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Time: 09:00-09:45
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The Challenges of Travel Medicine in the 21st Century

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Travel medicine has emerged as a new field of medicine, moving to an evidence based body of knowledge concerning risk assessment and measures to protect the health of travellers. Most of travel medicine concentrates on tourists from North America and Europe leaving for international destinations, many being low or middle income countries involving a higher risk of acquiring infectious diseases. This paradigm is changing rapidly. With the increasing mobility of populations, whether migrants, tourists, businessmen, students, soldiers, humanitarian workers, pilgrims, refugees or medical tourists, it is becoming evident that the diversification of globally mobile travelers is posing new challenges to the travel medicine community. Perception of risk, behaviour, exposure to risks and access to health services vary enormously. Nonetheless all contribute to the global circulation and potential spread of known or emerging pathogens. From an epidemiological and public health perspective a more global encompassing approach to health issues related to population mobility is urgently needed.
With globalisation new emerging economies are growing in many parts of the world, new patterns of travel and mobility appear. The sharpest increases in travel are observed in Asian and in Latin American regions where intra-regional and in-country travel is rising. The majority of these new travellers are urban dwellers often unaware of the existing risks gradients within their own country when they move to rural destinations. Thus travel medicine has to expand from the current international/across boarders approach to a practice based on risk assessment analysis and prevention across different prevalence gaps, wherever and for whomever they are of relevance. Climate change, security issues, economic fluctuations, demographic shifts and the threat of emerging diseases will also reshape the future of travel and mobility trends. All will influence travelers' health and pose new challenges to travel medicine in the forthcoming decades.

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Development of Travel Medicine in Latin America

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Approach to pre-travel consultation

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La consejería pre-viaje debe considerar varios aspectos: la persona que consulta por lo general no está enferma, no entiende muy bien la necesidad de una consulta médica.
El Médico debe considerar condiciones del viajero (edad, sexo,posible embarazo, patologías previas y condiciones actuales, medicamentos que ingiere alergias, etc).
Es relevante el itinerario antes de llegar al destino y actividades en zona a visitar, condiciones de alojamiento, comida, y transporte.
El Centro debe contar con Vacunatorio ad-hoc , productos necesarios para profilaxis de Malaria, picadura de mosquitos, botiquín del viajero, purificadores de agua.
Se debe estar en conocimiento de la geografía del destino y los posibles riesgos de salud y la maneras de prevenirlos

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Traveling with Kids

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Travelling with kids is a great adventure that offers opportunities for fun and to possibility to broaden ones cultural outlook. But travel is not just fun, some risks related to the travel exist and the whole family should be prepared to prevent them or to have early treatment. Preparing a trip with kids involves considering several aspects, such as age, underlying diseases and destination. The main aspects we are going to review are: safety travel (motor vehicles, safety water and food, air travel, sun protection, motion sickness, high altitude, animal bites), immunization, prevention of arthropods borne diseases and diarrhea. Air transportation can produce boredom and ear pain. No pharmaceutical interventions have been proved to be good at preventing painful earache. Sedation is controversial but if it is required, diphenhydramine is considered a safe drug. Children should have their immunization schedule updated at the time of the trip. Insect borne disease can be prevented by using DEET repellents. DEET concentration 30-35% is safe for use in children. It should not be applied around the eyes, mouth or on the hands and forearms of young children. Malaria chemoprophylaxis can be used in children and are licensed for infants. Mefloquine, chloroquine and malarone are the alternatives for children under 9 years old. Doxycicline can be used after that age. Maternal chemoprophylaxis is not enough for breastfed infants. Difficulties for children using chemoprophylaxis include bad taste, luck in pediatric preparations and toxicity risks. Diarrhea prevention includes safety in water and food consumption. Therapy should center on oral hydration. Self-treatment of travelers' diarrhea with antibiotics should be considered, but antimotility agents should be avoided. Travel offers good experiences for children and their families. Pre-travel evaluation and protective interventions can reduce the health risks of travel.

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The Elderly Traveler

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Old age has been divided into different groups: biological, physiological, emotional and functional. Advances in science and technology, as well as improvements in health services available, have played an important role in the increasing number of elderly in the world. The 20 th century saw an increase in both anticipated and actual life expectancy figures, a phenomenon described as the 'aging population' . In the year 2020, life expectancy at birth is predicted to reach 70 .Travel satisfies old age people needs for adventure in many ways. Most personal problems stem from rushing to meet a schedule of pleasure and joy. And during travels everything is permitted, specially food and sedentary activities, most of them due to physical and health limits. But how far can they go traveling? If they have to share their travel with prescribed medicines; diabetes; neurological problems; obesity and diets; vision and hearing loss; walking limitations *versus* jet lag; altitudes problems; airport/aircraft long stay/ pulmonary thromboembolism risks; lazy attitudes during cruises; infection disease risks and adult immunization status.

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Type: Invited Presentation

Central America and the Caribbean: Dengue and P.Vivax malaria

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In recent decades, the incidence, distribution and clinical severity of dengue have increased dramatically in most tropical and subtropical areas worldwide. As a consequence, and due to the expanding international tourism, health care providers in travel clinics of developed countries are increasingly confronted with dengue, reflecting its global impact. No specific prophylactic or therapeutic agents exist for dengue infections.
All four serotypes of dengue viruses are widespread in Central America and the Caribbean basin. Dengue is most common in cities but can be found in rural areas. It is rarely found in mountainous areas above 4,000 feet.
Dengue fever is the most common cause of fever in travelers returning to the USA from the Caribbean and Central America. In some case studies, dengue has been the second most common cause of hospitalization (malaria is the most common) among travelers returning from the tropics. Infection rates (based on anti-dengue serology) among febrile travelers returning from those areas may range from 2.9% to 8.0%. Similar results have been reported in travelers returning to Europe.
Persons travelling to areas where dengue is endemic should avoid exposure to mosquitoes, and health care providers should consider dengue as a differential diagnosis in febrile travelers returning from the tropics after discounting malaria. Surveillance of imported dengue is crucial to monitor the risk of infection for travelers and to strengthen clinical awareness of the disease.
The risk for a traveler acquiring malaria differs substantially from different areas within the region and from traveler to traveler, even within a single country. In a large series of 10,745 cases of malaria among U.S. residents reported to CDC from 1997 through 2006, 1,427 (13.3%) were acquired in the Caribbean and Centra/South America. Malaria has been reported in about 1 per 100,000 European travelers to Central America and the Caribbean.
The risk of vivax malaria may be relatively high in some Central American countries, including several large or middle size cities. Travelers to malaria-risk areas, including infants, children, and former residents of Mexico and Central America, should take an antimalarial drug. There is no chloroquine resistance in Central America, so this drug can still be recommended for travelers to these countries.
Malaria is not a risk in most of the Caribbean islands, but *P. falciparum* is endemic to most of Haiti and some areas of the Dominican Republic, where there is variable to low risk. Malaria in these areas is still sensitive to chloroquine, which is therefore recommended for prevention.

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Hantavirus and Bartonellosis

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Yellow Fever transmission in Brazil

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Yellow fever (YF) is an arboviral disease caused by a virus from *Flaviviridae* family and genus *Flavivirus* endemic in tropical regions of Africa and South America. Transmission occurs after infected mosquito bite, genera *Aedes* and *Haemogogus*. Urban YF was eradicated in Brazil in 1942, since than sporadic wild transmission has been maintained in country endemic area. From 1989 to 2008, 546 human confirmed cases YF were reported including 241 deaths (case fatality rate 44, 1 %) in Brazil. During this period north and midwestern region were responsible for the highest number of cases registering human cases almost every year. Beginning in 1999, YF virus underwent a geographic expansion into southeast, south and midwestern region - Federal District, Goias, Sao Paulo, Minas Gerais, Parana and Rio Grande do Sul states – related to outbreaks in areas that were silent for several decades and outside Amazon area. This study describes the re-emergence of YF virus in enzootic cycles involving mosquitoes, primates and humans cases in midwestern, southeast and south region during 2008 and 2009. During this period and explosive recording of monkey's death was registry by health authorities with laboratory confirmed epizootics. Human cases were associated with leisure and work activities in rural areas and occurred among unvaccinated person. Brazilian Ministry of Health considered it as a public health event of national concern according to the International Health Regulations (2005). Epidemiological control measures were adopted including entomologic control and assessments, monkey deaths surveillance investigation and mass vaccination campaigns were implemented. YF vaccine-associated viscerotropic and neurotropic disease were reported. Those activities were important to establish an effective intervention to control and prevent future outbreaks. Public health authority's interest has been awakened by reporting early identification of YF virus circulation to understand the potential geographic virus expansion and re-emergence.

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The Amazon II: Leishmaniasis and Chagas Diseases

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Chagas disease and leishmaniasis are the most important vector-borne protozoan NTDs. Almost all of the 8-9 million cases of Chagas disease (with approximately 50,000 new cases annually) occur in poor rural and, increasingly, many new urban and peri-urban areas of Latin America. Of these cases, an estimated 5.4 million people will develop chronic Chagas heart disease, while 900,000 will develop megaesophagus and megacolon. In LAC, the burden of disease caused by *Trypanosoma cruzi* infection is between five to ten times greater than malaria. Chagas disease is disproportionately represented among people living in poverty. The disease has also emerged or re-emerged in areas of conflict in Chiapas State, Mexico and Colombia. The major approaches to control including improved case management and vector control programs, together with housing improvement through regional programs. In LAC, both cutaneous and visceral forms of leishmaniasis result primarily from zoonotic transmission from either canine or sylvatic reservoir hosts. The most important determinants for the emergence of both new world zoonotic cutaneous leishmaniasis (ZCL) and zoonotic visceral leishmaniasis (ZVL) include poverty, urbanization, and human migration. *Leishmania mexicana*, *L. amazonensis*, *L. braziliensis*, *L panamensis*, *L. peruviana*, and *L. guyanensis* are the major species that cause new world ZCL. Approximately 62,000 cases of ZCL occur primarily in Brazil, Colombia, and Venezuela, where urbanization near *Lutzomyia* sandfly breeding sites have led to an increase in the number of cases. In addition, the emergence of ZCL in Colombia is linked to several decades of armed and guerilla internal conflict fueled by cocaine production and trafficking. In northeastern Brazil, ZVL (*L. chagasi*) has become an important infection in the *favelas* of Forteleza, Salvador do Bahia, and other urban centers; ZVL has also emerged in Rio de Janeiro and Belo Horizonte. A regional leishmaniasis control action plan is now being implemented.

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Type: Invited Presentation

Assessment in travelers coming from Latin America

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In recent years has been an important increase in international travel including Latin America. Travelling involves a series of risk depending of the travel destination, the standards of accommodation as well as the lifestyle and host characteristic (healthy versus pre existing condition, pregnancy, infants). Most illnesses reported by ill travelers are mild but some are serious enough to seek medical attention.
A systematic approach to the assessment of the ill returned traveler with knowledge of the most common, region-specific pathogens and recent outbreaks of infection will aid diagnosis and treatment.
The detailed travel history is the cornerstone of the post travel screening process, including travel destination, the particular area within a country, urban or rural areas were visited, season (dry or rainfall) , purpose of travel, hygiene standard (food and water exposures), duration of stay, accommodation, pre-travel vaccination, prophylaxis adherence and personal protection measures, illness of any travel companions, history of unprotected sexual contacts with new partners or casual sex, date of return in relation to onset of symptoms and type of symptoms. The physical examination may yield useful information.
According GeoSentinel surveillance, the most common syndromes in returned travelers from Latin America are chronic and acute diarrhea especially parasitic causes (Giardiasis), dermatological problems (larva migrans, myasis and leishmania), respiratory tract illness and fever (dengue and malaria).
Diarrhea remains the most frequent illness among travelers visiting Latin America. Dengue is a reemerging illness in the region as well and is the main cause of viral fever in returned travelers. Malaria should be considered if exposures and clinical findings are consistent with the diagnosis. Initial laboratory investigation should be performed depending upon exposure and other factors that prompt consideration of a particular disease.

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Fever and their etiologies

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The practice of Travel Medicine (TM) has 3 stages at which you can work: the pre-travel, the intra-trip and the post travel assistance. Many services only deal with pre-travel, strongly related to preventive measures, including vaccinations and malaria prophylaxis, and transfers to centers of Tropical Medicine, Internal Medicine Clinic or the Infectious Diseases Consultations ill patients encountered during the trip or upon returning. The need to cover all these stages in the centers of TM is controversial, even within their own ISTM. Our service, in the context of an Infectious Disease Hospital, allows comprehensive care of travelers in any of the 3 instances.
The most frequent reasons for consultation in returning travelers are the dermatological disease, fever, diarrhea and eosinophilia. The fever is about 30% of all searches, and the most common etiology is for malaria, followed by dengue, typhoid fever and rickettsial diseases. The diagnoses may vary according to geographic destination and the traveler's risk exposure. It is important not to forget cosmopolitan disease and non-infectious causes in the differential diagnosis.
The febrile syndrome after a trip to tropical areas is a medical emergency, because it can be *falciparum* malaria, or a viral hemorrhagic fever among others etiologies, which can endanger both the patient and health staff involved with him, and potentially to the community of the host country of the traveler.

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After a trip: the souvenirs in the skin

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Dermatoses are one of the most common reason for medical consultation after returning from a trip. The first consideration to take into account is that the spectrum of skin diseases that affect immigrants, long term travelers and expatriates may be different than those suffering from other travelers.
According to two large scale international studies performed by the GeoSentinel Surveillance Network involved 17,353 and 25,500 ill returned traveler encounters respectively at globally dispersed travel or tropical medicine clinics, between 1996 and 2006, the dermatosis were the third reason for consultation in frequency, after fever and diarrhoeal illness, and represented 17-18% of all diagnoses.
Independently of these studies and other series, dermatoses are likely to have higher incidence because they often resolve spontaneously or sometimes the patients require medical assistance outside the Travel medicine or Tropical disease units which have conducted the most research on these topics.
In assessing dermatoses in travelers, it is important to consider some factors such as the geographical destination visited,places visited en route, length of stay, purpose of travel and activities.
Dermatoses can be noninfectious and infectious/infestation, which can be cosmopolitan or from tropical origin.
The most common diagnoses are cutaneous larva migrans, soft tissue bacterial infection, arthropod bite, allergic reaction, myiasis, cutaneous leishmaniasis and tungiasis.
It is important to remember that skin lesions may be manifestations of systemic infectious diseases such as dengue rash, Chicungunya viruses, rickettsial infection, or non-infectious diseases such as those related to previous medical history, drug allergies, climate or sea related dermatoses.
Appropriate investigations and consultation with tropical or tavel medicine experts may be needed in order to make the correct diagnosis and provide correct management of these diseases. It is also necessary to emphasize preventive measures related to skin diseases in pre-travel advice.

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Ten Most Common Imported Diseases in Florida

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Emerging infectious diseases in Latin America

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In the last four decades new infectious diseases have been recognized almost every year, assuring emerging infectious diseases (EID) as a priority for global health. Some of these diseases, such as AIDS, SARS and the influenza pandemic, have threatened the global health due to their capacity to cross geopolitical boundaries. To respond to this new scenario the countries affiliated with the World Health Organization (WHO) approved a new revision of the International Health Regulations (IHR) in 2005. The IHR is a binding legal instrument, which aim to provide a proper public health response to the international spread of disease avoiding unnecessary interference with international traffic and trade. The new IHR, which have been enforced since June 2007, holds a broader framework, shifting its focus from a small list of notifiable diseases to any event that can become a public health emergency of international concern (PHEIC). Furthermore, the new IHR established a global sensitive mechanism to detect PHEICs using both official notification and media news.
The study analyses the events considered as potential international concern for the Americas under the IHR 2005 framework, from June 2007 to December 2009. The source of data was the World Health Organization Event Management System (WHO-EMS).
During the period studied, 243 events were considered as PHEIC in the region of the Americas. Despite the political commitment provided by the countries to approve the new IHR, 39.9% were initially detected through news media and 30.0% were notified by the National Focal Point (NFP) within the Ministries of Health. These figures reflect the countries' remaining tendency to hold the notification until finishing the verification process. 189/243 (77.8%) were infectious disease outbreaks, 8.2% were food safety events and 7.8% were animal health (epizootics) events. The study analyzes the main characteristics of these events and their implication for global health.
The IHR 2005 provides a useful framework for early detection and risk assessment of EID with potential international spread. Each country needs to accomplish the core capacities to perform surveillance and response activities in order to strengthen the global health security.

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Customizing Immunization to Travelers

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Immunization of travelers is a very important challenge for travel medicine practitioners. It should be tailored to each particular situation. Destination, duration of stay, activities and individual health, among others, influence these recommendations. The key point is to determine the travel **risk**. Selection of recommended immunizations should be based on epidemiological evidence, taking into account **incidence rates** and s**everity** of certain infections. Other factors to influence recommendations include: time, shots, availability, costs, interactions and vaccine side effects. Yellow fever remains the only **required** vaccine by Who. Special requirements are taken for those pilgrims on Hajj, where vaccination against meningococcal ACWY is mandatory and also polio vaccine is required to some travelers.
Routine vaccines are always updated in pre travel evaluation. Influenza remains one of the most frequent vaccine preventable infections**. Recommended** immunization for travelers includes common vaccine preventable diseases, as the main food and drinks related infections like hepatitis A and typhoid fever, as well as the life threatening disease rabies. Protection against hepatitis B is high through vaccination and should be considered in long term and frequent travelers. Our experience in Travel Vaccines will be showed.

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Routine Immunization

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Routine immunization has become among the most common preventive tools use by medical practitioners all over the World. Vaccinations have proven to eradicated and control many preventable diseases such as smallpox, polio, measles, tetanus and diphtheria among others. Globally, children vaccines calendars are most familiar for all developed and underdeveloped countries. However, only until recently that adolescents and adult vaccinations are known for many underdeveloped countries. Travel medicine is a good way to promote immunization calendars for all and should be a goal for our performance because there is an intrinsic synergistic relationship between them. The World Health Organization (WHO) has an important role in recommending routine immunizations for all groups of ages (children, adolescents and adults), diverse regions, and certain risk populations. WHO initial main program was the Expanded Program in Immunization which included vaccines for the maternal and children population under one year of age. Now among other goals are integrating immunizations' in the health systems and immunizing within a global health interdependence context are global objectives. Most countries follow the basic program for children and must comply with mandatory travel vaccines by the new International Health Regulations (2005). However, still the risk of life-threatening illness is very high especially in underdeveloped regions because still the vaccines coverage is low, therefore; the risk for reemerging diseases and spreading consequently with illnesses, disability and deaths. Also, there are new technologies and vaccines available which make difficult to financially provide the service for all. New biological products developments and technologies, vaccines primary series, interval of doses, and boosters must be learned by travel medicine practitioners. Also, adverse reactions and contraindications, particularly for those travelers with special needs or conditions in order to provide good advice during their pre-travel consultation.

