, Hardjo, Pomona, Canicola, Ballum had highest titers in Mat, respectively.

CONCLUSION Diagnosis of leptospirosis was confirmed in the laboratory for 327 of 788 cases. This suggests a high incidence of human leptospirosis. Part of the leptospirosis cases can be attributed to the intensive contact with domestic animals but rice farming seems to be the main cause of leptospirosis. The disease is mainly occurred in warm months of year (between May to October) with a peak in September (during harvesting of rice), and also mainly in middle aged group.
Leptospirosis is a main widespread zoonosis in the world. In 2005, we tested 788 single serum samples from patients admitted to the Razi hospitals in Guilan, Iran, with symptoms consistent with leptospirosis. The commercial IgM-ELISA (serion Elisa classic, Germany) was performed according to manufacturer’s recommendation. The in house IgM/IgG ELISA was performed by using plates which were coated with a local Icterohaemorrhagiae serovar. A (reciprocal) titer $\geq 160$ was regarded positive in house-IgM ELISA and titers $\geq 20$ u/ml was regarded positive (as company instruction) in commercial assays. MAT was performed by using plates which were coated with a local Icterohaemorrhagiae, Grippotyphosa, Hardjo, Pomona, Canicola, Ballum). An initial titer $\geq 160$ against one or more pathogenic serovars was scored positive.

RESULTS A total of 327 serum samples which were positive in MAT were selected for the study. Accuracy of in-house IgM-ELISA compared to commercial IgM-ELISA was studied. Sensitivity, specificity, positive and negative predictive values for the in house IgM-ELISA were 87.1%, 73.1%, 51.7%, and 94.5% consequently. For the commercial IgM-ELISA the values were 98.6%, 12.2%, 26.7%, and 95.8%. The sensitivity of in house IgM-ELISA was 81.3% for days 1–5 and 92.1% for days $\geq 6$. The sensitivity of commercial IgM-ELISA was 96.7% for days 1–5 and 100% for days $\geq 6$. The specificity of the in-house ELISA was 68.3% for days 1–5 and 73.3% for days $\geq 6$ but 6.5% and 16.9% for the commercial ELISA

CONCLUSION We evaluated two IgM-ELISA assays on single samples from patients with severe, acute leptospirosis. Both assays performed equally well. The average sensitivity of the commercial ELISA was higher than that from the in-house ELISA but sensitivity of both assays for samples of days $\geq 6$ were comparable. The specificity and positive predictive values of the commercial ELISA was less than that from the in-house ELISA for all days, IgM ELISA is a suitable alternative for the diagnosis of leptospirosis in circumstances where facilities for MAT are lacking.

Prognostic factors of severe leptospirosis in hospitalized patients, northern Iran, 2003 to 2005

A. Heidarzadeh1, A. Heidarzadeh2

OBJECTIVES Leptospirosis is one of the most common zoonosis worldwide that is more prevalent in tropical and subtropical regions. The disease is very common in the flat area of Guilan, Northern of I.R.Iran, in which, climate is humid temperate and rice farming is main agricultural activity in rural areas. This study is conducted to evaluate the prognostic factors of severe leptospirosis in hospitalized patients. METHODS In this cohort study, 788 individuals with suspected leptospirosis hospitalized in the Razi Rasht Hospital, between June and September during 2003 till 2005 were recruited into the study and followed for at least 15 days. Two blood samples were taken at days 1 and 15 and centrifuged sera were frozeed in -24 °C. The disease diagnoses were made by IgM-ELISA (quantitative,
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Leptospirosis: indications of changes in clinical presentation in Northern Iran, Guilan province, 2003 to 2005

A. Heidarzadeh1, H. Honarmand2 and S. Ghadjarjan2

1. Guilan Medical University, Community Medicine, Rasht, Iran, Islamic Republic of Iran; 2. Guilan Medical University, Microbiology, Rasht, Iran, Islamic Republic of Iran; 3. Guilan Medical University, Talented Students Office, Rasht, Iran, Islamic Republic of Iran

OBJECTIVES Leptospirosis has protean clinical manifestations. Leptospirosis remains underreported in I.R.Iran because of ignorance and the broad spectrum of clinical manifestations. This study aimed to find the common clinical manifestations and laboratory changes in Leptospirosis to make a better feature of this endemic disease in Northern Iran, Guilan province.

METHODS In this study, suspected clinical cases of leptospirosis who were hospitalized in the Razi Rasht Hospital, between June and September months of the years 2003 till 2005 were included in the sample and investigated. They were assessed by a structured questionnaire at the admission time and on each day until release. The clinical and laboratory data were collected daily by physician’s visits. The disease confirmation were made by IgM-ELISA (quantitative, serion ELISA Classic Leptospiral IgM) more than 20 IU/ml. All laboratory tests were done by the Razi Hospital Laboratory. The data were analysed by STATA 8.0 software. Cluster analysis was used to find the cluster of clinical manifestations.

RESULTS From 788 suspected cases, 327 ones were confirmed, the mean duration between first manifestations and admission time was 3.6 ± 2.6 days. The patients with more delay in admission had significant increase in complication rate (logistic regression <0.001). The most common presentations in confirmed patients were fever (96.9%), shiver (93.3%), headache (83.7%), myalgia (82.8%) and abdominal pain (82.8%). The most common laboratory findings were abnormal platelet, AST and ALT levels around 62.2%, 42.3% and 36.5% respectively. Just 35% of patients had icter at the admission time. Approximately half of confirmed patients could not fulfill the world health organization (WHO) criteria for suspected leptospirosis at the admission time. This criteria showed only 41.3% accuracy to predict a true diagnosis. The clusters of clinical manifestation and laboratory data were showed in Figure 1 and 2.

CONCLUSION Although prompt recognition of the characteristic presentations of leptospirosis and appropriate treatment could dramatically save patients’ lives, but the great difference between common manifestations of leptospirosis in Guilan province and WHO criteria could increase misdiagnosis in early approaches to patients which presents an enormous need to new criteria applicable in disease surveillance of health system of this area.

Malaria Treatment

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Synthesis and antimalarial activity of new isotebuquine analogs

A. J. Lin1, O. Miroshnikova2, T. Hudson2, L. Gerena3 and D. Kyle2

1. Walter Reed Army Institute of Research, Division of Experimental Therapeutics, Silver Spring, USA; 2. Walter Reed Army Institute of Research, Experimental Therapeutics, Silver Spring, MD, USA

OBJECTIVES To search for new Mannich bases with less liver toxicity.

METHODS Amodiaquine (AQ) and tebuquine (TQ) are 4-aminquinoline antimalarials with Mannich base side chain and are highly effective against chloroquine-resistant strains of Plasmodium falciparum. Clinical use of AQ has been severely restricted because of hepatotoxicity and agranulocytosis side effects associated
with its long term use. Lysosomal accumulation and bioactivation to generate reactive quinoneimine metabolite are implicated to be the cause of the observed AQ toxicities. To avoid the quinoneimine formation and thus the toxicity, a series of isotebuquine analogs and their N-O-oxides with hydroxy group meta to the amino rather than para position of the aniline moiety were prepared. In vitro antimalarial activities of the new compounds were assessed in CQ-sensitive (D6) and CQ-resistant (W2 and TM91C235) cell lines of *P. falciparum* and their *in vitro* toxicity was measured in a murine monocyte-like macrophage line J774.

**RESULTS** The new Mannich bases are highly active against both CQ-sensitive (D6) and resistant (W2 and TM91C235) clones of *P. falciparum* with IC50 in the range of 0.3–120 ng/ml. New compounds are 1000 fold less toxic (IC50 = 0.7–6 μg/ml) to mouse macrophage cell line than to parasite cell lines. In general, mono-Mannich bases are more active than bis-Mannich bases. Mono-Mannich base WR294542 (IC50 = 0.3 ng/ml) is the most active among the compounds tested and is twenty fold more active than the corresponding trifluoromethyl analog WR294688. The key intermediates which possess no Mannich base function are also highly active in the test against chloroquine sensitive clone D6 with IC50 of 8.8 and 15 ng/ml respectively, but showed cross-resistant to CQ in W2 clone.

**CONCLUSIONS** No appreciable difference in *in vitro* toxicity or antimalarial activities was observed between the new Mannich bases (*m*-hydroxyaniline derivatives) and the corresponding *p*-hydroxyaniline derivatives (tebuquine and tebuquine N-oxide). Though the new isotebuquines can not form toxic quinoneimine metabolite, they can be converted to another toxic metabolite, o-quinone methide which is potentially an alkylating agent.

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**QSAR Studies of antimalarial mefloquine analogs**

J. Bhonsle1, T. Heady2, G. Dow2 and D. Huddler3

1Walter Reed Army Institute of Research, Medicinal Chemistry, Division of Experimental Therapeutics, Silver Spring, Maryland, USA; 2Walter Reed Army Institute of Research, Parasitology/Experimental Therapeutics, Silver Spring, USA; 3Walter Reed Army Institute of Research, Medicinal Chemistry, Division of Experimental Therapeutics, Germantown, Maryland, USA

The Quantitative Structure Activity Relationship (QSAR) study involves reported 4-quinoline carbinolamine derivatives that are analogous to mefloquine. A catalyst pharmacophore based QSAR model reported. Out of the 11 possible chemical functions in catalyst, the data set had nine. Catalyst hypothesis can be computed with at most five chemical functions. So, the five chemical functions could be selected from the available nine in 9C5 ways, which is 126. Thus first, we computed the functional features of all the compounds. The following abbreviations are used for the various chemical functions.

- HBA – Hydrogen bond acceptor
- HBAL – Hydrogen bond acceptor – Lipid
- HBD – Hydrogen bond donor
- HDP – Hydrophobic
- HDP-Ali – Hydrophobic aliphatic
- HDP-Aro – Hydrophobic aromatic
- Neg-Chg – Negative charge
- Neg-Ion – Negative ionizable
- Pos-chg – Positive charge
- Pos-Ion – Positive ionizable
- R-Aro – Ring aromatic

We selected the best combination by using chemical intuition. Any of the chemical functions to be relevant for the pharmacophore QSAR model has to be surface accessible. Further, chemical functions such as HDP-Ali and HDP-Aro are proper subset of HDP, and HBA is a subset of HBAL. We selected several different combinations of the chemical functions and guided the refinement based on the computed correlation coefficient and the hypothesis bit costs. The combination of Pos-Ion, HBAL, HBD, R-Aro, and HDP with one excluded volume gave the best hypothesis with correlation coefficient of 0.743, total cost of 1455, fixed cost of 47 and null cost of 3118. The bit distance between total (tc) and fixed (fc) is 1408 (tc-fc), while distance between fixed and null (nc) is 3119 (fc-nc). The ratio of (tc-nc)/(fc-nc) of the final best hypothesis is 2.22. The correlation coefficients vary from 0.743 to 0.693, whereas the total cost vary from 1456 to 1682 bits. The final best hypothesis predicted 18 compounds within an error factor of 2, six compounds within error factor of 3, and the rest of the six compounds within error factor of 10. The final pharmacophore QSAR model has two hydrophobic features, one positive ionizable, and hydrogen-bond acceptor lipid and one ring aromatic. The model predicts all of the compounds within an error factor of 2.6. The predictive correlation coefficient is 0.923 for the four test compounds.

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**Chloroquine (CQ) and sulphadoxine/pyrimethamine (SP) efficacy in the treatment of acute uncomplicated *Plasmodium falciparum* malaria and the prevalence of genetic mutations in Central Sudan**

H. Schallig1, A. Mohamedani2, O. Saeed3, A. A. Gebrel1, G. Schoone1, Y. Abd Alla3 and B. Neur3

1Royal Tropical Institute, Biomedical Research - Parasitology, Amsterdam, Netherlands; 2Faculty of Medicine, University of Gezira, Pathology and Microbiology, Wad Medani, Sudan; 3Faculty of Medicine, University of Gezira, Medicine, Wad Medani, Sudan; 4Blue Nile Research and Training Institute, University of Gezira, Case Management, Wad Medani, Sudan; 5Blue Nile Research and Training Institute, University of Gezira, Parasitology, Wad Medani, Sudan

**OBJECTIVES** To study the current situation of CQ and SP efficacy in the treatment of uncomplicated malaria. To identify the role of *Plasmodium falciparum* multi-drugs resistance 1(Pfmdr1) and P. falciparum chloroquine resistant transporter (pfcrt) genetic mutations in CQ resistance. To identify the role of dihydrofolate reductase (DHFR) and dihydropteroate synthase (DHP5) genetic mutations that are highly predictive for SP resistance.

**METHODS** During September 2002 to April 2004, 102 patients infected with uncomplicated falciparum malaria were selected and divided into two groups. Then each group allocated to a supervised standard therapeutic dose of CQ and SP. Clinical and parasitological assessment were evaluated for 28 days using the WHO *in vitro* protocol (2002), and mutation specific polymerase chain reaction (PCR) analysis in combinations with restriction enzyme analysis was performed for determining the prevalence of two (pfcrt & Pfmdr1) and four genes (dhfr & dhps) conferring CQ and SP resistance respectively.

**RESULTS** In the 51 CQ group, 3/51(5.9%) of the enrolled patients were withdrawn and 48/51 (94.1%) reached the end point of the 28-day follow-up. Twenty-seven of the 48 patients (56.2%) revealed an adequate clinical response (ACR). While the 7(14.7%), 11(22.9) and 3(6.2) presented early treatment failure (ETF), late clinical failure (LCF) and late parasitological failure (LPF) respectively and are representing 21/48 (43.8%) as an overall *in vivo* CQ resistance, and gametocytes were detecting...
Efficacy of artemisinin derivatives in treating severe malaria in children: a systematic review

G. PrayGod1 and A. de Frey2

1National Institute for Medical Research, Public Health Sciences, Mwanza, United Republic of Tanzania; 2University of the Witwatersrand, School of Public Health, Johannesburg, South Africa

OBJECTIVES Evidence suggests that the efficacy of intravenous quinine, which is the mainstay for treating severe malaria in children, is decreasing in Asia and Africa. Artemisinin derivatives have the potential to replace quinine. The objective of this review was to assess the efficacy of parenteral artemisinin derivatives vs. quinine in treatment of severe malaria in children.

METHODS Using systematic review design, we searched literature for published and unpublished randomized trials in all major databases and then two reviewers independently selected the trials and assessed their methodological quality using pre-determined criteria. Data were independently extracted and analysed using STATA. Effect measures were calculated using pooled Relative Risks (RR) and Weighted Mean Difference (WMD). Mortality was the primary outcome where as parasite clearance time, fever clearance time, coma resolution time, 28th day cure rate, incidence of neurological sequelae and incidence of adverse effects were the secondary outcomes.

RESULTS Eleven trials were included (1455 subjects), nine from Africa and two from Asia. Allocation concealment was adequate in seven trials (1238 subjects). Overall there was no difference in mortality between treatment with artemisinin derivatives and quinine (RR = 0.89, 95%CI 0.71–1.1), sensitivity analysis gave similar results for adequately concealed and inadequately concealed trials (RR = 0.93, 95% CI 0.74–1.16 and RR = 0.66, 95% CI 0.36–1.22 respectively). Also parasite clearance time (PCT), tended to be shorter in artemisinin derivatives compared to quinine (WMD among studies which reported PCT as mean was -4.76 with 95% CI -9.68 to 0.17 and all three studies which reported PCT as median showed that artemisinin derivatives cleared parasites faster than quinine, each had P < 0.0001). Other secondary outcomes were not conclusively more efficacious in artemisinin derivatives.

CONCLUSION The available evidence suggests that parenteral artemisinin derivatives are not superior to quinine in the treatment of severe malaria in children.

Point mutations associated with sulfadoxine–pyrimethamine resistance in Plasmodium falciparum isolates in Southeast Iran

H. Keshavarz1 and A. Heidarzadeh2

1Tehran University of Medical Sciences, Department of Medical Parasitology, Tehran, Iran; 2Ministry of Sciences, Department of Medical sciences, Tehran, Iran

OBJECTIVES The spread of chloroquine-resistant *P. falciparum* has led to an increasing use of the antifolate combination of SP in Iran. Mutations in DHFR and DHPS genes strongly associated with *in vitro* and *in vivo* resistance and are related with SP usage. This study was performed in order to detection prevalence of point mutations in two mentioned above genes by SSOP-ELISA Nested PCR in southeast of Iran.

RESULTS Field isolates were collected from 50 resident subjects in southeast of Iran. Five *P. falciparum* laboratory isolate (3D7, FCR3, 7G8, DD2 and T518) were applied to determine the specificity of the technique and used as a standardized control panel in experiments. Amplification was used in 96 well PCR plates. Two microlitre of the diluted PCR products was added to each well of the ELISA plate. Optical density (OD) was detected, at 492 nm in ELISA reader.

RESULTS The prevalence of the wild type DHFR Asn-108 mutation, DHFR Arg-59 mutation, DHFR Ile-51 mutation, DHFR Leu-164 mutation, DHPS Gly-537 mutation, DHPS Mr-581 mutation and DHPS Gly-381 mutation were 100%, 81.1%, 1.9%, 1.9%, 32%, 85% and 5.7% respectively. Multicolonfection was found in three samples. Ninety six percent individuals infected with *P. falciparum* carried at least two dhfr/dhps mutations.

CONCLUSION The quintuple mutant alleles have been reported for the first time in Iran. This may indicates accumulation and emerging new mutation in DHFR and DHPS genes in the area. Presence of high prevalence of DHFR and DHPS mutation in *P. falciparum* isolates from malaria patients in low endemic region of Iran is of great concern.
previously reported S769N mutation was not detected in any of the isolates inspected. In addition, no gene amplifications were detected in a subset of eight isolates.

**CONCLUSION** Overall, this work shows that artemisinin derivatives display good *in vitro* activity locally and that the *pflagp* gene is distinct from that reported in French Guiana, suggesting that the latter haplotypes have not been introduced regionally.

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The use of *Anopheles dirus* and sporozoite-induced *Plasmodium berghei* mouse malaria model for testing exoerythrocytic antimalarial drugs

M. Gettsayazin1, J. Sattabongkot2, P. Hansukjariya1, A. Tungtaeng1, Y. A. Van Gessel1, C. A. Lanter1 and D. E. Kyle4
1 Armed Forces Research Institute of Medical Sciences, Veterinary Medicine, Bangkok, Thailand; 2 Armed Forces Research Institute of Medical Sciences, Entomology, Bangkok, Thailand; 3 Walter Reed Army Institute of Research, Experimental Therapeutics, Silver Spring, USA; 4 University of South Florida, Department of Global Health, South Florida, USA

**OBJECTIVES** Four drugs known to have exoerythrocytic (EE) antimalarial activity were validated in a new mouse model recently developed at AFRIMS.

**METHODS** Primaquine (PQ), azithromycin (AC), proguanil (PG) and atovaquone (AQ) were tested in four experiments of 45, 6- to 7-week-old, female ICR mice. Each experiment consisted of one control group and eight experimental groups (*n* = 5). PQ and AC were tested at 20, 40, 80 and 160 mg base/kg/day; and PG and AQ at 5, 10, 20 and 40 mg base/kg/day. The control group received phosphate buffered saline subcutaneously (SC). Test drugs were administered orally or SC on days 1, 0, 1 and 0. On day 0, mice were inoculated by intravenous injection of 100 000 *P. berghei* (ANKA strain) sporozoites. Blood smears were obtained on days 3 to 10, 13, 15, 17, 20, 22, 24, 27, 29 and 31 for identification and quantification of parasitemia. Mice were observed twice daily for 31 days for clinical signs. All mice that died or euthanized were necropsied.

**RESULTS** All control mice became parasitemic between days 3 and 5 post-inoculation with resulting 100% mortality within 7–17 days. PQ, AC and AQ demonstrated causal prophylactic activity (protection from malarial infection) with minimal effective dose (MED) by the SC route at 40, 160, and 5 mg base/kg/day respectively. By the oral route, MED of PQ and AQ were 40 and 20 mg base/kg/day respectively. Oral PQ was effective in four of five mice at 40 mg/kg but also caused acute toxic death in one mouse. PG was toxic at 20 and 40 mg base/kg by SC route. Gross necropsy of all mice with positive blood smears revealed splenomegaly and dark-grey swollen liver consistent with fulminant malaria infection.

**CONCLUSION** This validated model is useful and currently used for screening new drugs for potential EE activity.

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Medicines for malaria: a changing landscape

P. Olliaro1, S. Nwaka1 and P. Ambrose-Thoma2
1 UNICEF/UNEP/WB/WHO Special Programme for Research & Training in Tropical Diseases (TDR), Geneva, Switzerland; 2 Académie Nationale de Médecine, Paris, France

The environment and prospects for antimalarial treatments have changed significantly in the past few years. There are more funds, new operational paradigms and actors, and more products in the pipeline. A study of the Malaria R&D Alliance shows a 270% increase in investments in malaria R&D since 1996, but current funds are only 10% of the projected need for malaria R&D. The London School of Economics assessed the new paradigm created in the past few years by the emergence of PPPs and the roles of large and small pharmaceutical companies and academia. This renewed interest has resulted in a richer R&D portfolio, which will be analysed and discussed against the needs of malaria control. The limited novelty of the products in clinical development means that increased emphasis needs to be placed in the discovery of new chemical entities for sustainable malaria control, which is largely based on oral treatment of uncomplicated malaria. Artemisinin-based combinations (ACTs) are recommended by the WHO and there are several ACTs under clinical development. Total synthetic alternatives to naturally-derived artemisinin are being explored. Rectal formulations are also options to control progression to severe malaria. Limited R&D is currently being conducted on injectable formulations for treating severe malaria. For projects in clinical development the success rates are estimated to range widely between 6–22% (Glickman, 2006; Di Masi, 2002). This means that 5–17 products are needed in clinical phases to successfully register one drug. The implications of this information will be discussed.

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Polymorphisms of drug metabolising, nuclear receptor and drug transport genes among malaria patients in Zanzibar

P. Ferreira1, M. I. Veiga1, I. Cavaco1, J. P. Martins1, B. Andersson2, M. Mesellem3, K. Rynae4, K. Diderot5, V. Ribeiro5, A. Bjorkman5 and J. Giff6
1 Karolinska Institutet, Stockholm, Sweden; 2 Karolinska University Hospital, Karolinska Institutet, Malaria Research Unit, Department of Medicine, Stockholm, Sweden; 3 University of Algarve, Centre of Molecular and Structural Biomedicine, Faro, Portugal; 4 Karolinska Institutet, Programme for Genomics and Bioinformatics, Department of Cell and Molecular Biology, Stockholm, Sweden; 5 Ministry of Health, National Malaria Control Programme, Zanzibar, United Republic of Tanzania

**OBJECTIVES** Artemisinin-based combination therapy (ACT) is becoming the main option for malaria control in Africa. Zanzibar introduced this new treatment policy already in 2003. We have studied the prevalences of the main functional SNPs in major genes associated to the elimination of the ACT compounds in use in Zanzibar, to determine the frequencies of subgroups of patients predicted to be at high drug exposure and hence at higher risk of toxicity.

**METHODS** A total of 103 unrelated children with uncomplicated malaria from the Unguja and Pemba islands of Zanzibar were enrolled. Using PCR-RFLP and Real Time PCR based allele discrimination methods we have analysed the CYP2B6 (G1563TT), CYP3A4 (A-392G), CYP3A5 (A6986G, G14690A, 27131-132 insT, C3697T) SNPs, and the ABC transporter gene MDR1 SNPs C3435T, G2677T/A and T-129C. PCR product sequencing was applied to regulatory regions of MDR1 and to exons 2 and 5 of PXR, a gene coding for a nuclear factor activated by artemisinin and associated with the transcription of all the studied genes.

**RESULTS** Homozygous subjects for alleles coding for low activity proteins were found at the following frequencies: (i) MDR1: 2.9%; (ii) CYP2B6: 9.7%; (iii) CYP3A5: 14.1% and (iv) CYP3A4: 49.5%. No functionally relevant allele was found in the analysed regions of PXR. A new MDR1 SNP was found (T-138C). Importantly, ten subjects were found to be predicted low metabolizers simultaneously for CYP3A4 and CYP3A5.

**CONCLUSION** A non-negligible prevalence of subjects is predicted to be at higher exposure to the antimalarial compounds included in ACT underlying the importance of pharmacovigilance to identify potential adverse drug events.
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A simple test for the demonstration of artemisinin drugs
T. A. Egelte, T. P. C. Dorio and P. J. de Vries
Academic Medical Center, Infectious Diseases, Tropical Medicine & AIDS, Amsterdam, Netherlands

With the increasing resistance to the existing antimalarial drugs, the use of artemisinin compounds has become elemental in the treatment of malaria. Artesunate has already been successfully used in South East Asia for more than 10 years, but this has led to an unfortunate situation that this market has now been flooded with fake artesunate drugs. Also in Africa counterfeit artemisinin drugs have already been found on the market. As delay in proper treatment will increase the risk of severe malaria, further spreading of these products needs to be stopped and tests which can detect the fakes on the spot without the need of a well equipped laboratory are urgently needed. The Fast Red test used so far for the detection of counterfeit artesunate can also be used for artemisinin and dihydroartemisinin but is less suitable for artemether and arteether (1). A new test has now been developed which is faster and less cumbersome than the Fast Red test using cheap available chemicals and showing a distinct colour. The test works for all the artemisinins. For qualitative purposes the test can be directly used on tiny scrapings from the tablets and requires only the addition of a few drops of the reagents. All artemisinin compounds contain a peroxide moiety which is essential for their activity. Much attention has been given to the interaction of iron with the peroxide moiety in relation to the mechanism of action of the artemisinins. The new test is based on the reaction of a peroxide with Fe²⁺ and measuring the formed Fe³⁺ through complex formation. Test conditions were optimized using artemisinin. Colour formation is directly proportional to the amount of complex formation. Test conditions were optimized using artemisinin drug and the test can therefore be used for quantitative purposes. 1. Green MD, Mount DL, Wirtz RA Authentication of artesunate and dihydroartemisinin antimalarial tablets using a simple colorimetric method. Trop Med Int Health. 2001;6:980–2.