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Vaccines Recommended for Global Travelers

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Individuals travel for many reasons, including holidays, recreation, business, visiting friends and relatives, health treatments, educational experiences or others purposes. The World Tourism Organization predicts that international tourist travel may top 1 billion by 2010. Given the growth of international travel, the area travel medicine has expanded of the worldwide. The vaccination is one of the steps that health providers for giving travelers, and the vaccines recommended prior to international travel can be divided into three fases: those that are routine, those that may be required and those that are recommended on the basis an individual risk assessment for the traveler. Considerations in choosing vaccines include destination; season and duration of travel; activities planned; severity of disease; whether the trip will be urban, rural, or remote from medical care; time remaining before departure; vaccine availability, cost, and the number of doses needed; history of allergy to vaccines or their components; medications currently being taken; pregnancy; chronic illness; and underlying medical conditions such as a compromised immune system. Vaccines recommended for travelers and that will be discussed: cholera, hepatitis A, Typhoid fever, Japanese encephalitis, meningococcal disease, rabies and Tick-borne encephalitis. **Conclusion**: Vaccination is a highly effective method of preventing certain infectious diseases. Travel medicine practitioners must be care when to evaluate immunization status of the traveler with goal to consider or not to vaccine for patient. Travelers should be informed about the risks of contracting disease, as well as, the risks of adverse events from immunizations.

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Yellow fever vaccine

C. Biscayart
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The purpose of this talk is to briefly address some highlights about the illness and its burden in relation to travel, new epidemiological aspects, particularly focusing on the Caribbean and South American situation in 2008-9. Conceptual points regarding yellow fever vaccine will be reviewed, focusing specially on severe adverse events described in the last 10 years, which have put the actual vaccine risk/benefit relation under close scrutiny. Some practical situations regarding its indication that could lead to controversy will be also discussed.

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Final Abstract Number: 07.001
Session: Travel medicine and the influenza pandemic
Date: Tuesday, March 9, 2010
Time: 15:45-17:45
Room: Ballroom 2: Monroe/Flagler
Type: Invited Presentation

From the Americas to the World

J. Sotelo Morales
National Autonomous University of Mexico, Mexico City, Mexico

In April, 2009 a new influenza virus, from porcine origin, was detected in Mexico City and blamed as responsible for the death of young adults with pneumonia. The patients were seen within the brief lapse of a week at the National Institute of Respiratory Diseases of Mexico; three main factors contributed to trigger the awakening call from the Mexican Health authority that evolved, within a few weeks, into an unprecedented international epidemiological alert orchestrated by the World Health Organization which culminated with the “Pandemic alert grade VI”; it meant that the disease had already disseminated worldwide; the factors were: a) the presence of various cases of severe influenza in healthy adults, b) the presence of the disease in the middle of spring, an abnormal timing for seasonal influenza and c) the identification by molecular methods of a brand new influenza virus from porcine origin infecting humans. According to the standards settled by the WHO these characteristics represented the much feared possibility of an influenza pandemic of potential catastrophic consequences; thus, the Ministry of Health of Mexico implemented at measures which had already been planned two years before in the case of facing such event. The Minister of Health appeared on national TV indicating the closure of schools at all levels in Mexico City and various other actions aiming to social distancing and medical alert in all health institutions, together with the development of technical skills for the reliable detection of the new virus in specialized laboratories. Through the epidemic in Mexico several new factors were learned, the capacity of society to deal with similar events was put to test. From this experience, several scientific reports from our Institutes have been published; they provide a new framework for more efficient responses in future events.

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Clinical Spectrum of Disease. Influenza AH1N1 2009

J. Dabanch Pena
Hospital Militar de Santiago, Santiago, Chile

In Chile, the first case of 2009 pandemic influenza A H1N1 virus infection was detected on May 17 . Since then all influenza like illness cases were notified to Chilean Health Secretary. A total of 367.041 cases were reported, 1585 required hospitalization (0.56%) and 130 died.
The surveillance in Chile shows that the majority of those infected had a mild disease.
The most affected age group was between 5 and 14. Febrile respiratory infection was the most common clinical manifestation and range from self limited to severe illness. In the outpatient group, 97% had fever, 97% headache, 93.5% myalgias, 90% cough, 88.3% sore throat, 84% rhinorrhea, 43.8% join pain, 36% nausea, 29.4% diarrhea. Time between onset symptoms and second case was 3.6 days (range 1 – 9).
Of the 1585 admitted to hospital, 52% were females, median age 33 years (range11 to 94), 56% had underlying medical condition, average time from the onset of illness to hospital admission was 3.6 days. Symptoms at presentation included fever 83%, cough 92.7%, dyspnea 83%, myalgias 63%, hypoxia 50.8%, cyanosis 27.4%, hypotension 18.6%, and 8.3% seizures. Pneumonia was the diagnosis in 77% patients.
130 patients died, all has been admitted to and ICU. The median age was 44 years (range 4 months to 89 years), 87.5% had underlying medical condition. The cause of death was severe respiratory failure in 34%, septic shock in 19%, bilateral pneumonia 17% and multi organic failure in 16%. Almost all patients received antiviral treatment.
Surveillance in Chile of the 2009 influenza A H1N1 cases allow to characterize the clinical spectrum of the disease in this first pandemic wave.

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Interim lessons from 2009

J. Alves
Institute for Infectious Diseases Emilio Ribas, Sao Paulo, Brazil

Through the epidemiological week 37/2009, WHO reported more than 300,000 confirmed cases and almost 4,000 deaths produced by pandemic influenza H1N1 in 191 affiliated countries. During the peak of transmission in 2009, the Southern Cone countries, Chile, Argentina and Southern regions of Brazil, reported the highest number of cases. According to PAHO, through the week 20/2009, 92,773 H1N1 cases were confirmed in Latin America as well as in Caribbean islands and a total of 2,494 deaths had been reported. Brazil accounted for the highest number of deaths and an elevated mortality rate when compared to countries like Chile. Initial containment measures, such as screening symptomatic people in airports and aircrafts and isolating patients who had recently traveled and presented flu-like symptoms, proved ineffective. Different strategies developed in each country showed that the early identification and treatment of high risk patients were responsible for reducing mortality. Although some demographic differences and distinctive clinical outcomes were noticed in different countries, various reports demonstrated that patients with underlying conditions such as asthma, diabetes, cardiac and lung diseases as well as pregnant women were more susceptible to complications. General experience made the benefit of early use of antiviral drugs clear. Based on what had been learnt during the pandemic and in line with WHO directives, Latin America countries are working on a vaccination program targeting the most vulnerable populations. These countries had to deal with a high number of cases earlier than other regions and before the impact on health care systems could be observed. Cooperation between countries requires clear and quick exchange of information in order to control any disease that presents the risk of spreading internationally.

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Prospects on Influenza Vaccines

G. Baracco
University of Miami, Miami, FL, USA

The influenza pandemic of 2009 has brought renewed interest in the development of new technologies for the production of influenza vaccine. This presentation will discuss the traditional production methods and available clinical data of monovalent H1N1 influenza vaccine. New advances in the field of influenza vaccine manufacture include increasing the speed of production and delivery and expanding the breadth of immunologic coverage in the search for a "universal target". We will discuss different strategies being developed to achieve those goals, including the use of adjuvants, utilization of reverse genetics, and DNA vaccines. Lastly, we will discuss barriers to successful immunization coverage and strategies to overcome them.

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Session: Rabies, bites and envenomations
Date: Tuesday, March 9, 2010
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Room: Ballroom 3: Tuttle
Type: Invited Presentation

Rabies, the Emerging Challenge
D. Warrell
University of Oxford, John Radcliffe Hospital, Oxford, United Kingdom

Classic rabies (genotype 1) and 6 other rabies-related lyssaviruses have proved capable of infecting humans. Antibodies to unspecified lyssaviruses are being discovered in bats in Europe, Asia and Africa. A case of Duvenhage (genotype 4) infection acquired from a bat in Kenya illustrated the hidden menace, unlikely to be revealed except by chance exposure of "sentinel humans" in whom a precise diagnosis is possible.
Wild mammal vectors/reservoirs: New wild mammal vectors and reservoirs are being identified, such as ferret badgers (*Melogale moschata*) in SE China. The importance of bats is increasingly recognised. Bites by rodents and monkeys are generally considered to carry a negligible risk of rabies but in Brazil, pet marmosets (*Callithrix jacchus*) have transmitted rabies.
Rabies control in domestic dogs: This is the most economical way of preventing human rabies. Potent and inexpensive tissue culture vaccines (TCVs) are available. In India, a single injection may protect stray dogs throughout their short lives. Oral vaccination is being extended from wild mammals to feral dogs.
Tissue culture vaccines for human use: Phasing out nervous tissue vaccines has encouraged manufacture of TCVs in India, China and Brazil but quality regulation is difficult. Vaccine shortages in USA forced a shortening of the conventional 5-dose Essen im regimen by deleting the day 28 dose.
Economical multi-site intradermal vaccination: economical and rapidly-immunogenic multi-site intradermal regimens such as a new 4-site id regimen can be used. Less than 2 vials of vaccine and only 3 clinic visits are required.
Pre-exposure prophylaxis in travellers: In USA, the vaccine shortage prevented pre-exposure prophylaxis and, in these circumstance, id use may be condoned in the future.
Cure of human rabies encephalomyelitis: recovery of an un-immunised American girl infected by a bat was attributed to the "Milwaukee regime", but this approach has failed in at least 17 subsequent cases.

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Type: Invited Presentation

Envenomation by Latin American arthropods

C. Malaque
Vital Brazil Hospital, Sao Paulo, Brazil

In Latin America, the most dangerous venomous arthropods are scorpions, spiders, bees and caterpillars. Scorpion stings are especially common in urban areas of Mexico, Amazonia and Brazil. Although intense local pain is often the only symptom, scorpion stings can cause death from heart failure/acute pulmonary edema, especially in children. In cases of systemic involvement, antivenom and symptomatic treatment must be administered quickly. *Loxosceles* spider bite can cause dermonecrosis or, more rarely, intravascular hemolysis and renal failure. Accidents can occur when a spider is compressed against the body of a person, especially during dressing or sleeping. The timing of administration and the effectiveness of specific antivenom in neutralizing local effects are controversial. Accidents with *Phoneutria* (the “armed” or “banana” spider) are most common in southern and southeastern Brazil. *Phoneutria* are found near dwellings, under logs, in crevices, in woodpiles and among bananas. Most victims suffer only local pain. Autonomic nervous system involvement (requiring administration of specific antivenom) is most common in children. *Latrodectus* bite can cause local, regional, remote or generalized pain, occasionally causing muscle cramps/spasms. Specific antivenom is reserved for severe cases. Mass bee attacks occur in warmer Central and South American regions, potentially causing rhabdomyolysis, intravascular hemolysis, renal failure, respiratory distress, hepatic dysfunction or myocardial damage. *Lonomia* caterpillar accidents can produce hemorrhagic disorders (effectively reversed with *Lonomia*-specific antivenom), acute kidney injury, chronic renal failure or death. Whole blood/fresh frozen plasma transfusion has been associated with worsening and slower recovery of the hemorrhagic syndrome. Most *Lonomia* accidents occur in Venezuela and southern Brazil. Since *Lonomia* often cluster on fruit trees, accidents are most common near rural residences. Ecotourism has increased *Lonomia* accident rates in parks/reserves. Although most arthropod accidents have a benign course, travelers to endemic areas should be aware of the risks associated with envenomation.

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Date: Tuesday, March 9, 2010
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Room: Ballroom 3: Tuttle
Type: Invited Presentation

Diagnostic and Treatment of Snake Bites

F. Franca
Vital Brazil Hospital in Butantan Institute, Sao Paulo, Brazil

Snake bites are very common in many rural areas of Africa, Asia and Latin America. The victims, in general, are young adult males bitten during agricultural activities. Snake bites envenoming is one of the major neglected diseases of the 21st century. The data about the morbidity and mortality are limited but it's estimated, globally, at least 421,000 envenoming and 20,000 deaths each year and also that almost 1.2 million to 5.5 million snake bites could occur annually. The snakes related with the most severe cases of snake bite envenoming belong to Elapidae (cobras, kraits, mambas, Australasian species and sea snakes) and Viperidae (rattlesnakes, lance-headed pit vipers and true vipers) families. The families Atractaspididae and Colubridae are responsible for a small fraction of the snake bites with medical importance in Africa, Middle East and Central Asia. The genus *Echis* sp. (saw-scaled vipers) in northern Africa, *Naja* sp. (cobras) and *Bungarus* sp. (kraits) in Asia and *Bothrops* sp. in Latin America are responsible for significant numbers of severe cases and deaths. The snake venoms are a complex mixture of many families of toxins as haemorrhagins, neurotoxins, serinoproteases, phospolipases, myotoxins and others. The most frequent emergencies in snake bites are caused or a consequence a result of clotting and bleeding disturbances, rhabdomyolisis, intravascular haemolysis, muscle paralysis, local and systemic acute inflammation and consequent complications like severe hemorrhage, acute renal failure, acute respiratory failure, hypotension and shock, septicemia and severe local complications as compartmental syndrome, necrosis and amputation. The correct quantity of specific antivenom by the intravenous route, as soon as possible and supportive treatment are essential. The main challenges to control snake bites accidents are the production and large distribution of high quality antivenoms and extensive and systematic training of the health care workers about diagnosis and treatment of snake bites.

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Type: Invited Presentation

Immunobiologicals in South America
J. Murillo
University of Miami, Miami, FL; USA

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Session: Plenary 3
Date: Wednesday, March 10, 2010
Time: 09:00-09:45
Room: Ballroom 1: Brickell
Type: Invited Presentation

Edward H. Kass Lecture

The Discovery of HIV

F. Barre-Sinoussi
Institut Pasteur, Paris, France

Soon after, the first report of AIDS in the United States in 1981, similar cases were observed in France. In December 1982, a working group of clinicians contacted retrovirologists at the Institut Pasteur to work on the hypothesis that a retrovirus might be the cause of AIDS. Together, they define a successful strategy to isolate HIV from a patient at risk of AIDS. This discovery was the start of a collective adventure, which mobilized clinicians, multidisciplinary researchers and patients, altogether. Such a networking turned out to be very efficient for providing scientific evidences and for translating them rapidly into diagnosis, prevention and treatment of HIV infection. Since these early days, we have learnt that HIV infection is much more complex than initially thought. We have gained significant insights into the HIV biology and pathogenesis. Early virologic and immunologic events, particularly at mucosal sites, including the early virus dissemination, the establishment of viral reservoirs and the very rapid immune dysfunctions are critical in both HIV acquisition and/or disease progression.
Despite all the enormous progress made during the last 27 years at international level, HIV/AIDS epidemic still there. Research priorities still remain care, treatment and prevention. One of the major scientific challenges is to develop an efficient HIV/AIDS vaccine. Conventional immunization strategies may not be sufficient to elicit protection. We clearly need to elucidate the precise mechanisms that are governing the induction of protective immunity against HIV, taking into consideration the most recent advances in innate immunity and insights on early innate effectors that HIV can alter, including at mucosal sites. Lessons learned from distinct models of protection in human and non-human primates and new approaches, including systems biology will certainly contribute to novel concepts for future HIV vaccine research and development.

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Final Abstract Number: 10.001
Session: MRSA: Disease mechanisms and control
Date: Wednesday, March 10, 2010
Time: 10:15-12:15
Room: Ballroom 1: Brickell
Type: Invited Presentation

Inducible Dormant MRSA

G. Bearman[1], A. Rosato[2], K. Elam[2], M. Edmond[3]
[1]Richmond, VA, USA, [2]Virginia Commonwealth University, Richmond, Va, USA, [3]Medical College of Virginia Campus, Richmond, VA, USA

Inducible Dormant (ID) MRSA are mecA gene-positive *S.aureus* isolates that change from initial MSSA phenotype to CA-MRSA phenotype after β-lactam antibiotic exposure .They can be identified by SCC *mec* type. ID-MRSA has been reported in both hospital and community settings.
In healthcare facilities, transmission of ID-MRSA from a HCW to a patient has been postulated. In an earlier report, a HCW was colonized with MRSA after treatment with cephalexin. Exposure to the antibiotic was the purported inducer of phenotypic resistance. Until recently, there have been no prior epidemiological reports of ID-MRSA in the non-healthcare setting. A prospective epidemiologic surveillance study identified ID MRSA in a cohort of healthy university students
The potential impact of ID-MRSA colonization on CA-MRSA colonization and subsequent development of skin and soft tissue infections or invasive disease is not known. As in the hospital setting, ID-MRSA colonization may serve as a reservoir, thereby promoting cross-transmission within a household, dormitory, athletic team or social unit. Colonized individuals may theoretically cross transmit ID-MRSA isolates to close contacts. Additionally, ID-MRSA colonization or transmission may result in MRSA phenotypic conversion if the appropriate selective antibiotic pressure is applied. Furthermore, individuals persistently colonized with ID-MRSA may play an important role in households with high rates of CA-MRSA infections. Further studies are needed to better define both mechanisms of resistance and the epidemiologic significance of ID-MRSA.

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The Role of PVL in Severe Disease - What is the Evidence?

K. Christiansen
Royal Perth Hospital, Perth, Australia

ST8-MRSA-IV (USA300), ST80-MRSA-IV (European clone), ST59-MRSA-IV (Taiwan clone) and in Australia ST93-MRSA-IV (Queensland clone) and ST30-MRSA-IV (Oceania clone) are all PVL positive. Data from Australia where CA-MRSA has been described since the late 1980's show that disease severity and demographics vary widely between PVL positive and negative clones. Demonstrating the actual role of PVL in disease has been controversial. Mouse and rat animal models using PVL positive and negative clones or PVL deleted mutants have provided some support for a role in muscle damage, skin abscess and lung necrosis but there are studies that fail to show any association of PVL with pathogenesis of CA-MRSA disease. In contrast rabbit models have demonstrated a role in lung necrosis, dermatonecrosis and osteomyelitis - a reflection of the greater sensitivity of rabbit polymorphonuclear (PMN) leucocytes to PVL than murine PMNs.
As with most biological systems one single factor is rarely the explanation for a complex disease. Other virulence factors have been described for CA-MRSA including core genomic factors such as alpha haemolysin, secreted proteases, phenol-soluble modulins (PSMs), increased expression of the accessory gene regulator (*agr*) and especially for USA300 the possession of the arginine catabolic mobile element (ACME) that has a role in pH homeostasis, fitness and possibly transmission. More recently PSMs that are associated with the SCC*mec* have been described.
Conclusion: PVL is not necessarily a driver of the CA-MRSA epidemics being seen worldwide but is more likely a determinant of significant skin and soft tissue infection with abscess formation as well as more severe disease such as necrotising pneumonia, necrotising fasciitis and osteomyelitis.

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MRSA Control Programs in the UK: Impact on Quality of Care, Nosocomial Infection, and Public Perception

I. Gould
Royal Infirmary, Aberdeen, Saudi Arabia

Driven largely by public and hence political pressure, the NHS has made good progress in reducing MRSA bacteraemia. By the end of June 2009, they had fallen to 26% of 2003-04 levels in England and Wales. Little data however, is available on background MRSA colonisation rates or other types of infection although HAI audits suggest MRSA is still the dominant cause of postoperative wound infection. Signifiant resource is now being invested in universal admission screening and early signs are that this is being successful with signigicant reduction in colonization rate at admission, overall burden on isolations rooms, clincially diagnosed infections and laboratory clinical isolates. The little evidence available suggests that the public is happy with screening programmes. Nevertheless, significant concerns remain at public health level about the use of these resources for MRSA screening and at an ethical level about the enforced isolations of patients with possible detrimental effects on quality of care.

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Room: Ballroom 1: Brickell
Type: Invited Presentation

MRSA epidemiology and Control in Developing Countries

V. Rosenthal
International Nosocomial Infection Control Consortium (INICC), Buenos Aires, Argentina

International infection control consortium (INICC) reported data from January 2003 through December 2008 in 173 ICUs in Latin America, Asia, Africa, and Europe. During the 6-year study, using CDC NNIS/NHSN definitions for device-associated healthcare-associated infection, we collected prospective data from 155,358 patients hospitalized in the consortium's hospital ICUs for an aggregate of 923,624 days.
Although device utilization in the developing countries' ICUs was remarkably similar to that reported from U.S. ICUs in the CDC's NHSN, rates of device-associated nosocomial infection were markedly higher in the ICUs of the INICC hospitals: the pooled rate of CVC-associated BSI in the INICC ICUs, 7.6 per 1000 CVC days, is nearly three-fold higher than the 2.0 per 1000 CVC-days reported from comparable U.S. ICUs, and the overall rate of ventilator-associated pneumonia (VAP) was also far higher, 13.6 vs 3.3 per 1000 ventilator-days, as was the rate of catheter-associated urinary tract infection (CAUTI), 6.3 vs. 3.3 per 1000 catheter-days.
Most strikingly, the frequencies of resistance of *Staphylococcus aureus* isolates to methicillin—MRSA (84.1% vs 56.8%), *Klebsiella pneumoniae* to ceftazidime or ceftriaxone (76.1% vs 27.1%), *Acinetobacter baumannii* to Imipenem (46.3% vs 29.2%), and *Pseudomonas aeruginosa* to piperacilline (78.0% vs 20.2%) were also far higher in the consortium's ICUs, and the crude unadjusted excess mortalities of device-related infections ranged from 23.6% (CVC-associated BSI) to 29.3% (VAP).

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Session: Seasonal flu vaccines: Current status and future directions
Date: Wednesday, March 10, 2010
Time: 10:15-12:15
Room: Ballroom 2: Monroe/Flagler
Type: Invited Presentation

Influenza vaccination: Where do we stand?

A. E. Fiore
National Center for Infectious Diseases, CDC, Atlanta, GA, USA

In the United States, influenza causes an average of 36,000 deaths and 226,000 hospitalizations yearly. Rates of infection are highest among children. Rates of serious illness and death are highest among persons aged ≥65 years, children aged <2 years, and persons of any age with medical conditions that place them at higher risk for complications from influenza.
Annual influenza vaccination is the most effective method for preventing influenza virus infection and its complications. Influenza viruses undergo frequent antigenic change (antigenic drift); patients need an annual vaccination against the influenza viruses that are predicted on the basis of viral surveillance data. Trivalent inactivated influenza vaccine (TIV) can be used for any person aged ≥6 months, including those with high-risk conditions. Live, attenuated influenza vaccine (LAIV) may be used for healthy, nonpregnant persons aged 2–49 years.
The 2009 novel influenza A (H1N1) pandemic required a separate monovalent vaccine to be rapidly developed, with different vaccination recommendations from those for seasonal vaccines. The initially limited supply of vaccine required that early vaccination efforts target children and young adults, adults <65 years old with chronic medical conditions, pregnant women, and healthcare personnel. By January 2010, monovalent vaccine supply had increased sufficiently to allow all persons who wanted vaccination to receive it.
Vaccination coverage has remained low in most groups for a variety of reasons, including the need for annual revaccination, the complexity of vaccination recommendations, and a lack of knowledge among patients and healthcare providers. In recent years, simpler age-based recommendations have been added for persons 50-64 years old, and children ages 6 months through 18 years, and in 2009, >85% of the US population had an indication for annual vaccination. As more manufacturers have entered the market, seasonal vaccine supply has met demand. A universal vaccine recommendation for all persons aged 6 months or older is feasible and has been proposed as a way to increase vaccine coverage in all age groups.
Current influenza vaccines are safe in all age and risk groups and quite effective in healthy children and younger adults. Lower effectiveness among seniors and persons with chronic medical conditions, and lower immunogenicity (requiring 2 doses) among previously unvaccinated infants and children highlight unmet challenges. More effective vaccines are needed that can be more rapidly produced and can overcome challenges such as immunosenescence, annual revaccination, and lower protection against drifted viruses. Ideally, better vaccines would stimulate longer-lasting cross-reactive immunity against multiple strains. Vaccines must be effective in protecting the very young, the chronically ill, and the elderly, who bear the largest burden of influenza illness. Also needed is a better understanding of how to motivate people to seek annual influenza vaccination.

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Session: Seasonal flu vaccines: Current status and future directions
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Room: Ballroom 2: Monroe/Flagler
Type: Invited Presentation

Overcoming limitations of seasonal vaccines

A. S. Monto
University of Michigan School of Public Health, Ann Arbor, MI, USA

Among the limitations of seasonal influenza vaccines are limited breadth of immunity, short duration of protection, lower protection in older individuals and immunocompromised patients, problems with needle inoculation such as needle phobia and medical waste disposal, and dependence on the egg supply. Because antigenic drift (poor antigenic match between the vaccine and circulating strains) is associated with a fall in efficacy, there is a need for vaccines that will induce an immune response to both identical and related strains. In an effort to produce broadened immunity, new adjuvanted vaccines with different oil components have been formulated, and the concept of a universal influenza vaccine continues to be explored. It is not clear whether producing a higher titer postvaccination will result in longer duration of protection, as that requires specific evaluation involving major practical difficulties. Improved technology for influenza vaccines may result in vaccines intended for specific population segments, such as younger children and the elderly. A quadrivalent vaccine may be developed containing the two A subtypes and the two B lineages, which would be most useful in children. To combat the issue of immunosenescence, a high-dose vaccine has recently been approved for use in older patients. Some studies suggest that unvaccinated older individuals may be more ill but because of their disability, underutilize the healthcare system; in contrast, vaccinated older individuals may be healthier because they are in care, indicating bias in analyses. It may be possible that these new vaccines will produce protection in the immunocompromised, but this will need to be evaluated specifically. To address problems associated with needle inoculation, new delivery systems and alternative routes to intramuscular administration have been developed, such as a nasal vaccine approved in the United States in 2007 and an intradermal vaccine approved recently in Europe. Cell culture production of influenza vaccines may improve vaccine efficacy and would reduce the system’s dependence on the egg supply and provide greater production flexibility.

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Emerging Trends: Vaccines in late development
R. L. Atmar
Baylor College of Medicine, Houston, TX, USA

A number of strategies are being pursued to increase the availability of and to improve the immunogenicity, efficacy, and effectiveness of seasonal influenza vaccines. Many of these approaches have led to vaccine candidates that are in the late stages of clinical evaluation (i.e., Phase 3 trials) or that have been recently licensed. Approaches to increase the availability of influenza vaccines in the United States include the licensure of vaccines approved in other countries and the production of influenza virus antigens by cell culture (eg, canine kidney cells and Vero cells) rather than by growth in embryonated eggs. Some cell culture-derived vaccines are approved in Europe. The influenza hemagglutinin is partially purified from whole virus in currently licensed vaccines. Another approach is the production of influenza virus hemagglutinin with a baculovirus expression system. Alternative routes of immunization have also been explored, and an intradermally administered vaccine has recently been approved for use in persons 60 years of age and older in Europe. Improved vaccine immunogenicity and efficacy may be attained through the use of adjuvants or higher doses of hemagglutinin. Although several adjuvanted influenza virus vaccines are approved in other countries, none are licensed in the United States. However, oil-in-water adjuvants are in advanced stages of evaluation. A high-dose (60 mcg hemagglutinin) trivalent influenza vaccine has recently been licensed based upon its superior immunogenicity compared with the standard dose (15 mcg hemagglutinin), to be used in persons 65 years of age and older. Phase 4 studies of the high-dose vaccine are under way to determine whether the improved immunogenicity is associated with increased vaccine efficacy and effectiveness.

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Final Abstract Number: 12.001
Session: Traveler's diarrhea and enteric diseases of Latin America
Date: Wednesday, March 10, 2010
Time: 10:15-12:15
Room: Ballroom 3: Tuttle
Type: Invited Presentation

Epidemiology of Traveler's Diarrhea

A. McCarthy
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This presentation will provide a review of etiologies and risk factors for diarrhea in those visiting Latin America and will provide some comparison with travelers to other destinations.

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Traveler's Diarrhea: Prevention and Treatment
R. Steffen
University of Zurich, Zurich, Switzerland

Different options for the prevention of travelers' diarrhea (TD) exist. Risk reduction is possible by implementing the Hazard Analysis Critical Control Point System or by improvement of the local infrastructure. To abandon travel plans or to abstain from potentially contaminated food and beverages is not attractive. Both a cholera and a candidate LT-ETEC transcutaneous patch vaccine have been shown to prevent TD by LT-ETEC strains, possibly by other pathogens. Among drugs suggested for chemoprophylaxis, probiotics showed at best a low protective efficacy rate; bismuth subsalicylate was modestly effective. Many older antibacterial agents are obsolete because of antimicrobial resistance by prevalent enteric bacterial pathogens. The fear of systemic reactions has limited the prescription of fluoroquinolones. Poorly absorbed antibiotics, mainly rifaximin, are more attractive for compliant travelers.
As no current prophylactic measure is satisfactory, (self)-therapy of TD remains an important option (travel kit!). Only few still recommend to wait for spontaneous cure; rapid relief is often important as incapacitation and the necessity to change travel plans have a great impact. Probiotics and charcoal have been demonstrated to offer no clinically relevant benefit. Oral rehydration solutions have no effect on the duration or amount of diarrhea, but they are essential in paediatric patients and senior travelers. Antimotility agents offer fast relief, but they are contraindicated in dysentery, also they are often followed by a period of constipation. Antimicrobial agents, mainly quinolones and particularly in SE-Asia also azithromycin, have been used in this decade, although there is only limited recent data on the frequency of resistance from analysis of TD stool samples on all continents. The non-absorbed rifamycin-derivative rifaximin – with a broad antimicrobial spectrum and a tolerance profile similar to placebo – has been demonstrated in patients with TD to be as effective as ciprofloxacine, but this only in non-invasive cases of TD.

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Helminths of Latin America
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Albert Einstein College of Medicine, Bronx, NY, USA

This session will focus on intestinal helminths. *Ascaris lumbricoides* is among the most prevalent of parasitic infections in humans. Most patients are asymptomatic or experience mild abdominal pain. Children have the highest intensity of infections and generally present with more severe clinical manifestations. The most common clinical syndromes of ascariasis are pneumonitis, intestinal, biliary and pancreatic obstruction. Ascariasis adversely affects growth, development, and nutritional status of children. Another helminth, Hookworm, is particularly troubling for children and women of reproductive age who are vulnerable to the effects of hookworm anemia. Trichuris is an important helminth in which most cases of are asymptomatic. Heavy infections can result in the Trichuris dysentery syndrome (TDS). This syndrome includes chronic dysentery, rectal prolapse, anaemia, poor growth, and clubbing of the fingers. The severe stunting in TDS now appears likely to be a reaction at least in part to a chronic inflammatory response and concomitant decreases in plasma insulin, plasma insulin-like growth factor-1 (IGF-1), increases in tumor necrosis factor-α(TNF-α) in the lamina propria of the colonic mucosa and peripheral blood (which likely decreases appetite and intake of all nutrients) and a decrease in collagen synthesis. Improvements in cognitive performance have been found after treatment for relatively heavy infections in school age children. Synergistic associations between hookworm and other helminths has been described. In a recent study from Brazil, 61% of individuals harbored mixed helminth infections. Multivariate analysis indicated significant positive associations for co-infection with hookworm and *S. mansoni* and for co-infection with hookworm and *A. lumbricoides*. Co-infection with hookworm and Ascaris resulted in higher egg counts for both, suggesting a synergistic relationship between these species, although, the intensity of *S. mansoni* or *A. lumbricoides* co-infection did not differ from that of mono-infection. Another study from from Brazil looking at Hookworm and Ascaris infection and the impact of polyparasitism on cognitive performance in Brazilian schoolchildren suggested that hookworm may be associated with poorer concentration and information processing skills while *A. lumbricoides* infection may be associated with poorer general intelligence. Polyparasitized children seem to experience worse outcomes that children with only one helminth infection. In yet another study, multivariate analysis revealed that stunting was significantly associated with ascaris infection among children and adolescents, whereas low body mass was significantly associated with hookworm infection among adults and the elderly.
Strongyloides stercoralis can cause acute infection, chronic infection and hyperinfection syndrome. Hyperinfection syndrome has been associated with a variety of risk factors and predisposing conditions, including new immunosuppressive therapy therapies; HTLV-1 infection; cadaveric transplantation; immune reconstitution syndrome; hematological malignancies (especially lymphoma). Co-infection with with HTLV-1 results in decreases in IL-5, and parasite specific IgE responses in patients with strongyloidiasis consistent with a relative switch from Th1 to Th2 response leading to an increased risk of autoinfection resulting in hyperinfection syndrome. Co-infected patients with HTLV-1 and strongyloides may not respond as well to anti-helminth treatment. In addition to HTLV-1, corticosteroid use remains one of the most frequent risk factors for hyperinfection syndrome. Hyperinfection syndrome presents with diverse symptoms and signs often leading to misdiagnosis on the clinicians part. It is associated with a high mortality rate (15-87%). Therefore, increased recognition is important for clinicians caring for at-risk patients.
Of the five major species of Schistosomiasis pathogenic to humans the only one endemic in South America is *Schistosoma mansoni*. Despite the efforts in carrying out integrated control programs during the last 25 years, there are still regions where the prevalence of *S. mansoni* is over 50%. Heavily infected, susceptible individuals are at risk for developing hepatosplenic disease. Pulmonary involvement in *S. mansoni* is reported in acute schistosomiasis and in chronic disease. Recent studies from Brazil suggest that pulmonary hypertension may be more common than previously thought in individuals with hepatosplenic disease due to *S. mansoni*. Similarly, recent studies suggest that hepatopulmonary syndrome also occurs in patients with *S. mansoni* who also have periportal fibrosis and portal hypertension. Although CNS involvement is rare, it is well described. Transverse myelitis or seizures have been described in both acute and chronic infection.

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Food-borne Toxins

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Food-borne toxins are an important cause of morbidity in the unwary traveler. In rare situations, deaths may occur. Education is the key to prevention and a careful history is usually the key to diagnosis.
Ingestion of contaminated fish and shellfish is one of the commonest causes of poisoning and the risk from marine toxins appears to be increasing as a result of multiple factors such as global warming, coral reef damage and spread of toxic algal blooms. Important examples include ciguatera poisoning from ingestion of large carnivorous coral reef fish, puffer fish poisoning and various shellfish poisonings such as paralytic shellfish poisoning. Scombroid poisoning occurs in open ocean fish such as tuna and mahi mahi that contain histidine in the flesh. Inadequate chilling after capture results in conversion of histidine to histamine and symptoms that resemble an acute allergic reaction.
In most cases the presence of toxin does not affect the appearance, smell or taste of seafood and it is not destroyed by cooking, smoking, freezing or drying. Onset of illness typically occurs soon after ingestion of contaminated food and produces gastrointestinal symptoms such as diarrhea, nausea, vomiting and abdominal pain often followed by a variety of neurological and cardio respiratory symptoms. Paradoxical dysesthesiae such as temperature reversal (hot objects feel cold and cold objects feel hot) are very characteristic of ciguatera and neurotoxic shellfish poisoning.
Treatment is usually symptomatic and supportive. In the case of scombroid poisoning antihistamines provide specific treatment and in the case of ciguatera poisoning intravenous mannitol may reduce the severity and duration of some of the neurological features.
Diagnosis is usually based on a careful history. Test kits that detect ciguatoxin in contaminated fish are commercially available.
Ackee poisoning and cassava poisoning are examples of food poisoning from non-marine sources. Ackee poisoning occurs after eating unripe ackee fruit and results in vomiting and life threatening hypoglycemia. Acute and chronic cyanide poisoning may occur after ingesting cassava root products containing cyanogenic glycosides. Acute poisoning causes diarrhea, vomiting, mental confusion and death. Chronic intoxication causes abnormal thyroid function and various neurological disorders.