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Interaction of 3,6-diamino-1'-dimethylamino-9-anilinoacridine with hematin and antagonism of its antimalarial effect by concanamycin A
S. Auparakkitanon1, S. Chapoomram1, T. Chirachariyavej1, W. A. Denny2 and P. Wizaret3
1Division of Toxicology, Department of Pathology, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand;
2Department of Biochemistry, Faculty of Science, Mahidol University, Bangkok, Thailand; 3Cancer Research Laboratory, School of Medicine, University of Auckland, Auckland, New Zealand

OBJECTIVES Worldwide resistance of Plasmodium falciparum to chloroquine (CQ) has stimulated search for alternative compounds that are not subject to parasite CQ-resistance mechanism, but act on the same target as CQ, namely, hemozoin formation. We have previously shown (Auparakkitanon S et al. (2003) Antimicrob Agents Chemother 47: 3708) that 3,6-diamino-1'-dimethylamino-9-anilinoacridine (DDAA) has IC₅₀ of 30 nM against both CQ-sensitive and CQ-resistant P. falciparum in culture, but does not appear to bind hematin using a Job plot involving absorbance measurement. We now demonstrate DDAA can bind hematin by using a fluorescence quenching method and it is located in the parasite acidic food vacuole by the ability of concanamycin A, a macrolide antibiotic inhibitor of vacuolar H⁺-ATPase derived from Streptomyces sp., to antagonize DDAA action against P. falciparum in culture.

METHODS Fluorescence measurements were made by mixing at room temperature equal volume of 1 µM hematin and DDAA in 100% DMSO and recording fluorescence spectrum of the mixture in a Shimadzu spectrofluorometer at DDAA excitation wavelength. Determination of the effect of drug combination was conducted by measuring IC₅₀ values of one drug in the presence of a series of fixed concentrations of the other drug. Results were expressed as the mean sums of the fractional inhibitory concentrations (FIC), defined as (IC₅₀ of concanamycin A in mixture/IC₅₀ of concanamycin A alone) + (IC₅₀ of DDAA in mixture/IC₅₀ of DDAA alone) for each fixed concentration. Antagonism is defined when sum of FIC >1. Determination of IC₅₀ was based on inhibition of [3H]-hypoxanthine incorporation into P. falciparum K1 isolate (CQ-resistant) grown under ‘candle-jar’ condition.

RESULTS Hematin quenched fluorescence of DDAA, indicating interaction of the two compounds. Sums of FIC of combination of DDAA and concanamycin A ranged from 1.2 to 1.4, indicative of antagonism between the two.

CONCLUSION We have shown that fluorescence quenching may provide a more sensitive method to demonstrate interaction of hematin with antiplasmodial DDAA and that DDAA is targeted to the malaria parasite food vacuole.

PB 63
Pharmacodynamics/pharmacokinetics of a new pharmaceutical form of fixed-dose artesunate/amodiaquine (Trimalact®) for the treatment of patients with uncomplicated malaria in Africa
D. Parzy1, V. Sinou1, C. Kinsama2, S. Sese2, R. Lwaivo2, L. Tshilolo3, M. Desbordes1, M. Martelloni1, D. N. Yan1 and A. Benais4
1Institute of Tropical Medicine, Army Health Department, UR1P, Marseille Armées, France; 2Centre Hospitalier Monkole, Maladies Infectieuses, Kinshasa, Congo, Democratic Republic Of; 3Saokim Pharma, Hanoi, Viet Nam; 4Geneva University, Department of Pharmacology, Geneva, Switzerland

To facilitate drug administration during artemisinin-based combined therapy (ACT), and to reduce the time required for stability trials on the interaction between the two active compounds artesunate/amodiaquine (AS/AQ), a new pharmaceutical formulation consisting of three-layer orally administered tablets has been developed (Swiss Patent CH692299A5/13.5.06) for adults (100 :300 mg AS/AQ) and children (50 :135 AS/AQ), secable tablet. After overnight fasting, evaluation of parasitaemia by microscopic investigation and Paramax3 test and body temperature measurement, 12 patients with uncomplicated Plasmodium falciparum malaria each received two Trimalact® tablets per day for a three-day period according to WHO guidelines (2006). Blood samples were taken via a permanent cannula until 52 h post-administration, and artesunate (AS), dihydroartemisinin (DHART), AQ and monodihydroamodiaquine (DEAQ) levels were measured in the plasma by HPLC technique at various time intervals over the 52-h period. In the majority of cases (nine out of 12), parasitaemia and fever were no longer observed 48 h after initiation of treatment. The AS and DHART values were equivalent to those reported in similar studies – AS: Cmax 80 ng/ml at 90 mn, DHART: Cmax 220 ng/ml at 120 mn. No AQ in unchanged form was detected in any patient up to 52 h post-administration, but the DEAQ value was 620 ng/ml at the last determination i.e at 52 h. In conclusion, this study demonstrated that the new pharmaceutically formulated and dosage schedule provided excellent therapeutic results. Trimalact®: Trademark of the new AS/AQ pharmaceutical formulation manufactured by Saokim Pharma, Hanoi, Vietnam.
PB 64  
**Piperazine absorption not affected by food intake in healthy Vietnamese volunteers**  
S. Friberg Hietala, T. N. Ha, N. V. Huong and M. Ashton  
1Göteborg University, Pharmacology, Gothenburg, Sweden; 2NIMPE, Hanoi, Viet Nam  

**OBJECTIVES**  
To investigate the influence of a standard Vietnamese meal on the extent of absorption and the absorption profile of orally administered piperazine in healthy adults.  

**METHODS**  
Thirty-two healthy Vietnamese adult subjects were included in the study. Following an overnight fast they received two tablets of Artekin®, each containing 40 mg dihydroartemisinin and 320 mg piperazine phosphate as a single dose under supervision of assigned study personnel. Subjects were randomly assigned to remain fasting for another 4 h following drug intake (n = 16) or take the study drugs together with a standardized Vietnamese meal (n = 16). Frequent blood samples were obtained on days 1 and 2 followed by weekly samples for 2 months.  
Piperazine was separated from plasma components by solid phase extraction and the concentration was determined with HPLC. The pharmacokinetic parameters AUC0–∞, Cmax, Tmax and half-life were determined by non-compartmental analysis in WinNonLin (v5). The difference in pharmacokinetic parameters between fasting and fed conditions was assessed using the Mann–Whitney test in SPSS (v 12.0.1).  

**RESULTS**  
The geometric mean (95% CI) AUC0–∞ was 17.1 h mg/l (10–6.27–4) and 19.7 h mg/l (12.1–32.1) for fed and fasting subjects respectively. The geometric mean Cmax (95% CI) was 216 µg/l (175–266) and 139 µg/l (95; 205) for fed and fasting subjects respectively. There was no statistically significant difference in pharmacokinetic parameters between fed and fasting subjects. The absorption profiles were similar, exhibiting multiple peaks under both fed and fasting conditions.  

**CONCLUSION**  
A typical Vietnamese meal does not influence the extent of absorption or the absorption profile of orally administered piperazine.  

PB 65  
**Pharmacokinetics of pyronaridine: artesunate (Pyramax®) for treatment of children with acute uncomplicated *Plasmodium falciparum* malaria**  
L. Fleckenstein, M. Ramharter and P. G. Kremmer  
1University of Iowa, College of Pharmacy, Iowa City, USA; 2Albert Schweitzer Hospital, Medical Research Unit, Lambarene, Gabon  

**OBJECTIVES**  
Pharmacokinetics of tablet and granule formulations of the fixed combination of pyronaridine:artesunate [PA] (Pyramax®) was studied in an open label, dose escalation, single site study in children aged between 2–14 years with acute uncomplicated falciparum malaria (1000–200 000 asexual parasites/µl blood).  

**METHODS**  
Four groups of 15 patients received pyronaridine:artesunate doses of 6.2 mg/kg, 9.3 mg/kg and 12.4 mg/kg tablets or a paediatric granule drug formulation of 9.3 mg/kg. An independent safety review was conducted prior to dose escalation. Plasma samples were assayed for artesunate (AS) and dihydroartemisinin (DHA) pre-dose and at 0.25, 0.5, 1, 1.5, 2.5, 4, 8, 12, 24 h (pre-dose), and 48 h (pre-dose). For pyronaridine (PP), blood draws were made pre-dose, 0.5, 1, 1.5, 2.5, 4, 8, 12, 24 (pre-dose), 48 (pre-dose), 72, 168, 336 and 504 h. Plasma AS and DHA were determined by LC/MS (sensitivity 1 ng/ml) and whole blood PP was measured by LC/MS (sensitivity = 5.7 ng/ml).  

**RESULTS**  
AS was extensively converted to DHA. The Cmax for DHA after the first PA dose was linear and dose proportional for AS doses between 2–4 mg/kg. Mean Cmax values ranged from 425.1–917.2 ng/ml. The Cmax for PP after the first PA dose was also linear and dose proportional for PP doses between 6–12 mg/kg. Mean Cmax values ranged from 76.9–291.6 ng/ml. Comparable levels of AS, DHA and PP were seen between the tablet and granule formulations of PA in terms of AUC, Cmax, time to peak concentration and half-life.  

**CONCLUSION**  
This is the first report of PP pharmacokinetics in paediatric patients with malaria. Pharmacokinetic analyses support the once daily administration of pyronaridine:artesunate for the treatment of uncomplicated falciparum malaria in paediatric patients.  

PB 66  
**Population pharmacokinetics of amodiaquine and desethyldesamodiaquine in pediatric patients with uncomplicated *falciparum* malaria**  
1Göteborg University, Pharmacology, Gothenburg, Sweden; 2Karolinska Institute, Medicine, Stockholm, Sweden; 3Zanzibar Malaria Control Program, Zanzibar, Tanzania, United Republic Of; 4Divine Word University, Faculty of Health Sciences, Madang, Papua New Guinea; 5Tokyo Women’s Medical University, International Affairs and Tropical Medicine, Tokyo, Japan  

**OBJECTIVES**  
The study aimed to characterize the population pharmacokinetics of amodiaquine (AQ) and its major metabolite N-desethylamodiaquine (N-DEAQ), and to assess the correlation between exposure to N-DEAQ and treatment outcome.  

**METHODS**  
Blood samples from 86 children in two studies in Zanzibar and one in Papua New Guinea were included in the pharmacokinetic analysis. The children had been treated with AQ in combination with artesunate or sulphadoxine-pyrimethamine. The population pharmacokinetics of AQ and N-DEAQ were modeled using the non-linear mixed effects approach as implemented in NONMEM. Bayesian post hoc estimates of individual pharmacokinetic parameters were used to generate individual profiles of N-DEAQ exposure. The correlation between N-DEAQ exposure and effect was studied in 212 patients and modeled with logistic regression in NONMEM.  

**RESULTS**  
The systemic exposure to AQ was low in comparison to N-DEAQ. N-DEAQ half-lives ranged between 3 to 12 days. There was a statistically significant, yet weak, association between N-DEAQ concentration on day 7 and treatment outcome.  

**CONCLUSION**  
The age based dosing schedule currently recommended in Zanzibar appeared to result in inadequate exposure to N-DEAQ in many patients.
adults and children with uncomplicated falciparum malaria treated with two different dosage regimens of the ACT combination dihydroartemisinin-piperazine (DHA-PQ).

METHODS Ninety-eight patients \( (n = 98) \) aged 3–55 years, who were either Burmese or of the Karen ethnic group, with symptomatic uncomplicated falciparum infection were enrolled in the study. DHA-PQ (Artelin®) was administered to achieve a total treatment of 7 mg/kg bodyweight of DHA and 55 mg/kg bodyweight of PQ phosphate. Drug administration was divided into four doses (DP4) at 0, 8, 24 and 48 h or into three doses (DP3) at 0, 24 and 48 h. A total of 480 sparsely drawn venous blood samples, drawn over 63 days, were analysed for PQ by a high-throughput method utilising solid phase extraction and liquid chromatography with UV detection. Population pharmacokinetic parameter estimates for PQ were obtained by nonlinear mixed effects modelling using NONMEM.

RESULTS The measured concentrations of PQ were described by a two-compartment disposition model with first-order absorption and inter-individual random variability on all parameters with an additive random residual error. The population pharmacokinetics of PQ [population mean (95%CI)] were characterised by a low oral clearance [\( CL/F = 66 (60–73) \text{l/h} \)], a large oral steady-state volume of distribution [\( VSS/F = 38100 (34400–41800) \text{l} \)] and a long terminal half-life [\( t_{1/2,Z} = 28, (23–33) \text{ days} \)]. Bodyweight was included in the final model as a linear co-variate explaining the variability in oral clearance and central volume of distribution (2.6% and 2.7% increase in clearance and central volume of distribution, respectively, per kg bodyweight increase from median weight). PQ pharmacokinetic parameters did not depend on dosage regimen.

CONCLUSION In this, to date the largest, patient study on PQ pharmacokinetics, a common structural model with bodyweight as covariate on clearance and central volume, described the variable pharmacokinetics of PQ in children and adults. The current study supports further the use of a simplified once daily treatment regimen to improve treatment adherence and efficacy. Children \( (n = 11; \text{<12 years}) \) appeared to have a markedly prolonged terminal half-life but lower concentrations at the beginning of the terminal phase which might have an impact on post-treatment exposure and sub-therapeutic resistance selection pressure. This requires study in a larger cohort of children to elucidate if a difference is present.

PB 69
Criteria for safe outpatient treatment of falciparum malaria
J. Clerinx\(^1\), E. Bottieau\(^1\), R. Colebunders\(^1\), E. Vanden Ende\(^2\), H. Demey\(^1\), R. Wouters\(^1\), M. Van Esbroeck\(^1\), T. Vervoort\(^1\), A. Van Gompel\(^1\), J. Van den Ende\(^1\), ITMA, Clinical Sciences, Antwerp, Belgium; \(^2\)UZA, intensive care, Antwerp, Belgium

OBJECTIVES There are as for now no firmly established criteria to define patients with falciparum malaria who can be safely treated as outpatients. The absence of any clinical and paraclinical criteria of severe malaria at diagnosis according to the revised definition proposed by the WHO in 2000 is not sufficient, as some patients develop complications in the following days despite adequate treatment. In a recent study we observed that a normal bilirubinemia (\(<1.3 \text{mg/dl}) \) and a parasite level \(<1\% \) were two strong independent predictors of uncomplicated malaria. In this study we have constructed an easy to apply model based on clinical and laboratory criteria to fit best the requirements for a patient infected with \( P. \) falciparum to be safely treated as an outpatient.

METHODS From 4-2000 to 9-2006, we enrolled prospectively all patients diagnosed with \( P. \) falciparum infection at our referral centers. We sought to establish the best combination of bilirubin level and \( P. \) falciparum parasitemia to define a patient to be safely treated as an outpatient. Complicated malaria was considered present when any complication according to the 2000 World Health Organization criteria of severe malaria occurred at diagnosis or within 3 days thereafter. Only non-vomiting patients were considered fit for ambulatory (oral) treatment. Among non-vomiting patients with normal bilirubin level, various levels of parasitemia were studied in relation with an uncomplicated course following treatment.

RESULTS \( P. \) falciparum malaria was diagnosed in 450 patients, of whom 133 (30%) were already on anti-malarial therapy. Vomiting was noted in 153/450 (34%) patients. Severe malaria was diagnosed in 80/450 (18%) patients. Bilirubin levels were available for 388/450 patients. Only two of 213 patients with normal bilirubinemia (\(<1.3 \text{mg/dl}) \) and a parasite level \(<1\% \) had a complicated course. Among these, none of the nonvomiting patients \( (n = 153) \) developed any complication during treatment. Only 5/122 (4%) of those individuals who were first treated as outpatients were subsequently hospitalized, all because of minor events not related to severe malaria.
CONCLUSION Ambulatory treatment is safe in non-vomiting patients with falciparum malaria provided that parasitemia is lower than 1% and that bilirubin level is normal.

PB 70
Pharmacokinetic evaluation and metabolite characterization of the antimalarial piperaquine in the rat
J. Tarning1, N. Lindegardh1, S. Sandberg1, N. Day2, N. White3 and M. Ashton1
1 Sahlgrenska Academy at Göteborg University, Department of Pharmacology, Göteborg, Sweden; 2 Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

OBJECTIVES To evaluate the pharmacokinetic properties of piperaquine (PQ) in the rat after intravenous and oral administration. Further, to identify and characterize the main PQ metabolites in rat plasma, urine, feces and bile after intravenous administration.

METHODS Male Sprague-Dawley rats were administered PQ as a micro-emulsion (water/oil/surfactant, 65:25:10) orally (n = 12) or intravenously (n = 10). Venous blood for pharmacokinetic evaluation was frequently withdrawn from an indwelling jugular vein catheter for up to 60 h after dose. Urine and feces were collected for up to 70 h in 12 h intervals after intravenous administration of PQ to rats (n = 4) kept in metabolic cages. Bile was collected for up to 8 h in 1 h intervals after intravenous administration of PQ to anesthetized rats (n = 4). PQ plasma, urine and bile concentrations were quantified using solid phase extraction (SPE) and a triple quadruple LC-MS system. Metabolite identification and structural characterization was performed on an iontrap LC-MS system with MS3 capability. Individual and population pharmacokinetic parameter estimates were obtained by compartmental and non-compartmental analysis using WinNonlin and by nonlinear mixed effects modelling of the pooled concentration-time data using NONMEM.

RESULTS The measured concentrations of PQ were best described by a three- and two-compartment disposition model with first-order absorption after intravenous and oral administration, respectively. A rapid initial distribution phase was evident after intravenous but not oral administration. The population pharmacokinetics of piperaquine were characterised by a low clearance (CL), a large steady-state volume of distribution (VSS) and a long terminal half-life (t1/2,Z). The absolute bioavailability (F) of PQ after oral administration was approximately 40–80% with extensive variability. PQ displayed a low biliary clearance and was predominately eliminated by metabolism with less than 1% of total dose recovered in urine.

CONCLUSION Despite extensive clinical use, very little non-clinical and animal in vivo data of PQ is available, none addressing metabolism or pharmacokinetics. PQ exhibited multiphasic pharmacokinetics in the rat, similar to humans. The rapid initial decline in plasma concentrations after intravenous administration is reminiscent of chloroquine suggesting that this route of administration should be avoided for PQ considering the dangerous side-effects seen after intravenous chloroquine. The principal PQ metabolite formed in humans was formed in the rat. Taken together, these results indicate the rat to be a suitable specie for non-clinical PQ studies.

PB 71
Diagnoses and therapy for the treatment of malaria in illegal immigrant sub-Saharan patients who arrived on the island of Tenerife in 2006
M. Velez Tobarias1, E. Llabrés Valenti2, M. R. Sánchez Flores3, J. J. Ruiz Lacombrã, D. García-Rosado, P. Laynez Cerdeña1, M. Miguez Morales1, M. Hayek4 and M. R. Aleman Valls5
1 Hospital Nª S. de Candelaria, Internal Medicine, Santa Cruz de Tenerife, Spain; 2 Hospital Nª S. de Candelaria, Oncology, Santa Cruz de Tenerife, Spain; 3 Hospital Nª S. de Candelaria, Microbiology, Santa Cruz de Tenerife, Spain; 4 Hospital Universitario de Canarias, Internal Medicine, La Laguna, Spain

OBJECTIVES The proposition was to run a diagnostic and therapeutic algorithm of malaria, adapted to the clinical and epidemic characteristics of the immigrant sub-Saharan patients and to the medical resources available in the Public Hospitals of Tenerife island (Spain).

METHODS Descriptive study of all cases of malaria (n = 56), diagnosed from July to November of 2006, using diagnostic and therapeutic parameters established by official organisations (CDC, WHO). Patients were classified using clinical criteria and density parasite (DP) in complicated malaria (DP>20%) vs. non-complicated malaria (DP<20%). Blood smear was used as a quality indicator.

RESULTS 100% were males between 14 and 30 years of age, from sub-Saharan countries. 94.6% compatible with non-complicated malarial diagnosis, 7.5% (4p) of which were admitted due to clinical criteria. 5.3% (3p) with complicated malaria, one of them had Intensive Unit Care criteria. 80.3% (45p) of all the cases were admitted for average 6.8 days, the rest of them were admitted in emergency for 2 days on average. 25% (14p) gave a control blood smear before being discharged. 26% (15p) were treated with atovaquona–proguanil for 3 days, 5% (3p) with quinine sulphate (3 days) + doxycyline (7 days), 57% (32p) with quinine sulphate (7 days) + doxycyline (7 days), and 1% (1p) with quinine+doxycyline+atovaquona–proguanil because of a lack of quinine.

CONCLUSION More than 60% of cases should not have been hospitalised. There was no uniform attitude about the drug election and treatment duration. In most cases, the answer to treatment was not valorated by blood smear control before discharge. To comply with the recommendations set out by organisations, in relation to the type of treatment, duration of stay and admittance procedure in malaria cases, we have concluded that there is an urgent need for a revision to our approach for treating this disease.
PB 72
Comparative study of total cost of malaria management in illegal sub-Saharan immigrants on the island of Tenerife
1Hospital Nªsra de Candelaria, Internal Medicine, Sta. Cruz Tenerife, Spain; 2Hospital Nªsra de Candelaria, Oncology, Sta. Cruz Tenerife, Spain; 3Hospital Nªsra de Candelaria, Microbiology, Sta. Cruz Tenerife, Spain; 4Hospital Universitario de Canarias, Internal Medicine, Sta. Cruz Tenerife, Spain; 5Hospital Universitario de Canarias, Internal Medicine, La Laguna, Spain;

OBJECTIVE Analyse the total cost of treatment and hospital admittance of sub-Saharan immigrants who arrived to the island by small boat from July to November of the year 2006 and where admitted in public hospitals of the island of Tenerife (Spain) and the estimated reduction of cost using a diagnostic-therapeutic algorithm.

METHODS Observational study of all cases of malaria (n = 56) which are classified in complicated or not complicated using a diagnostic and therapeutic algorithm with official parameters. We calculate the real cost of treatment and hospital admittance using official fares of our autonomous region and we compare with the estimated cost if we had used the algorithm. Test performance are not included in admittance fares. Treatment fares only include antimalaric drugs. The only case of admission in Intensive Care Unit has not been considered.

RESULTS 78.5% (44p) were hospitalised by Internal Medicine Unit an average of 6.8 days with a cost of 2265.95 euros/person. 19.6% (11p) stayed in emergency unit an average of 2 days with a cost of 309.5 euros/person. Total admission cost per person: 1874.66 euros. 57.1% (32p) were treated with quinine sulphate + doxicicline (7 days); 5% (3p) with quinine sulphate (3 days) + doxicicline (7 days); 26.7% (15p) atovaquona-proguanil for 3 days; 1% (1p) with quinine sulphate+doxicicline+atovaquona-proguanil because of a lack of quinine. Total cost of treatment: 21.5 euros/person. Results using the algorithm: 87.5% (49p) were diagnose of non-complicated malaria with criteria of observation in Emergency Unit during 3 days and treatment with quinine sulphate (3 days) and pirimetamina-sulfadoxina (unique dose). 10.7% (6p) were diagnosed of complicated malaria with criteria of admittance in Internal Medicine Unit during 7 days and treatment with quinine sulphate and doxicicline. Estimated cost of admittance: 1102.7 euros/person. Estimated cost of treatment: 15.5 euros/person. Absolute (relative) reduction in admission: 771.96 euros (41.2%). Absolute (relative) reduction in treatment: 6 euros (27.9%)

CONCLUSION Using a diagnostic-therapeutic algorithm in management of malaria there is a significant reduction of cost in antimalaric drugs and admission in hospital. Massive immigration from sub-Saharan countries reveal our lack of experience in imported malaria and makes necessary standardized clinical criteria to diagnose and treat it.

PB 73
ENU mutagenesis for the discovery of novel targets of cerebral malaria
D. Togbe, V. Boissy, V. Nalesso, V. J. F. Quesniaux, B. Ryffel and Y. Herault
CNRS – UMR 6218 Transgenose Institute, Immunology, Orleans, France

Cerebral malaria (CM) represents a major complication of malaria infection killing too many patients worldwide every year. Investigations in man and mice revealed that parasitized erythrocytes induce a variety of pro inflammatory cytokines, the release of endothelial micro particles and adhesion molecules leading to sequestration of erythrocytes and monocytes with microvascular obstruction causing CM. We have established the murine model of CM by injecting Plasmodium berghei ANKA (PbA) parasitized erythrocytes, which kills the parasitized mice within 7 days with acute CM symptoms. Further, we confirm a critical role of TNF family members in the pathogenesis of CM as reviewed (Hunt and Grau, 2003). To identify novel key proteins regulating CM we have initiated a large scale screen for resistance towards CM using mutant mice derived from the ethyl-nitroso-urea (ENU) chemical mutagenesis program at CNRS (called PhenHoMut). In our standard infectious protocol mice resistant to CM survive about 20 days and eventually succumb to generalized hypoxia due to severe anemia with parasitemia of about 70%. So far we have identified five pedigrees of mutant mice resistant to CM carrying recessive mutations with Mendelian inheritance. The genetic mapping of those families is ongoing and may lead to the identification of novel proteins involved in the pathogenesis of CM and possibly open the way to new therapeutic approaches.