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Type: Invited Presentation

Epidemiology of Chronic Viral Hepatitis in Latin America

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Chronic viral hepatitis caused by Hepatitis B or C viruses are major health problems in this beginning of the 21st century. Estimated prevalence in the world population in different regions range between less than 1% to more than 3% for HCV and between less than 2% to more than 8% for HBV, affecting more than 400 million people in the world. In Latin America, prevalence estimates are flawed. For HCV it varies from less than 1% to 2%, and for HBV from less than 1% to more than 8%. Numbers can be as high as 15% in the Amazon region.
In Latin America, some surveys report HBV prevalence as high as 21.4% in Dominican Republic and 7.9% in Brazil, followed by 3.2% in Venezuela and 2.1% in Argentina. Low prevalence was found in Mexico (1.4%) and Chile (0.6%). For HCV, rough estimates project more than 10 million infected people. Many surveys were conducted by blood banks, but results are biased by sampling problems.
In Brazil, HCV prevalence studies estimates had found a wide range, varying from 0.4% to 5.9%. A population based study in 2007 found a HCV antibodies prevalence of 0.28% to 2.61% and a HCV-RNA from 0.02% to 0.9% in different regions of the country. From 1994 to 2005, the Ministry of Health database has registered 52,440 HCV cases. Recently, a national survey was conducted by the Ministry of Health, but results are not published yet.
In São Paulo state, there were 30,299 HCV cases registered from 2002 to 2008 and 14,810 HBV cases in the same period. In the city of São Paulo it is estimated a mean prevalence of 1.42% (95% confidence interval 0.7 – 2.12%).
Diagnosis can be done with blood tests, but availability is a concern in poor countries. Treatment is expensive and fairly effective, implying in high morbidity, mortality and costs. Chronic hepatitis is a great challenge for the health systems in Latin America.

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Update on Hepatits B Therapy

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Tha main goal for the treatment of chronic hepatitis B (CHB) is to prevent advanced hepatic disease: cirrosis,hepatic failure and hepatocellular carcinoma (HCC) . The first aim of treatment is to achieve sustained suppresion of HBV replication as well as the remission of liver disease.The sustained supression of virological replication varies widely,depending on the population on treatment, therapeutic agent s , treatment duration and less clearly from genotype. Since 1992 ,eigth therapeutic agents have been approved worlwide (INF alfa, lamivudine, adefovir, entecavir, PegINF alfa-2ª thymosin alfa1, ,telvibudine and tenofovir) but only some of them are used in different countries according to national regulation. . When and how to treat an CHB depends on the HBV DNA levels, ALT and status of HBeAg. For HBeAg(+) patients,the endpoint of treatment is HBeAg seroconvertion. Therapy is considered in GHB with HBV DNA leves of 20.000 IU/ml or higer (HBeAg positive patient) or 2.000 IU/ml (HBeAg negative) , although lower HBV DNA levels migth be selected when evidences of progresive disease are identified. ALT normalization and HBV DNA suppression are the measures of reponse to therapy. Oral nucleoside analogs (NA) is a significant contribution for treatment in the last years,but a major concern with this agents is the selection of antiviral resistant mutations. This may be identified prior to virological breakthrough or at the same time. Peginterferon alfa-2ª, entecavir and tenofovir are currently included in the first-line treatment choice on the basis of their potency as well as the low rate of antiviral drug resistance. The strategy of drugs combination in CHB treatment for achieving a sustained virological response and some end points has beeen explored and the level of HBV DNA suppression . This combination theraphy is encouraging in some clinical trials.

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Type: Invited Presentation

Hepatitis C Treatment Today and the Future

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Therapy of chronic HCV infection is based on the use of the combination of pegylated interferon and ribavirin. Sustained virological response (SVR), a negative HCV RNA 24 weeks following discontinuation of therapy, is the most important surrogate parameter to achieve. Actually, SVR is obtained in about 50% of patients with genotypes 1/4 and in 80% of the patients with genotypes 2/3.
Patients infected with genotypes 1 or 4 must be treated for 48 weeks. But, if the patient achieves a rapid virological response (RVR), defined as a negative HCV RNA at week 4, we can consider a shortening of treatment. In patients with a slow response to treatment (HCV RNA only negative between weeks 12 and 24) the length of therapy must be extended to 72 weeks. For patients infected with genotypes 2 or 3 treatment should be planned for 24 weeks.
New drugs are needed for non-responders and for those who are not good candidates to treatment.
Several new oral agents, more potent, less toxic and allowing for shorter duration of treatment are being developed. These new drugs are designed to inhibit several viral enzymes. Results of recent clinical trials using inhibitors of NS3/4A protease or inhibitors of NS5B polymerase in combination with peginterferon/ribavirin are promising. These studies demonstrated that adding telaprevir or boceprevir (the protease inhibitors in the most advanced phases of evaluation) to peginterferon/ribavirin improved the rates of SVR in treatment-naïve and treatment-experienced patients. From these and other trials it was possible to conclude that the use of these new agents in monotherapy, owing to its relative low genetic barrier, was associated with a rapid development of resistance to the drugs and that the use of ribavirin was always necessary. These new agents will be available for general clinical use in the next years but they must be used as a complement of current therapy.

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Management of HIV and Hepatitis C Co-infection
M. Brito
University of Illinois, Chicago, IL, USA

The rate of coinfection of HIV with Hepatitis C is high in countries where the mode of transmission is predominantly intravenous drug abuse. The success of highly active antiretroviral therapy (HAART) in decreasing HIV related morbidity and mortality has shifted the focus of care for people living with HIV. More attention is being paid to the management and prevention of chronic ailments such as cardiovascular, liver and renal disease. Thus, it is important for the clinician treating HIV infected patients to recognize the clinical presentations, spectrum of disease, efficacy of treatment and principles of management for coinfected patients. Patients coinfected with the HIV and Hepatitis C viruses have an increased risk of liver related morbidity and a more rapid progression to end-stage liver disease. The treatment of these patients is complex owing to the significant side effects and limited efficacy of Peg Interferon and Ribavirin. This lecture will review the epidemiology, natural history, diagnosis, management and newer treatment modalities in HIV/HCV coinfection.

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Time: 10:15-12:15
Room: Room Orchid B/C/D
Type: Invited Presentation

Infectious diseases and infection control after natural disasters.

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University Hospitals of Geneva, Geneva, Switzerland

Infections are frequent complications after natural catastrophes. Previous reports suggest a high prevalence of colonisation and infection with multi-resistant Gram-negative pathogens in victims of natural disasters.
Literature regarding infections and infection control measures after natural disasters was reviewed from 1986 through the end of 2009, with special emphasis on the 2004 tsunami. Local microbiology of patients followed in our institution was also reviewed.
Patients admitted after natural disasters often have polymicrobial infections with atypical bacteria and fungi. Moreover, they are usually colonised or infected with multi-drug resistant organisms. These pathogens are acquired either nosocomially or environmentally. Several studies have suggested that Gram-negative bacteria are more prevalent than Gram-positive bacteria. A high incidence of colonisation and infection with extended spectrum β-lactamase-producing bacteria, multi-resistant non-fermenting Gram-negative rods and difficult to treat fungal infections are found in these patients and may pose challenges in routine hospital care.
According to published date and our own experience, we recommend pre-emptive contact isolation for victims of natural disasters during hospitalisation until results of microbiological cultures become available. If respiratory symptoms are present, droplet isolation must be included. These measures should also be applied during the air transportation of these patients. Considering the different multi-resistant colonisers, cohorting patients must be avoided whenever possible. In cases of life-threatening infections, empiric antibiotic therapy must cover multi-resistant non-fermenting Gram-negative rods. Clinicians must be aware of unusual microbiological findings in these patients.

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Type: Invited Presentation

Infectious diseases and war conflicts in the Middle East

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Infectious diseases and war have been witnessed for as long as human life. Historically, infectious diseases have been responsible for the majority of deaths during war; however, numerous medical and military advances have reversed this trend, resulting in more deaths from battle than infectious diseases in the 20th century. Wounds incurred in war are grossly contaminated with bacteria and most will become infected unless appropriate treatment is initiated quickly.Common infections include respiratory as well as gastrointestinal infections. Endemic diseases are also reported during the war and they include Brucella, Q-fever, Malaria, Sandfly fever and Leishmaniasis. Non-battle injuries such as mental and combat stress are common; while battle associated infections such as trauma- related complications are extensively reported.
Multidrug resistances (MDR) Gram negative bacilli have been reported in war wound infections, particularly Acinetobacter spp, Enterobacter spp.and Pseudomonas spp. and therefore empirical treatment for infected war wounds should be given to cover MDR. Other war related infections such as malaria , MDR tuberculosis, chronic Q fever and brucellosis may become apparent after returning home and therefore they should be considered due to their lengthy reactivation periods. In addition to this, vaccines have proven to be an important breakthrough to help prevent the spread of several infectious diseases.
War wounds are predisposed to infection due to environmental conditions on the battlefield, devitalized tissue, and foreign bodies in the wound as well as delays in evacuating causalities. Knowledge of likely pathogens for particular infections and sites, as well as optimal antibiotics to eradicate those pathogens will aid battlefield healthcare providers in averting and treating infections appropriately.

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Type: Invited Presentation

Infectious diseases and earthquakes in Peru

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Because of the presence of the Nazca tectonic plate, Peru is a risk area for earthquakes. The surveillance system for infectious diseases confirms that respiratory infections (bronchitis, pneumonia, etc.) are frequent. This probably occurs because people sleep in provisional places and in unsanitary conditions. Cutaneous infections (pyodermitis, cellulitis, etc) are therefore also frequent. Allergy to dust is sometimes confused with respiratory infections.
If there is sufficient water of good quality, there are no outbreaks of cholera, typhoid fever or salmonellosis. In Peru, although there have been more than 15 earthquakes over the past 20 years, there were not any outbreaks of food- or vector- borne diseases.
It takes time to mount a vaccination campaign: it is very difficult to vaccinate during the first weeks after a disaster and there is no immediate effect. No vaccination plan has shown to be useful. On the contrary, vaccinations can be associated to unusual or adverse effects. The experience of vaccination against yellow fever in Ica- Peru in 2007, which was motivated only by the possibility of ecological change, showed more adverse effects than benefits.

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Disaster Relief in Haiti

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Hurricanes hits Caribbean region every year, strangest rains are excepted in August and September. Year 2008 was catastrophic because the Hispaniola Island (Haiti and Dominican Republic) have been affected twice in a start period (2 weeks). First hurricane hit south of Haiti in middle and second whole island at the end of august 2008 and caused subsequent floads which persistent in north, affecting mainly the city Gonaives with more than 100 000 people for several month. During this period, non-falciparum malaria and diarrhoeal disease increased 2,5 - 3 times. However, no major outbreaks of hepatitis and leptospirosis have been noted in this area because of Governmental UN humanitarian assistance and reconstruction of water supply. Our hospital in Mole st. Nicolas and clinic in Baiedes Hennes have noted increasing incidence of malaria but not significant increase of diarrhoeal disease, because in rural area, where are located, are wells protected against floads. Large cities/urban areas near rivers are much more affected by hurrican related floads then coastal regions.

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Room: South Hall
Type: Invited Presentation

Treating Resistant Filamentous Fungi Infections

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Resistance to treatment can be caused by intrinsic resistance to antifungal drugs, and also by the angioinvasive nature of some of these mycoses, which causes distal pulmonary infarction. As blood flow is blocked, antifungal drug penetraiton is decreased. Both considerations must be addressed.
With the development of infarction, there is decreased penetration of polyenes and presumably all antifungal drugs into tissue. Inadequate delivery of antifungal drugs is one reason which causes *in vitro* susceptible pathogens, like *Aspergillus* species (triazoles) or zygomycetes (polyenes) to progress in the presence of antifungal therapy which "should be effective". Management of clinical resistance in these patient can be improved at the outset, by accelerating the speed of diagnosis and initiating treatment more promptly. Tools for this include a) rapidlly identifying patients at high risk and b) intensive surveillance with serum (and now bronchoalveolar lavage) galactomannan, beta-D-glucan, and PCR. The former allows identification of groups for antifungal prophylaxis, and the latter allows for identifcation of patients ever earlier in the course of disease. There is room for considerable improvement in rapid diagnosis.
Intrinsically high resistance to antifungals can be predicted for many (not all) isolates simply by identifying the fungal species. This is straightforward for polyene resistance of *Aspergillus terreus*, or almost pan-antifungal resistance of *Scedosporium prolificans*. Others, such as *Fusarium or Paecilomyces* species, are very challenging, but may respond to high levels of certain antifungals. For these patients animal studies and small clinical series may provde guidance. There is great temptation to use combinations of antifungal drugs, especially when synergy is suggested by *in vitro* studies. This area is complicated by the rarity of such isolates and inability to collect large series of infected patients. For some, recommendations may need to be individualls tailored.

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Room: South Hall
Type: Invited Presentation

The endemic systemic Fungal Infections in Latin America

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Corporacion para Investigaciones Biologicas (CIB), Medellin, Antioquia, Colombia

Three endemic mycoses, coccidioidomycosis (C), histoplasmosis (H) and paracoccidioidomycosis (P), have relevance in Latin America as they occur in most countries of the region although their distribution is not homogenous. The etiologic agents are the soil-related dimorphic fungi Coccidioides immitis, Histoplasma capsulatum and Paracoccidioides brasiliensis, which in their saprophytic mold form and under certain environmental conditions produce microconidia (< 5mμ). These propagules become air-born and are accidentally inhaled by man; once in the lungs they convert to the tissue e forms. Most patients are adult males engaged in aerosol-generating activities (agriculture, forestry, masonry, speleology), with women and children being afflicted less often. The three mycoses initiate their pathologic expression in the lungs but extra-pulmonary dissemination is common mainly to mucous membranes, skin, lymph nodes, liver, spleen, adrenals, bones, CNS and others; these entities are systemic and one-organ affection is rare. Signs and symptoms may be related to the respiratory tract but are more often referred to secondary lesions making it difficult to confirm suspicion on clinical evidence alone. Image studies vary depending on the diseases' course and include infiltrates, nodules, cavities, pleural retraction, fibrosis and calcifications. Definitive diagnosis is established only on mycological grounds through biopsies, direct examinations and cultures. The three etiologic agents' differential characteristics under the microscope plus the type of propagules produced in cultures, allow their precise identification. Availability of several indirect tests to determine circulating antibodies and antigens and also of several DNA-based tests serve to confirm diagnosis and facilitate follow-up studies. These mycoses are difficult to treat requiring prolonged courses and careful medical supervision. Treatment has greatly improved with the advent of the new triazoles (itraconazole, voriconazole, posaconazole) but amphotericin B remains a major therapy; recovery is contingent on prompt diagnosis, patient's immune status and stage of the mycosis at therapy initiation.

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Fungal Skin Infections in the Tropics

R. Hay
International Foundation of Dermatology, London, United Kingdom

The main challenges confronting us in the tropical mycoses are 1) rapid and accurate diagnosis 2) the availability of appropriate therapy and 3) a rising incidence of certain infections. Diagnosis is dependent on the logical association between the clinical appearances and appropriate laboratory steps. However key features of fungi that aid their recognition are their size and the simple cultural and histological techniques used to detect them. Use of conventional histopathology or immunopathological techniques is highly effective in many cases but molecular tools are now used for some conditions including dermatophytosis and sporotrichosis. With some mycoses the process is simpler. In mycetomas, for instance, histological or cultural evidence can be obtained directly from sinuses or by biopsy.
Most new antifungals have not been profiled with tropical mycoses in mind and there are few evidence-based clinical trials to establish usage or duration of therapy . The commonest of these infections that present major therapeutic problems are the mycetomas and chromoblastomycosis. Fungal mycetomas seldom respond to normal doses of antifungals; whereas those caused by bacteria, actinomycetomas, respond to a range of antibacterials such as dapsone, amikacin, fusidic acid, imipenem etc unless they are very extensive. There is only limited reporting of the use of newer azoles, posaconazole and voriconazole in these mycoses. Mycoses where there have been changes in epidemiology, suggesting, spread include tinea capitis. Spread of *Trichophyton tonsurans* infections to South America and West Africa are examples. Whereas HIV in many countries is controlled through the use of antiretrovirals in infected individuals late recognition is a feature in many areas of the tropics and therefore there is a continuing risk of systemic fungal infections presenting with skin lesions as their first and most obvious clinical manifestation. Being alert to these changes provides a rapid means of dealing with these infections.

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Final Abstract Number: 15.004
Session: Update on fungal infections
Date: Wednesday, March 10, 2010
Time: 10:15-12:15
Room: South Hall
Type: Invited Presentation

Prevention and Treatment of Nosocomial Candidiasis

M. Nucci
Univ. Fed. Rio de Janeiro, Rio de Janeiro, Brazil

Candidemia is an important nosocomial infection, with high incidence and mortality rates. Strategies for the management of candidemia include prophylaxis and treatment of established infection. Prophylaxis is more likely to benefit groups of patients with high incidence of candidemia, such as premature neonates, allogeneic hematopoietic stem cell transplant recipients and high-risk liver transplant recipients. For the treatment of candidemia, various studies have been conducted comparing different drugs, such as fluconazole, voriconazole, deoxycholate and liposomal amphotericin B, and the echinocandins caspofungin, micafungin and anidulafungin. In general, the echinocandins represent the best option for the initial treatment of candidemia. In addition to prophylaxis and treatment, attempts to define a group of patients that may benefit from early empiric or preemptive have been developed. These include the development of prediction rules and the use of serum biomarkers such as 1,3-beta-D-glucan and polymerase chain reaction-base techniques.

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Final Abstract Number: 16.001
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Date: Wednesday, March 10, 2010
Time: 14:15-15:01
Room: Ballroom 1: Brickell
Type: Invited Presentation

The Changing Patterns of Global Migration and the Impact on Infectious Diseases

M. Cetron
CDC, Atlanta, GA, USA

Human migration has always been associated with disease translocation. Over the last century the speed and volume of international travel and migration has reached unprecedented levels bringing the impact of globalization into every sector of society- economic, environmental, political, socio-cultural, and health. As a consequence, the threat of geographic expansion from emerging and traditional infectious diseases has increased. UNESCO defines an international migrant as a person living outside their birth country for >= 12 months. The global patterns of human migration have changed substantially in the last half century: 1) increased # countries sending and receiving migrants, 2) accelerated rates of migration, 3) bi-directional migration and migration transitions, 4) diversification of migrant types, and 5) changes in gender patterns of migrants. Along with these profound changes in demography, volume, speed, and purpose of migration come unique challenges in detection, diagnosis, response and management of infectious diseases. Even in the 21st Century infectious diseases account for ~25% of the global mortality burden as well as substantial morbidity. Increasingly these diseases are blind to geopolitical borders. Cyclical pandemics like influenza traverse the globe more rapidly than ever; newly emerged pathogens like SARS represent a constant challenge to public health preparedness and response. Even old diseases like tuberculosis emerge in more lethal drug-resistant forms e.g. XDR-TB. These challenges demand new paradigms to global disease control in governance, surveillance and response. The 2005 International Health Regulations and a range of newly formed international networks and partnerships are a testament to the challenges posed by the new era of migration. Our success in combating these microbial threats will depend on our collective effort to organize and respond on "supra_national" level.

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Session: Will the next generation end AIDS?
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Time: 15:45-17:45
Room: Ballroom 1: Brickell
Type: Invited Presentation

Role of innate immunity in the control of HIV infection

G. Alter
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While the immunological correlates that contribute to slower HIV disease progression are still unknown, epidemiologic data strongly suggest that particular major histocompatibility complex (MHC) class 1 alleles (including -B27, -B57, and others that fall within the HLA-Bw4 family of HLA-class I B alleles) are highly enriched in subjects who maintain undetectable viral loads in the absence of antiretroviral therapy, Elite controllers. While these MHC molecules interact with T-cell receptors found on cytotoxic CD8+ T cells, they also interact with innate immune receptors, such as the Killer Immunoglobulin like receptors (KIR) found on the surface of innate cytotoxic Natural Killer (NK) cells. Furthermore, the protective effect of MHC class I alleles is amplified in subjects that co-express particular KIRs, with which they are able to interact, resulting in slower progression to AIDS in these individuals compared to those that only possess the KIR or MHC allele alone. Thus it is plausible that NK cells may play a central role in the control of HIV infection. NK cells expand rapidly following acute infection, and specific populations of KIR+ NK cells expand preferentially in subjects that co-express protective KIR/MHC class 1 combinations. This specific KIR3DS1+ NK cell clonal expansion persists for up to 1 year in the peripheral circulation, and is associated with more aggressive containment of HIV-viral replication in vitro, these NK cells exhibit a more polyfunctional cytokine profile, and kill MHC class 1 target cells more more aggressively than NK cells from individuals that do not have the protective KIR/HLA combined genotype. However, despite this early epansion of NK cells in the periphery, these cells do not gain access to secondary lymphoid organs, thus providing a safe haven within which the virus is able to replicate unabated by the innate immune system, potentially allowing the virus to establish a chronic infection. These data strongly suggest durable control of HIV infection is associated with an early aggressive deployment of highly licensed antiviral NK cells in the periphery that may provide specific and non-specific control of HIV viral replication in acute infection, while producing large quantities of cytokines and chemokines required for the induction of high quality adaptive immune responses that may then maintain control of HIV replication most likely in contained tissue sites.

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Time: 15:45-17:45
Room: Ballroom 1: Brickell
Type: Invited Presentation

The Role of T Cell Immunity in the Control of HIV Infection

N. Goonetilleke[1], M. K. Liu[2], V. Ganusov[3], E. Giorgi[3], J. Salazar[4], H. Li[5], J. Kirchner[6], E. Turnbull[1], V. Bourne[1], S. Moore[1], H. Yang[7], B. Keele[4], P. Borrow[1], M. Cohen[8], A. Perelson[3], F. Gao[6], B. Hahn[4], G. Shaw[4], B. T. Korber[3], A. J. McMichael[1]
[1]University of Oxford, Oxford, United Kingdom, [2]Oxford University, Oxford, United Kingdom, [3]LANL, Santa Fe, NM, USA, [4]University of Alabama, Birmingham, AL, USA, [5]University of Alabama, Birmingham, AB, USA, [6]Duke University, Durham, NC, USA, [7]Unversity of Oxford, Oxford, United Kingdom, [8]UNC Chapel Hill, Chapel Hill, NC, USA

The window between transmission and peak viremia, prior to the establishment of viral reservoirs, is the narrow but critical period in which a HIV-1 vaccine must control viral replication, prevent extensive CD4 T cell destruction and curb generalised immune activation. We recently published the results of T cell studies in 4 patients, showing that the first HIV-1 specific T cells detectable just prior to peak viremia can select for complete virus escape in as little as 14 days. Mathematical modeling of these very rapid rates of T cell escape showed that the contribution of CD8+ T cell mediated killing of productively infected cells was earlier and significantly greater than previously described; calculating that T cells in acute HIV-1 kill as much as 35% of virus-infected cells per day. These first T cell responses often waned rapidly following virus escape leaving, or being succeeded by, T cell responses to epitopes that escaped slowly or were invariant. Here, we present data from an additional 10 patients that extend these observations and demonstrate that early rapid escape from primary HIV-1-specific T cell responses occurs in the majority of patients studied, suggesting that T cells are major contributors to the control of viremia in acute HIV-1 infection. Additional data will be presented on functional avidity, phenotyping and kinetics across the group over the first 6 months of infection. Discussion will focus on how these results, together with the studies investigating new immunogens may direct more effective design of HIV-1 T cell vaccines. Supported by the NIAD Center for HIV/AIDS Vaccine Immunology grant # U19 AI067854

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Room: Ballroom 1: Brickell
Type: Invited Presentation

Understanding Anti-HIV Antibody Targets

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HIV-1 subtype C viruses elicit potent but highly type-specific neutralizing antibodies within the first year of infection. In order to determine the specificity and evolution of these autologous neutralizing antibodies, we examined neutralization escape in four individuals infected with HIV-1 subtype C from the CAPRISA 002 cohort in Durban, South Africa. Early neutralizing responses recognized a very limited number of epitopes, with antibodies that recognize new epitopes evolving sequentially. In addition, only two regions of the envelope were targeted by these antibodies, suggesting there might be common vulnerabilities in the HIV-1 subtype C transmitted envelope. We have shown that type-specific responses have a short term affect on viral load which is lost with the emergence of viral escape mutants. Factors that contribute to the development of broadly cross-reactive neutralizing antibodies, those which would ideally be elicited by an HIV vaccine, are largely unknown. We have examined the evolution of neutralization breadth in the CAPRISA 002 cohort, and shown that cross-neutralizing antibodies develop in about a quarter of infected individuals by 3 years post-infection. Generally breadth develops incrementally suggesting the possibility that multiple antibodies mediate breadth, and/or that breadth is conferred by the maturation of a single specificity. In one case, the development of breadth could be attributed to a single neutralizing antibody specificity. In the CAPRISA 002 cohort, as well as in a cross-sectional cohort of chronically infected individuals, we have explored the targets of cross-reactive antibodies which mediate breadth using an array of methodologies including peptide and protein adsorptions and the use of chimeric viruses. We have shown that multiple epitopes on the envelope glycoprotein are involved in the cross-reactive neutralization elicited during natural HIV-1 infection, many of which are yet to be determined.

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Room: Ballroom 1: Brickell
Type: Invited Presentation

The Hope and Progress in Microbicides and Pre-Exposure Prophylaxis to Prevent HIV

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Even with a growing recognition that HIV doesn't discriminate by race, gender, socioeconomic status or sex orientation, the developing world accounts for 90% of the global HIV burden. Sub-Saharan Africa, which accounts for two-thirds of the global HIV infections, Injecting Drug Users, Men who have Sex with Men, and Commercial Sex Workers bare a disproportionate burden of the HIV epidemic. Recent HIV surveillance studies in African countries at best show stabilization of the epidemic or at worst, slight increases in countries like Uganda.
Clearly, the HIV research community recognizes that additional new biomedical prevention modalities are required to augment existing HIV prevention strategies.
Incidence modeling based on as relatively low efficacy as 30% for a Pre-Exposure Prophylaxis (PrEP) regimen or a topical Microbicide has provides a glimmer of hope based on number of new HIV infections prevented through such new modalities. However, scientists need to prove efficacy for these new regimens first.
Several international collaborations with the developing world have been formed to enable us conduct clinical research that meets international standards. Phase IIB and phase III HIV PrEP and Microbicide trials are being conducted in nine countries globally, involving over 20,000 participants in the various high risk groups and across different HIV transmission routes. Each study is being overseen by regulatory agencies both within the developing and the developed world.
The major lessons learned to date are that; North-South collaborative partnerships are critical to realizing the hope of finding new prevention modalities to be added to the HIV prevention tool kit for the most-at-risk groups. Secondly, with these collaborations, the developing world has developed capacity to conduct of clinical research that conforms to international standards for licensure of new products or change of indication of existing drugs/products in the developing world.

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Session: The H1N1 influenza pandemic
Date: Wednesday, March 10, 2010
Time: 15:45-17:45
Room: Ballroom 2: Monroe/Flagler
Type: Invited Presentation

Historical perspective: Lessons Learned from past Pandemics

D. Morens
NIAID, NIH, Bethesda, MD, USA

It has been exactly 500 years since the first recognized influenza pandemic appeared and spread around the world in 1510. Since that time, at least 13 additional influenza pandemics have been studied by countless historians, physicians and scientists. Influenza and its complications have been well characterized clinically, much has been learned about pandemic epidemiology, and a lore about influenza pandemic behavior has developed over these past five centuries. This includes ideas about pandemic genesis, pandemic cycling, and pandemic wave-like behavior. However today, in the genomics era, much of what we thought we knew is beginning to unravel, and we are quickly discarding old ideas to replace them with rapidly expanding new knowledge. Pandemic influenza was examined using historical research approaches incorporating modern scientific methods to develop a comprehensive overview.
In recent years we have come to understand that there are at least several different mechanisms by which pandemic influenza viruses may be generated, that pandemic cyclicity is probably partly if not wholly a myth, that pandemics may be regional or global, that for most of the past 500 year domestic animals have played a major role in influenza epidemiology, that wave-like pandemic behavior is not inevitable and probably not wholly a viral property, and that influenza co-pathogenesis with common colonizing nasopharyngeal bacteria probably accounts for most influenza-related deaths.
Much remains to be learned about pandemic influenza, and we can expect an explosion of knowledge in the coming decade. It is truly a time to fasten our seatbelts, because the roller coaster is leaving the platform.

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Room: Ballroom 2: Monroe/Flagler
Type: Invited Presentation

The H1N1 Outbreak in Mexico

S. Ponce de Leon
Mexico, Mexico

On April 23rd 2009, health authorities in Mexico informed that a new virus was causing an increasing number of severe pneumonia cases in adults with unusually high mortality. After three weeks of intensive clinical and epidemiological research, a new influenza virus was identified as the unknown pathogen in most of the clinical samples sent by Mexico to labs in Winnipeg and Atlanta. The WHO was notified on the night of the 22nd, as soon as the information on etiology was available. At the same time, strict distancing measures were initiated in Mexico City and its suburbs; schools were closed and noncritical activities suspended.
The problem was first evident at the Emergency Room of the National Institute of Respiratory Diseases, and confirmed by simultaneous reports received from San Luis Potosi and Oaxaca. We focused our analysis on cases with severe viral pneumonia and thus overestimated the mortality of the virus during the first weeks of the outbreak – the full picture was apparent only afterwards. The initial response was timely as oseltamivir, educational materials, and protective medical equipment were ready to be sent thanks to Mexico's national preparedness plan for a pandemic. 1340 cases fulfilled the case definition during the first month. Mexico's strict social distancing measures had a significant impact on the number of cases but were later relaxed. The epidemic curve shows a sharp increase, followed by a decrease in the number of cases, with growth during June and July due to a high number of cases in the southeast region. More recently, another wave of increased transmission was present in the metropolitan area.
A significant feature of this outbreak has been the increased mortality in patients between 15 and 55 years old, some previously healthy, with no increase in the young and the old population. Pregnancy and obesity have also been identified as risk factors for severity. Previous immunity probably plays a role in the severity related to age.
Many lessons should be learned from this epidemic: Collaboration, preparedness, transparency, and the importance of being alert towards the unexpected.

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Time: 15:45-17:45
Room: Ballroom 2: Monroe/Flagler
Type: Invited Presentation

Global Surveillance of the H1N1 Pandemic

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WHO, Geneva, Switzerland

Pandemic surveillance can be viewed from two perspectives, the need to detect the emergence of a novel strain of influenza virus and the need to monitor the progression of spread of the virus. In monitoring pandemic progression, the primary goal is to describe and detect changes in several important epidemiological characteristics of the event. These include severity, both in terms of virulence and impact on society, transmission dynamics, risk groups, and the clinical characteristics and spectrum of disease. Several methods are used for doing this at the global level. These include the existing network of National Influenza Center laboratories through FluNet; monitoring of reports from ministries of health both on web sites and formal submissions; monitoring of media reports, formal communications through WHO country offices and national focal points for International Health Regulations; formal networks of epidemiologists, virologists, and clinicians; and through informal networks of friends, colleagues, and acquaintances. Several shortcomings have been highlighted by the current pandemic including lack of standardization for reporting of a variety of parameters, lack of standard surveillance methods for severe disease, lack of a requirement for reporting of data once initial notification occurs, and the challenge of getting timely data when countries are busy responding to a public health emergency. WHO has proposed a system of sentinel surveillance for severe acute respiratory infections which will be reported country by country onto a global platform which will allow more systematic monitoring of both pandemic and seasonal influenza.

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Room: Ballroom 2: Monroe/Flagler
Type: Invited Presentation

International response to the H1N1 pandemic

A. S. Monto
University of Michigan School of Public Health, Ann Arbor, MI, USA

Heightened global concern about an influenza pandemic can be dated back to 2003, when the SARS outbreak was followed by the spread of highly pathogenic A (H5N1) infections in poultry with occasional spread to humans. These illnesses had a high case fatality ratio, which increased the worry of the potential effect of a pandemic caused by this subtype. The WHO developed a variety of tools for countries to use and made preparations for vaccine stockpiling. Plans were developed to contain any focal outbreak with antivirals. Pandemic phases were established to define extent of adaption of an animal virus to humans and subsequent spread. Severity of the pandemic was not quantified in a scale. Fortuitously, modification of the phases had been put in place well before transmission of pandemic H1N1 virus was recognized in April, 2009.

The H1N1 pandemic has been very different from that anticipated based on the virulence of the H5N1 virus. Paradoxically, this was initially a problem, since some countries' plans were geared only to severe pandemics. Some borders were effectively closed for a time, even though this was against the pandemic IHR recommendation. There was also confusion between containment and mitigation, in part because of the rapidity of spread of the virus.

Overall, preparations for a more severe pandemic had positive results. Many developed countries had antiviral stockpiles, which they used in different ways. Development of a monovalent pandemic vaccine moved ahead rapidly. Not only were adjuvanted and nonadjuvanted inactivated vaccines used but live attenuated vaccines were employed as well. Technology transfer will make these approaches available in more countries. The need for only one inoculation of vaccine will make more vaccine available to risk or priority groups in developing countries. Equity issues clearly need to be addressed as we go forward. The time periods between pandemics have been irregular, and the next might not wait 40 years to occur.

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Session: Malaria in the Americas
Date: Wednesday, March 10, 2010
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Room: Ballroom 3: Tuttle
Type: Invited Presentation

Epidemiology and Intensity of Transmission
K. Carter
PAHO, Washington, DC, USA

Malaria transmission was eliminated from a number of territories in the Americas but still occurs in 21 countries in the Region. The presentation focuses on past and present strategies and goals to combat malaria in the Region, trends, the present situation and challenges as well as on financial resource mobilization including that for operational research.
After the Global Malaria Eradication Strategy was abandoned, it was replaced by the Global Malaria Control Strategy in 1992 and the strengthening of efforts to reduce the global burden of the disease was catalyzed by the Roll Back Malaria Initiative (RBM) which was launched in 1998. The goal of the RBM initiative was to reduce the burden of disease by 50% by 2010. The United Nations Millennium Development Goals were launched in 2000 with Goal 6 calling “to halt and begin to reverse the incidence of malaria by 2015”. At the World Health Assembly in 2005, Resolution WHA58.2 called for an additional 25% reduction from the RBM target; with the goal of reducing the burden between 2000 and 2015 by 75%.
The burden of malaria reported in the Americas by Member States decreased from over one million cases and over three hundred deaths in 2000 to just under 573 thousand cases representing a 52% reduction in cases and 57% reduction in malaria related deaths between 2000 and 2008.
Plasmodium vivax is the leading cause of malaria in the Region, accounting for approximately 75% of all cases with *P. falciparum* being the cause of almost all other cases and a small number due to *P. malariae*. In the countries sharing the Amazon rain forest, similar proportions are observed while in Mexico, Central America, Argentina and Paraguay *P. vivax* accounts for over 90% of the cases. In Hispaniola, the only endemic island in the Caribbean shared by the Dominican Republic and Haiti; almost 100% of the cases are due to *P. falciparum.*
There has been a reduction in the overall malaria incidence in recent years but the disease still constitutes a public health problem in the region with a disparity in outcome of efforts in different countries related to a number of factors including variations in ecological conditions, diagnostic and treatment coverage, weaknesses in health systems and technical capacity issues. Operational research is important for evidenced based decision making.
The greater part of the financial resources for national malaria efforts to combat the disease is provided by national governments but there has also been additional resource mobilization in the Region including that of the Amazon Network for Monitoring Antimalarial Drug Resistance with funding available through the United States Agency for International Development’s (USAID) Amazon Malaria Initiative (AMI). Additionally, individual country projects in Bolivia, Guatemala, Guyana, Haiti, Honduras, Nicaragua and Suriname have been financed by the Global Fund to combat HIV/AIDS, Tuberculosis and Malaria (GFATM) as has been a multi-country Andean proposal by the Organismo Andino de Salud (ORAS) to the GFATM for Colombia, Ecuador, Peru and Venezuela. Towards the end of 2009, proposals by Brazil, Colombia, the Dominican Republic and Ecuador were approved by the GFATM. The Global Environment Facility / UN Environmental Program also supported a project for the prevention of the reintroduction of DDT use in malaria vector control in Mexico and Central America.
With reduction of the malaria burden in different geographical regions worldwide, there have been calls for renewed efforts to eliminate malaria. The presentation includes suggestions for lessons learnt from the eradication era to be borne in mind.

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Room: Ballroom 3: Tuttle
Type: Invited Presentation

Need for chemoprophylaxis for travelers to the Americas: Yes

P. Arguin
CDC, Atlanta, GA, USA

International travelers may sometimes acquire infectious diseases such as malaria during their journeys. This session will be a debate about the usefulness of malaria chemoprophylaxis for travel to the Americas. Malaria can be a fatal disease even when it is diagnosed early and treated correctly. It is preferable for persons at risk of infection with malaria to prevent the infection.