PB 74
Towards malaria eradication: a multifaceted multimodal malaria control programme
C. Rousseaux and Xenores Malaria Research Institute, Kampala, Uganda
Department of Pathology and Experimental Medicine, Faculty of Medicine, University of Ottawa, Wakefield, Canada

OBJECTIVES To propose and give a rationale for a novel multifaceted control programme for malaria in Sub-Saharan Africa.

METHODS Previous efforts to treat complex diseases, such as AIDS, with one modality have been fraught with difficulties and poor efficacy. Since multimodal therapy has been introduced as a cocktail, the success rate and longevity of life of affected individuals has increased. Using a similar concept, a multifaceted multimodal treatment regimen will be undertaken in ‘quarantined’ areas in the Apac, Kibale, and Kamuli regions of Uganda. These areas correspond to hyper-endemic, endemic and epidemic areas. The treatments used will include identification and treatment of clinical cases with standard WHO recommended medication, prophylaxis for children and pregnant women, residual insecticide application in homes, use of insecticide treated bed nets, biological larvicidal control and drainage of breeding grounds, and education of the population with respect to the programme.

RESULTS Field trials using the biological larvicide Bacillus thuringiensis var israelensis have shown 100% efficacy in Ugandan mosquito breeding grounds without any notable environmental effects. All other modalities have been shown to be effective in this region.

CONCLUSION We conclude that the proof of concept has demonstrated that the individual modalities proposed are effective in Uganda. Next year we hope to report on the results of multifaceted multimodal trials in areas of endemic and epidemic malaria in Uganda. Successful completion of these large scale trials will illustrate that this programme can then be introduced to other regions of the world affected by malaria.
Meningitis

PB 75
Epidemiology of travel-related cerebro-meningeal infections
C. Rapp, O. Aoun, C. Picko, P. Imbert, R. Barruet and T. Debord
Begun Military Hospital, Infectious and Tropical Diseases, Saint-Mandé, France

OBJECTIVES To assess the aetiological spectrum of travel-related cerebro-meningeal infections in adult patients.

METHODS From 1998 to 2005, all adult patients presenting to our infectious diseases department or the intensive care units of Begin military hospital with a cerebromeningitis and a history of travel in the previous month were recorded.

RESULTS A total of 56 patients (21 females, 35 males) with a median age of 29 years (16-83) were included. Twenty-five patients were classified as tourists (44.6 %), 15 as military (26.8 %), nine as immigrants (16.1 %) and seven as expatriates (12.5 %). Travel destinations were: Africa (n = 32; 57.2 %), Europe (n = 11; 19.5 %), Asia (n = 7; 12.5 %), Caribbean (n = 2; 3.6 %), Indian Ocean (n = 2; 3.6 %), Pacific Ocean (n = 1; 1.8 %) and South America (n = 1; 1.8 %). The median duration of travel was 24 days (5-550). The median duration between return from travel and onset of symptoms was 3.5 days (0-180). The median time to presentation from the onset of symptoms was 4 days (0.5-96). Initial clinical presentation was encephalitic in 18 cases, a typical meningeval syndrome was observed in 26 cases and in 12 cases the symptomatology was incomplete (headaches or fever). The diagnoses were: viral infections (n = 38, among which 24 confirmed cases (enteroviruses: 12, arboviruses: 2, Herpesviridae: 8, HIV: 2), bacterial infections (n = 4; Neisseria meningitidis, Mycoplasma pneumoniae, Brucella melitensis, Salmonella typhi), parasitic infections (P. falciparum malaria [n = 12], Cysticercosis [n = 1]) and fungal infections (n = 1; Cryptococcus neoformans). The median duration of hospitalization was 9.5 days (3-63). One death by HSV-1 meningo-encephalitis was recorded. Four patients had neurological sequelae.

CONCLUSION Cerebro-meningeal infections are a rare cause of morbidity in travellers. Except malaria in endemic areas, the return from travel should not mislead: cosmopolitan diseases are widely predominant (particularly viral infections). Therefore, they should be considered in the diagnostic approach of travel-related cerebro-meningeal infections, which must be focused on curable causes.

Military Medicine

PB 77
Immune response against saliva from malaria and arbovirus vectors in tropical Africa travelers
Institut de Médecine Tropicale du Service de Santé des Armées, Parasitology, Marseille Armées, France

The exposure to malaria and arbovirus vectors has been evaluated among French soldiers by the comparison of their IgM and IgG immune responses against the saliva of Anopheles gambiae and Aedes aegypti before and after a trip in Gabon and in Ivory Coast. The immune responses IgG (principally IgG3 and IgG4) and IgM against anopheles and aedes saliva increased significantly in about 50% and 30% of the individuals, respectively and decreased 2 months after their return in France. The characterization of anopheles and aedes saliva proteome by a gel-based approach and lack of correlation between the immune responses against anopheles and aedes saliva after the exposure suggest a genus specificity. The immune response against the saliva of vectors may be used as an epidemiological marker of exposure of travellers to arthropod born infections, even if they are under chemoprophylaxis.

PB 78
Entomological risk assessment during EUFOR DR CONGO: first record of Aedes albopictus in Gabon
A. KRUGER and R. HAGEN
Bundeswehr-Krankenhaus Hamburg, Department Tropical Medicine, Hamburg, Germany

OBJECTIVES According to German/EU military preventive medicine standards for operations in the tropics, measures have been undertaken to re-assess the vector situation in Libreville (Gabon) during the EUFOR RD CONGO mission. Major attention was given to vectors of mosquito-borne diseases such as malaria and arboviruses.

METHODS During the short rainy season in November 2006 vector collections were carried out at several locations in the city, using CDC miniature light traps and a BG-Sentinel trap as well as ovitraps at sites near the international airport in the North (‘Taïti’) and near the harbor in the South (‘Owendo’).

RESULTS Throughout Libreville, adult specimens of Aedes (Stegomyia) aegypti ssp. formosus were detected. Simultaneously, Aedes aegypti eggs could be obtained from ovitraps. At Owendo near the harbor as well as at another site near the Low River several adult Aedes (Stegomyia) albopictus were also caught at two occasions.
Abstracts of the 5th European Congress on Tropical Medicine and International Health

PB 79
Lessons from the participation of the French real-time surveillance system ASTER/2SEFAG in an international disease surveillance exercise.

H. Chaudet1, J.-B. Meynard2, G. Tezcur3, L. Pellegrin4, B. Queyriaux5, C. Hupin6 and J.-P. Boutin7
1IMTSSA/DESP et LIF – UMR CNRS 6166, Marseille Armées, France; 2Institut Pasteur de Guyane, Cayenne, France; 3IMTSSA, DESP, Marseille, France; 4LIF – UMR CNRS 6166, Marseille, France

OBJECTIVES During Spring 2006, the French real-time surveillance system ASTER/2SEFAG has been involved in an international disease surveillance exercise organized by NATO. The aim of this exercise was to test in real size, from outbreak detection until countermeasure applications, an inter-allied real-time surveillance for biological threats.

METHODS During the virtual deployment of a joint French and British NATO contingent in Northern Afghanistan, a natural outbreak (dysentery) and a biological attack (anthrax) were simulated. The two countries used their own surveillance system (ASTER/2SEFAG and PRISM/RMS) for the collection and analysis of data, which were a mix of usual patient declarations coming from real operations and additional cases related to the outbreaks. Simultaneously, data were sent to a NATO Central Analysis Center in Munich for a joint semi automated analysis. From the French point of view, we used this exercise for testing the interoperability of our system, its capacity for an early detection of natural and intentional outbreaks, the organizational requirements and the human factors demands for the outbreak detection, investigation, and the counter-measure building in a context of real-time surveillance.

RESULTS The adaptation requisites for ASTER concerned essentially the geographic information system and the specific building of epidemiological baselines, raising the need for a methodology for constructing such baselines where French Forces have no history of presence. ASTER allowed NATO to directly access to authorized data in real time, proving the technical interoperability of our solution, but showing the need for a semantic interoperability of medical information. The system was able to make an early warning for the two outbreaks, within two hours (including the building of counter-measures) for the anthrax outbreak. However we found that alert investigations, situation diagnostic, and counter-measure building need electronic collaborative infrastructures and very specific epidemiological and clinical decision-making assistance that not currently exist.

CONCLUSION This exercise showed that ASTER/2SEFAG was able to early detect natural or intentional outbreaks, but raised several new methodological problems that have yet never been addressed, mainly a methodology for building epidemiological baselines without historical references, and specific decision-making tools for epidemiological investigation and countermeasure building. Molecular Epidemiology of P. vivax and P. falciparum.

PB 80
Prevalence of Plasmodium vivax in different age groups in Karachi-Pakistan

S. A. Qamar and I. Ahmad
University of Karachi, Department of Zoology, Karachi, Pakistan

OBJECTIVES More than half of the world’s populations in approximately 100 countries are exposed to malaria. A malaria prevalence study was carried out among different sex and age groups in the areas with high mortality and morbidity rates.

METHODS To access the validity of clinical and field criteria, we investigated the patient’s blood from different districts of Karachi-Pakistan during 2002–2004. The study based on microscopic examination of human blood having fever, chill, headache and vomiting for the detection of various species of Plasmodium by thick and thin films. Thin films after being fixed with methyl alcohol (methanol) was stained with Giemsa stain.

RESULTS Out of 3821 thick and thin Giemsa stained blood smears 11.04%, 20.40% were identified as having P. vivax infection during the year 2002, 2003 and 2004 respectively. A total of 8.65% slides were interpreted during 3 years as having mixed infection. Whereas in children between 2–12 years infected, 14.25%, 20.64% and 9.32% slides were interpreted during the above mentioned periods.

CONCLUSION The study concluded that there were marked variations in the intensity of P. vivax infections, deaths and fever symptoms. P. vivax malaria increasing in last 2 years. These cases appeared increased during April to September and decreased after September.

PB 81
Analysis of Plasmodium vivax merozoite surface protein-I gene sequences in isolates collected from Dashte Moghan, Iran

Pasteur Institute of Iran, Parasitology, Tehran, Iran, Islamic Republic of Iran

OBJECTIVES The emergence of Plasmodium vivax cases in Dashte Moghan in north western Iran has become a major concern for Iranian’s health officials. Knowledge of genetic make up of the P. vivax populations in this area would give us an insight into the origin of the prevalent infections and the routes they are introduced.

METHODS The analysis of a variable region between the two interspecies conserved blocks (ICBs) of 5 and 6 of MSP1 gene in 12 isolates from Dashte Moghan has been done by amplification by PCR and sequencing of products.

RESULTS The results revealed that all the amino acid sequences of 12 isolates were similar to an Azari Belem-like type with 21 glutamine (Q) in the repeated residues as compared to 23 in Belen allele.

CONCLUSION The present study supports the findings from recent epidemiological studies that resurgent malaria has primarily been introduced from Azerbaijan in this area. This put an emphasis on implementation of a tougher surveillance of malaria in people moving between two countries.
Non Communicable Diseases and Nutrition

**PB 82**

Investigation of cadmium content in Iranian rice (*Oryza sativa*): its weekly intake

A. Malek1, M. A. Zazoli2 and R. Ebrahimi1

1Kurdistan University of Medical Sciences, Health Facuty, Sanandaj, Iran; 2Islamic Republic of Iran

**OBJECTIVES** Cadmium (Cd) is one of the dangerous heavy metals which its presence in nature and entrance to humans food chain, causes the serious damage in kidneys, lungs, bones, and also anemia and sometimes hypertension. The major source of cadmium intake is rice for rice eating countries such as Iran. Cadmium in rice comes from soil through plant roots. Thus, rice may be the best indicator for the environment mentoring of cadmium especially in rice eating countries. The most important sources of soil pollution to cadmium are industrial sludge sewage discharge for increasing its fertility, applying superphosphate fertilizers and etc. This investigation surveyed Cd content of tarrom rice.

**METHODS** A total of 60 samples were collected from four areas of Qaemshahr region in north of Iran (Mazandaran province). The samples were collected in during harvesting of rice in filed. The first step, grains of rice were digested by acid digestion method and then were analyzed for Cadmium by atomic absorption spectrometer.

**RESULTS** The results showed that average concentration of Cd in rice was 0.41 ± 0.17 mg/kg dry weight. Notably the Cd content in the rice samples was found to be upper the FAO/WHO Guidelines.

**CONCLUSION** We concluded that a substantial exists in Cd contents in the rice of four areas and hence health risk is maximum and this risk will increase to eating other foods such as vegetable, fish etc., and also the situation could worsen in the future. Treatment and remediation of polluted soils and environment, decreasing ease of fertilizer using could reduce Cd intake by plant and consequently health risk.

**PB 83**

Leptin, soluble leptin receptor, lipid profiles, and Ob-R gene polymorphisms in Thai children and adolescents

S. Popruk1, R. Tungtrongchitr2, S. Peemrip1, P. Pongsaw1, T. Harnroongroj1, S. Pouwadong1, B. Phonrat1, U. Yamborisut1, N. Chongviriyaphan1 and A. Tungtrongchitr2

1Mahidol University, Department of Tropical Nutrition and Food Science, Bangkok, Thailand; 2Mahidol University, Department of Tropical Nutrition and Food Science, Faculty of Tropical Medicine, Bangkok, Thailand;

**OBJECTIVES** To evaluate the relationships between leptin, soluble leptin receptor, lipid profiles, and ob-R gene polymorphisms in child and adolescent Thai subjects.

**METHODS** Cross-sectional study of Thai children and adolescents was investigated. Subjects comprised 116 male and 65 female at risk for overweight/obese child and adolescent Thai subjects, and 33 male and 62 female healthy child and adolescent Thai subjects (age 5–19 years). The Mann-Whitney U test was used to calculate any statistical difference between the two groups. The statistical difference in genotypic frequencies of the two groups was assessed by chi-square test.

**RESULTS** The median ages of at risk for overweight/obese were significantly lower than the healthy weight group. All anthropometric parameters, except height, were significantly higher in at risk for overweight/obese when compared with the healthy weight group. Statistically significantly higher levels of cholesterol, triglyceride, and LDL-C were observed in at risk for overweight/obese than in the healthy weight group. HDL-C was significantly lower in at risk for overweight/obese than the healthy weight group. Serum leptin levels were significantly higher in at risk for overweight/obese than the healthy weight group. On the other hand, there were significantly lower soluble leptin receptor levels in at risk for overweight/obese than the healthy weight group. The allele frequencies of ob-R gene polymorphisms were compared between at risk for overweight/obese and the healthy weight group and no significant differences were found between groups. Subjects with Lys656Asn homozygous wild type had significantly higher cholesterol and LDL-C levels than those with Lys656Asn heterozygous mutant type and Asn656Asn homozygous mutant type. In contrast, subjects with Lys656Lys homozygous wild type had significantly lower leptin levels than those with Lys656Asn heterozygous and Asn656Asn homozygous mutant type. There were statistically significant associations between BMI and hyperleptinemia (OR = 2.49, P = 0.000). When compared by sex, females had more increased risk of hyperleptinemia than males (OR = 15.74, P = 0.004). Serum soluble leptin receptor levels were significantly negatively correlated with leptin.

**CONCLUSION** The present study is the first report of Lys656Asn polymorphism having association with cholesterol, LDL-C, and leptin levels in Thai children and adolescents, and it provides a genetic basis for ob-R gene research in children and adolescents. Further studies should identify whether other ob-R gene polymorphisms are associated with biochemical parameters and obesity which may help develop more effective strategies for the prevention and treatment of childhood obesity.

**PB 84**

Haematological impact of sesame leaves consumption on adult male Sprague Dawley rats

L. A. J. Shitu1, M. Bankole4, R. E. Shittu1, O. Ogundipe3, M. Bankole4, T. Ahmed6, A. Tayo1 and Sesame research group 1Lagos State University, College of Medicine (Lasuco), Anatomy, Lagos, Nigeria; 2College of Medicine, University of Lagos, Medical Microbiology and Parasitology, Lagos, Nigeria; 3Bolomedics Laboratory, Medical Microbiology, Lagos, Nigeria; 4Obafemi Awolowo University, Biochemistry, Ille-Ife, Osun state, Nigeria; 5Nigerian Institute of Medical Research, Diarrhoea Unit, Microbiology Division, Lagos, Nigeria; 6Drug Quality Control Laboratory / LASUTH, Medical Mmicrobiology, Lagos, Nigeria; 7Lagos State University, College Of Medicine (Lasuco) & LASUTH, Obst. & Gynae., Lagos, Nigeria

**OBJECTIVES** Sesame diet has constituted one of the staple foods of Africans especially in Togo and Nigeria (south west and middle belt areas) since ancients’ times. Concern about the potential effects of estrogenic endocrine disruptors (EDs) in the environment on human health has been expressed and the heavy death burdens from infectious diseases such as malaria has been increasing also in the last decade especially in the holoendemic regions like Nigeria for example. However, little attention is paid on the dietary haematological impact of sesame leaves consumption in our regular diets over the years now.

**METHODS** Setting: The study was carried out under controlled animal environment in the animal house of the Anatomy Department. Subjects: Thirty adult male rats were divided into three

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groups of 10 rats each. The treated groups received oral garavage of 28.0 mg/kg bwt/day and 14.0 mg/kg bwt/day of aqueous extract of sesame leaves respectively for 6 weeks. The control group received equal volume of 0.9% normal saline per day.Intervention: Full haematological profiles involving the red cells, white cells and platelets indices were assessed using the Coulter counter.Type of statistics: SPSS analyses of data were generated with P < 0.05 being considered statistically significant.

RESULTS Significant (P < 0.05) evidence of normal red cells indices, white cells profiles and reduced platelets indices (with exception of the mean platelet volume, which is within the normal range) were found in both treated groups in a dose related manner when compared to control. However, no evidence of toxicity is seen which may be as a result of the beneficial effect of the dietary interaction of its active nutritive ingredients. Hence, it can prevent anaemia of nutritional origin and prevent platelet aggregation thereby enhancing the cardiovascular status and complications arising from anaemia.

CONCLUSION Sesame leaves consumption improves the haematological profiles in a dose related manner.

PB 85
Nutrition behavior, body activity and health interactions
H. Javandei and F. Berahmandpour

INTRODUCTION Today, the nutrition behaviors are very different from 50 years ago. Women spend more hours out of home and for this reason fast foods have main rule in family nutrition. In the other hand the young, especially young women have more attention in body activities, which has a basic effect in their health. The rapid progress in nutrition industry in production and maintenance routines affects the nutrition behaviors. In this paper, nutrition behavior and body activities and their effects on health are discussed.

DISCUSSION The basic in nutrition behavior is the suitable energy intake from eating. If the energy intake is enough, the suitable nutrients will be taken by food. Nutrition behavior depends on some of the parameters such as age, sex, weight, etc. But the main interaction between nutrition and body activity is weight control. It is shown that body activity with suitable nutrition behavior is the best way for weight control and more important for health progress. In the other hand, the sport men or sport women can progress their performance by a good and effective food regime and suitable nutrition behavior.

CONCLUSION It can be concluded that: New and modern technology has a basic effect in nutrition behavior. Body activity with good diet can improve the health both for high active persons or other one. Nutrition Behavior directly depends on the nutrition needs. Weight control also can be a key parameter in nutrition behavior and body activity improvement.

Onchocerciasis
PB 86
Impact of 3 years of biannual ivermectin treatment on onchocerciasis in Yanomami tribe of Roraima, Brazil
D. Banic, R. Calvao-Brito1, V. Marchon-Silva2, A. Tava1, M. Costa-Alves2, J. Batista-Vieira3 and M. Masa-Herzog4

INTRODUCTION AND OBJECTIVES This work reports the first evaluation of the impact of 3 years of biannual ivermectin treatment on onchocerciasis in Yanomami communities (Roraima, Brazil) that were considered a hyperendemic area. The control of onchocerciasis, in the endemic areas, is based mainly upon the large-scale distributions of ivermectin. Ivermectin-based elimination efforts have been under way in Brazil for the past decade but only achieving all communities in 2002 due to the difficult access to these remote communities and the semi-nomadic habits of them.

METHODS The study population consisted of 113 Yanomami Amerindians inhabiting two communities Arathau and Xiriana (Roraima State). Biannual mass ivermectin treatments were initiated in April 2001 and six rounds were given until April 2004. Patients were treated with ivermectin at a dose of 150–200 mg/kg of body weight by the Ministry of Health. Physical evaluation and parasitological examination were conducted immediately before each drug administration.

RESULTS The coverage of six ivermectin rounds of treatment in Yanomami communities during the study varied between 89% to 92%. After six rounds of treatment, a remarkable reduction of prevalence of individuals with positive skin snips was observed, from 87% to 42% and the skin infection intensity was dramatically reduced in iliac crest (from 30 to 4.4 mf/skin snip) and in scapula (from 43.1 to 3.6 mf/skin snip). However, following six rounds of ivermectin treatments, no significant differences were observed in the prevalences of palpable nodules (from 45% to 41%) and of onchodermitis (from 17% to 20%).

CONCLUSIONS Six biannual mass ivermectin treatments reduced the prevalence of individuals with positive skin snips by 42% and the average of mf densities in skin snips by 89%, demonstrating the strong microfilaricidal effect of this drug. Nevertheless, further research is needed to understand why 42% of the studied population remained skin snip positive.

PB 87
Tuberculosis patient centered approach (PCA): methodological approach and first results in Senegal
S. Fall1, A. H. Diop2, T. Ndoye2, P. Huygens2 and B. Dujardin1

OBJECTIVES Demonstrate that TB patient centered approach (PCA) enables a better patient consideration along the diagnosis-treatment process.

METHODS Two surveys (qualitative and quantitative) have been made. Socio-anthropological study of patients, care providers and families: observation in situ in six detection and treatment centers (DTC), about hundred semi-structured and twenty focus groups, aimed at understanding the determinants of therapeutic recourses. In identifying detection and treatment determinants by going through 255 consultation registers, the quantitative survey completed the qualitative information.

RESULTS Restraints to accessibility are linked to the complexity of the therapeutic itinerary faced by the patient. In addition, the lapse of time linked to the recognition of symptoms by health professionals is not in favor of an early diagnosis. The restitution of results to the actors involved has permitted their validation and is at the origin of: interventions focused on treatment decentralization, implementation of a network of support to the patient, community involvement in the fight against stigmatization, training of first line care providers, health care services reorganization, creation of new care centers and implementation of structures improving the patient-care provider interface. For 2006, the first results of the districts of Bamby and Diourbel show a favorable trend in the abandonment rate of
Abstracts of the 5th European Congress on Tropical Medicine and International Health

Tropical Medicine and International Health

VOLUME 12 SUPPL I PP 147–255 MAY 2007

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Molecular characterization of Cryptosporidium parvum isolates from human and cattle using 18s rRNA gene in Tehran, Iran

M. Pirestani, J. Sadraei, A. H. Dlimi and M. Zavvar

1Department of Parasitology & Tropical Medicine, School of Medicine, Tarbiat Modares University, Tehran, Iran, Islamic Republic of Iran; 2Department of Parasitology, Tarbiat Modares University, Tehran, Iran, Islamic Republic of Iran; 3Razi Ins. & Department of Parasitology at Tarbiat Modares University, Tehran, Iran, Islamic Republic of Iran; 4Tarbiat Modares University, College of Medicine & Tehran National University, College of Medicine, Parasitology & Clinical Microbiology and Tropical Medicine, Tehran, Iran, Islamic Republic of Iran

OBJECTIVE Cryptosporidiosis is a widespread cause to diarrheal disease of humans, young calves and many other mammals caused by infection of intestinal epithelial cells with the protozoal agent Cryptosporidium parvum. The disease occurs in humans of all ages. C. parvum is one of the causes of diarrhea in travelers, and is frequently transmitted among young children in day care centers. Disease in these groups, while unpleasant and sometimes severe, is usually self-limiting. In contrast, cryptosporidiosis in immunocompromized patients is persistent, severe and often life-threatening.

METHODS The Cryptosporidium isolates in which this study obtained from patients who suffering from diarrhea. Morphologically Cryptosporidium oocysts were identified as C. parvum and isolated from 17 men and 23 bovines in Tehran. The samples were amplified by Nested-PCR using 18s rRNA gene. So far the yield was digested by SspI and VspI to recognize the genotypes.

RESULTS Nested-PCR/RFLP patterns for all bovine samples have identical patterns that refer to C. parvum genotype 2. In contrast, the DNA profiles for human samples show two distinct genotypes: genotype 1 and genotype 2.

CONCLUSION Genotype 2 isolated from 15 patients appears zoonotic infection cycle in Tehran.

PB 89

Pneumonia by Rhodococcus equi in patient infected with HIV-AIDS

D. Saevedra Castellanos

Centro Provincial de Higiene y Epidemiologia de Ciudad de la Habana, Laboratorio de Referencia Provincial de Microbiologia, Ciudad de La Habana, Cuba

INTRODUCTION Rhodococcus equi is a microorganism that initially was defined as cause of infections in patients with a severe immunological deficiency. This microorganism has reported every time with more frequency in patients with AIDS, in which it produces pneumonia recurrent with pulmonary injuries similar to the tuberculosis.

OBJECTIVES The reason for this work is to report the study made in patients with HIV-AIDS, taken care of in the Hospital of the Tropical Medicine Institute Pedro Kouri.

METHODS Samples received of sputa for bacteriological study from nine patients (seven men and two women) who presented/displayed respiratory pictures, as well as, other clinical characteristics and epidemiologists of pneumonia recurrent.

RESULTS The nine patients presented/displayed clinical signs like fever, cough and thoracic pain. The average count of CD-4 at the moment of the diagnosis was of 33 mm$^3$. The microbiological diagnosis was made from bacteriological culture of sputa with a confirmation of 88% of positivity to R. equi. The test of antimicrobial susceptibility showed a sensitivity following antibiotics: vancomycin 100%, erythromycin 100%, ciprofloxacin 100% and azlocilina 100%. A clinical answer with the disappearance of the present clinical signs was observed in the 33.3% of the cases. The complete clinical answer was observed in the 22.2% of the cases. Nevertheless, in 44.4% of the cases the answer to the treatment was difficult.

CONCLUSION These results suggest that infection by R. equi is a complication, and although it is not frequent, it must be considered in the diagnosis of pneumonia recurrent in the course of the infection by HIV-AIDS. Of this study, it is deduced that the infection by R. equi has settled down like an opportunistic organization in the patients affected with HIV-AIDS and is evident that this increases is the reason why the laboratories of microbiological diagnosis must think about the identification of this microorganism for antimicrobial therapeutic adapting.

PB 90

Identification of a new Pneumocystis species derived from Mongolian gerbil based on its, 5.85r DNA and mt LSU rDNA sequences

S. Q. Lu, X. Feng and Z. Li

Capital University of Medical Sciences, Department of Parasitology, Beijing, China

OBJECTIVES To identify a new species of Pneumocystis (Pc) derived from Mongolian gerbil (Meriones unguiculatus) based on ITS1 (1 and 2), 5.8S DNA and mt LSU rDNA sequences.

METHODS Fifteen Mongolian gerbils were immunosuppressed by subcutaneous injections of dexamethasone. Lung impression smears of the infected animals were made and stained with Wright-Giemsa’s compound stain. Genomic DNA of Pneumocystis organism was extracted from the lung tissues. The Pc DNA was amplified by one step PCR (at the mtLSU rRNA gene) and nested PCR (at the ITS1-5.8rDNA-ITS2). The PCR products were cloned and sequenced. The sequences were compared with the related ones from members of other fungi and protozoa accessed in GenBank. Sequences were aligned using DNAStar softwares and edited manually. The genetic distances were calculated by MEGA 3.1 software utilizing parameters of p-distance and pairwise deletion. Neighbour-joining (NJ) trees were constructed with MEGA 3.1 and 1000 replications were performed for each tree to evaluate the reliability of the topology.

RESULTS Numerous cysts and trophozoites were observed with microscope in the lung impression smears of the infected animals and the infective rate reached to 93% (14/15). A length of 550 bp fragment was amplified from the DNA specimens extracted from the gerbils lung tissue. The nucleotides of ITS1, 5.8S rRNA and ITS2 gene were 1585bp, 1573bp and 172bp respectively. A 340 bp fragment of mt LSU rDNA was also amplified. Both ITS1-5.8rDNA-ITS2 and mtLSU rRNA sequences of Pneumocystis from the gerbils were not reported previously and had been accepted by GenBank database under the accession number AY873972 and DQ452954 respectively. The phylogenetic tree based on ITS1-
5.8S rDNA-ITS2 sequences showed that *Pneumocystis* species from human, monkey and rodents (rat, mouse, rabbit, and gerbil) formed a group, in which those from human and monkey were closest. Those from rat, mouse, rabbit and gerbil formed the other group with bootstrap values reached 99%. Moreover, the tree showed all the fungal members from genus Ascomycota expect *Pneumocystis* clustered one group. The tree based on the sequence of mLSU rDNA showed that 11 species were systemetically aligned into three major clades: (i) *Pneumocystis* from two primates (humans and macaques), (ii) *Pneumocystis* from five rodents (rat, mouse, rabbit and gerbil), and (iii) three fungal members from genus Ascomycota. expect *Pneumocystis*.

**CONCLUSION** Mongolian gerbil be considered a new host of *Pneumocystis* organism and *Pneumocystis* derived from this should be a new species of *Pc*.

**PB 91**

**Anti-malarial chemoprophylaxis by cotrimoxazole in HIV-infected pregnant women in West Africa**

V. Patria, S. Piguet, J. Simporé, L. R. Tomasoni, S. Caligaris, S. Bigoni, M. Manfren, M. Guilletta, A. Massei, and F. Castelli

1. University of Brescia, Institute for Infectious and Tropical Diseases, Brescia, Italy; 2. Centre Medical Saint Camille, Ouagadougou, Burkina Faso; 3. Centre de Recherche Biomoleculaire Pietro Annigoni, Ouagadougou, Burkina Faso; 4. Medicus Mundi, Brescia, Italy

**OBJECTIVES** Co-trimoxazole has a well-defined parasitocidal effect against *Toxoplasma gondii* and other coccidian protozoan, such as Plasmodia. In malaria endemic areas, daily administration of cotrimoxazole might then serve to either malaria chemoprophylaxis and prevention of opportunistic infections in HIV-infected pregnant women.

**METHODS** St Camille Medical Center (SCNC) is a large urban mother-and-child structure run by the Camillian Order in Ouagadougou, where over 6000 deliveries take place every year. The University and Speciai Civili General Hospital of Brescia, Italy and Medicus Mundi Italy collaborate with the Camillian Order in the fight against HIV/AIDS since 2003 in the frame of the ESTHER project. HIV-infected pregnant women with CD4+ cell count below 200 cells/μl have been administered 960 mg cotrimoxazole daily from 13’week of gestation (group A). After informed consent, HIV-infected pregnant women with higher CD4 cell count have been administered either 960 mg cotrimoxazole daily (group B) or pyrimethamine-sulfadoxine (SP) single dose at 13 and 25 week of gestation (group C). Primary outcome of the study was the incidence of parasitological malarial infection during pregnancy in the cotrimoxazole group (groups A & B) and SP group (group C), assessed monthly by haemocytoscopy.

**RESULTS** During the period June-November 2006 (high malaria incidence in Burkina Faso), 137 HIV-infected pregnant women were identified. Of them, 110 were enrolled into the study and 27 were excluded (24 were close to delivery, two were anaemic and one was lost to follow-up after the first visit). Altogether, we were able to perform 138 follow-up visits in the cotrimoxazole groups (n = 54; A & B) and 144 follow-up visits in the SP group (n = 56; C). Malaria parasites were detected in 10/144 (6.9%) and 10/138 (7.2%) of follow-up visits in the cotrimoxazole and SP groups, respectively. No significant adverse event was observed in either groups.

**CONCLUSIONS** Co-trimoxazole prophylaxis of opportunistic infections is well tolerated and may serve as anti-malarial prophylaxis in HIV-infected pregnant women. Larger study is needed to assess equivalence with SP prophylaxis.

**PB 92**

**Oesophageal candidiasis in children infected by HIV: what are the challenges of diagnosis and management in resource-constraints settings?**

A. Azondekon, A. Sessou Keitchion, A. Sagui, A. Toudonou Singbo and A. M. Kora Zime Monzorgui

Military Teaching Hospital, Care Unit for Children Exposed to or Infected by HIV, Cotonou, Benin

**OBJECTIVES** Oesophageal candidiasis is the most common cause of oesophageal symptoms in children with AIDS. The aim of this study is to investigate epidemiologic trends, clinical features and outcome of oesophageal candidiasis in a resource-constraints setting in a population of children infected by HIV.

**METHODS** Records of a prospectively monitored population of children infected by HIV, followed at the Care Unit for Children Exposed to or Infected by HIV (Military Teaching Hospital, Cotonou, Benin), from 1998 to 2006 were reviewed for a history of oesophageal candidiasis. Oesophageal candidiasis was defined as proven (clinical and/or endoscopic findings of oesophageal candidiasis) or probable (opharyngeal candidiasis and oesophageal symptoms or difficulty of feeding). The medical records of all patients fulfilling these criteria were reviewed for demographic, clinical and laboratory features at presentation, as well as therapeutic interventions and outcome.

**RESULTS** Of 156 children infected by HIV, 25 had oesophageal candidiasis. They developed 43 episodes, two were proven whereas 39 were probable oesophageal candidiasis. 100% of all patients had a history of prior oral or pharyngeal candidiasis. Children <2 years were concerned in 17 of 25. Clinical manifestations were oropharyngeal candidiasis (95%), nausea or vomiting (60%); fever (57%) and difficulty of feeding (72%). CD4 cells counts at the time of diagnosis were less than 15% for 37 of 43. Upper endoscopic investigations were done for two patients because only dysphasia was the clinical manifestations. Treatment consisted of oral fluconazole (tablets) or oral amphotericin B (suspension). Relapse was observed for patients treated by amphotericin B and death occurred for three patients, during the period fluconazole and HAART were not available. Clinical cure was observed for 22 patients and symptom resolution was observed within two weeks for 95%, especially when fluconazole was used.

**CONCLUSION** Oesophageal candidiasis has to be considered in children infected by HIV when history of oropharyngeal candidiasis is known with severe immunosuppression. Fluconazole and HAART have changed outcome of this disease and hence reduced mortality especially in children <2 years.

**Pathology**

**PB 93**

**Relation between P. falciparum asymptomatic infection and malaria attacks in a cohort of Senegalese children**

A. Le Port, M. Coz, J. F. Esard, O. Gaye, F. Migo-Nabias 5 and A. Garcia 6

1. IRD, UR010, Cotonou, Benin; 2. IRD, UR010, Paris, France; 3. IRD, Lyon, France; 4. University Cheikh Anta Diop, Dakar, Senegal; 5. Institut de Recherche pour le Développement, UR010: Santé de la mère et de l’enfant en milieu tropical, Cotonou, Benin

**OBJECTIVES** Whether or not the presence of malaria parasites in peripheral blood of individuals is a predictor of clinical malaria attack remain an important question for both clinicians and National Control Programs. The aim of this study was to determine how an asymptomatic positive thick blood smear could
be related to the occurrence of a mild malaria attack (MMA) during the nine following days in a children population.

**Methods** The study was conducted in a strictly seasonal transmission area, at the beginning (September) and at the end (November) of the transmission season. Asymptomatic carriers (AC) were defined during enrollment as parasitaemic children, without fever or any clinical sign. Children were followed-up and their axillary temperature was measured every 3 days. A MMA was defined as fever (>37.5°C) associated with parasitaemia over 2500/μl. Survival analysis was performed and risk estimates were calculated by Cox proportional hazards model.

**Results** At the beginning of the transmission season, 5.4% (8/147) of MMA occurred among ACs vs. 1% (4/382) among non-carriers (RR = 3.32, IC = 1.36–8.15, P = 0.008), independently of their age. No clinical MMA was detected during the 9 days following period at the end of the transmission season.

**Conclusion** Asymptomatic carriage is a predictor of MMA at the beginning but not at the end of the transmission season. This difference could be related both to the acquisition of immunity and the evolution of the genetic diversity of parasite strains in the course of the transmission season. The existence and significance of asymptomatic carriage could represent a major challenge at the time when intermittent preventive treatment for malaria is under evaluation.

**Primary Health Care**

**PB 94**

**Rapid assessment to understand current maternal and neonatal health status in district – Gorakhpur, Uttar Pradesh, India**

A. Jha

*Catholic Relief Services, Health & HIV/AIDS, Lucknow, India*

**Objectives** Rapid assessment to understand current MNH situation and practices in district – Gorakhpur, Uttar Pradesh, India.

**Methods** Methods and site selection purposive sampling methodology was used for the selection of blocks and villages. Total Blocks: 19• RA Blocks: 10• Two sites having minimum 5000 population was selected in each of the 10 blocks. • One site having proximity to PHC (near site) while other distant (far site) from PHC. Findings: Current MNH situation and practices foremost of the Rapid Assessment process was to investigate existing household and community practices on MNH. Assessment process brings out the fact that many traditional practices are common feature in rural Gorakhpur but only a few may be termed at best as harmless while many current practices are harmful and risky according to widely approved medical protocols of mother–neonate health. Their status needs clarification because such practices aggravate mother–neonate mortality and morbidity. However changing practices is a long term and sensitive process. Low status of ANC, TT immunization, IFA consumption and strong preference for home based deliveries by unskilled service providers dispel the myth that existence of formal health care system will guarantee its use. Many women deliver without the assistance of a skilled attendants. Many midwives who can manage normal deliveries and treat the life-threatening complications of pregnancy and childbirth and refer women for appropriate care during emergencies. Physical, financial, and socio-cultural barriers often prevent women and their families from getting public health care services. Existing practices of neonatal care shows risky cord care, lack ofcolostrums feeding and usage of undesirable supplements like goat’s milk and honey. At several stages of the journey through pregnancy and childbirth, women face delays in receiving skilled care. These delays pose barriers to embracing motherhood. Women and their families or caregivers may not recognize the warning signs of life-threatening complications, difficulty reaching a decision to seek medical care due to financial constraints. Community also articulated rude treatment, high fees and substandard care at formal health facilities. Traditional practices and village based semi skilled and unskilled service providers like TBAs, RMPs & even quacks play indispensable role in shaping up the issues concerning MNH. Some of the current practices of community have their own wisdom but most are harmful and act as deterrent to save mother and child.

**PB 95**

**The effect of depth and distance from Zayandehroud on microbial quality of ground water in neighbor zone in Iran**

S. Dobaradaran1, B. Bina2 and M. Hatamzadeh2

1Faculty of Health, Boushehr University of Medical Science, Environmental Health, Boushehr, Iran, Islamic Republic of Iran; 2Isfahan University of Medical Sciences, Isfahan, Iran, Islamic Republic of Iran

**Objectives** The location of a well relative to surface drainage ways is important in determining the potential for groundwater contamination from surface water flow. Locating a well in a safe place takes careful planning and consideration. For determining the effects of well depth and distance from Zayandehroud on water quality, wells up to 4 m depth and 100 m distance from river were selected in Falavarjan. Geologically, the earth in this zone composed of clay (more in surface) and sand (particular in the depth higher than 1 m). Flow direction of river with comparison static level of wells and bottom of river is toward wells.

**Methods** For determination microbial quality of well water, coliform indicator and fecal coliform in three tubes method and according standard method was used.

**Results** Finally a total of 100 samples were taken and analyzed. Results of this study showed that the TC and FC showed a range of 3–460 and 0–29 MPN/100 ml respectively.

**Conclusion** We observed that TC and FC decreased with increasing well depth and distance from river.

**PB 96**

**Trauma and post-traumatic stress disorder in a rural primary care population in South Africa**

K. Pelzer

HSRC, Pretoria, South Africa

**Objectives** The aim of this study was to assess trauma events experienced and PTSD among primary care patients in South Africa.

**Methods** A total of 250 consecutive rural primary clinic patients (all Black Africans, 24% male and 76% female, Mean age 31.1 year, SD = 11.8, range 18–65 years) were interviewed using the Trauma History Questionnaire and the PTSD Checklist-Civilian Version interview-administered.

**Results** Results indicated that the mean number of traumatic events reported was 3.5 (SD = 2.9, range = 0–19) and was significantly higher among men (Mean = 4.9, SD = 3.5) than women (Mean = 3.0, SD = 2.6). Among the most frequently endorsed traumas among men were seen someone seriously injured or killed (60%), serious accident (43.3%), and seen dead bodies (43.3%), and among women natural disaster (mostly floods) (51.6%), news of a serious injury, life-threatening illness or unexpected death of someone close (31.1%), and seen some...
A current indicative diagnosis of PTSD of 12.4% and W. Kipp
In a selective pilot programme
Candidate drugs related to the lead compound
We conclude that the attempt to extend a selective
If compared with the standard of the initial programme,
values than the congeneric phenylpropiophenones. Never-
volume 12 suppl 1 pp 147–255 may 2007
A questionnaire was distributed to a random sampling
The knowledge level of medical students and general
European Congress on Tropical Medicine and International Health
Tropical Doctor 1998; 73–77). The
233
These substances were subsequently evaluated for
values were found in both the
value in the low
West Uganda.
programme to a greater population of 60 000 in Kabarole district,
others that AED treatment is feasible and accepted in the setting of
epilepsy prevalence, we have recently confirmed the findings of
that AED treatment is feasible and accepted in the setting of
rural Africa (Kaiser et al., Tropical Doctor 1998; 73–77). The
present study compares two approaches to extend the initial pilot
programme to a greater population of 60 000 in Kabarole district,
West Uganda.
METHODS First, AED were made available in two health units
(HU) of the District Basic Health Services (BHS), where patients
received treatment from the health workers in charge (HU-
Approach). SECOND, in an area beyond the catchment area of a
HU, patients received treatment with a 6-monthly outreach from
the district capital, following the example of the pilot programme
(Pilot-Outreach-Approach). BHS cooperated with a committee of
the local community for active mobilisation of patients and AED
distribution.
RESULTS If compared with the standard of the initial programme,
quality of care was found low with the Pilot-Outreach-Approach.
On the other hand, the quality of patient/health worker contact and
treatment practice was considered sufficient with the HU-
Approach. Although continuity was affected by drug shortage in
both approaches, HUs appeared to be more resilient than the Pilot-
Outreach-Approach which was fully interrupted when greater
amounts of AED needed at one given time were not available.
CONCLUSION We conclude that the attempt to extend a selective
pilot programme for AED treatment to a greater population was
not successful. On the other, AED treatment appears to be
appropriate for integration into primary care in the frame of a
rural African district.

Proteomics
PB 98
Structure activity relationship studies of a novel class of
antimalarials derived from the class 1c antiarrhythmic drug
propafenone
O. Tasanor1,2, M. Errus3, P. Starzengruber1, G. F. Ecker1, H. Noedl1 and P. Chiba3
1Medical University of Vienna, Institute of Specific Prophylaxis and Tropi-
cal Medicine, Vienna, Austria; 2Medical University of Vienna, Institute of
Medical Chemistry, Vienna, Austria; 3University of Vienna, Department of
Medical Chemistry, Vienna, Austria
OBJECTIVES Candidate drugs related to the lead compound
propafenone are highly effective inhibitors of \( P. falciparum \) growth
with 50% inhibitory concentrations (IC\(_{50}\)) in the submicromolar
range. The parental compound propafenone is a cardiac sodium
channel blocker which is in clinical use for the treatment of
ventricular arrhythmia. For a first series of structure activity
relationship studies 25 analogues were selected from a proprietary
compound library of more than 400 compounds based on
structural diversity.
METHODS These substances were subsequently evaluated for
their growth inhibitory potential in the chloroquine sensitive 3D7
and the chloroquine resistant DD2 strain in vitro, using the
histidine-rich protein 2 drug sensitivity assay.
RESULTS Comparable IC\(_{50}\) values were found in both the
chloroquine resistant and sensitive strain, indicating a different
mode of action of propafenone analogues and 4-aminooquinolines.
Propafenone analogues contain an inherently photoactive aryl-
carboxyl substructure, which allows their use in target identifica-
tion studies. Labelling efficiency is increased for compounds in
which the phenylpropionophenone core structure is replaced by a
benzophenone substructure. However, the phenylpropionophenone
substructure represents part of the pharmacophore of the com-
pounds. Benzophenone-type analogues invariably show higher
IC\(_{50}\) values than the congeneric phenylpropionophenones. Never-
theless, one of the photoligands has an IC\(_{50}\) value in the low
micromolar range in both the chloroquine sensitive 3D7 and the
chloroquine resistant DD2 strain.
CONCLUSIONS Use of this photoligand is expected to allow
identification of molecular target structures by mass spectrometry,
following two dimensional separation of the plasmidodal proteome.
The Malaria Genome Project has advanced our understanding of
parasite biology and development of novel drugs can mount on
data made available by the recently completed sequencing effort of
\( P. falciparum \). The lead compound propafenone is a registered
drug and this compound class might therefore have a major
potential as an antimalarial drug, either alone, or in combination
with conventional antimalarials.Funded by Austrian National
Bank Grant12099

Quality of Care and Clinical Guidelines: Policy Making
PB 99
General practitioners and medical student’s knowledge and
perspectives regarding influenza (treatment and prevention)
R. Ghasemian and N. Najafi
Mazandaran University of Medical Science, Infectious Disease, Sari, Iran,
Islamic Republic of Iran
OBJECTIVES Influenza is a viral disease of the upper respiratory
tract and has a high prevalence in autumn and winter. Although
influenza medical treatment has improved, but a considerable rate of
mortality (especially in high risk group) occur each year during the
influenza epidemics. Influenza vaccination rate in high risk group is
very low (<5%). It sounds that lack of knowledge or attention to
influenza prevention and management in our physicians.
METHODS A questionnaire was distributed to a random sampling
of general practitioners and medical students in three teaching
hospitals of Mazandaran University of medical science. Questions
were asked regarding, general information about influenza, treat-
ment, current use of influenza vaccines, medical prevention, and
knowledge regarding avian influenza. Answers were scored as
correct based on published literature and CDC recommendations.
The data were statistically analyzed using SPSS (ver 10) and we use
Chi-square to compare two groups.
RESULTS The knowledge level of medical students and general
practitioners regarding flu and vaccination indications was com-
parable. The majority of physicians were not aware of the severity of
influenza infection in young children, could not correctly identify all
contraindications to receiving vaccination and their knowledge regarding chemoprophylaxis was not acceptable. However, on medical treatment and prevention general physicians had higher level of knowledge ($P < 0.01$), while medical students were better in avian influenza ($P < 0.001$).

**CONCLUSION** Given the lack of adequate knowledge of GPs and medical students on the two important parts of medical treatment and influenza prevention and considering the high prevalence of this disease, it seems that physicians will need a greater understanding of the severity of influenza management coupled with an increased knowledge of indications for vaccine administration and chemoprophylaxis. As for avian influenza, it seems, educational sessions are necessary for both groups.

**PB 100**
**Organ donors and rabies transmission**
J. Bronnert, M. Fischer and R. M. Hagen

**BWK Hamburg, Fachbereich Tropenmedizin am Bernhard-Nocht-Institut, Hamburg, Germany**

**OBJECTIVES** After seven recipients of transplanted organs died of rabies infection in the last 2 years, standards and algorithms in potential organ donors have to be re-evaluated. The American donor was bitten by a bat, while the German donor had a recent travel history to India where she reportedly was bitten by a dog. Both donors had neurological and behavioral symptoms and signs consistent with rabies. These were disregarded or attributed to other causes.

**METHODS** There are highly sensitive and specific tests for the post- and ante-mortem diagnosis of rabies. Organ transplants are carried out at tertiary care centers which have instant access to fluorescent microscopy and molecular technology. Laboratory studies such as antibody testing in serum and cerebro-spinal fluid (CSF), reverse transcription-polymerase chain reaction (RT-PCR), nucleic-acid sequence based amplification (NASBA) detected rabies virus RNA either in saliva, urine, CSF or in extracted hair follicles. A corneal smear and magnetic resonance imaging can be helpful but is not pathognomonic for rabies. If tests don’t give a definitive result to exclude rabies, an immediate postmortem open or trans-orbital brain biopsy should be obtained to determine the diagnosis.

**RESULTS** PubMed research revealed that during the last two decades 15 published cases of organ transplanted cases of rabies occurred, seven of them in the US and Germany in the last 2 years.

**CONCLUSION** Because there is no intravitam serological or molecular test for rabies that has been shown to carry 100% sensitivity, all currently available diagnostic means including brain tissue examination have to be applied. Only then a potential organ donor should be cleared for transplantation. The authors suggest that laboratories at tertiary transplant center should be able to carry out FAT on brain as well as molecular studies within hours.

**Safe Motherhood**

**PB 101**
**Obstetric ectoscopy – visualizing maternal ill-health outside hospital gates**
S. Bergstrom

Division of International Health, Department of Public Health Sciences, Stockholm, Sweden

The article ‘Obstetric ectoscopy – an eye-opener for hospital-based clinicians’ was published in 2005. The intention was to draw attention to the fact that obstetricians and gynaecologists demonstrate a disproportionate interest in high-tech instruments aimed at advanced diagnostic exercises inside women’s bodies of affluent societies, often with a very clear overriding goal of commercialization. This inward-looking and hospital-based trend of high technology is gaining ground simultaneously with our growing insight that the 5th Millennium Development Goal (MDG 5) is by far the one least on a track of all MDG: to reduce by 75% the maternal mortality ration by the year 2015, taking 1990 as a point of departure. Anyone participating in any world congress of obstetrics and gynaecology can witness the enormous overflown of ‘endoscopies’ while little is talked of maternal mortality. This is absurd. Let us have a look to make a tentative comparison of what I would like to call ‘obstetric endoscopy’ (e.g. looking in utero to visualize the human fetus to draw blood for analysis) and ‘obstetric ectoscopy’ (looking outward of the hospital gates to see the obstetric pathology of poverty among deprived and dying mothers). Many medical schools in low-income countries copy their undergraduate training and post-graduate training in obstetrics from high-income countries, where maternal mortality is extremely low. In the latter countries, community obstetrics is a peripheral, if not trivial, ingredient in the discipline of obstetrics. This bias has negative repercussions on their identification with and interest in efforts to reduce maternal mortality. There is a tension between inward-looking (‘endoscopic’) and outward-looking (‘ectoscopic’) obstetrics. It is an alarming sign that obstetricians of our time show this disproportionate lack of interest in one of the major challenges today: maternal mortality. 