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Time: 15:45-17:45
Room: Ballroom 3: Tuttle
Type: Invited Presentation

Need for Continuous Prophylaxis for Travelers to the Americas: No

M. Boulos
University of Sao Paulo, Sao Paulo, Brazil

The risk a traveler becomes infected by malaria will depend on the overall rate of malaria transmission in the area to be visited and the extension of the traveler's contact with infected mosquitoes.
Topics like: 1. Wearing long-sleeve shirts and long trousers; 2. Applying insect repellent; 3. Spraying aerosolized insecticides in living and sleeping places; 4. Sleeping in a screened or air-conditioned rooms; 5. Sleeping on netted bed; and 6. Use mosquito coils containing pyrethroids are consensual measures in all malaria transmission areas, and the use of chemoprophylaxis are not consensual in low endemic areas (Wyler, NEJM 1993)
My aim is convincing you that the routinely use of malaria chemoprophylaxis is not needed in America.
The use of anti-malarial chemoprophylaxis should be carefully directed at high risk travelers when the benefit of using anti-malarial drug regimens outweighs the risk of adverse events. The risk for adverse events during the anti-malarial drugs for prophylaxis is in the range of 30-40%.
Everyone knows that malaria is a disease of low incidence in America and most of these cases are in topic areas where tourists only occasionally reach.
A retrospective study conducted on Italian travelers found that malaria incidence was 1.5/1000 for trips to Africa, 0.11/1000 for trips to Asia, and 0.04/1000 for trips to Central and South Americas. Another study among Swedish travelers found a number four times lesser among travelers to America (Croft AM. BMJ 2007).
The use of chemoprophylaxis against malaria in this scenario, where contra-indications overlap the benefits, show us the inadequacy of routinely use of drugs to prevent malaria in Americas.
In a restrict number of cases when the travelers must stay in remote malaria transmitting areas in America, for long period o time, we recommend standby treatment.

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Room: Ballroom 3: Tuttle
Type: Invited Presentation

Choice of Drugs for the Prophylaxis of Malaria in the Americas

A. Magill
Walter Reed Army Institute of Research, Silver Spring, MD, USA

Preparing a traveler for a trip to the Americas often includes a discussion about the prevention of malaria with personal protection measures to minimize mosquito bites and the recommendation to use a drug for chemoprophylaxis when appropriate. The characteristics of malaria in the Americas that differ from many other areas of the world include the relatively low transmission rates, the predominance of vivax malaria in most locations, and the relatively wide availability of quality medical care for tourists. Use of all current approved malaria chemoprophylaxis drugs will be discussed with special emphasis on primaquine, the only currently available drug that can prevent vivax malaria.

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Date: Wednesday, March 10, 2010
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Room: Room Jasmine
Type: Invited Presentation

Escherichia coli

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Escherichia coli is a remarkably versatile organism able to easily acquire antimicrobial resistance as well as virulence determinants. *E. coli* is the leading pathogen causing urinary tract infections and one of the most common organisms implicated in bloodstream infections. Its ubiquity in the community and hospital setting, together with antibiotic overuse, have delineated a scenario in which multidrug resistant isolates are not infrequent and appear as a foremost challenge for clinicians to achieve therapeutic success.
Beta-lactam resistance owing to the presence of extended-spectrum-beta-lactamases (ESBLs) is globally spread among *E. coli*, particularly due to CTX-M-type enzymes, and coexistence of more than one beta-lactamase in the same isolate has also been observed. Moreover, co-resistance to non-beta-lactam antimicrobials is a common feature among ESBL-producers as resistance genes to unrelated antimicrobial compounds such as aminoglycosides, tetracyclines, sulfonamides, trimethoprim, and chloramphenicol are simultaneously harboured by conjugative plasmids carrying transposons and/or integrons where these genes are located. The prevalence of certain phylogroups exhibiting these multiresistant phenotypes has recently been associated with a genetic island that comprises genes encoding antibiotic resistance and virulence in particular *E. coli* clones such as the ST131 clone. Concomitant resistance to fluoroquinolones due to mutated topoisomerases in many of these isolates is an alarming reality.
Incidence of *E. coli* isolates carrying plasmid-AmpC cephalosporinases is raising in many countries and, although carbapenems are still broadly active against *E. coli*, the incidence of carbapenemases merits strict supervision mainly in geographic areas where this resistance appears to be endemic in other species such as *Klebsiella pneumoniae.*
Other resistance traits have been described in *E. coli* clinical isolates as plasmid-mediated quinolone resistance due to *qnr* and *aac(6')-Ib-cr* genes, and the efflux pump QepA. Moreover, production of plasmid 16S rRNA methylases has recently drawn attention as a novel aminoglycoside resistance mechanism in pathogenic gram-negative bacteria including *E. coli*. It confers high-level resistance to all aminoglycosides that are currently available.
Multiresistance in *E. coli* affects almost all antimicrobial families, it is easily transmitted through successful and virulent clones and can be spread from and among not only humans but animals and food. The role of continuous antimicrobial pressure in this phenomenon is unquestionable and requires control measures to curtail the spread and maintenance of these multiresistant isolates with high likelihood of causing serious and almost untreatable infections.

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Session: Current issues in multi drug resistant gram-negatives
Date: Wednesday, March 10, 2010
Time: 15:45-17:45
Room: Room Jasmine
Type: Invited Presentation

Multidrug resistance in *Klebsiella pneumoniae*

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Hospital-acquired and clinically-important Gram-negative pathogens remain mostly *Enterobacteriaceae, Pseudomonas aeruginosa* and *Acinetobacter baumannii*. Among those Gram negatives, *Klebsiella pneumoniae* remains an important source of hospital spread of multidrug resistance. Wide-spectrum β-lactamases are increasingly reported in *Enterobacteriaceae* being either clavulanic-acid inhibited extended-spectrum β-lactamases (ESBLs) or carbapenem-hydrolyzing β-lactamases (CHBLs). Although first reported in *Klebsiella pneumoniae* mostly from 1980's to 2000's, ESBLs are developing rapidly among community-acquired *Escherichia coli*. These novel ESBLs of the CTX-M-type are reported worldwide with important structural and genetic diversity. Those ESBL genes may be transmitted from *E. coli* to *K. pneumoniae* providing a novel source of hospital-acquired multidrug-resistant *K. pneumoniae* since there are associated to other plasmid-mediated resistance determinants. The CHBLs identified in *Enterobacteriaceae* are mostly metallo-β-lactamases (Ambler class B enzymes) of the VIM/IMP-types in hospital-acquired *K. pneumoniae*. The Ambler class A carbapenemases of the KPC-type are also identifed mostly in *K. pneumoniae*, first from the USA and then worldwide. The latest reported CHBL in *K. pneumoniae* is OXA-48 mostly from Mediterranean countries. All this carbapenemase producers are difficult to detect in a clinical laboratory and may the source of multidrug resistance leading to therapeutic deadend*. K. pneumoniae* will remain the most important enterobacterial species as a source of multidrug resistance in hospital-acquired Gram negative isolates.

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Pseudomonas aeruginosa

G. Cornaglia
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NO ABSTRACT RECEIVED

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Evolution of antimicrobial resistance in *Acinetobacter baumannii:* Factors affecting multiresistance

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Acinetobacter baumannii are an important cause of nosocomial infections mainly in patients in the intensive care units. In this presentation I will analyse the evolution of antimicrobial resistance, the molecular bases associated with the increase in antimicrobial resistance, the factors affecting multiresistance and the current treatment of *Acinetobacter* infections.
Antimicrobial resistance has steadily increased in the last decade. Nowadays *A. baumannii* clinical isolates resistant to all antimicrobial agents even to colistin (panresistant) have been isolated in the nosocomial setting. Three major factors favour the acquisition of multiresistance: 1. Intrinsic resistance, mainly related to the interplay between decreased permeability (small number of porins) and constitutive expression of efflux pump(s) (AdeIJK, CraA); 2. Persistence in the environment, in this sense, biofilm-producing *A. baumannii* clinical isolates survive in inanimate surfaces longer than those non-producing biofilm. 3. Acquisition of genetic elements. It has recently been shown that resistance islands with a variable composition of resistance determinants interspersed with transposons, integrons and other genetic elements play an important role in the acquisition of multiresistance. However, this is not an universal contributor to multiresistance since target mutations, overexpression of efflux pumps, and IS elements located upstream from some resistance genes have also been found to be implicated in multiresistance.
Although some clinical isolates are still susceptible to carbapenems and colistin, and therefore these antimicrobial agents can continue to be used, few options are available to treat infections caused by this microorganism. Tygecycline has been used to treat infections caused by *A. baumannii.* However, emergence of resistance to this antimicrobial agent has been reported during treatment when this monotherapy.
This microorganism, albeit with slight differences depending on the country**,** presents resistance to multiple antimicrobial agents, occasionally including resistance to colistin, hence, it can be considered the paradigm of nosocomial multiresistant bacteria.

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Type: Oral Presentation

Incidence and trends of imported malaria in the Netherlands: 2000-2007

G. Van Rijckevorsel[1], G. J. B. Sonder[1], R. B. Geskus[1], P. J. J. Van Genderen[2], M. Keuter [3], R. J. Ligthelm [4], L. G. Visser[5], J. C. F. M. Wetsteyn [6], J. A. R. Van Den Hoek[1]
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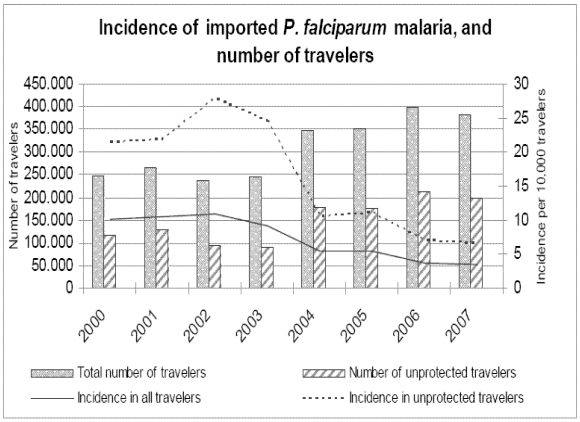
Background: To describe the epidemiology and trends of imported malaria in the Netherlands from 2000 until 2007.
Methods: National surveillance data on all notified infections of imported malaria, diagnosed between January 2000 and January 2008 were analyzed. Incidence and trends in imported malaria were estimated using the number of Dutch travelers visiting malaria endemic countries as denominator. In addition, the annual number of prescriptions for malaria chemoprophylaxis collected from pharmacies in the Netherlands was used to estimate the number of unprotected travelers.
Results: The annual number of imported malaria infections (all species) fell from 535 in 2000, to 197 infections in 2007. Most infections (72%) were acquired in Sub-Saharan Africa, and 75% were caused by *Plasmodium falciparum*. In the same period, travel to malaria endemic countries increased from 247,000 to 384,000 travelers per year. The number of prescriptions for malaria chemoprophylaxis increased from 131,400 to 186,300 (53% and 48% of all travelers respectively) per year. Yet, the absolute number of unprotected travelers rose from 115,600 to 197,700. The overall incidence in imported *falciparum* malaria per 10,000 unprotected travelers fell from 21.5 to 6.6. The incidence of imported *falciparum* infections is greatest from Middle and West Africa, and decreased from 121.3 to 36.5 / 10,000 travelers. The import of malaria from this region by immigrants visiting friends and relatives (VFR) decreased from 138 infections in 2000, to 69 infections in 2007.



Conclusion: The annual number of imported malaria shows a continuing declining trend, even with an increasing number of travelers visiting malaria endemic countries. This decline is not readily explained by the increased use of malaria chemoprophylaxis, but could also be explained by a reduced risk of infection due to lessening local malaria transmission as observed in some malaria endemic areas. VFR import less malaria than previously, and contribute largely to the declining incidence seen. Although the incidence in imported malaria has decreased, the increasing number of travelers not using malaria chemoprophylaxis remains worrisome.

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Type: Oral Presentation

Predictors of primary multiple drug resistant tuberculosis (MDR-TB) transmission in Lima, Peru

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Background: The emergence of MDR-TB strains is considered among the greatest threats to global TB control. Despite a well-established national directly observed therapy (DOTS) TB control program with high treatment compliance rates and a low burden of HIV co-infection among cases, Peru has among the highest MDR-TB incidence rates in the Americas. Understanding primary MDR-TB transmission is essential for developing effective control strategies and preventing further emergence.
Methods: Using a semi-structured questionnaire, we conducted a case-control study of risk factors for primary MDR-TB in San Juan de Lurigancho (SJL), a Lima district with the highest TB rates in Peru. Consecutive, consenting TB cases (drug sensitive (DS) and primary MDR-TB cases) followed in SJL clinics and randomly selected healthy community controls were enrolled. Questionnaire data were analyzed using Chi-square tests and logistic regression comparing primary MDR-TB cases with DS-TB and healthy community controls.
Results: Sixty MDR-TB cases, 80 DS-TB and 80 community controls enrolled. MDR-TB cases were significantly more likely to have a household contact diagnosed with TB compared with DS-TB cases (OR 3.20 p=0.003) and community controls (OR 16.0 p<0.0001) in the 3 years prior to their own diagnosis. While MDR-TB cases and DS-TB cases were equally likely to have had a TB diagnosis in their workplace, 40% of MDR-TB cases reported being unsure if there was a TB diagnosis at work in comparison to 20% of drug sensitive TB cases (OR. 3.18 p=0.006). Spending time in hospitals or clinics, methods of transportation, visiting the prison and geographic location within SJL were not statistically associated with MDR-TB. Further analyses are required to confirm the strength of the effect after considering potential confounders, however preliminary multivariate models show that household and workplace contact with TB remain significant predictors of primary MDR-TB.
Conclusion: These results support ongoing community transmission of primary MDR-TB in SJL. Though a basic contact tracing program is in place for household contacts aged ≤ 15 years old and others are encouraged to present for care if they develop symptoms, control measures in addition to DOTS are likely needed to stem community transmission of primary MDR-TB.

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Type: Oral Presentation

Foodborne *Campylobacter* infections have a low impact on human health: A community-based cohort study in Yucatan, Mexico

M. B. Zaidi[1], F. D. Campos[1], F. Martinez[1], F. Gutierrez[1], A. Polanco[1], M. Leon[1], S. Patzi-Vargas[2], T. Estrada-Garcia[2], J. J. Calva[3]
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Background: In recent years, antimicrobial-resistant *Campylobacter* has become a major public health concern. There is a need for conducting community-based integrated food chain surveillance to determine the impact of resistant *Campylobacter* on human health in highly endemic settings.
Methods: A 15-month cohort study was conducted in Buctzotz, a small, well-nourished, agricultural community in Yucatan, Mexico. Household visits were performed twice a week to detect diarrheal episodes, collect fecal specimens and give health education for 126 infants less than 3 years and 120 elders over 74 years. Ten samples each of food-animal intestines and raw retail meat were tested weekly. Isolates were speciated into *C. jejuni*, *C. coli* and *Campylobacter* spp. and tested for antimicrobial susceptibility according to standard methods.
Results: *C. jejuni* was most commonly found in chicken intestine (65% of samples) and chicken meat (29%), while *C.coli* was frequently recovered from swine and chicken intestine (45% and 30%) and their retail meats (23% and 27%). A total of 432 diarrheal episodes occurred in infants and elders, of which *Campylobacter* was the fourth cause of bacterial diarrhea (4.4% of all episodes) after diarrheagenic *E.coli* (13.4%), *Salmonella (12.3%)*, and *Shigella (5.3%)*. *C. jejuni* and *C.coli* were isolated with equal frequency from human diarrheal samples. The annual incidence of diarrhea of any etiology was 2.1 episodes/infant and 0.7 episodes/elder. Annual incidence of *Campylobacter*-associated diarrhea was 111 episodes/1000 infants and 13 episodes/1000 elders. *Campylobacter*- infected infants presented more frequent vomiting and fever than those infected with *Salmonella* and *Shigella* (21%vs. 10% and 14%; and 43% vs. 18% and 38%), but less frequent bloody stools and a shorter duration of diarrhea than *Shigella* (21% vs. 50% and 5 vs. 8 days). None of the episodes resulted in dehydration or hospitalization. Resistance rates in human *C. jejuni* isolates were 0% to gentamicin, 5% to erythromycin, 46% to tetracycline, and 68% to ciprofloxacin. For human *C. coli* isolates, resistance rates were 0%, 10%, 14% and 48%, respectively.
Conclusion: Despite continuous exposure to *Campylobacter*, - including fluoroquinolone-resistant strains, the incidence and health impact of symptomatic infections in this community were relatively low; this suggests an efficient and persistent protective naturally-acquired immunity. Although there is a general need for containing antimicrobial resistance in foodborne pathogens, efforts should focus on those with the greatest public health impact.

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Room: Room Orchid B/C/D
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DNA-Level diversity and relatedness of *Helicobacter pylori* strains in Shantytown families in Peru and transmission in a developing-country setting

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Background: The efficiency of transmission of a pathogen within families compared with that between unrelated persons can affect both the strategies needed to control or eradicate infection and how the pathogen evolves. In industrialized countries, most cases of transmission of the gastric pathogen *Helicobacter pylori* seems to be from mother to child. An alternative model, potentially applicable among the very poor in developing countries, where infection is more common and the sanitary infrastructure is often deficient, invokes frequent transmission among unrelated persons, often via environmental sources
Methods: In the present study, we compared the genotypes of *H. pylori* from members of shantytown households in Peru to better understand the transmission of *H. pylori* in developing-country settings. *H. pylori* cultures and/or DNAs were obtained with informed consent by the string test (a minimally invasive alternative to endoscopy) from at least one child and one parent from each of 62 families.
Results: The random amplified polymorphic DNA fingerprints of 57 of 81 (70%) child-mother strain pairs did not match, nor did the diagnostic gene sequences (>1% DNA sequence difference), independent of the child's age (range, 1 to 39 years). Most strains from siblings or other paired family members were also unrelated.
Conclusion: These results suggest that *H.pylori* infections are often community acquired in the society studied. Transmission between unrelated persons should facilitate the formation of novel recombinant genotypes by interstrain DNA transfer and selection for genotypes that are well suited for individual hosts. It also implies that the effective prevention of *H. pylori* infection and associated gastroduodenal disease will require anti-*H. pylori* measures to be applied communitywide.