<table>
<thead>
<tr>
<th>Obsteric endoscopy</th>
<th>Obstetric ectoscopy</th>
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<td>High tech</td>
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<td>High cost</td>
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<td>Accessing few, wealthy women</td>
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<td>No impact on maternal mortality</td>
<td>Impact on maternal mortality</td>
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<td>Highly ‘prestigious’</td>
<td>Little ‘prestigious’</td>
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<td>Attractive to many doctors</td>
<td>Attractive to few doctors</td>
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**Schistosomiasis**

**PB 102**
**Cytokine profiles after somatostatin therapy in Schistosoma mansoni infected high pathology mice**
S. Chatterjee1, T. Panis1, A. Bernal2, C. Bridts2, W. Stevens2 and E. Van Marck1

1Pathology Lab. Antwerp University, Antwerp, Belgium; 2Immunology Lab. Antwerp University, Antwerp, Belgium

**OBJECTIVES** Our previous work has delineated an association between fibrosis and low endogenous levels of the neuropeptide somatostatin in S. mansoni infected Senegalese subjects [1]. Parallel experiments have revealed an antifibrotic effect of somatostatin therapy on S. mansoni infected outbred mice, suggesting that exogenous somatostatin may reduce the secretion of fibrosis inducing-mediators [2], one of which being IFN-gamma [3]. This study investigated whether somatostatin therapy modu-
lates cytokine expression in *S. mansoni* infected, inbred mice strains - C57BL6 (develop light pathology via balanced T1/T2 immune reactions) and the C3H mice (infection triggers serious pathology via strong T1 and T2 responses).

**METHODS** Somatostatin (Somatostatin-ucb®) therapy (90 µg/day for 2/5 days) was given to *S. mansoni* infected inbred mice. Biochemical assessment of fibrosis was done by the hydroxyproline protocol [4]. Radioimmunoassay (Gut Hormone lab. KUL, Louvain), was used to study evolution of inherent somatostatin levels in mice strains. A week after somatostatin therapy, mice spleens were extracted, cells stimulated in culture with Con A, and a Cytometric Bead Array (R & D) kit used to screen for levels of IFN-gamma, TNF-alpha, IL-2, IL-4, and IL-5 in the culture supernatants.

**RESULTS** In outbred Swiss and inbred C3H mice, *S. mansoni* infection increased endogenous somatostatin levels at acute stage (8 weeks) of infection, that were reduced at chronic stages (16 weeks) (*P* = 0.01). In the low pathology C57BL6 mice, the reverse trend was noticed. In infected C57BL6 mice, somatostatin therapy provided no relief from *S. mansoni* caused pathology. In contrast, a marked modulation of fibrosis was noted in infected C3H mice strain. Here, somatostatin treatment caused a significant decrease in hydroxyproline levels at week 8 (2.03 ± 0.16 µmol) and at week 16 (2.88 ± 0.18 µmol) (*P* < 0.0001), when compared to respective values in untreated animals. Splenic T cells isolated from somatostatin treated, 8 weeks infected C3H mice were triggered by Con A to secrete IFN-gamma, TNF-alpha, IL-2, IL-4, IL-5, levels of which were comparable to that obtained from T cells from untreated animals. However at 16 weeks of infection, somatostatin therapy caused a significant decrease in IFN-gamma and IL-2 levels secreted by splenic T cells from C3H mice. No significant variations were observed in the levels of other cytokines.

**CONCLUSION** The anti-inflammatory effects of somatostatin may occur via a selective inhibitory effect on IFN-gamma production in infected C3H mice.

Urinary schistosomiasis among children in Danjarima, a rural community of Kano state of Nigeria

P. Sarkinfada, O. Azeez-Akanle, I. B. Amin, S. I. Abubakar, Z. Ilyasu

Department of Medical Microbiology and Parasitology, Bayero University, Kano, Nigeria

OBJECTIVES The prevalence of urinary schistosomiasis among children in rural communities in Nigeria is a consequence of inadequate health education, indigenous beliefs and water contact activities. A cross-sectional survey on the prevalence of urinary schistosomiasis was conducted in Danjirima community of Kano State, Northern Nigeria. The objective of this survey was to determine the prevalence of urinary schistosomiasis among children and the associated social factor that relate to its prevalence in the community.

METHODS A stratified sample of 890 subjects comprising children (5 years and above) were included in the study. Examination of urine samples for detection of ova of *Schistosoma haematobium* was carried out using sedimentation technique. A semi-structured questionnaire was administered to the selected subjects in order to determine knowledge and perception of the residents about urinary schistosomiasis modified to suit local epidemiology and cultural attitudes of the subjects.

RESULTS Out of 890 subjects examined, 370 (41.6%) were infected. The highest (54.4%) prevalence rate of infection by sub-village was recorded in Zaura and the lowest (6.4%) in Sabon-Fegi. More males, (361 out of 646, 55.9%) than females (9 out of 244, 3.7%) were infected and the difference was statistically significant (*P* < 0.01). The age group 10–14 years recorded the highest rate of infection (*P* = 0.05) in both males (80.9%) and females (10.3%).

CONCLUSION Lack of adequate knowledge and health education are factors responsible for high prevalence of *S. haematobium* infection in Danjirima community.

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Co-infection by hepatitis C but not hepatitis B virus aggravates hepatic periportal fibrosis and its clinical outcomes in subjects infected by *Schistosoma mansoni*


University of Buea, Douala, Cameroon; AL Zaiem Al Azhari University, Omdurman, Sudan; Unité des Virus Emergents, Laboratoire de Virologie Transfusionnelle, Tropicale et Moléculaire, Faculté de Médecine, Marseille, France; Institute of Nuclear Médecine, Molecular Biology and Oncology, University of Gezira, Wad Medani, Sudan; Immunologie et Génétique des Maladies Parasitaires, Institut National de la Santé et de la Recherche Médicale, INSERM U399, Laboratoire de Parasitologie Mycologie, Faculté de Médecine, Marseille, France

OBJECTIVES Periporal hepatic fibrosis (PPF) affects some of subjects infected by *Schistosoma mansoni* endemic in areas. The high prevalence of Hepatitis C and B viruses (HCV and HBV) in these regions of Africa raise the possibility up that these viruses may aggravate hepatic and splenic diseases in schistosome infected subjects.

METHODS We performed a study on 593 subjects from Sudan, an endemic area for *S. mansoni*. The clinical parameters and their measurements were assessed by ultrasound. Serum samples were assayed for anti-HBc IgG, HBsAg and anti-HCV IgG by ELISA and for HCV genotypes by REL. The association of covariates with different clinical parameters was performed by stepwise linear regression accounting for the effects of other covariates that could affect the progression of disease.

RESULTS Severe PPF was observed in 10.1% of subjects, whereas 58.6% and 31.2 % exhibited no fibrosis or periportal inflammation with light fibrosis respectively. Anti-HBV Ab, HBs Ag and anti-HCV Ab were found in 41%, 11% and 12% of the subjects respectively. Only HCV infections were found associated with an increase in number of cases of severe PPF (*P* < 0.01; OR = 2.3; IC = 1.2–5.4), with splenomegaly (*P* = 0.01) and portal hypertension (*P* < 0.01). None of the six identified genotypes was associated with the aggravation of PPF.

CONCLUSION HCV aggravates PPF in schistosomiasis patients, either acting directly on the level of the fibrogenic/fibrotic process or indirectly by increasing Th-2 response associated to disease; since co-infections *S. mansoni* / HCV were not found associated with an increased parasite burden. That effect might be underestimated due the earlier death of young subjects with co-infections. It must be expected that in the near future, the number of schistosomes infected patients with severe clinical presentation will increase due to the incessantly increasing incidence of HCV infections in this area and in other areas of South.

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endemic areas of Schistosomiasis even if they do not present symptoms or suggestive signs of parasitisation.

PB 108
Evaluation of control of Schistosomiasis mekongi in Lao PDR
1National Institute of Public Health, Vientiane Capital, Lao People’s Democratic Republic; 2Research Institute, International Medical Centre of Japan, Department of Appropriate Technology Development and Transfer, Tokyo, Japan; 3Dokkyo University School of Medicine, Department of Tropical Medicine and Parasitology, Tochigi, Japan; 4Hokkaido University, Department of Veterinary Parasitology, Sapporo, Japan; 5Fukuoka University, Department of Social and Environmental Medicine, Fukuoka, Japan, Department of Appropriate Technology Development and Transfer, Tokyo Gakugei University, Department of School Nurse Education, Tokyo, Japan

OBJECTIVES In Lao PDR, the morbidity rate of Schistosomiasis mekongi is more than reduced to less than 1% by MDA (Mass drug administration) control measure at Khong district in Champasak province till 1999. However, resurgence of the disease was reconfirmed in the same district in May 2003 (Vongsouvan, 2003) and high prevalence was confirmed among school children in March 2004 (Nakamura et al. 2004). Subsequently, the government of Lao PDR sent a therapeutic mission to tackle the situation in September 2005. Hence, we conducted a small-scaled evaluation survey to confirm the efficacy of the therapeutic status of Schistosomiasis mekongi among the people at relatively higher infested villages in the area.

METHODS Field survey was conducted at 2 villages in Khorn Island in Khong district, Champasak province in April 2006. The villages are Khorn Thai (population: 537 in 2003) and Khorn Noi (487). The prevalence of the infection of Schistosomiasis mekongi in village was 47.2% and 50.0%, respectively in 2004. The efficacy of the drug therapy was evaluated mainly on school children by stool examination using modified formalin detergent technique. A serological technique (ELISA) was also employed complementally to detect specific antibodies to the parasite in human serum sample. Moreover, the related knowledge on the schistosomiasis: symptom, vector snail etc. were evaluated by questionnaire survey, at the same time.

RESULTS A total of 183 stool samples and 199 questionnaire survey cases on the pupils were obtained. The results of stool examination conducted at these 2 villages revealed 28% and 48% of each, Strikingly, in 117 sampled cases, almost all the children had been exposed by the schistosome, which was confirmed with the ELISA. The curative rate was about 60% among 101 drug administered cases in 2004, which showed that the drug treatment in this area was inadequate. The other helminthes infections, hookworm infection were the most prevalent among the dwellers in this area. According to the results of the questionnaire survey, more than 70% of the pupils did not know the schistosomiasis in the area.

CONCLUSIONS Our evaluations clearly show that schistosomiasis mekongi is still important disease in the Mekong in the border of Lao PDR and Cambodia. Systematic and sophisticated public relation methods on the disease control should be urgently introduced to the area, which should conduct under the collaboration of border countries, especially Lao and Cambodian governments tightly.

PB 109
Treatment of Schistosoma spp infections with multiple cycles of praziquantel in a cohort of immigrants followed in Milan, Italy
D. Ratti, G. Gaiera, N. Ceserani, M. Cernuschi, A. De Bona and A. Lazzarin
IRCCS H San Raffaele, Infectious Disease, Milan, Italy

OBJECTIVES Schistosomiasis is a growing disease in Milan, due the increase of immigration from endemic countries. We describe a cohort of immigrants infected by Schistosoma and the difficult management of the therapy with the poor criteria of diagnosis and follow up.

METHODS From 1993 on 2006, 107 patients infected by Schistosoma, are followed in Infectious Diseases of San Raffaele Hospital in Milan, Italy. As diagnosis we use haemagglutination test reactive for antibody anti S. mansoni, hemoglobin, intercalatum (positive for Ab > 1:160) or the direct examination of faeces, urine or biopsy for the eggs research. In addition we investigate the presence of hypereosinophilia, increase of IgE and HCV coinfection. The monitoring of the infection is every 3-6 month in compliance patients.

RESULTS About 93% of the patients are from Egytpe, the other from Eritrea, Sudan, Nigeria. The most are young male and 52% are coinfected with HCV, mainly genotype 4. At the first examination, 58% of the patients didn’t receive a treatment for the schistosomiasis in their life, the other a unkowned treatment or with praziquantel. Only the 12% have positive microbiological tests, the others have a positive serological test with a median of 3 dilutions (1:640), IgE among between 101 and 500 UI/ml and eosinofilia mainly in the range. 61% have a normal abdominal ultrasound, 23% is without it. 97 patients (77%) take praziquantel 40mg/Kg/die, 61% of them during for 3 days and the remain for 1 day only. On the average, every patient take 2 cycles of praziquantel until to entry in the follow up or get drop out. 68 patients are in the follow up and the median of Ab anti schistosomiasis and the level of IgE decrease slowly on the time.

CONCLUSIONS In developed countries, schistosomiasis is not endemic and its eradication is the objective of the treatment to avoid several complication of the chronic schistosomiasis. The lack of studies in these areas doesn’t allow to have a common protocol of treatment and, above all, valuable criteria to evaluate the really eradication of the infection and to reduce its cost. Therefore is necessary to find new laboratory methods for the diagnosis and the follow up of the schistosomiasis, as antigen (CAA or CCA) or genomic (PCR) investigation in the blood.

PB 110
The combined profile tests of circulating Sj14-3-3 and its antibodies for the diagnosis of schistosomiasis
J. Shen and Y. Yu
Anhui Medical University, Dept. of Parasitology, Hefei, China

OBJECTIVES To evaluate the immunodiagnostic value of the profile test with detection of both circulating antigen Sj14-3-3 and its antibodies in the patients with schistosomiasis.

METHODS The rSj14-3-3 expression in E.coli was induced and purified through affinity chromatography. Monoclonal and polyclonal antibodies against rSj14-3-3 were produced. Sera of patients with acute and chronic schistosomiasis were detected with rSj14-3-3 in indirect ELISA, double antibody sandwich ELISA( using anti-rSj14-3-3 monoclonal and polyclonal antibodies), and the combined detections of Sj14-3-3 and its antibodies.

RESULTS The positive rates of the three methods in 70 cases of acute schistosomiasis were 72.9%, 75.7% and 91.4%, while in 110 cases of chronic schistosomiasis were 46.4%, 61.8%, and
The profile test of both circulating antigen Sj14- and A. Sie falciparum, in 8 isolates. Parasite densities significantly increased in Angola, cessation of war led to better accessibility to health facilities and accuracy of reporting systems. This fact revealed that sickle-cell-anemia is very frequent and no records exist about G6PD-deficiency, a common X-linked enzymopathy. This study aimed to assess the impact of these human determinants on malaria disease outcome in this setting.

METHODS Finger-prick collections were performed from 250 children, 0.5-14 years-old, in the Luanda Paediatrics Hospital Emergency, after the clinician examination and before anti-malarial therapeutics and/or blood transfusion. Malaria outcome was defined as Severe (SM), Mild (MM) and Asymptomatic (AM); a group of non-infected children (NI) was also studied. Detection and identification of Plasmodium species were done by nested-PCR; multiplex- and RFLP-PCR were used to determine HbB and g6pd genotypes. These were grouped according to the associated enzymatic activity as G6PD+ (normal), G6PD± (intermediate) and G6PD- (deficient). Comparisons of proportions and means were done using Pearson’s χ², Mann-Whitney-U and Kruskal-Wallis tests.

RESULTS Plasmodium ovale was detected, jointly with Plasmodium falciparum, in 8 isolates. Parasite densities significantly decreased with increasing malaria severity. Densities were significantly higher in the HbAA and lower in the HbSS individuals in overall population but not within clinical groups. No differences occurred among g6pd genotypes. From a total of 228 individuals, 68% were HbAA, 13% HbAS and 21% HbSS. SM, MM cases and NI individuals distributed significantly different among the HbB genotypes. HbS overall allelic frequency was 0.27, being similar in the SM and MM (0.19 and 0.17) and higher in the AM and NI groups (0.32 and 0.47). From a total of 223 individuals (117 males, 106 females), 91% were G6PD+ (in both genders), 3% G6PD± (6% of the females) and 7% G6PD- (9% and 4% of the males and females). Malaria cases and non-infected individuals did not significantly differ among the genotypes. Allelic frequencies of B, A and A- were 0.74, 0.18 and 0.08, being similar in the malaria and non-infected groups.

CONCLUSIONS The occurrence of P. ovale in Angola was controversial. In this study, we present the first unequivocal report of this species in Angolan isolates. Association between absence of symptoms or even non-infection with the HbSS genotype and the inverse, clinical cases (severe and mild) with the HbAA genotype was found. The sickle-cell trait, traditionally associated with protection against severe malaria, predominated in this study in the asymptomatic and non-infected individuals and occurred similarly in the clinical cases, independently of disease severity.

**PB 112**

**Clinical presentation and complications of imported** Falciparum malaria from Africa in two populations: travellers and immigrants


1 Hospital Clinic, Centre de Salut Internacional, Barcelona, Spain; 2 Hospital Sant Joan De Déu, M, Manresa, Spain

OBJECTIVES Falciparum malaria is the most aggressive form of this disease, 90% occurring in Africa. Only natives from malaria endemic areas can acquire some immunity. Complicated malaria occurs among children, pregnant women and people from non endemic areas. For a long time, there has been the hypothesis that natives lose immunity when they leave endemic areas, but some recent articles reflect this may not be true.

METHODS Retrospective study of cases of imported falciparum malaria from Africa in Hospital Clinic (Barcelona, Spain), from 1999 to 2005. We compared clinical, epidemiological, chemotherapy compliance and parasitemia between travellers and African immigrants. Statistical analyses were made using Chi Square, T Student and Ranksum tests.

RESULTS There were 187 falciparum malaria cases during that time, 102 (54.5%) from non endemic areas and 85 (45.5%) from endemic areas. Time of residence in non endemic country was more than 5 years in 70% of African immigrants. Use of chemoprophyaxis and compliance was higher in traveller group (p=0.043). There were 18 complications (WHO criteria), only one of them (a pregnant woman) was from endemic area (p=0.0001). There were 5 fatal cases, all from non-endemic areas. Parasitemia was higher (2.4%) in the complicated group than the non-complicated group (0.17%) (p=0.0001).

CONCLUSION The most relevant data of this study was that immigrants had fewer complications than travellers despite the majority of immigrants had been living in non-endemic areas for more than five years and their lesser use of chemoprophyaxis. This data could change the idea about loss of immunity among African immigrants, after a long time period of living in non-endemic areas. Parasitemia is a predictive factor of complicated malaria. The poor use and compliance of chemoprophyaxis observed in this study is another important fact, perhaps travel providers should be tougher in their counselling for prevention of a potential fatal disease, especially for people from non malaria endemic areas.

**PB 113**

**Household characteristics and severe malaria in Nouna, Burkina Faso**

S. Yamamoto, R. Sauerborn and A. Sie

1 University of Heidelberg, Department of Tropical Hygiene and Public Health, Heidelberg, Germany; 2 Centre de Recherche en Santé de Nouna, Nouna, Burkina Faso

OBJECTIVES To assess different housing characteristics of participants’ homes as risk factors for severe malaria.

METHODS This retrospective case-control study examined different housing risk factors among the homes of families with
women (15-45 years) and/or children (9 years) in conjunction with severe malaria incidence during the wet season in Nouna, Burkina Faso. Cases were matched to controls on age, sex, ethnicity and geographic location. An extensive survey of several potential housing risks factors was conducted for each participating household. Conditional logistic regression for a matched case-control study was used in the analyses with SAS 9.1 (SAS Institute Inc., Cary, NC).

RESULTS Electrification of the home, number of rooms greater than or equal to four and running water source in the home or neighbourhood were statistically significant variables for severe malaria in women and children (OR=3.00, p=0.02, 95%CI=1.23-7.30, OR=0.58, p=0.03, 95%CI=0.36-0.94, OR=0.23, p=0.07, 95%CI=0.05-1.15, respectively); however, when added to a regression model and a backwards elimination performed, only electricity remained significant (adjusted OR=5.03, p=0.04, 95%CI=1.08-23.46). Likewise, different housing materials for roofs (metal: adjusted OR=1.26, p=0.64, 95%CI=0.48-3.31) and walls (semi-dur or earthen bricks covered with cement: adjusted OR=0.99, 95%CI=0.44-2.20) were not statistically significant. Only banco flooring (earthen brick) was a statistically significant protective factor (adjusted OR=0.55, p=0.02, 95%CI=0.15-0.83).

CONCLUSIONS These initial results suggest that electricity may be a risk factor for severe malaria among women and children. Electrification of the household could reduce the amount of traditional fuels used and therefore the amount of smoke in the homes, rendering environments more favourable for mosquitoes. We were not able to determine that the type of roof or wall material used in dwellings were either risk or protective factors, although banco floors were associated with a strong protective effect. Homes with banco floors may have cooler indoor temperatures and therefore fewer mosquitoes. Additional analyses with a larger number of cases and controls could provide stronger statistical evidence and offer a clearer picture of the relationship of these factors to severe malaria.

Sexual and Reproductive Health

PB 114
Integrated health services in a rural community: reproductive and child health, STIs/HIV Prevention and family planning: lessons learned
U. Mohammed
Sri Venkateswara University, Department of Population Studies and Social Work, Tirupati, India

The focus of this paper is on successful provision of integrated health services viz., reproductive and child health, prevention of STIs/HIV and family planning to women in a rural community in Andhra Pradesh, India among whom prevalence of STIs/HIV was very high.

OBJECTIVES To improve the overall health status of the women. To prevent STIs/HIV in the community To bring about behavioural change in the entire community. To achieve cent per cent Condom use during illicit sex by the tribals. To provide general health, maternal and child health, family planning, STI/ HIV preventive services – all under one roof. To increase family planning adoption.

METHODS AND MATERIALS A cluster of 80 villages with a population of about 2,00,000 consisting of tribals was selected for the programme in the year 2003. The programme was carried-out with the help of trained social workers, doctors and paramedics.

PROGRAMME INTERVENTIONS Community education and mobilization Information, education and communication programmes on STIs/HIV/Family Planning Enactment of dramas Folk media Distribution of literature on STIs/HIV/AIDS MCH/Family Planning/Condom Group discussions Meetings One-to-one meetings STI/HIV prevention counseling HIV-pretest counseling HIV-testing HIV-post-test counseling Pre-natal, natal and post-natal care at the doorstep and at the hospital Treatment for STIs and common ailments General health services Condom promotion Free Condom distribution Prevention of Mother-to-Child Transmission of HIV Immunization of pregnant women and children Family planning services Applied nutrition programme for pregnant and lactating mothers and children Medical termination of pregnancy (in certain cases) Social care and support Involvement of husbands in the MCH Programme

RESULTS Owing to the impact of the programme in the study area, as many as 45,600 women utilized different services provided by the NGO during 2003-2006. There was considerable increase in the knowledge of the women on the health aspects in the study area. Prevalence of STIs/HIV had decreased. The number of women attending MCH clinic has increased. Institutional deliveries have become popular. All pregnant women and infants were immunized as per the immunization schedule. Morbidity and mortality among infants and women decreased considerably. The overall health status of women had increased. The adoption of family planning had picked-up in the community. Many more achievements of the programme have been detailed in the full length paper.

CONCLUSIONS The programme is worth replicating in all the developing countries where similar situation exists.
After this day-care, the caregivers are in most cases responsible for looking after these children, but there are also other people regularly supporting the respondents with their child care duties like partners, grandparents, friends etc. However, HIV-infected caregivers declare the need of support in performing parental care, but they also demand for assistance with financial planning, in case of legal problems and integration in the job market. For most of the caregivers parenting is a positive experience. More than half of the caregivers have observed one or more conspicuous behaviour on the part of their children, indicating a challenging situation. Standard multiple regression analysis shows that less support (β=-0.30, p < 0.001), younger children (β=0.19, p < 0.01) and less physical complaints (β=-0.16, p < 0.05) increase the caregivers’ self-efficacy (adj. R-Square=0.16, p < 0.001).

CONCLUSIONS Physicians should address caregivers living with HIV on the subject of their parenting responsibilities and provide the necessary scope for this subject in their consultation sessions. Physicians are able to draw their patient’s attention to available service offers at their disposal.

PB 116
Reproductive health care in disabled women
E. Hajikazemi1, S. Abedi2, S.F. Hosseini2 and F. Fahidi3
1 Iran University of Medical Sciences (IUMS), Faculty of Nursing and Midwifery, Community Health & Mother & Child Health, Tehran, Iran, Islamic Republic of Iran; 2 Iran University of Medical Sciences and Health Services (IUMS), Tehran, Iran, Islamic Republic of Iran

OBJECTIVES Determination the reproductive health care services received by women with mobility impairment during disability period

METHODS All 241 handicapped women between the ages of 15-49 years who were the members of Iranian Handicapped Society contributed in this study. It was descriptive study in which data were collected through questionnaires.

RESULTS Findings revealed that 2.9% of the samples had received sexual counseling before and after marriage. Less than 50% of them had received family planning services. Prenatal exams (except blood and urine tests) were done for less than 40% of samples and necessary education was done for less than 35% of them. All periodical prenatal care (except dentist visit) was done for about 60% - 75% of disables women. Those who had had Pap smear test, breast self exam instructions, and breast physical exam by health staff were respectively 14%, 4.6% and 6.2%. Beside mammography was done for nobody in the group of more than 40 years old.

CONCLUSION According to the results it is estimated that only small percentage of women with mobility impairment received reproductive health care. Therefore further studies to explore obstacles faced by disables women are recommended. It is also suggested that available necessary services for cited citizens to be made.

Sexually Transmitted Infections

PB 117
Human papillomavirus (HPV) detected in anogenital condyloma of HIV-infected men
O. Blanco González, M. Munique, S. Acosta, B. Blanco, M. E. Toledo, V. Capó and M. E. Rodríguez
Instituto de Medicina Tropical Pedro Kouri, Ciudad de la Habana, Cuba

INTRODUCTION Sexually transmitted diseases continue to rise constituting a serious health, economic and social burden. It’s control is crucial in other to improve the reproductive health of the community becoming one of the greatest challenges for mankind. In the developed countrys these are at the moment the most common group of infectious diseases. Among them, genital warts are probably the ones with the highest incidence. In the general HIV-infected population in Cuba, there is few data on the prevalence of HPV in men and due to it’s frequency in this particular sector and it’s viral oncogenicity, it becomes necessary to detect and typify the serotypes related with condyloma lesions in these patients, therefore becoming the main object of these investigation.

METHODS Detection of HPV was carried out in 30 anogenital condyloma lesions from HIV-infected men who had assisted to consults at our Department of Dermatology during the period between January 2002 and January 2004. HPV characteristics and sexual behaviour assessed through semi-directive questionnaire were collected. Detection of HPV DNA was done using consensus-primer PCR and typing was made by hybridization with 32 low and high-risk HPV DNA biotin-labelled probes. Clinics, epidemiologic and immunologic features of these patients were analyzed.

RESULTS AND CONCLUSIONS HPV DNA was detected in 100% of the lesions. Associated to the condyloma lesions, HPV 6 and 11 (low oncogenicity) were detected in 19 of 30 cases (63.3%) and HPV 26 was found in 16 of 30 patients (53.3%). Multiple infections with high-risk HPV types, predominantly HPV 16 and 18 were observed in 20 samples being found up to 11 different genotypes in the same patient. The studied population was represented mostly by single, unoccupied and white skin people, coming from urban area, and with an average of age 27, 4 years. Condylomas were more frequently localized in perianal region and in patients with a lymphocyte CD4 count < 500 cell/mm. Trichloroacetic acid (TCA) or Dichloroacetic acid (DCA) 80%-90 was the more used and effective therapy.

PB 118
Chlamydial trachomatis prevalence in Iranian women attending obstetrics and gynaecology clinics
1 Reproductive Biotechnology Research Center, ARI, Reproductive Infections, Tehran, Iran, Islamic Republic of Iran; 2 Monoclonal Antibody Research Center, ARI, Reproductive Immunology, Tehran, Iran, Islamic Republic of Iran; 3 Reproductive Biotechnology Research Center, ARI, Tehran, Iran, Islamic Republic of Iran; 4 Shahid Beheshti University of Medical Sciences, Social Medicine, Tehran, Iran, Islamic Republic of Iran; 5 School of Public Health/Teheran University of Medical Sciences, Epidemiology and Biostatistics, Tehran, Iran, Islamic Republic of Iran; 6 Reproductive Biotechnology Research Center, ARI, Reproductive Infections, Tehran, Iran, Islamic Republic of Iran; 7 University of Sheffield Medical School, Division of Genomic Medicine, Tehran, Iran, Islamic Republic of Iran

OBJECTIVES This study was designed to estimate the prevalence of Chlamydia infection in women attending Obstetric and Gynaecology clinics in Tehran.

METHODS Women attending Obstetrics and Gynaecology clinics aged 16–40 were recruited by Sequential Random sampling. Those who had not passed urine in the last hour were eligible. Informed consent was obtained and a questionnaire completed after being interviewed by a midwife. First void urine was collected and after DNA extraction, PCR tests was performed in Iran; urine DNA samples were restested by strand displacement amplification (SDA) for Chlamydia confirmation in Sheffield university.
RESULTS 12.6% (133/1052) tested positive for Chlamydia by PCR. Of these PCR positive samples, 86 were available for re-testing by SDA and 67 were positive giving a correlation between the tests of 78%. This gave an overall true prevalence of 6.4% which is however, underestimated. No statistical differences were seen between patient age groups, details of personal and reproductive history and combined PCR and SDA positivity for C. trachomatis.

CONCLUSION A 12.6% prevalence of Chlamydia trachomatis was found by PCR testing which is cost effective to screen and treat. Despite limitations in re-testing PCR-positive samples by SDA, a 78% correlation between tests confirms a high prevalence of C. trachomatis. Non-invasive screening of women was therefore a success in this group of patients. As this was the first time that more sensitive molecular methods were used for detection of C. trachomatis in such a big sample size, the results are considerable. However, we suggest further such testing. This study supported by WHO/EMRO (grant no R6/18/3, ID RPC 02/86), Reproductive Biology Research Center, Avesina Research Institute, Iran & Sheffield University, UK.

PB 119
Asymptomatic trichomoniasis
Z. Valadkhani1, M. Assmar1 and N. Hassan1
1Pasteur Institute of Iran, Parasitology, Tehran, Iran, Islamic Republic of Iran

OBJECTIVES Trichomoniasis is an extremely common infection worldwide and is associated with important public health problems, including amplification of HIV transmission. This disease has found to be in forms of symptomatic and asymptomatic in women and may depend on host as well as parasite variables. Thus the aim of this study was to evaluate the patients attending gynecology clinic with different symptoms and checked them for Trichomonas vaginalis infection.

METHODS The vaginal secretion and urine samples of the patients attending gynecology clinic, Imam Reza hospital, Amol city, have been checked by direct smear and cultured in TYI-S-33 culture media. Isolates obtained from patients complaining of vaginal discharge and/or pruritis, dysuria, and dyspareunia were considered as symptomatic patients isolates. Those who attended the clinic for routine checkup, infertility or some other gynecology problems with no complain of above mentioned symptoms were considered as asymptomatic patients isolates. Data were analyzed by using Epi-info software.

RESULTS Results showed that the numbers of asymptomatic patients for trichomoniase were 1.3 times more than infected samples belong to symptomatic ones. Per speculum examination revealed that 75% of T. vaginalis positive subjects had normal appearance of vagina and cervix.

CONCLUSION Most of the physicians according to the symptoms complain by the patients, without checking by different laboratory methods, prescribing the drugs for the patients as well as their partners. While as we checked more than 70% of the suspected patients had other problems, but not trichomoniasis. Thus laboratories could play important role for diagnosis of infection and help the physicians for proper treatment. According to the epidemiological aspects, these asymptomatic patients are very important as healthy carriers, and T. vaginalis infections are commonly associated with other STDs and are a marker of high-risk sexual behaviour. Therefore, if these women are not screened, the diagnosis will be missed.

PB 120
Sexually transmitted infections in Kosovo
H. Gashi1, N. Ramadani1, A. Kalveshi1 and S. Gashi-Nalca1
1Department of Epidemiology, Kosovo National Institute of Public Health, Pristina, Albania; 2Medical Faculty, Forensic Institute, Pristina, Albania

OBJECTIVES To present epidemiological situation regarding IST, HIV and AIDS in Kosovo

METHODS Epidemiological surveillance data and retrospective method.

RESULTS Epidemiological occurrence of RTI/STI in Kosovo during the period 1990–2006 did not present the reality of the epidemiological situation because of lack of reporting of RTI/STI cases. It was reported in total 1169 cases. Reporting through this surveillance system identified 24 syndromic diagnoses and nine cases of Neisseria gonorrhoeae in 2001. As laboratory diagnostics are extremely limited, it is not possible to state the etiologic profile or prevalence of STIs. Since 1986 until December 2002, 41 confirmed AIDS cases with 22 deaths were registered in the National Institute of Public Health (NIKH) in Pristina, Kosovo. In 2001, 12 AIDS cases were reported; in 2000, six AIDS cases, four in 1999 and between 0 and 3 cases during the previous 12 year period. Two-thirds of reported cases were males. In 2006, six new cases of syphilis were reported.

CONCLUSION A specific RTI/STI Programme is being established on march 2003. Gaps were identified in various components of STI prevention and care. Gnostics are not at uniform current standards. Providers perceive a lack of privacy and confidentiality in STI care themselves. Due to limited supplies and reagents, STI diagnostics is limited. A long-term plan of data needs is essential to direct program work.

PB 121
Prevention and management of STIS/HIV among female sex workers in India: a success story
U. Mohammed1
1Sri Venkateswara University, Population Studies and Social Work, Tirupati, India

INTRODUCTION The focus of this paper is on successful Sexually Transmitted Infections (STIs)/HIV prevention programmes for female sex workers currently in operation in India through non-governmental organizations. Owing to abject poverty in India, the number of women entering into commercial sex is on the increase day by day. The prevalence of STIs/HIV among them was very high (63%) and a very few among them use condom. Sex workers are one of the potant sources for fast spread of STIs/HIV in India. Thus to curb the spread of STIs/HIV through them to others and also to make them to use condom regularly for safer sex, this programme was initiated in the year 2004. The programme is still in operation.

OBJECTIVES Increase awareness on STIs/HIV among sex workersPerceptible change in behavioural patternReduction in STIs/HIV infection and re-infectionIncrease health seeking behaviourPromote safe sexual practicesBring them to in mainstream.

METHODS AND MATERIALS The STI/HIV prevention and developmental programme for sex workers is currently carried-out with the help of trained sex workers who work as peer educators. Programme interventionsNetworking of sex workersPersonal meetingsGroup discussionsWorkshopsCounsellingPeer promotionPolice protectionInformation, education and communication programmes on STIs/HIV and development programmesFree distribution of literature on STI/HIV/AIDSCondom availability and promotionProvision of free health services for STIs and common
Aims: Free distribution of medicines; Provision of educational facilities to the children of sex workers; Promotion of self-help groups among sex workers; Take-up of economic activities; Provision of loans to start cottage industries; STIs/HIV prevention counselling; HIV pre-test counselling; Post-test counselling; General health services; Education; Promotion of yoga and meditation; Literacy and educational programmes.

Results: These interventions helped to bring down the STI/HIV prevalence to a greater extent (24%) among the sex workers. Today, eight out of ten among them are using condom as a safer sex practice. Majority of the sex workers insist their clients on compulsory use of condom. The use of condom by men during illicit sex has also increased in the country. Some of the sex workers are coming out the profession and starting cottage industries/business. Many more achievements are given in the full paper.

Conclusions: The programme interventions are worth replicating in both developed and developing countries.

PB 122

STI sentinel surveillance in Kosovo

L. Gashi1, E. Deva2, N. Ramadani1, S. Gashi-Naka3, S. Syla4 and A. Kalaveshi1

1Department of Epidemiology, Kosovo National Institute of Public Health, Pristina, Albania; 2Ministry of Health, Office of HIV/AIDS, Pristina, Albania; 3Medical Faculty, Forensic Institute, Pristina, Albania; 4World Health Organisation, Office in Pristina, Pristina, Albania

Objectives: Determine the HIV, HBsAg and Syphilis prevalence among women attending Antenatal Clinic (ANC) and STI patients attending the Clinics of Venerology (Venerology Department/STI Ward); Monitor the trends of HIV, HBsAg and Syphilis in selected sentinel sites during the serosurvey period.

Methods: The survey has been conducted at ANC and Dermatology Clinics (Venerology Department/STI Ward) of the UCCK in Pristina. This is a cross-sectional serosurvey, based on Unlinked anonymous testing with informed consent, which included pregnant women attending the ANC in public sector for the first time and STI patients who visited the Clinic of Dermatovenerology (STI ward) during the serosurvey period (until the desired sample size was achieved).

Results: There were 357 blood samples collected with the questionnaire. All blood samples were tested for HIV, HBsAg and Syphilis. In ANC were the desired sample size of 300 was reached, none of the pregnant women tested positive for HIV, nor for Syphilis. Of 300 pregnant women 2% tested positive for HBsAg, identified as a chronic carrier of hepatitis B and 15% were tested positive for AntiHBs, indicating that they may have been either vaccinated (post-HBV-vaccine immunity) or exposed naturally to HBV (Figure 3). While of 300 pregnant women 13% tested positive for AntiHBc, which indicates that these are chronic carriers, none tested positive for HBeAg. Analyzed by age-groups, of women who tested positive for HBsAg, three belong to age-group 20–29 and three to 40–49, while one belongs to age-group 30–39. Of those who tested positive for AntiHBs, 28 belong to age-group 30–39, 16 to age-group 20–29, four each to age-groups 10–19 and 40–49, while only one is older than 50. From 45 pregnant women who tested positive for AntiHBc, 28 belong to age-group 30–39, 17 to 20–29, 4 to 40–49, 3 10–19 and one belongs to age-group older than 50.

Conclusion: This was the first HIV/STI sentinel serosurvey conducted in Kosovo and in the Western Balkans region. The results of the study in two sentinel sites, show that among pregnant women and STI patients, which are considered as good proxy for general population, the HIV and Syphilis prevalence in Kosovo is underdetermined in order to take further concrete steps in HIV prevention among general population. Taking into consideration the result as from survey, in the future should be focused on groups with higher risk for exposure to HIV and other STIs, already identified in HIV/AIDS Prevention Strategy for Kosova (2004–2008).

TB Treatment

PB 123

Will mycobacteria fall for the TROIAN-Trick?

J. de Steenwinkel1, W. Van Vianen1, M. ten Kate1, A. Van Belkum1, H. Verbrugh1, R. Schijve2, G. Storm3, M. Van Agmael3, D. Van Soolingen4 and I. Bakker-Woudenberg5

1Department of Medical Microbiology and Infectious Diseases, Erasmus University Medical Centre Rotterdam, Rotterdam, Netherlands; 2Department of Pharmaceutics, Utrecht University, Utrecht Institute for Pharmaceutical Sciences, Utrecht, Netherlands; 3Department of Internal Medicine, Free University Medical Centre Amsterdam, Amsterdam, Netherlands; 4National Institute of Public Health and the Environmen, National Reference Laboratory for Mycobacteriology, Bilthoven, Netherlands

Objectives: Using a site-specific and site-avoidance drug delivery tool (carrier), the objective of this study is to improve treatment in mycobacterial infections by reduction of treatment duration, using existing antimycobacterial agents. The application of this drug delivery-based therapy in this study indicated as the Targeted Reduction Of Infectious Agents Numbers-therapy or short: TROIAN-therapy.

Methods: In vitro, different antimycobacterial agents were compared on their bacteriostatic vs. bactericidal activity against Mycobacterium avium, in relation to the time of exposure and the mycobacterial growth phase. In vivo, a disseminated Mycobacterium avium infection was established in C57B/6 mice, and antimycobacterial treatment was administered over a period of at most 6 months. Therapy efficacy was assessed by quantitative cultures from lung, spleen, liver, mesenterial- and inguinal lymphnodes at various time intervals.

Results: The in vitro study revealed a rapid and high killing capacity of Amikacin. In the experimental Mycobacterium avium infection, addition of the TROIAN-therapy with Amikacin to the conventional treatment, effected a rapid decrease of mycobacterial load in the infected organs and complete elimination of mycobacteria after 12 weeks. This in contrast to the conventional therapy alone, which resulted in a substantial decrease in the mycobacterial load but not in complete elimination of mycobacteria even after 24 weeks of treatment.

Conclusion: The addition of the TROIAN-therapy, allows a reduction of the treatment duration from 24 weeks to 12 weeks in Mycobacterium avium infection in mice. In addition, all infected organs were free of mycobacteria, and relapse did not occur. These results open new ways in the treatment of tuberculosis and studies of this new treatment approach in our mouse model of pulmonary tuberculosis are ongoing.

PB 124

Effect of decision thresholds on blackstone like error ratio in pulmonary tuberculosis: an example from a national reference level in Rwanda

J. Van den Ende1, J. Mugabe1, J. Moreira1, E. Seryange1, P. Basinga1, Z. Bisoffi2 and M. Boelaert2

1Centre Hospitalier Universitaire Kigali, Institute of Tropical Medicine Antwerp; 2Institute of Tropical Medicine, Antwerp, Belgium

Objectives: The threshold concept represents the probabilistic standard of proof from patients’ perspective, the Blackstone-like...
error ratio gives the ratio between erroneously treated and erroneously not treated patients in a population. \(1,2\) This study intends to explore the effect of using different hypothetical therapeutic thresholds on the error ratio in pulmonary tuberculosis patients.

**METHODS** In a cohort of 300 patients with chronic cough we estimated the post-test probability of tuberculosis of individual patients, based on a latent class analysis. With bacteriological proof as reference test we calculated crudely and weighted error ratios, the latter based on hypothetical harm of commission vs. omission. We calculated the effect of the application of different thresholds on both error ratios.

**RESULTS** Lowering the threshold from 80% to 20% would have added 58 patients (+64%). Applying a threshold based on international data (2.7%) would have resulted in treating almost all patients. \(3\) An error ratio of one matched a threshold of 0.30, and a weighted error ratio of one matched a threshold of 0.11.

**CONCLUSION** For pulmonary tuberculosis a decision solely based on the patient’s perspective leads to a very low threshold. The individual perspective cannot be the only one, as it could lead to an excess prescription which could affect the overall availability of treatment in a poor-resource setting. On the other hand, in our study, a (weighted) error ratio driven decision would be sufficiently conservative from the individual perspective, as a very small proportion of true TB cases would be left without treatment.

**REFERENCES**

**PB 125**

Tuberculous meningitis: does lowering the treatment threshold result in many more treated patients?

J. Moreira\(^1\), F. Alarcón\(^1\), Z. Bisoffi\(^1\), J. Riviera\(^1\), R. Salinas\(^1\), J. Menten\(^2\), G. Dueñas\(^3\) and J. Van den Ende\(^4\)

\(^1\)Institute of Tropical Medicine, Clinical Sciences, Antwerp, Belgium; \(^2\)Hospital Eugenio Espejo, Neurología, Quito, Ecuador; \(^3\)Ospedale Sacro Cuore, Centro Malattie Tropicale, Negrar (VR), Italy; \(^4\)Hospital Metropolitano, Neuroradiología, Quito, Ecuador

**OBJECTIVES** To estimate the effect of lowering the treatment threshold for tuberculous meningitis (TBM) on the number of patients who would be treated.

**METHODS** From 1989 until 2004 findings of patients with symptoms for more than 1 week and inflammatory changes of cerebrospinal fluid (CSF) were prospectively collected. Several models of latent class analysis were tested. Cumulative numbers of cases were plotted against different cut-offs for post test probability.

**RESULTS** The retained model of Latent Class Analysis included four clinical indicators: culture or autopsy positive, consciousness impairment, altered cerebral images and CSF glucose-40 mg/dL. In a cohort of 232 patients the prevalence of TBM was estimated at 79.2% (95% CI 67.9–87.7); post test probability of TBM above 80% was reached in 171 (73.7%) patients. Lowering the threshold from 80% to 20% would bring the number of patients at 200 (86.2%); increase 12.5%). A further lowering to 5% brings the number at 212 (91.3%; increase 17.6%).

**CONCLUSION** Analysis shows that, in this setting, three quarters of patients showing suggestive symptoms for more than 1 week

and CSF changes had a high probability (>80%) for tuberculous meningitis. The number of patients that would be treated does not increase linearly when lowering the threshold.

**TB-HIV**

**PB 126**

No evidence for hypoadrenalism as a cause of early mortality in a high HIV/ TB prevalence population starting anti-tuberculosis treatment (ATT) in Malawi

M. Besisworth\(^1\), J. VanOosterhout\(^2\), M. Diver\(^2\), B. Farragher\(^4\), A. Shenkin\(^5\), H. Mwandumba\(^1\), S. Khoos\(^1\), T. O’Dempsey\(^2\), B. Squire\(^2\) and E. Zijlstra\(^5\)

\(^1\)School of Tropical Medicine, Tropical and Infectious Diseases Unit, Liverpool, UK; \(^2\)Department of Medicine, College of Medicine, University of Malawi, Blantyre, Malawi; \(^3\)Department of Clinical Chemistry, University of Liverpool, Liverpool, UK; \(^4\)School of Tropical Medicine, Liverpool, UK; \(^5\)Department of Pharmacology and Therapeutics, University of Liverpool, Liverpool, UK

**OBJECTIVES** Early mortality following commencement of anti-tuberculosis therapy (ATT) is high, particularly in HIV co-infected individuals. The reasons for this are unclear but may include late diagnosis or presentation, HIV co-infection, malnutrition or missed opportunistic infections. Additionally, hypoadrenalism associated with tuberculosis (TB) and HIV which is further exacerbated by the use of rifampicin may also contribute to excess mortality.

**AIM** To assess the prevalence of adrenal dysfunction and its relation to outcome (early mortality, at 1 month) of patients with TB following initiation of ATT.

**METHODS** Consecutive adult patients with proven TB presenting to a large teaching hospital in Blantyre, Malawi were prospectively enrolled. A synacthen test was undertaken at baseline, then at 2 weeks after initiation of ATT. Clinical follow-up was undertaken until 3 months after completion of TB therapy.

**RESULTS** A total of 51 patients were enrolled, 29 (56.9%) were female, and 22 (43.1%) male. Median age was 32 years (range 18–62). Of the 43 patients tested, 38 (88.3%) were HIV seropositive. Seven (17.9%) died within the first month. At 3 months, 11 (21.6%) were known to have died. Adequate cortisol levels were found in (49/51) (95.9%) before commencement of rifampicin. Neither of the two patients with reduced response died. All 34 samples taken at 2 weeks revealed adequate cortisol responses. Seventeen declined or had died at 2 weeks.

**CONCLUSION** In this first prospective study in Africa assessing adrenal function and outcome prior to and after rifampicin induction, in a high HIV prevalence population, of TB patients no evidence of hypoadrenalism was found. Urgent studies are required to identify other possible aetiologies.

**PB 127**

The cost of collaborative TB/HIV interventions in Ethiopia

A. Vassali\(^1\), A. Semé\(^2\), F. Meheus\(^3\), P. Compagnolle\(^4\), S. Adnew\(^4\), T. Aibicho\(^4\), Z. Tadesse\(^1\) and D. Haile Mariam\(^4\)

\(^1\)Royal Tropical Institute, Amsterdam, Netherlands; \(^2\)Department of Community Health, University of Addis Ababa, Addis Ababa, Ethiopia; \(^3\)Hosanna Hospital, Hosanna, Ethiopia; \(^4\)Ministry of Health, National Tuberculosis and Leprosy Control Programme, Addis Ababa, Ethiopia

**OBJECTIVES** To identify and quantify the health service (provider) and patient cost of TB/HIV services from three pilot sites in Ethiopia.

**METHODS** Provider costs were measured using secondary data and standard techniques. Patient costs were measured through facility based interviews.

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RESULTS The provider cost of TB/HIV services was found to be comparable with costs from higher income settings. The high cost was primarily due to the hospital setting of the TB/HIV pilots. Patient costs were also found to be substantial compared to income levels, but were broadly comparable to other studies measuring the patient costs of TB and HIV/AIDS in similar settings.

CONCLUSION Our provider costs provide the basis for estimates of the costs of scaling up TB/HIV within hospital settings in Ethiopia. Our patient cost results highlight the need to mitigate the economic burden of both TB and HIV/AIDS in Ethiopia. Although our study shows that the economic burden of both diseases is likely to fall during treatment, patients incur substantial direct costs prior to treatment. In the early stages of treatment, the combination of high levels of income loss and the additional costs of accessing treatment were found to reach catastrophic levels. Collaborative TB/HIV services may provide an opportunity to reduce pre-treatment costs by providing an additional channel for the early diagnosis of HIV and AIDS. Costs and economic impact may be further reduced by providing both diagnostics and therapies free of charge and providing social support.

Treatment Adherence

PB 128
Compliance and adherence to prescribed regimen in diabetic patients seeking treatment at the out-patient clinic of Kenyatta National Hospital, Nairobi, Kenya

J. Kebaso¹ and A. Orago²
¹African Population and Health Research Centre, Research, Nairobi, Kenya; ²Kenyatta University, Public Health, Nairobi, Kenya

OBJECTIVE To determine the compliance to the prescribed regimen in the treatment and control of diabetes in diabetic patients seeking treatment at Kenyatta National Hospital.

METHODS Over a period of 6 months, during routine diabetes care in the clinic, a questionnaire was issued randomly to 100 patients to evaluate their level of compliance. Follow up trips were made to the patients places of residence to determine the actual compliance to their regimens.

RESULTS A total of 80 diabetic patients were included, 52% were females and 48% were males. We found that a majority of diabetic patients (90.0%) had poor knowledge about the disease, 83.7% had poor knowledge about the complications associated with diabetes and 96.3% had poor awareness of how to control the disease. The poor level of knowledge that diabetics have about their disease suggests that health care providers need to be trained in the areas of information, education, and research.

Conclusion The results of this study demonstrated that those patients who adhered to the physician/nurse advise and prescribed regimen, achieved better glycemic control. Income and formal education levels influence compliance. Patients in low income class cited unaffordability of the drugs and the required dietary arrangements as a major reason for their non compliance with their regimens. Age, sex, tribe, marital status, occupation and duration of the disease, did not affect patient Compliance to their prescribed regimen.

PB 129
How to give an impulse to women’s health care seeking through popular theatre - experience of Mopti health district on tuberculosis control in Mali

L. F. Traoré¹, F. Maguragµ¹, I. Godin² and B. Dujardin²
¹Centre National d’Appui à la lutte contre le Maladie FORESA3, Bamako, Mali; ²Université Libre de Bruxelles, Politiques et Systèmes de Santé, Bruxelles, Belgium

OBJECTIVES The health district of Mopti has a TB detection rate of 54% (2006), but the sex ratio of male to female TB cases is 3:1. The purpose of the study is to use popular theatre to reduce such discrepancy in TB detection.

METHODS The main reasons of non access to health care are identified within the community (with focus group and community interviews) and are used to create the scenario for popular theatre. The scenario is taking gender issues into account. A debate-focus group is organized after the sketch representation to the community. Qualitative and quantitative analysis are made.

RESULTS The analysis of group discussions between spectators and researchers will allow determining the effect of the sketch on men and women; how they want to use the information acquired to instruct others and what they want to change in their behaviours. The data collected in the health centres will show the effect on their utilization rate.