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Type: Oral Presentation

Etiology of childhood pneumonia in Tacloban, the Philippines

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Background: Pneumonia kills 3 milion children annually, but considered as “The Forgotten Killer of Children”(UNICEF/WHO). Our previous study showed the presence of human metapneumovirus and human bocavirus among Filipino children with influenza-like illness. But their clinical importance, in line with other common respiratory viruses, is yet to be elucidated. On the other hand, bacterial may be another important pathogens in those age groups. This study is to elucidate the causative agents of sever pneumonia among children in the Philippines.
Methods: From May 2008 to May 2009, 891 patients, who fulfilled diagnosis of severe pneumonia by Integrated Management of Childhood Illness and visited outpatient clinic in Eastern Visayas Regional Medical Center in Tacloban City, Leyte, were enrolled. Two nasopharyngeal swabs were taken from patient; one swab for rapid antigen detection for influenzavirus A and B (BD Flu Examen, BD Japan) and RS virus (BD RSV Examen, BD Japan), and the other swab for PCR targeting common respiratory viruses. Sequencing was performed for confirmation of PCR result as well as genotyping of the viruses. Blood culture was performed for all cases, and drug sensitivity test was done for all isolates.
Results: The number of cases peaked in October, the rainy season in the Leyte. 57% were aged under one year-old. 86% recovered, but 8.5% died during hospitalization. The rhinoviruses were the most common virus (HRVA:16%, HRVB:3%, HRVC11%), followed by RS virus (RSV-A:24%, RSV-B:0.6%). Seasonal influenzaviruses, Human metapneumovirus, human coronaviruses, human WU/KI polyomovirus, and human bocavirus were detected. The mean age for HRVB was 8 month-old and that of RSV-A was 10 month-old. S. pneumoniae, H. influenzae, S. aureus, and Salomonella were cultured from blood. Viral pathogens detected from fatal cases were proportional to that among over all study population. One fatal case was positive for MRSA and RSVA. None of those pathogens had statistical association with wheeze, respiratory distress, or outcome (survived / died) in logistic regression.
Conclusion: Rhinovirues and RSV may be the two major pathogens account for severe pneumonia among children in Leyte. We may need another integrated strategy in order to save children below 6 month, who should have protected by maternal antibody.

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Room: Room Orchid B/C/D
Type: Oral Presentation

Population-based surveillance for pneumonia, sepsis and meningitis in all ages in The Gambia: Implications for pneumococcal vaccine introduction and surveillance in Africa

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Background: WHO recommends that introduction of pneumococcal conjugate vaccine is accompanied by disease surveillance. Surveillance for pneumonia, sepsis and meningitis has been established in rural Gambia and 7PCV was introduced in August 2009.
Methods: In and outpatient surveillance among a population of 148,000 began May 2008 following pilot surveillance which began September 2007. 24/7 surveillance for suspected pneumonia, sepsis and meningitis involves those aged ≥2 months. Suspected cases are confirmed by clinicians followed by standard investigations. Pneumococcal isolates are serotyped using latex agglutination.
Results: From May 2008 until March 2009, 1463 cases (1225 <5 years, 238 ≥5 years) of suspected pneumonia, sepsis and meningitis were detected. Age-specific proportions of those <5 years with suspected disease were 43% (n=530) 2-11 months, 32% (n=387) 1 year, and 25% (n=308) 2-4 years. Of those aged ≥5 years, 42% (n=100) were <15 years and 58% (n=138) were ≥15. 7% (95/1385) of blood cultures grew pathogens; 38% (36/95) pneumococcus and 20% (19/95) *Staphylococcus aureus*. 80% (76/95) of invasive bacterial disease occurred <5 years of age. 86% (25/29) of IPD <5 years of age was associated with pneumonia and there were seven cases of bacterial meningitis. All cases of IPD ≥5 years of age were associated with pneumonia and there were two cases of bacterial meningitis. The estimated incidence of IPD per 100000 person years was 362 (2-11 months), 295 (1 year), 56 (2-4 years), 4 (5-14 years) and 9 (≥15 years). The serotype distribution of 90 IPD episodes since initiation of pilot surveillance was: serotype 1: (28), 6A: (11), 5: (9), 14: (9), 19A: (3), 4: (3), 23F (2), 6B (2), 7F (2), other (21). The proportions of IPD covered by different vaccines were: 7PCV 20%, 7PCV+6A 32%, PHiD10CV 63%, PHiD10CV+6A 76%, 13PCV 79%.
Conclusion: The burden of childhood pneumococcal disease in rural West Africa is substantial. The relative burden among older children and adults is much less. Vaccines of greater valence than 7PCV will cover substantially greater proportions of IPD. Ongoing high quality surveillance is critical to document the effectiveness of vaccine introduction and to provide data to inform immunization programs in resource limited settings.

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Room: Room Orchid B/C/D
Type: Oral Presentation

Controlling persistent cholera outbreaks in Africa: Lessons from the recent Cholera Outbreak, West District Unguja Zanzibar, Tanzania, 2009

S. Masauni[1], M. Mohammed[1], G. H. Leyna[2], F. Mosha[1], J. Mghamba[1], K. Omar[3], H. Ali[4], F. Abdallah[5], O. Oleribe[1], P. Mmbuji[6]
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Background: Cholera is a diarrhoeal disease caused by infection with the bacterium *Vibrio Cholerae*. It affects both children and adults. It has a short incubation period and potent enterotoxins resulting in severe dehydration and death within a few hours to days if treatment is delayed. In Africa, Cholera is a major cause of preventable morbidity and mortality. With eight different outbreaks in 2009 alone, Cholera epidemics have become a recurring public health challenge in 7 regions of Tanzania namely Tanga, Kigoma, Mwanza, Singida, Dar Es Salaam, Zanzibar and Mara. Of recent, a cholera vaccine trial is being piloted in Zanzibar with the aim of reducing the burden of disease. The objective of the study was to investigate the risk factors for the recent cholera outbreak in Zanzibar so as to plan for control measures which will be applicable to other regions in Tanzania
Methods: Unmatched case-control study was carried out in the West Unguja District of Zanzibar in October 2009. Stool specimen from cases and water samples from the nearby river, taps, boreholes and wells were collected for laboratory analysis. Data analysis was done using Epi Info.
Results: Factors found to be associated with cholera infection included use of water from bore holes OR= 9.1 (p = 0.000) and the river OR = 14.9 (p = 0.000), storage of water in buckets OR = 15.5 (p = 0.002) and jerry cans OR = 5.5 (p = 0.000) and living in a dirty environment (p = 0.000).Boiling of water OR = 0.11(p = 0.002), storage of water in plastic bottles OR = 0,1(p = 0.017), education (p = 0.000) and washing of hands after use of toilet (p = 0.000) were found to be protective. There was no statistically significant difference between those that had vaccination against cholera and others (p=0.74).
Conclusion: Following the conclusions of our epidemiological studies, a drastic change of strategy was proposed which concentrated in community awareness, personal hygiene and provision of clean and safe water. Vaccination has never been found to be an effective public health intervention in cholera outbreak as shown in this study.

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Type: Oral Presentation

High-risk travelers in the Boston Area Travel Medicine Network: Demographics, trip plans and vaccinations

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Background: Given increased international travel by high-risk groups (immunocompromised persons and those with medical comorbidities), there is need for better characterization of these travelers and their travel risks. Our objective was to describe the demographics, travel plans and vaccination requirements of immunocompromised travelers and those with medical comorbidities.
Methods: Boston Area Travel Medicine Network (BATMN) is a research collaboration of five travel clinics in the greater Boston area that sees ~7,500 travelers per year. We compared immunocompromised travelers (e.g., those with HIV/AIDS, malignancy, etc) to those with underlying medical conditions (e.g., cardiovascular and pulmonary disease), and “healthy” travelers (without known comorbidities) in the BATMN cohort.
Results: Of 9,254 travelers evaluated, 349 (3.8%) were immunocompromised and 969 (10.5%) had medical comorbidities. In the immunocompromised group, 196/349 (64.2%) had cancer and other non-HIV immunodeficiencies, 79 (22.6%) autoimmune disease, and 53 (15.2%) HIV/AIDS. Among those with medical comorbidities, 433/969 (44.7%) had lung disease, 409/969 (42.2%) cardiovascular disorders (both coronary artery disease and history of arrhythmias) and 180 (18.6%) diabetes. Immunocompromised travelers and those with co-morbidites were older than healthy travelers (median 57, 47 and 33 years respectively; p-values <0.001); 24.6% of the immunocompromised group were elderly (>65 years) vs. 5.8% of healthy travelers (p<0.001). High-risk persons traveled more for tourism and less often to visit friends and relatives than healthy travelers; they also travelled less to countries endemic for malaria (26.2% vs 30.3%) or yellow fever (YF) (23.7% vs 30.1%). Among travelers to YF-endemic areas, 41/87(47.1%) immunocompromised travelers, 126/229 (55.0%) of those with co-morbidities, and 1407/2391 (58.8%) healthy travelers received the YF vaccine. Among elderly travelers to YF-endemic countries, 15/25 (60.0%) immunocompromised travelers, 20/36 (55.6%) of those with co-morbidities and 53/112 (47.3%) healthy travelers were vaccinated.
Conclusion: High risk travelers tend to be older and are usually tourists. While fewer high-risk persons go to endemic countries, there are nevertheless moderate numbers of immunocompromised and elderly patients visiting regions where immunization with YF may be required. Given their underlying medical conditions, clinicians need to be aware of the potential risk for adverse events associated with YF vaccination in these high risk populations.

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Final Abstract Number: 21.009
Session: Pathogens in populations
Date: Wednesday, March 10, 2010
Time: 15:45-17:45
Room: Room Orchid B/C/D
Type: Oral Presentation

Factors determining performance of integrated disease surveillance strategy in Kenya, 2008

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Background: Integrated Disease Surveillance and Response (IDSR) is a strategy that was adopted by WHO /AFRO member countries in 1998 following the recognition that existing disease surveillance systems in the continent were not working effectively to measure health impact of major diseases intervention programmes nor in detecting disease outbreaks for early response. The main aim of IDSR strategy is to assist national health systems detect and respond to diseases of epidemic potential, public health importance and those targeted for eradication and elimination. The main objective of the study was to identify the factors that determine the performance of Integrated Disease Surveillance (IDS) strategy in Kenya.
Methods: A Comparative Cross Sectional study was carried out in 10 districts. Five districts had indicators below the 80% target while the other five districts had indicators above the target. Four provinces were selected using inclusion/exclusion criteria while the 10 districts were selected randomly. Stratified random sampling method was used to select health facilities. Quantitative and qualitative data was collected from 138 facilities in September-October 2008. Univariate, bivariate and multivariate analysis was done.
Results: The performance of IDS weekly indicators is largely influenced by; **Stock out of tools,** facilities which had low stocks of reporting tools were performing better than those that had stock outs 6 months before the study (P=0.00). **Training,** health facilities that had been trained staff in IDSR performed better compared to those that had no trained staff (P=0.017). **Mode of Communication**; Facilities that were using SMS as a mode of transmitting data were performing better that those using other modes (P=0.024). **District Health Manager's support supervisions,** were not found effective in influencing performance.
Conclusion: Trainings for health workers in IDSR at all levels are necessary for successful implementation. District's support supervision had no influence on performance, the quantity was adequate, but the quality was questionable. The channels of data transmission need to be re-focused, new technologies on cell phone based data communication are yielding better results. Other existing challenges include overburdened health facility staff; poor communication; poor incentives; coordination capacity and insufficient financial resources for an effective IDSR system.

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Type: Oral Presentation

Molecular analysis of excised valves in the diagnosis of blood culture negative infective endocarditis (BCNE) in a Cardiac Surgery Referral Center in Rio de Janeiro, Brazil: 1998 to 2009

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Background: BCNE remains a diagnostic and therapeutic challenge, especially in developing countries, due to lack of appropriate serologies and molecular tools. We sought the causes of this condition on valves collected at surgery over a 12 year period in a reference cardiac surgery hospital.
Methods: Formalin-fixed valves were tested by PCR for the detection of *Coxiella burnetii, Bartonella sp., Tropheryma whipplei, Staphylococcus aureus, Streptococcus oralis* group*, Streptococcus bovis* group*, Enterococcus sp., and Mycoplasma sp*.Immunohistochemistry was also performed on all valves of the study.
Results: Forty-one patients with BCNE had surgery in the 12 year study period; of those 29 (78%) had valves available for analysis. 9/29(31%) had organisms detected by PCR: *S.oralis* 5, *S.oralis+S.gallolyticus* 1, *S.oralis+Bartonella* 1, *Bartonella* 1, *C.burnetii* 1. Mitral(M) and aortic(A) valves were involved as follows: 1 native M, 2 native A, 3 native MA, 1 M bioprosthesis (11 years old), 1 A bioprosthesis (1.5 y) and 1 mechanical M (29 y). Mean patients' age was 39.7 ± 17.0 years (amplitude 9 to 70). Five patients were male, 4 female. All had subacute presentations and community acquired infections. Antibiotics were not given before blood culture (BC) collection in only 3 of 9 patients (*C.burnetii* 1, *S.oralis* 2). Mean time of antibiotics given before valve surgery was 29±15 days. Predisposing conditions were interventricular septum 1, rheumatic valvulopathy 4, prosthesis 3. All transesophageal echocardiograms showed major criteria, but all cases were only clinically possible by the modified Duke criteria. All cases were definite by surgical and histopathological and immunohistochemistry findings. Clinical features showed fever in 4/9, new valvar regurgitation in all, splenomegaly in 1/9, emboli to skin in 1/9, elevated CRP in 6/6, and elevated ESR in 5/7 patients. Two patients died, both in refractory heart failure.
Conclusion: The gold standard to establish the etiology of BCNE is study of the excised valves. Nearly a third of cases of BCNE in this cardiac surgery hospital had its etiology defined by PCR of paraffin-embedded valves. This is the first data from Brazil relying on molecular biology of valves for the diagnosis of BCNE, with viridans, *Coxiella* and *Bartonella* documented. Of note, 7 of the 9 cases involved *S.oralis* underscoring antibiotics prior to BC collection as a major factor in BC negativity.
Supported by FAPERJ, Brazil

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Final Abstract Number: 22.001
Session: Successful short antibiotic treatment of childhood pneumonia - Myth or reality?
Date: Wednesday, March 10, 2010
Time: 15:45-17:45
Room: South Hall
Type: Invited Presentation

Determinants of Bacteriologic Eradication in Respiratory Tract Infections

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Understanding of the relationships between pharmacokinetic (PK) and pharmacodynamic (PD) parameters and bacteriological and clinical outcomes of infections has resulted in appreciation of the correlation between in vitro potency and in vivo efficacy of antimicrobial agents. PK and PD principles can be applied to the development of new antibacterials and optimising the formulation of existing agents to help address the increasing prevalence of antibacterial resistance. Antimicrobial agents can generally be divided into those that have time-dependent activity, such as beta-lactams, and those that have concentration-dependent activity, such as macrolides, lincosamides and quinolones. For beta-lactams, the unbound serum concentration of the drug exceeding the minimum inhibitory concentration of the causative pathogen for 40-50% of the dosing interval (40% for penicillins and 50% for cephalosporins) is predictive of bacteriologic efficacy and can be used to determine a PK/PD breakpoint for specific dosing regimens. For concentration-dependent agents, the unbound serum area-under-the-curve (AUC) to MIC ratio exceeding 30 for macrolides, lincosamides and quinolones is generally predictive of bacteriologic efficacy and can be used to determine a PK/PD breakpoint for these agents. Amoxicillin and amoxicillin/clavulanate are examples of agents that have been studied and PK/PD principles applied to develop new and enhanced formulations, allowing these agents to remain significant antibacterial agent in the management of respiratory tract infections despite development of resistance. While intrinsic and acquired resistance is common in respiratory pathogens, in vitro susceptibility can be accurately interpreted based on PK/PD parameters. PK/PD principles can be used to develop effective dosing regimens, develop new formulations and dosage regimens, contribute to guideline recommendations, establish susceptibility breakpoints, and validate bacteriologic outcome in clinical studies. However, PK/PD principles do not relate to length of therapy, which is mainly influenced by disease severity, presence of comorbid conditions and patient compliance.

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Final Abstract Number: 22.002
Session: Successful short antibiotic treatment of childhood pneumonia - Myth or reality?
Date: Wednesday, March 10, 2010
Time: 15:45-17:45
Room: South Hall
Type: Invited Presentation

What Are the Benefits of Short Antibiotic Treatment?

H. Goossens
University Hospital Antwerp, Edegem-Antwerp, Belgium

Most antibiotics prescribed for outpatients are written for treatment of respiratory tract infections. Many of these prescriptions are necessary for curbing spread of infection and preventing development of harmful sequelae. Less attention has been paid to the role of duration of antibiotic therapy to treat respiratory tract infections, particularly pneumonia in children, for the judicious use of antibiotics. In fact, prescribing the appropriate duration of a course of antibiotic therapy is as important as eliminating prescriptions for nonbacterial illnesses in practising judicious use of antibiotics.
How long is enough and how long is too much? Therapeutic courses need to be of sufficient duration to result in a clinical cure to return patients as rapidly as possible to normal functioning and to prevent the progression of disease and the development of dangerous sequelae. However, unnecessarily lengthy courses of therapy may prevent the realization of these treatment goals by heightening the risk of development of bacterial resistance and side effects and by reducing compliance with the therapeutic regimen. In children, the latter is however not relevant. We investigated the direct impact of antibiotic exposure on resistance at the individual level in healthy cohorts, treated with azithromycin, clarithromycin, or a placebo in a randomised, double-blind trial. Both macrolides significantly increased the mean macrolide-resistant proportions of viridans streptococci compared to the placebo at all time-points. Our study showed that selection of resistance occurs very rapidly after the exposure to antibiotics, peaking in the immediate post-therapy period. In conclusion, decrease of side-effects could be the main benefit of shorter antibiotic treatment.

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Final Abstract Number: 22.003
Session: Successful short antibiotic treatment of childhood pneumonia - Myth or reality?
Date: Wednesday, March 10, 2010
Time: 15:45-17:45
Room: South Hall
Type: Invited Presentation

Short Treatment and the WHO Pneumonia - What are We Treating?