CONCLUSION The poor access to health care is due to many different factors in the women’s population. Popular theatre is identified here as a tool for providing information at the community level. Concerning the particular case of TB, the fear of the disease is due to the lack of adequate information. Improving information aim at reducing stigmatization of the patient.

FORESA3 Project, EuropAid Contract N° SANTE/2004/078590

Tropical Neurology

PB 130
Apoptosis onset and bax protein distribution in spinal motoneurons of newborn rats following sciatic nerve axotomy

M. J. Rezaei¹ and T. Traibi²
¹Kurdistan University of Medical Sciences, anatomy and Histology, Sanandaj, Iran, Islamic Republic of Iran; ²Departments of Anatomical Sciences and Pathology, Tarbiat Modarres University, Tehran, Iran, Islamic Republic of Iran

OBJECTIVES Extensive apoptosis in spinal cord motoneuron was reported to occur in the newborn following sciatic nerve axotomy. The purpose of this study was to evaluate the onset of cell death at early stages of axotomy, and the changes in Bax protein distribution pattern in the apoptotic cell.

METHODS Newborn rats were divided into seven groups, axotomized at day 5 postnatal and sacrificed at the following time points: 1, 3, 6, 12, 24, 48, and 72 h after surgery. The left sciatic nerve was transected while the right side was kept as a control. Three experiments were made for morphometric, immunohistochemical, and ultrastructural studies.

RESULTS Morphometric study showed sustained reduction in the number of neurons in the ventral horn. Neuronal losses onset occurred at the first hour after axotomy and the highest loss
Cardiac autonomic imbalance in the digestive form of Chagas' disease

INTRODUCTION Chagas' disease still represents a public problem in the majority of countries of Latin America. The impairment of the autonomic nervous system is easily diagnosed in the digestive form of the disease. Several studies have pointed out that, serum levels of antibodies against muscarinic-colinergic and beta-adrenergic neurotransmitters, are elevated in this form of Chagas' disease.

OBJECTIVES Evaluate the cardiac autonomic function by using the computerized analysis of the heart rate variability in patients with the digestive form of Chagas' disease.

METHODS We studied 74 patients, gender-and age-matched, 26 (digestive group), 25 (indeterminate group) and 23 (control group). A continuous ECG recording in DII lead was performed in supine rest and during cold face and passive tilt tests. The overall R-R intervals were acquired and the variability of R-R series was assessed in the time and frequency domains using autoregressive power spectral analyses.

RESULTS The groups were similar regarding to gender and age. In baseline conditions, there was no difference between the groups regarding to the R-R intervals, variance and power spectral areas of low and high frequencies. In the cold face test the digestive group showed a statistically significant decrease of the normalized high area compared with the two groups ($P = 0.02$). During tilt tests, the digestive group showed a statistically significant decrease in low frequency and normalized low frequency areas, compared with indeterminate and control groups ($P = 0.018$ and $P < 0.001$). A decreased of the high frequency/low frequency ratio was observed in digestive group compared with indeterminate and control groups ($P < 0.001$) in the tilt test.

CONCLUSION Patients with exclusive digestive form of Chagas' disease showed predominant cardiac parasympathetic autonomic impairment as compared with individuals of the indeterminate and control groups.
METHODS Groups of 12–15 healthy rats were given single oral doses of racemic eflornithine HCl of 750, 1500, 2000 and 3000 mg/kg body weight in saline solution. Another group of 8–10 rats were given single intravenous doses of either 375 or 1000 mg/kg body weight. The selections of dose levels were based on allometric scaling and the lower limit of quantification (LLOQ) for the enantioselective assay. Spurrose blood samples (300 μl plasma) were obtained from rats in each dose group. Eflornithine enantiomers were separated quantified with liquid chromatography and evaporative light-scattering detection (ELSD). The LLOQ for each individual enantiomer was 83 μM (300 μl plasma sample). Frequent blood sampling (50 μl plasma per sample) in another group of rats allowed characterization of the complete plasma profile of racemic eflornithine which was quantified with a sensitive HPLC-UV method with a LLOQ of 5 μM (50 μl plasma). Pharmacokinetic data analysis was by mixed effects modelling on the combined racemic and stereospecific drug levels.

RESULTS Upon intravenous administration, the plasma concentration-time profile of eflornithine was bi-phasic with no apparent difference between enantiomers. Absorption after oral administration was zero-order suggesting active processes. The pharmacologically more potent stereoisomer L-eflornithine was less well absorbed than the less active D-eflornithine. Oral bioavailabilities were 30–58% and 71–78%, respectively, with an increase with dose for L-eflornithine especially.

CONCLUSION Eflornithine exhibited enantioselective absorption with the more potent L-form less favoured. These data may help explain why oral, in contrast to intravenous, treatment with racemic eflornithine is associated with poor response and gastrointestinal adverse effects. Oral treatment could become a therapeutic alternative if ways to improve the bioavailability of L-eflornithine are found.

PB 134
Women’s dependence from health attention during pregnancy in a sanitary area of Madrid, Spain
M. Blazquez1, Gender and Health
1Instituto de Salud Carlos III, Escuela Nacional de Sanidad, Madrid, Spain

OBJECTIVES Show the high demands of health attention during pregnancy by Spanish women. Hypothesis: The high number of visits during pregnancy it is not related with the risk on pregnancy. It is related with sanitary personal’s belief’s about its helpful and women’s belief.

METHODS These data are part of the information of a qualitative research. This study is developed with anthropological methodology: participatory observation and personal interviews such as women as health professionals. The study take place in Primary Care and Specialized Care, in a sanitary area of Madrid (Spain). The number of women observed have been 456.

RESULTS The visits media in this sanitary area is seven visits in no risk pregnancy. The women with low level education, immigrant and unhealthy style of life are the women who have got more visits. However, women with high level education demand more control and they assisted beside to private health centers. Their reasons are that they have the necessity to know that all is ok, the scare to the risk and boarding and to look for security.

CONCLUSION With the results of this research, we can know that women and health professionals promote the medical control of pregnancy like an issue mainly biological and pathological.

PB 135
HIV/AIDS infection among injection drug users and harm reduction in Indonesia
A. Nurhidayat
1The Drug Dependence Hospital-RSKO Jakarta, Amsterdam, Netherlands

OBJECTIVES Indonesia, with a population of 225 million, is experiencing public health problems associated with injection drug use (IDU) and increasing numbers of HIV/AIDS cases. Harm reduction strategies has been implemented in an attempt to reduce the spread of HIV infection among this group. This study was aimed at reviewing the HIV/AIDS infection among IDUs and harm reduction implementation in Indonesia.

METHODS A literature review utilizing 12 journal articles, official reports and documents from Ministry of Health, National Narcotic Board and Health Research Center-University of Indonesia.

RESULTS The total number of officially registered HIV/AIDS cases reaching 13,424 HIV/AIDS by the end of 2006, and the true number of HIV cases is estimated to fall between 169 000 and 216 000. The Ministry of Health reports that by the end of 2006, 50.3% of HIV/AIDS new cases were acquired through injection drug use. At present, there were estimated 3 million drug users in Indonesia. The true number of injection drug users (IDU) is estimated to fall between 191 000 and 248 000. Economic cost due to drug dependency is estimated around 23.6 trillion rupiahs (2.36 billion US dollar). 60% of IDUs used needles or syringes that someone else had used and share them with other people, and quarter of this group also had unsafe sex practices in the last practice. Among 100 respondents with HIV/AIDS, 63% of them still inject heroin in the last year, more than there is a need for harm reduction implementation. (Wibowo, 2004) Harm reduction has been listed by Ministry of Health in their guidelines for health providers, and implemented at 120 sites (prisons, NGO, Primary Health Care and seven Methadone Maintenance Treatment centers). It includes drug treatment, health education, HIV voluntary counselling and testing, outreach, sterile needle exchange, and substitution therapy. The challenge is how to socialize these strategies to stakeholders, and synchronize it with supply and demand reduction.

CONCLUSION The result of the study is in favour of the importance of harm reduction programs for injection drug users as high risk group. Integrated models of harm reduction are needed to address the increasing number of drug users today. The recent challenges are how to scaling up the willingness of IDUs to join the programs, and build network among institutions related to harm reduction strategies.

PB 136
Clinico-epidemiological differences between short term and long term travellers to Africa
P. Zamarrón1, E. Salvadó1, M. Navarro1, B. C. Jiménez1, J. A. Pérez-Molina1 and R. López-Vélez2
1Ramón y Cajal Hospital, Tropical Medicine, Infectious Diseases, Madrid, Spain

OBJECTIVES Compare clinical and epidemiological features between two groups of returned travellers from Africa: short term and long term travellers.

METHODS Descriptive study of two retrospective cohorts, Short Term (ST) and long term (LT) Spanish travellers returned from Africa.
Africa attended at a referral Tropical Medicine Unit from 1990 to 2006. ST were defined as a travel duration <3 months and LT>3 months. Statistical analysis was made by Chi Square test and when expected frequencies were <5 with Fisher’s exact test (P > 0.005 was considered non-significant, ns).

RESULTS A total of 1481 patients. 906 (61.17%) ST and 575 (38.82%) LT. Mean time from arrival until consultation was 3.97 months in ST and 8.11 months in LT. Average age: 35.7 years in ST and 37 years in LT. Average trip duration: 0.99 months in ST and 50.27 months in LT. Most common symptoms were: Fever: 404 (44.6%) ST and 169 (29.4%) LT (P = 0.000), Diarrhoea: 256 (28.3%) ST and 101 (17.6%) LT (P = 0.000), skin disorders: 228 (25.2%) ST and 140 (24.3%) LT (ns), respiratory symptoms: 80 (8.8%) ST and 61 (10.6%) LT (ns), urogenital symptoms: 73 (8.1%) ST and 72 (12.5%) LT (P = 0.005). Diagnoses obtained were: Malaria: 158 (17.4%) ST and 79 (13.7%) LT (ns), intestinal parasites 90 (9.9%) ST and 68 (11.8%) LT (ns), gastrointestinal infections: 141 (15.6%) ST and 56 (9.7%) LT (P = 0.001), extraintestinal parasitosis: 43 (4.7%) ST and 67 (11.7%) LT (P = 0.000), skin disorders: 65 (7.2%) ST and 42 (7.3%) LT (ns), viral infections: 13 (1.4%) ST and 5 (0.9%) LT (ns), respiratory infections: 48 (5.3%) ST and 16 (2.8%) LT (P = 0.020), STD: 7 (0.8%) ST and 11 (1.9%) LT (ns), urinary infections: 17 (1.9%) ST and 13 (2.3%) LT (ns), Mycobacterium tuberculosis infection 54 (6%) ST and 71 (12.3%) LT (P = 0.000), viral hepatitis 46 (5.1%) ST and 51 (8.9%) LT (ns), and HIV infection 0% (0%) ST and 2 (0.3%) LT (ns).

CONCLUSION Fever and diarrhoea were more common symptoms in ST and urogenital symptoms were more common among LT. Gastrointestinal infections and respiratory infections were more common diagnoses among ST, on the other hand, tuberculo-sis infection and extraintestinal parasitosis were more common diagnoses among LT. It is important to know what the most frequent symptoms and diagnoses among each traveller group are, because it changes the diagnosis orientation of the health provider.

PB 137
External review of outreach work with commercial sex workers (CSWs): an exploratory study on HIV/AIDS in Morocco
P. Huysgens,1 K. Alami2, I. Semini3 and O. Taiwi3
1Université Libre de Bruxelles, Politiques et Systèmes de Santé, Bruxelles, Belgium; 2Programme ONUSIDA/Maroc, Rabat, Morocco; 3UNAIDS Regional Support Team for the Middle East and North Africa [MENA – RST], Cairo, Egypt

OBJECTIVES Reviewing existing HIV/AIDS prevention/care experiences amongst CSWs; identifying significant anthropological characteristics of CSWs and understanding risk and dynamics of vulnerability; examining CSWs utilization of STI services; recommending best practices and strategies. This evaluation is in line with the review process of the national strategic plan and has been supported by UNAID.

METHODS Stakeholder and strategic analysis using operational qualitative research methods were used with about 30 actors key-players in the HIV/AIDS health care/prevention system. Health practitioners and politics, CSWs and outreach workers were interviewed through conversational interviews or during focus group-discussions. Qualitative data were indexed and organized before analysis.

RESULTS A wide range of social and professional profiles was found amongst CSWs of both genders. Vulnerability is explained through a variety of dynamics: stigmatization related to religion, law and morals, family dependence and marginalization, gender discrimination and rape, socioeconomic discrimination, migration and illegality, presence of international SW networks. Access to prevention and care is good but needs to be expanded in the country and especially towards more clandestine CSWs. A variety of channels and strategies have been proposed to improve access to prevention and care showing that the main obstacle was when focusing exclusively on SW.

CONCLUSION It is necessary to establish an approach centered on the needs and to reinforce the functional links between health and social actors by CSWs. Resources and competences are there but they need to be shared and distributed rationally at the national level. Intersectorial Regional Committees have to play a major role in decision making and planning. An innovative type of observ-atory has been proposed to support their work. Funded by UNAIDS and Belgian Co-operation Directorate.

PB 138
Abstract withdrawn.

Vector Control

PB 139
Molecular characterization of nitric oxide synthase in Anopheles culicifacies: a novel putative Plasmodium vivax immune responsive mechanism for refractoriness
H. K. Das1, S. Ray1, K. Raghavendra2, T. Adak1 and A. P. Dash3
1National Institute of Malaria Research (ICMR), Protein Biochemistry, New Delhi, India; 2National Institute of Malaria Research (ICMR), Molecular Entomology Division, New Delhi, India; 3National Institute of Malaria Research (ICMR), National Institute of Malaria Research (ICMR), New Delhi, India

BACKGROUND Innate immune-related anti-parasite defenses mounted by Anopheles can suppress the growth of Plasmodium in mosquitoes. Among the defense systems used by the mosquito against Plasmodium is the synthesis of nitric oxide (NO), catalyzed by an inducible NO synthase (iNOS). Nitric oxide produced by the action of an inducible Anopheles culicifacies NO synthase (AcNOS) may be central to the anti-parasitic arsenal of this mosquito. The recent demonstration that NOS gene elements kill malaria parasite in vitro and can be manipulated into the mosquito germ line to diminish their ability to transmit the malaria parasite offers new hope to explore the mechanism of refractoriness and fight against the disease.

RESULTS In the present study, we have identified and characterized expression of An. culicifacies NO synthase gene (AcNOS), which is highly homologous to characterized NOS genes and was detected in the midgut soon after invasion of the midgut by Plasmodium vivax at the beginning of blood feeding. Circulating levels of nitrite/nitrate in hemolymph, end products of NO synthesis, were found to be significantly higher in Plasmodium-infected An. culicifacies species B refractory mosquitoes. Increased levels of mRNAs (encoding iNOS) were observed 9–14 days after ingestion of an infected blood meal using RT-PCR analyses. Dietary provision of a NOS substrate L-arginine reduced action of an inducible NO synthase (iNOS). Nitric oxide produced by the action of an inducible Anopheles culicifacies NO synthase (Ac-NOS) may be central to the anti-parasitic arsenal of this mosquito. The recent demonstration that NOS gene elements kill malaria parasite in vitro and can be manipulated into the mosquito germ line to diminish their ability to transmit the malaria parasite offers new hope to explore the mechanism of refractoriness and fight against the disease.
parasite *Plasmodium vivax* and share anti-plasmodial defense with other *Plasmodium* species.

CONCLUSION Analysis of the molecular interactions between *Anopheles* culicifacies midgut epithelial cells and *Plasmodium vivax* parasites, as they migrate through midgut cells, revealed that AcnOS may be used as an additional effector gene to block the development of the malaria parasite in mosquitoes. Such responses may be important for the vectorial capacity of the mosquito, understanding of parasite-vector interactions and elucidate the mechanism of refractoriness.

**PB 140**

**Outcomes of delivery systems for ITNs: attributing coverage through a household survey in Ghana**

J. Webster1 and C. Marin2

1London School of Hygiene and Tropical Medicine, TARGETS Consortium, London, UK; 2Academy for Educational Development, NetMark, Washington, DC, USA

OBJECTIVES Mosquito nets and insecticide-treated nets (ITNs) for malaria prevention have been delivered through a wide range of systems, in both public and private sectors and mixes of the two. Despite considerable debate on which system or combinations of systems are most effective, no rigorous comparisons have been undertaken, and the debates are therefore not evidence based. We use data from a household survey in Ghana to develop a simple method of assessing the relative effectiveness of ITN delivery systems.

METHODS We reviewed net delivery systems in Ghana through published and grey literature. A household survey undertaken in five sites in five regions of Ghana (Accra, Keta, Kumasi, Wa, and Tamale) interviewed 1,500 women who were guardians of a child under 5 years of age. Questions were asked on source of net and used to link nets to the delivery sector (public, public-private, private, community) through which the net reached the household. We assessed coverage achieved by each delivery sector using three RBM indicators (household ownership, use by children under five, use by pregnant women). We also tested the validity of using cost and brand to distinguish between delivery through routine services and campaigns within the public sector. We used the equity ratio and concentration index to assess disparities in coverage across socio-economic quintiles.

RESULTS The survey identified 572 net-owning households owning 808 nets. Nets and ITNs have been delivered through a variety of channels in Ghana, all at a sub-national level and some of short duration. Levels of ownership and use of nets varied between survey sites and the delivery sector contributing to the greatest coverage also varied. Ownership and use was highest in Keta, with most coverage attributable to the commercial sector. Conversely, in Wa and Tamale, the public sector had the greatest impact. The socioeconomic disparities in coverage achieved through the public and private sectors were comparable. However, coverage with nets obtained through informal commercial sources was more equitable than through either formal commercial sources or routine services.

CONCLUSION We demonstrated that survey questions on source of net can be used to match nets in households to the sector through which they were delivered and therefore assess the relative effectiveness of different delivery systems. Attributing coverage measured in household surveys to specific delivery systems could provide the evidence base needed to inform international debates on the most effective and equitable systems for delivering ITNs to target groups.
OBJECTIVES Anopheles stephensi is considered as one of the major vectors of malaria in south and south west of Iran. In this study, we conducted a series of biochemical enzyme assay for detection of resistance and to define the underlined mechanisms involved in DDT and dieldrin resistance in An. stephensi.

METHODS Protein assay, Glutathion S-transferase (GST) activity and Monoxygenaze assay were measured. A one-way analysis of variance (ANOVA) was used to compare protein content and enzyme expression levels in susceptible and resistant strains.

RESULTS Results from biochemical assay on resistant strain to DDT and dieldrin and their comparison to sensitive one indicating the activity rate of GST enzyme is 8.66 and 1.64 respectively. Comparison of haem level of selected strains with DDT and dieldrin, which are representative of mixed function oxidae activity, indicating 2.28 and 1.22 fold increase in comparison to susceptible strain.

CONCLUSION GSTs have been reported to play a significant role in detoxification and resistance to DDT and other insecticides. The elevated MFO has relative contribution to DDT and pyrethroid resistance. The further studies are necessary to determine other mechanisms such as reduced penetration in DDT and dieldrin resistance.

PB 143 Insecticidal properties of tropical and temperate plants on mosquito malaria vector
D. K. Rocha1, O. C. Matos2 and A. J. S. Grácio1
1Instituto de Higiene e Medicina Tropical (IPMM), Medical Entomology, Lisboa, Portugal; 2Estação Agronômica Nacional, Fisiologia Vegetal, Oeiras, Portugal

OBJECTIVES Malaria prevention using anti-vectors measures is among the most important components of control strategies of malaria. However, the widespread and massive applications of insecticides frequently produce the risk of developing insect resistance and insecticidal residual for humans and the environment (WHO, 2005); Hence, plants can provide the wherewithal in the form of specific biodegradable alternatives to synthetic organic insecticides (Berenbaum, 1988; Jackson et al., 1990) in this study we evaluated the toxicity effects of plants with different geographical origin on the same species of insect.

METHODS We test ethyl acetate extracts of Thevetia peruviana from Cape Verde Island, Sambucus nigra from Portugal and essential oil of Azadirachta indica from Brazil and Juniperus communis from Portugal on third instars larvae of Anopheles atroparvus, the vector of malaria in Portugal. Data for the anti-mosquito potential were analyzed by means of computerized probit analysis, yielding a level of effectiveness at 50% and 90% mortality.

RESULTS The lethal concentration 50 values of T. peruviana extract was 0.13 mg/ml while that of S. nigra was 0.004 mg/ml, at 95% of confidence limits. Dilution of A. indica oil resulted in larvae mortality - CL50-200 μl/ml and J. communis oil - CL50 – 35 μl/ml, results obtained 24 h after exposition.

CONCLUSION The extract of S. nigra and the oil of J communis possess bioactive compounds which can cause 100% mortality 24 h after exposition. However, the phytochemical nature of these plants has to be explored and identified.

REFERENCES

PB 144 Water quality characteristics of Anopheles stephensi habitats and its resistance status to different insecticides in South part of Iran
A. Maleki1 and R. Ebrahimi2
1Department of Environmental Health, Kurdistan University of Medical Sciences, Sanandaj, Iran, Islamic Republic of Iran; 2Kurdistan University of Medical Sciences, Sanandaj, Iran, Islamic Republic of Iran

OBJECTIVES Malaria is one of the most important arthropod transmitted diseases in Iran, So that a series of studies on malaria transmission and control have been implemented in endemic malarious regions of Iran. In the present study, the chemical quality of water in the larval breeding habitats and the susceptibility levels of Anopheles stephensi to DDT 4%, dieldrin 0.4%, permethrin 0.75% and cyfluthrin 0.15% were investigated according to WHO methods in south part of Iran (Hormozgan and Fars provinces).

METHODS Water quality analyses were done according to standard methods for the examination of water and wastewater. The LT50 values of different insecticides were calculated using the probit regression line.

RESULTS The result of water chemical analyses of larval habitats showed that water pH range from 6.2 to 8.1, chloride from 0.7 to 132 mg/l, sulfate from 0.2–10.5 mg/l, nitrate from 0.2 to 4.3 mg/l, nitrate from 0.02–1.5 mg/l, and salinity from 91 to 122 mg/l. Results of the susceptibility tests showed that An. stephensi is resistant to DDT and dieldrin in both regions; however Hormozan strain showed the highest level of resistance to these two insecticides. The LT50 of Hormozgan strain against cyfluthrin with 5.2 and 3.4 min were the highest and the lowest values, respectively. The highest and lowest mortality rates of the Fars strain of An. stephensi were against permethrin with 6.3 and 0.73 min, respectively.

CONCLUSION It is concluded salinity is one of the important factors for breeding site. Furthermore, other chemical parameters of water also exerted some impact on mosquito larval population. Performing complementary tests with cyfluthrin on Hormozgan strain seems to be necessary.

PB 145 Analysis of D3 domain of 28S ribosomal DNA of Anopheles fluviatilis reveals two species of T and U in Iran
S. R. Naddaf Dezfoli1, M. R. Razavi1, M. Asmar4 and B. Ghazinezhad4, Malaria Research Group
1Puster Institute of Iran, Parasitology, Tehran, Iran, Islamic Republic of Iran

INTRODUCTION Anopheles fluviatilis is one of the known malaria vectors in India, Pakistan, Bangladesh and Iran. In India three cryptic species of this species designated as S, T and U have been identified based on polythene chromosomes examination. DNA-base method using ITS2 fragment analysis could reveal two
Human brucellosis is a common bacterial zoonosis. Immunotherapy with normal human gammaglobulin (intacglobin R) at doses of 100 mg/kg of weight subcutaneously and inter escapular. Results We found significant difference in the time of resolution of the active phase of the illness $P < 0.01$ when patients were compared with established therapy with antiparasitic and anti-inflammatory. The obtained results when we use hngg could also demonstrate spacing acute phases in the group of immunotherapy.

CONCLUSION Immunotherapy with normal human gammaglobulin (hngg) represent a new option for treatment in ocular toxoplasmosis.

PB 148
A new therapeutic management in acute uncomplicated brucellosis: comparison between three month Ofloxacin and Doxycycline based Regimens
A. Ali Khan1 and A. Heidarzadeh2

OBJECTIVES Human brucellosis is a common bacterial zoonosis in I.R. Iran and with current therapy has significant relapse rate and side effects. However, the optimal duration of therapy has not been determined and side effects cause poor compliance. This study focused on comparison between effects and complications of two therapeutic regimens.

METHODS In this single-blind randomized trial, 78 uncomplicated brucellosis patients were recruited and allocated into two tail of study by fixed block random allocation method. (39 number in each tail of trial). Patients of Doxycycline tail were treated with streptomycin, doxycycline plus rifampin (streptomycin plus Doxycycline for first month and Doxycycline plus rifampin for second and third months) and patients of Ofloxacin tail were treated with streptomycin, Ofloxacin plus rifampin (streptomycin plus Ofloxacin for first month and Ofloxacin plus rifampin for second and third months) for 3 months. Therapeutic outcome was evaluated by measuring efficacy, relapse rate and drug GI and skin side effects. Acute brucellosis diagnosed by serology (wright and 2ME tests) at the start, 3–6 month after drug therapy. The data were analyzed by Stata 8.0 software. The proportions were compared by Fisher exact test. Significance level was 0.05. The results were reports as proportion (standard error).

RESULTS At the end of study 75 patients (96.1%) were completed the treatment and follow up process (38 number in Ofloxacin and 37 number in Doxycycline tail). The curative results were similar in Doxycycline and ofloxacin tail (100%). The complication rate
had significant different in Doxycycline and ofloxacin tails, 48.6 (8.3) vs. 13.2 (5.5)% respectively. (P < 0.001, Fisher Exact test). The recurrence rate in both group during 6 month follow up after complete treatment process was zero.

CONCLUSION It seems that duration is more important factor in the management of the brucellosis. Treatment of acute uncomplicated brucellosis in human for 3 month had no relapse and decreased side effects with ofloxacin included regimen.

METHODS Four BALB/c mice were immunized by GAVAC vaccine and their spleen cells were fused with NS-1 myeloma cell line. The resultant clones were analyzed by ELISA and Western blot. Cell distribution of antigens was also checked by indirect immunofluorescent technique.

RESULTS Clone 4E11 reacted with 36 and 45 kDa molecules of midgut epithelial cells of Hyaloma anatolicum anatolicum in Western blot analysis. These molecules showed speckled distribution on tick midgut epithelial cells by indirect immunofluorescent technique.

CONCLUSION Our results displayed presence of two 36 and 45 kDa molecules in epithelial cells of Hyaloma anatolicum anatolicum which contain similar structures to Bm86. These Bm86-like molecules may contain similarities to HA98 (known Bm86-like molecule) which need further investigation.

### PB 149

**Serologic prevalence of Toxoplasma gondii infection in women 15–44 years old in Republic of Croatia**

M. Sviben1, D. Horvat-Krejči1, E. Minani-Missoni1, D. Karlovic-Marinkov1 and T. Vilbig-avlek1
1Croatian National Institute of Public Health, Zagreb, Croatia

**OBJECTIVES** In our work we present results of Toxoplasma gondii seroprevalence study in women of childbearing age from Zagreb, Croatia. Seronegative pregnant women have the risk of developing acute toxoplasmosis and their child risk to develop congenital toxoplasmosis.

**METHODS** During the year 2006 in our study we tested 471 women of childbearing age (15–44 years old) on Toxoplasma gondii specific antibodies. Three groups were analyzed according to their age: 15–24 years of age (151), 25–34 years (184) and 35–44 years of age (136 women tested). IgG ELISA kit for quantitative antibodies detection, produced by Nova Tec Immundiagnostica GmbH, Germany, was used for testing. Tests were done in accordance with producer’s recommendations.

**RESULTS** We found that 178 (38%) serum samples were positive on Toxoplasma gondii specific IgG antibodies. Age distribution of seropositive women was as follows: 15–24 years – 47 (31%) positive samples; 25–34 years – 64 (35%) positive samples; 35–44 years – 67 (49%) positive samples.

**CONCLUSION** The study showed that two-thirds of women in age group 15–34 years and one half of women in the age group 35–44 years don’t have specific antibodies against Toxoplasma gondii. Acute toxoplasmosis in seronegative women could end with congenital toxoplasmosis of a child. That could have devastating and permanent consequences on a child and family. By appropriate testing of women, especially pregnant ones, the congenital toxoplasmosis could be completely prevented if appropriate methods were used.

### PB 151

**Annual distribution of Lymnaea truncatula Muller, 1774 (mollusca, pulmonata, lymnaeidae) in Portugal**

P. M. Ferreira1, M. M. Calado1, C. C. Ferreira1 and M. A. A. Grácio1
1Instituto de Higiene e Medica Tropical, Medical’s Helminthology and Malacology Unit/UPMM, Lisbon, Portugal

**OBJECTIVES** Lymnaea truncatula Muller, 1774 (Mollusca, Pulmonata, Lymnaeidae) is a freshwater snail with a great interest, not only on the malacologic view, but also due to the role of this specie on parasite transmission (Bargues and Mas-Coma, 1997). In Portugal L. truncatula is the only intermediate host of Fasciola hepatica Linnaeus, 1758, a liver fluke with a great importance on medical and veterinary medicine (Grácio, 1992). The objective of the present study was to assess the annual distribution and abundance of Lymnaea truncatula in four Portuguese districts as well as the relationship with climatic/environmental factors. These results were obtained between January and December 2006.

**METHODS** Both water and mollusc samples were collected, in four Portuguese districts – Lisbon, Leiria, Évora and Coimbra. Whenever present, animal faeces were also collected to search for F. hepatica eggs. All habitats were followed up monthly between January and December 2006. In the laboratory, snails were identified, counted and exposed to artificial light to search for cercariae elimination. Some physico-chemical parameters and heavy metals were measured on collected water.

**RESULTS** Several habitat types were identified, ranging from small streams, rice fields and even water tanks. Lymnaea truncatula was collected in 25 of 38 (65.8%) identified habitats. It was observed an increase of the number of collected snails from January to March followed by a decrease until June/July. The number of collected snails starts rising again at the end of the summer/beginning of the autumn, September/October respectively, up to December. In spite of the physico-chemical variations observed on collected water, statistic analyses didn’t show any relation with the number of collected snails.

**CONCLUSION** The snail abundance and dynamics observed throughout the year seems to be dependent of the water levels in each habitat. Many of visited habitats were temporary and became dry at the summer months. The aestivation properties of these snails are crucial for their survival under unfavourable environmental conditions. Cercariae elimination was not observed from collected L. truncatula and all analysed faeces were negative for F. hepatica, nevertheless we should be on the alert and search for new habitats where infection can occur, considering that fascioliasis keep existing in both humans and animals in Portugal.

work supported by the funding from FCT/POCI/CLI/5797/2004.

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### PB 150

**Production of monoclonal antibody against Bm86 a known vaccine candidate molecule of Boophilus microplus tick to find similar molecules in other tick: Hyaloma anatolicum anatolicum**

A. Miree1
1Razi Vaccine and Serum Research Institute, Biotechnology, Karaj, Iran, Islamic Republic of Iran

**OBJECTIVES** This study was conducted to find vaccine Candidate molecules in Hyaloma anatolicum anatolicum by usage of monoclonal antibody against known vaccine molecule; Bm86, which is a vaccine molecule primarily found in midgut epithelial cells of Boophilus microplus. Immunological control by terms of vaccine against tick is developed within two recent decades and the known vaccine Candidate molecule; Bm86 has been widely used in commercial vaccines (GAVAC and TickGARD) with great success.
PB 152
The epidemiology and clinical presentation of Brucellosis in 29 patients referred to a private clinic (2006) in Rafsanjan, Southeast of Iran
N. Zia sheikholeslam1, F. Iranmanesh2, Z. Salem3 and M. Tashakori4
1Rafsanjan Medical University of Medical Sciences, Infectious and tropical medicine, Rafsanjan, Iran, Islamic Republic of Iran; 2Medical University of Rafsanjan, Neurology, Rafsanjan, Iran, Islamic Republic of Iran; 3Medical University of Rafsanjan, Social Medicine, Rafsanjan, Iran, Islamic Republic of Iran; 4Medical University of Rafsanjan, Rafsanjan, Iran, Islamic Republic of Iran

OBJECTIVES Brucellosis remains as an important zoonosis disease worldwide. Its clinical presentations can be extremely varied and definitive signs to indicate the diagnosis can be lacking. It still represents a major public health problem in many countries. In Iran also, it is common. This study represents the epidemiology and clinical presentation of brucellosis in 29 patients referred to a private clinic (2006) in Rafsanjan (south east of Iran).

METHODS This study was descriptive. A questionnaire was completed by an infections disease specialist of all of the patients referred to a private clinic and all of them were examined by that specialist.

RESULTS 29 patients were studied and all of them had positive Wright test. 55/2% of them was male, 41% had positive familial history, 75/9% had exposure to animals and 75/9% consumed non-pasteurized milk. 31% were housekeepers, 24/1%; husbandman, 17/2%; farmer and 27/7% were workers and students. Based on clinical presentation: in 89/7% of cases the course of the disease was chronic. 69% had chills, 89/7%; perspiration, 100%; bone pain, 75/9%: low back pain, 89/7%; arthralgia, 13/8%; urinary symptoms, 20/7%; abdominal pain, 3/4%; diarrhea, 27/6%; constipation, 19%; loss of appetite, 86/2%; malaise, 54/3% had tender- ness on lumbar vertebrae.

CONCLUSION Brucellosis is prevalent in Rafsanjan and patients have many different presentations. In order to prevent brucellosis, vaccination of animals must be done more seriously and more educational efforts should be done about consuming dairy products.

PB 153
Tick bite and lyme disease in Belgrade
N. Pavlovic1, V. Djerkovic1 and V. Babic-Dunic2
1Institute of Public Health Belgrade, Center for prevent and control disease, Belgrade, Serbia and Montenegro; 2Institute of Public Health Belgrade, Center of Microbiology, Belgrade, Serbia and Montenegro

OBJECTIVE To show demographic characteristics persons with tick bite who live in Belgrade and to compare the epidemiologic characteristics of those ones who have Lyme disease with those ones who do not have the disease.

METHODS We prospectively studied cohort of persons who got bitten in period of 3 years(1997–1999) in area of Belgrade. We have used data from the Central Registry for the cases of Lyme disease and of persons with tick bite (Institute of Public Health Belgrade) and clinicians reports. The criteria for diagnosis were: confirmed tick bite and/or being in endemic area; Erythema migrans or another typical clinical manifestation and serologic results (ELISA and Western Blot). To collect the relevant data we have used epidemiologic questionnaire. Results of serology tests were taken from the findings by authorized microbiologic laboratories.

RESULTS In the cohort was 331 persons with tick bite, both sexes (M: F = 1:2), in all age groups mainly aged over 40(63.5%). Mostly they were officers, pensioners and workers. The tick bite happened equal in the recreational activity and also everyday life activity. In Institute of Public Health were more calls from the urban area of Belgrade (86.7%) than from the rural. Those from the urban area had mostly bites from the lawns, parks and woods, and those from the rural areas had mostly bites from gardens and meadows. The biggest number of tick bite were in period April–July, with pick in June (34.9%). The most often ones were the tick bites on the legs. Ticks were remove from the skin usually in first 24 h after bite. Persons affected by the disease were in the bite time significantly more spending time in gardens, and healthy ones on lawns and parks. Unknown duration and duration of tick attachment on the skin from 25 to 48 h were significantly more registered with the ones with disease. Disease ended in first stage in 78.9% of the cases and Erythema migrans is most frequent clinical manifestation. In the second stage (21.2%) were involved skin (10.2%), heart (4.4%), nervous (3.6%) and locomotor system (2.9%). Antibodies to Borrelia burgdorferi were detected in 54.5% of the cases who had Lyme disease.

CONCLUSION Our results are showing of risk for Lyme disease after tick bite begin on green grass in urban area of the Belgrade, significantly more begin in the gardens than in the lawns, and if it has been past 25–48 h from the moment of attachment.

PB 154
Zoonoses in Kosovo
A. Kalaveshi1, L. Gashi1, N. Ramadani1, G. Mulliqi2 and T. Osmani-Vllasoll3
1National Institute of Public Health of Kosovo, Epidemiology, Pristina, Albania; 2National Institute of Public Health of Kosovo, Microbiology, Pristina, Albania; 3Medical Faculty, Clinic for Rehabilitation, Pristina, Albania

OBJECTIVES Aim of this study is to present epidemiological situation and characteristics of more common zoonoses in Kosovo.

METHODS For descriptive analysis were used the data of the Kosovo surveillance system (KO – Surv) as well statistic test (h2 test).

RESULTS Zoonoses have been known to be endemic in Kosovo since 1954. Between 1990–2006 in Kosovo, 2875 cases of zoonoses were registered and 59 deaths (case fatality ratio 2%). The cases are registered all over the territory. Statistical test (h2 test) shown us the significant difference (P < 0.01), 99.7%, before year 1999 and after 2000. The numbers of cases are increased after year 2000. The main route of transmission was meaty, milk, not adequately stored food and water from wells (uncontrolled and not disinfected). The most affected age-groups during these period (investigated group), n = 2875 were: age group 20–39 years with 1108 cases or 38.5% and age-group 40+ with 852 cases or 29.6%. The gender distribution was dominant among males 1560 cases or 54.2%. Seasonal distribution of frequency is the almost equal during all months.

CONCLUSION Kosovo is an endemic zone of this group of disease since 1954 where the first cases were registered. The most common zoonoses registered at Kosovo are Anthrax, Leptospirosis, Tularemia, Brucelosis, CCHF, HFRS. All age groups were affected. Males were more affected, accounting for 54.2% of total cases. Due to high infectiousness, severe clinical picture, and high lethality it was necessary to determine case
frequency, geographic spread and risk factors in order to initiate preventive measures.

**PB 155**
Protein analysis of plerocercoid larvae and juvenile worms of Spiorometra erinacei using 2D-gel electrophoresis
J.-h. Kim1, Y.-j. Kim2, Y. M. Bae3, S.-T. Hong1, M.-H. Choi1 and W.-M. Sohn2
1Seoul National University, Parasitology and Tropical Medicine, Seoul, Republic of Korea; 2Kyungpung National University, Parasitology and Institute of Health Sciences, Jinju, Republic of Korea

OBJECTIVES This study was performed to compare stage-specific protein expression between the two developmental stages, plerocercoid larvae (sparganum) and juvenile worms of Spiorometra erinacei, and to understand the genetic mechanism of cestode growth.

METHODS Plerocercoid larvae were collected from subcutaneous tissues of rats at 3 months of infection with plerocercoid, and juvenile worms were recovered from the small intestine of cats experimentally infected with plerocercoid larvae for 8 days, respectively. After homogenizing larvae and juvenile worms, supernatant were obtained using centrifugation. We determined isoelectric point (IEP) of proteins on immobilized pH gradient (IPG) strips and performed two-dimensional gel electrophoresis.

RESULTS Protein spots of larvae were observed within 6.5–175 kDa (pH 3–10) and those of juvenile worms were mainly 32–175 kDa (pH 3–10). Protein fractions showing different expression between the two stages were analyzed using the MALDI-TOF system and peptide protein fingerprints were analyzed using NCBI database. In larvae, eight proteins were identified, including 14-3-3 protein, methyl-accepting chemotaxis protein, and cystein-S-methyl-transferase and zinc finger protein. In contrast, fourteen proteins were identified from juvenile worms, including serine/threonine protein kinase, heat shock protein 70, zinc finger-like protein, multi-drug resistant protein and ubiquitin.

CONCLUSION Differentially expressed proteins between the two stages should be further evaluated to explain the growth of S. erinacei according to the stages.

**PB 156**
Chikungunya virus disease in Reunion Island: evolution of rheumatic manifestations during the first 12 to 18 months of infection
D. Sisoko1, F. Moscetti2, E. Ballesterd3, M. Ledrans4 and V. Pierre1
1InVS-Cire Reunion Mayotte, Saint Denis cedex, France; 2Dass Mayotte, Equipe SEROCHIK-MAY, Mamoudzou, France; 3Centre Hospitalier Mayotte, Laboratoire, Mamoudzou, France; 4Institut de veille sanitaire (InVS), Cire Reunion Mayotte, Saint Denis, France; 5Institut de veille sanitaire (InVS), Dpt International et tropical, Paris, France

OBJECTIVES Since its introduction in 2005, Chikungunya Virus (CHIKV) has expanded rapidly across the borders of southern west islands of Indian Ocean. The true extent of symptomless infections was unknown. As CHIKV, dengue virus (DENV) is mosquito-borne infection transited by Aedes species. Despite the circulation of (DENV) in this region, there are no estimates of DENV seroprevalence among the overall population of Mayotte. Our objectives were: i) to estimate CHIKV seroprevalence; ii) to determine the extent of asymptomatic infections in this population; iii) additionally, to assess the extent of previous exposure to DENV in Mayotte.

METHODS Design and setting: Cross sectional sero-survey in Mayotte Population sampling: we selected 1154 individuals more than 2 years old in using multi-stage cluster sampling procedure. Intervention: From November 9 to December 27, 2006, trained survey teams made one to three visits to each selected house. All eligible residents (or guardian for those <18 years old) were invited to participate by giving signed consent, responding to a questionnaire and providing a blood sample. Serum samples were tested for IgM and IgG antibodies (CHIKV), only IgG antibodies were tested for DENV. A clinical definition of CHIKV was based on self-reporting by the participant time period of the patient from March 2005 to day of enrollment. Our protocol was approved by the Committee for Protection of Persons (Bordeaux-Oversea).

RESULTS Of 1154 participants, 499 were male, the median age was 24 years. CHIKV: The overall prevalence of CHIKV was v-chik; and iii) consented orally to participate in the study. Data source: Patients were identified through outbreak surveillance database. All eligible patients with informed phone number were invited to participate. Intervention: Patients were interviewed by telephone on self-perceived of rheumatic symptoms over 12 to 18 months after v-chik illness onset.

RESULTS We recruited 147 subjects, 69% were female. The median age was 52 years (IQ 25–75: 43–63). At 30 days after onset, 63% of participants continued to have symptoms. Between 12 and 18 months after acute infection, 84 participants (57%) reported rheumatic symptoms. Of the 84 patients, 53 (63%) reported permanent trouble while 31 (37%) had recurrent symptoms. In univariate and multivariate analyzes, younger age < 45 years vs. age ≥ 45 years (OR = 3.0, 95% CI 1.9–4.7) and absence vs. presence of underlying illness (OR = 2.3, 95% CI 1.3–7.1) are predictors of achieving a full recovery.

CONCLUSION An unexpectedly high rate of persistent rheumatic symptoms was found in a unselected cohort of patients who experienced v-chik disease in Reunion Island. Efforts aimed at preventing v-chik infection should focus on older persons who are more likely to present long term sequela of this illness. Further studies are needed to more accurately assess the long term outcome particularly the disability related to this emerging virus infection.
Our findings suggest that a consequent number of congenital toxoplasmosis caused by the intracellular parasite Toxoplasma gondii is a serious infectious disease of man affecting both pregnant women and her offspring. Most congenital infections occur when a none-immune susceptible woman affected by the parasite during her pregnancy for the first time. Therefore, the knowledge of distribution of anti-Toxoplasma antibodies among women in child-bearing ages and/or during pregnancy is important. The present study was conducted to determine the seroprevalence of anti-Toxoplasma antibodies among the pregnant women of the province in first trimester of their pregnancy and to investigate the potential risk factors affecting the infection.

Methods Three hundred and eighty-four pregnant women in the first trimester of their pregnancy were selected randomly and their sera were examined by IFAT method. The specific conjugated Total anti-human-globulin was purchased from Dako Company, Denmark and the Toxoplasma antigens derived from RH strain were provided by Faculty of Health, Shahrekord University. Data processing was carried out by SPSS software ver.11.0.

Results One hundred and six sera out of 384 (27.6%) were positive for the Total anti-Toxoplasma antibodies with levels between 1/20-1/2560. There was a significant correlation between the sero-positivity of subjects and the variables, age, cat ownership and consumption of lamb meat (P < 0.05).

Conclusion The present study showed that only a small proportion of pregnant women living in this area have infected by the parasite and the majority of this population and women in child-bearing ages are susceptible to Toxoplasma infection whether during the rest of pregnancy or their further pregnancies. It may be concluded that the risk factors for Toxoplasma infection in pregnant women are increasing age, cat ownership and lamb meat consumption. Therefore, it is mandatory to reduce the potential risk of the infection in susceptible none-immune pregnant women and women in child-bearing ages through serological surveillance during pregnancy, implanting the health education programs for preventing the infection and avoiding from the sources of infection (e.g. cats or raw or undercooked lamb).

Leptospirosis

PB 159

Serological diagnosis of leptospirosis: peptide ELISA vs. MAT

F. Aviat1, S. Rocheserou-Roulet2, C. Branger1, J. Bellin1, C. Lefur1, J.-M. Estavoyer1, B. Chatre2, J.-L. Orsonneau3 and G. Andre-Fontaine1

1Ecole Nationale Vétérinaire de Nantes, Unité de Bacteriologie Medicale et Moléculaire des Leptospires, Nantes Cedex, France; 2Centre for Infectious Diseases, Biodesign Institute, Arizona, USA; 3CHU Saint Jacques, Maladies Infectieuses et tropicales, Besancon, France; 4Virbac, Carros, France; 5CHU Hotel Dieu, IBH, Nantes, France

Leptospirosis is a zoonotic disease with a worldwide distribution. Today, the golden standard method for the human serological diagnosis is MAT which detects agglutinating antibodies after at least two weeks of infection. Early diagnosis tests at the beginning of the disease are highly needed.

Objectives We identified a specific peptide, called herein ‘PP’, which can be used as antigen in ELISA. We compared specificity and sensitivity of this peptide ELISA, and MAT to confirm diagnosis of leptospirosis cases. Then, we compared PP-ELISA and MAT performed with serovars of Leptospira interrogans to ELISA and MAT performed with Leptospira biflexa Patoc.

Methods We tested by IgM and IgG PP-ELISA 162 human sera: 85 patients with a known history of leptospirosis and 77 sera without any known leptospirosis history (control group). We used a synthetic peptide ‘PP’ as antigen in ELISA. We compared specificity and sensitivity of this PP-ELISA (IgM, IgG) to MAT. We demonstrated that PP-ELISA was more precocious than MAT.

Results Concordances of PP-ELISA and MAT were studied on leptospirosis cases. In this study, PP-IgM-ELISA concordance with MAT was low (43%) but higher with PP-IgG-ELISA (85%). In other respects, in relation to hospitalization delay, we demonstrated that PP-ELISA was more precocious than MAT. We showed that MAT and ELISA performed with Leptospira biflexa Patoc compared to ELISA and MAT performed with leptospirosis diagnosis.

Conclusion The response of anti-Hap1 antibodies, and consequently anti-PP antibodies, is earlier than agglutinating antibodies against structural antigens. MAT and PP ELISA are complementary methods. The precocity of Hap1 expression by only pathogenic leptospires is a good marker of acute leptospirosis. PP-antigen is a real new promising tool which can be very helpful in the leptospirosis diagnosis.

References


PB 160

ABO histo-blood group phenotypes and falciparum malaria

M.-P. Lescartelas1, C. Donkor2, E. Senga3, S. Owen4, J. O’Donnell4, J. Bunn5, B. Bosch-Capblanch6 and B. Brabin1

1Liverpool School of Tropical Medicine, Child and Reproductive Health Group, Liverpool, UK; 2Liverpool School of Tropical Medicine, Child and Reproductive Health Group, Kumasi, Ghana; 3Department of Biochemistry University of Malawi College of Medicine, Blantyre, Malawi; 4Laboratories, Medical Research Council, Banjul, Gambia; 5Institute of Molecular Medicine, Trinity College Dublin Haemostasis Research Group, Dublin, Ireland; 6Department of Paediatrics, Medical College, Blantyre, Malawi; 7Liverpool School of Tropical Medicine, International Health Group, Liverpool, UK

Objectives The aim of this analysis was to estimate the association of ABO blood group phenotypes and P. falciparum malaria.
malaria in pregnant and not pregnant subjects, and to provide an overview of the mechanisms which underlie the contribution of ABO blood groups to malaria pathogenesis.

METHODS ABO phenotype and placental malaria risk was assessed from two cross-sectional studies in Malawi and The Gambia. ABO phenotype and severe malaria risk in children was assessed for 1012 children (6 months to 6 years) admitted with severe malaria in Kumasi, Ghana. The literature was reviewed to identify all studies of ABO phenotype and malaria. A meta-analysis using RevMan was completed.

RESULTS The risk of placental infection was significantly associated with the blood group O phenotype with a lower risk of active infection in blood group O multigravidae compared to primiparae. In Ghanaian children, we observed that blood group O was associated with reduced levels of blood lactate, (raised levels are a marker for disease severity). In the meta-analysis most studies reported significant differences that were consistent with the association of the A phenotype with a higher risk and the O phenotype with reduced risk for malaria severity. ABO phenotype was not significantly related to parasite prevalence. The geographic distribution of the O phenotype in Africa was consistent with selection pressure related to malaria transmission. In terms of mechanisms, several ABO associations with molecules involved with RBC invasion pathways suggested that ABO phenotype was central to the integrity of the RBC invasion process and could influence cytoadherence through effects on platelet function or endothelial adhesion mediators.

CONCLUSION There are clear associations between group A and clinical severity, and group O and milder disease in children. Both placental malaria datasets support an association in similar magnitude between blood group O and induction of parity-specific immunity to placental malaria in multigravidae. Research into the relationship between the ABO blood group phenotypes and malaria, may open a new insight into the glycomicrobiology of infectious diseases and contribute to a wider understanding of malaria pathogenesis.

PB 161 Identification of A2 proteins in Leishmania infantum from canine isolates ofMeshkinshahr, northwestern Iran

M. Farahmand1, H. Nahrevanian1, M. Assmar1, M. Mohebali1 and Z. Zarei1
1 Pasteur Institute of Iran, Department of Parasitology, Tehran, Iran, Islamic Republic Of

OBJECTIVE Visceral leishmaniasis (VL) is characterized by diversity and complexity of clinical manifestations ranging from asymptomatic infection to life threatening illness. In Iran, VL is endemic in some areas of northwest and south. Leishmania infantum is major parasite, children are susceptible and dogs are key reservoirs. Some stage specific antigens in VL parasites play a role in the pathology and or protection. A family of A2 proteins ranging from 42 to 100 KDa is located mainly in the cytoplasm, which is considered to be virulent for the survival of leishmania in the mammalian host. In the present study, the presence of A2 proteins was investigated in isolates of canine L. infantum from Meshkinshahr, northwest Iran.

METHODS An A2 protein was produced experimentally in cultured promastigotes by a combined temperature and pH shifts.

RESULTS Western blot analysis revealed three major bands with molecular weight ranging from 46.8 to 63.8 KDa in various VL strains.

DISCUSSION It is indicated that A2 proteins expressed predominantly in the amastigote stage of L. infantum isolates from canine isolates of Iran.
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