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It is estimated that there are 5-9 episodes of acute respiratory infections (ARI) per year / under 5 children, the vast majority of which are viral. Some 2-3% of these episodes represent pneumonia and between 7-13% (some 11-17 million acute lower respiratory infections are severe enough to require hospital admission.
Despite numerous advances in understanding the burden and epidemiology of childhood respiratory pneumonia, the disorder still accounts for almost 1.8 million child deaths annually, 98% in developing countries. It is widely stated that in developing countries, most pneumonia is bacterial and most acute respiratory infection related deaths are due to pneumonia, however, the exact proportion of these infections which are related to viral or bacterial infections is unclear. Given the high burden of deaths in young children, WHO has progressively developed algorithms for the diagnosis and management of acute respiratory infections based on clinical criteria of fast breathing and chest indrawing. These criteria have been used for the diagnosis and therapy of pneumonia in a range of settings. In recent years, the success of short course antibiotic therapy of such episodes has opened the possibility of improving community case management of such infections and reducing rates of resistance. However, a legitimate question has been raised as to the nature of acute respiratory infections diagnosed by the WHO algorithms. This presentation will review the current state of knowledge in relation to the etiology and outcomes of respiratory infections in children in developing countries and also discuss the implications for research and programs.
Our findings indicate that the current criteria for defining pneumonia as suggested by WHO are too broad and probably include a host of conditions, including viral infections and asthma, which do not require antibiotics. A much more effective and validated definition and clinical description of pneumonia is needed for programmatic settings

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Final Abstract Number: 22.004
Session: Successful short antibiotic treatment of childhood pneumonia - Myth or reality?
Date: Wednesday, March 10, 2010
Time: 15:45-17:45
Room: South Hall
Type: Invited Presentation

Can Short Antibiotic Treatment be Widely Used in Developed Countries

R. Dagan
Beer Sheva University, Beer-Sheva, Israel

Childhood pneumonia is the most common killer of children <5 years worldwide. Although in the developed world pneumonia does not commonly result in death, it is an extremely common disease. Treatment is almost universally with antibiotics. However, the lack of appropriate definition of pneumonia, the difficulty in diagnosing the pathogen and cultural differences make it extremely difficult to agree on the ideal treatment. A short antibiotic course is preferred to a longer one, since if equally effective, it should be associated with lower cost, less adverse events and lower rates of antibiotic resistance in the community. An extensive literature search using a combination of the words “pneumonia”, “community-acquired”, “treatment”, “drug”, “antibiotic”, short”, “shortened”, “day (s)”, and “child” resulted in a few articles only dealing with short duration treatment of pneumonia in children, all in the developing world and most dealing with pneumonia defined by the WHO criteria (used in locations where no modern medicine can be applied).
We undertook a prospective, double blind, randomized study, comparing high-dose amoxicillin (80 mg/kg) administered for 5 *vs.* 10 days in children with community-acquired alveolar pneumonia with the following inclusion criteria: 1) <5 years old; 2) radiologically proven alveolar pneumonia; 3) temperature ≥38.5°C; 4) peripheral WBC ≥15,000/mm3. We followed the children both clinically and with laboratory findings for a month. The study will be unblinded after January 31st and the preliminary results will be presented.
In conclusion: Paucity of data and difficulty in defining childhood pneumonia in the developed world result in confusion in regard to short treatment. However, the first studies will reveal, at least in some defined subgroups of pneumonia, the efficacy and the potential use of short-course treatment in childhood pneumonia.

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Final Abstract Number: 35.001
Session: Plenary 5
Date: Thursday, March 11, 2010
Time: 09:00-09:45
Room: Ballroom 1: Brickell
Type: Invited Presentation

Richard K. Root Memorial Lecture

Transmission and Prevention of Transmission of HIV: Clues from the Early 21st Century

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HIV is transmitted by blood and blood products, from HIV infected mothers to babies (before and during birth, and through breast milk) and by anal and vaginal intercourse. The sexual transmission of HIV has lead to the majority of infections worldwide and this route of transmission has great variability in efficiency (~1/10-1/1000 transmission events/sexual exposure). Transmission variability reflects viral concentration in the genital secretions of the infected host, inflammation in the index case or partner, and the sexual acts chosen. HIV prevention depends on complimentary behavioral and biological strategies. Condoms and male circumcision reduce the risk of HIV acquisition. No preventive vaccine has been developed, but a recent trial in Thailand has suggested potential limited protection from infection, albeit for a brief period of time. To date all first and second generation topical vaginal microbicides have failed to provide reliable and significant protection from HIV infection, but trials with antiretroviral agents are in progress. The use of oral or topical antiretroviral agents for HIV prevention is considered pre-exposure prophylaxis (PrEP). More than 20,000 study subjects are enrolled in trials with oral antiviral agents, especially the combination of tenofovir and emtricitabine. It is likely that HIV infected patients receiving antiretroviral therapy are less contagious and a large randomized controlled trial (HPTN052) has enrolled more than 1500 HIV discordant couples to address this question directly. The enthusiasm for ART as prevention has led to a “seek, test and treat strategy” now called “TLC PLUS”…which requires wider HIV testing (T), linkage (L) to medical care and delivery of ongoing care (C), PLUS emphasis on combined behavioral and biological prevention strategies for HIV positive people. Several pilot studies designed to implement TLC PLUS are underway worldwide. HIV transmission has been well-studied and prevenntion strategies are likely to be increasingly successful in the coming years

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Final Abstract Number: 36.001
Session: Strategies for Expanding Global Impact of Immunization Programs
Date: Thursday, March 11, 2010
Time: 10:15-12:15
Room: Ballroom 1: Brickell
Type: Invited Presentation

Growing burden of dengue in Latin America: A public health challenge

J. Mendez Galvan
Hospital Infantil de Mexico Federico Gomez, Mexico City, Mexico

The evolution of dengue fever and dengue hemorrhagic fever in the world in the last 50 years shows the lack to effective vector control. The re-emergence of dengue fever and the new dengue hemorrhagic form in The Americas has epidemiological, clinical, ecological, political and socioeconomic implications. Insufficient political commitment, inadequate financial resources, increased globalization and urbanization growth have contributed to change the dengue situation after 19 Latin American were certified to have eradicated *Aedes aegypti*. Difficulties begin with diagnosis (clinical and laboratory), which includes asymptomatic infections, undifferentiated febrile illness and differential diagnosis with other hemorrhagic diseases. Collection of appropriate epidemiological data and a true appreciation of the social and economic impact of dengue are essential to securing social, political and economic commitment for dengue control efforts, as well as increased scientific and social awareness. In addition, the estimation of cost-effectiveness is necessary in order to define the optimal division of resources between traditional dengue vector control and the eventual introduction of dengue vaccines. Furthermore, anticipating the coordination of all the efforts to facilitate the regulatory requirements and to develop vaccination strategies is essential.

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Final Abstract Number: 36.002
Session: Strategies for Expanding Global Impact of Immunization Programs
Date: Thursday, March 11, 2010
Time: 10:15-12:15
Room: Ballroom 1: Brickell
Type: Invited Presentation

Clinical development of tetravalent dengue vaccine for endemic areas

M. Saville
sanofi pasteur , Marcy L'Etoile, France

A vaccine to protect against dengue disease is sorely needed, particularly for children living in endemic areas who are most affected by the disease. The safety and immunogenicity of a tetravalent live attenuated dengue vaccine containing 5 log10 TCID50 of chimeric yellow fever (YF)/DEN1,2,3,4 viruses (TDV) was tested in children in the Philippines, where dengue is endemic, and in a region of Mexico, where dengue is non-epidemic.
In each of two randomized controlled blind-observer phase 1 trials (one per country), 126 subjects 2-45 years old were enrolled, including 72 2-11 yr olds/study. Subjects were divided into two groups receiving 1) 3 doses of TDV 2) 1 dose of either Stamaril® YF vaccine (Mexico) or Typhim Vi® (Philippines) followed by 2 doses of TVD. Vaccines were administered at months 0, 3–4, and 12. Baseline flavivirus serostatus was determined. Vaccine safety and immune response were evaluated after each vaccination.
No related serious adverse events were observed. The reactogenicity profile was comparable to that of the control vaccines. No increase in reactogenicity was observed: in children compared with adults, or after the second or third dose compared with the first. In both non-endemic and endemic populations, immune responses increased incrementally after each of the 3 doses of TDV and were balanced against the 4 serotypes after 3 doses.
TDV was well tolerated and immunogenic in children in both endemic and non-endemic areas with a 3 dose schedule.

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Final Abstract Number: 36.003
Session: Strategies for Expanding Global Impact of Immunization Programs
Date: Thursday, March 11, 2010
Time: 10:15-12:15
Room: Ballroom 1: Brickell
Type: Invited Presentation

Pertussis surveillance and testing: Recommendations from the GPI

C. H. Wirsing von König
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The Global Pertussis Initiative (GPI) was established in 2001 to evaluate the ongoing problem of pertussis worldwide and to recommend appropriate pertussis control strategies. In addition to primary vaccinations, the GPI currently recommends pertussis booster vaccination to pre-school children, adolescents, and those adults at risk of transmitting *Bordetella pertussis* infection to infants. The GPI actively encourages efforts toward global standardization of pertussis disease clinical definitions and diagnostics. At a meeting in Paris in January 2010, GPI members discussed pertussis surveillance and testing, and prepared recommendations on the implementation and utilization of these activities. Issues and projects discussed included:
- Advantages and limitations of various national surveillance systems;
- Seroprevalence studies;
- Ideal surveillance methodologies;
- Ongoing efforts in standardization of real time PCR, culture, serology and sample treatment;
- Likely future advances (eg, antibody detection in saliva).

Previous regional meetings of the GPI have confirmed that many countries have limited laboratory facilities for the detection of pertussis. The GPI hopes that the future introduction of increased laboratory capabilities and greater harmonization of clinical definitions and detection methods will lead to enhanced surveillance and a better estimate of the burden of pertussis infection worldwide.

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Room: Ballroom 1: Brickell
Type: Invited Presentation

Adolescent and adult Pertussis vaccination programs: Are they having an impact?

T. Tan
Northwestern University, Chicago, IL, USA

Pertussis disease in infancy remains a significant problem, with a high risk of serious morbidity and mortality in both developed and developing countries. Improved disease prevention strategies are imperative. In countries with established childhood vaccination programs, studies have shown that adults are the predominant source of infection for infants. Therefore strategies to protect infants now emphasise vaccination of adults, particularly those (eg, parents, close household contacts and health-care workers) at high risk of transmitting infection to infants. A cocoon strategy, in which all potential adolescent and adult contacts of infants are vaccinated, is probably the most cost-effective solution.

Postpartum vaccination program of new mothers are ongoing in the US.

The introduction of booster doses in adolescents has been an important step toward decreasing disease burden. For example, in areas of Canada where Tdap vaccine has been administered to 14- to 16-year-olds, marked reductions of pertussis have been observed in adolescents and younger age groups, possibly due to herd immunity.

Adult disease in itself is a concern, with the true adult burden estimated at more than 600,000 cases annually in the United States. Adults commonly have a persistent cough for up to 4 months, often requiring medical treatment for the associated morbidity and to reduce the risk of infection to others. Furthermore, it can have significant financial implications for the patient and society. Evidence suggests that implementation of adult vaccination programs could be highly cost-effective and even cost-saving. This presentation will review available data on pertussis vaccination of adults and adolescents, and assesses the potential impact of such vaccination, both now and in the future.

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Session: Infectious Disease and Vaccines Development
Date: Thursday, March 11, 2010
Time: 10:15-12:15
Room: Ballroom 2: Monroe/Flagler
Type: Invited Presentation

Meningococcal C in Latin America

E. Berezin
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Final Abstract Number: 37.002
Session: Infectious Disease and Vaccines Development
Date: Thursday, March 11, 2010
Time: 10:15-12:15
Room: Ballroom 2: Monroe/Flagler
Type: Invited Presentation

Tick-borne encephalitis: Clinical Development of vaccines for Children and Adults

E.M. Pöllabauer, A. Löw-Baselli, P.N. Barrett, H.J. Ehrlich
Baxter BioScience, Vienna, Austria

Tick-borne encephalitis virus (TBEV), a member of the family Flaviviridae, causes substantial morbidity and even mortality in endemic areas. The distribution of TBEV covers many countries in Europe and large parts of central and eastern Asia. Although most infections with TBEV are asymptomatic, more than 10,000 severe cases are reported annually, and the incidence has increased considerably during the last few decades. Up to 46% of patients are left with permanent sequelae such as cognitive or neuropsychiatric complaints, dysphasia, hearing defects and spinal paralysis. The severity of the disease and the lack of causal therapy emphasize the need for prevention of tick borne encephalitis (TBE) by vaccination. Inactivated, whole virus TBE vaccines (FSME IMMUN, Baxter and Encepur, Novartis) are widely used in Europe. In recent years a full clinical development program, including safety, immunogenicity and seropersistence studies has been conducted for FSME-IMMUN in all age groups. Antigen doses of 2.4µg and 1.2µg were identified as optimal for adults and children, respectively. In an ongoing study, the safety and immunogenicity of FSME-IMMUN 0.25 ml Junior and Encepur 0.25 ml Children are being investigated in children 1 to 11 years of age. A total of 150 and 152 subjects were enrolled in the FSMEIMMUN and Encepur group, respectively. Immunogenicity was assessed by two different ELISA assays using antigens homologous to the TBEV strains of either FSME IMMUN (IMMUNOZYM*), or Encepur (Enzygnost**). Four weeks after the second vaccination, in the FSME-IMMUN group, 100% of subjects were seropositive in both the IMMUNOZYM- (>126 VIEU/ml) and the Enzygnost ELISA (>10.32U/ml) compared with 94.0% and 96.7% respectively, in the Encepur group. Geometric mean concentrations (GMC) measured by IMMUNOZYM ELISA were 3026 in the FSME-IMMUN and 678 in the Encepurgroup. GMCs measured with the Enzygnost ELISA were 163.3 (FSME-IMMUN) and 93.7 (Encepur). Local reactions after the 1st vaccination occurred in 12.7% with FSME-IMMUN and in 28.9% with Encepur. The rate of systemic reactions was comparable: 9.3% (FSME-IMMUN) and 11.8% (Encepur). The presently marketed TBE vaccines represent highly effective tools for the prevention of this continuously spreading disease.
*IMMUNOZYM FSME IgG, Progen; **Enzygnost TBE, Dade Behring

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Session: Infectious Disease and Vaccines Development
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Time: 10:15-12:15
Room: Ballroom 2: Monroe/Flagler
Type: Invited Presentation

Strategies for the Development of New Vaccines

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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.
Success has also been achieved against some agents replicating on respiratory or gastrointestinal mucosae, 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.
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 major scientific problems to be solved are maintenance of immune memory, immaturity and post-maturity of the immune system, and adjuvants capable of stimulating selective cell types

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New Technology Update: Cell Culture derived seasonal and pandemic flu vaccine

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The Vero cell line is the most widely accepted continuous cell line by regulatory authorities and has been used since decades for the production of, e.g. polio-, rabies- and rotavirus vaccines. Here we report on the clinical characterization of Vero cell derived inactivated pandemic- and seasonal influenza vaccines.

A whole virus H5N1vaccine based on (Vietnam/1203/2004/H5N1, clade 1) was demonstrated to be safe and had an excellent tolerability profile. A dose of 7.5 µg of a non-adjuvanted vaccine formulation was highly immunogenic and induced antibodies neutralizing homologous strains as well as viruses from other H5N1 clades. A booster dose of a heterologous (clade 2) H5N1 vaccine 12-17 months later resulted in enhanced antibody responses against both the original (clade 1) and the booster (clade 2) strain, indicative of .cross-protective memory.

A vaccine against the current pandemic H1N1 strain is being studied in adults and children. In adults, two doses of 7.5µg antigen induced seroprotective HA antibody titers in 89% - 91% of subjects. An ongoing pediatric study demonstrated that after the second dose 100% seroprotection (HI assay) was attained in the 3-8 and 9-17 year old cohorts.

Vero cell derived trivalent seasonal influenza vaccines (split virion), using wildtype virus seed stocks were developed and extensively tested in human studies. Their immunogenicity met all licensure criteria, clinical efficacy was demonstrated and safety profile was comparable to egg derived vaccines[1)].

These data indicate that flexible and versatile Vero cell platform can successfully be in the production of pandemic and seasonal influenza vaccines.

1) This Project has been funded in whole with Federal (United States Government) funds from the Office of the Assistant Secretary for Preparedness and Response, Office of Biomdical Advanced Research and Development Authority, under contract NUMBER HHS0100200600013C to DynPort Vaccine Company LLC, a CSC company, under No.:S1008307 awarded to Baxter Healthcare Corporation

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Type: Invited Presentation

Febrile Illnesses

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Roughly 10% of travelers to developing countries experience a febrile illness during travel or on return. The likelihood of developing a medical condition during travel relates to an individual's past medical history, travel destination, duration of travel, level of accommodation, immunization history, adherence to indicated chemoprophylactic regimens, activities during travel, and history of exposure to infectious agents prior to and during travel. The risk for acquiring a tropical infection is primarily affected by the activities of the traveler. For example, immigrants from developing countries return home to visit friends and relatives (VFR) in their place of birth and usually don't take preventive therapy for malaria. Long-term expatriates, on the other hand, have unique risk profiles. Fever is a leading reason for post travel consultation. Careful questioning of patients about the pattern of fever and associated symptoms is useful. Several papers around the world have reported data about returning travelers with fever. The Geosentinel has reviewed its data on 24,920 travelers from 1997 to 2006. They reported that 28 % of returned travelers seen at clinics presented with fever as their chief reason for seeking medical care. Fever was a marker of a serious illness requiring hospitalization. In this report, causes of fever varied by region visited and by time of presentation after travel. The exposure history is crucial to the formulation of a differential diagnosis. Knowledge of infectious disease outbreaks like the novel H1N1 Influenza pandemics in a specific region where the patient has traveled is very helpful. Travelers to Latin America can be exposed to different infectious agents that can give a systemic febrile illness. The most common ones include respiratory tract infections, mononucleosis, dengue, malaria, and typhoid fever. Sometimes no specific cause is reported. Laboratory diagnosis has to be done promptly and efficaciously to avoid delays in treatment.

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Cutaneous Diseases in Returnee Travellers from Latin America

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Cutaneous diseases are very frequent in travelers. They are ranked in the three most common causes of health problems in returned travelers. Some destinations have a higher risk of cutaneous diseases in travelers, such as the Caribbean and Latin America. The origin of most of these dermatological disorders is due to infection, but some of them are due to solar allergies and envenomization. The main cutaneous diseases observed in travelers are cutaneous larva migrans, phytophotodermatitis, complicated mosquito bites, pyodermas, miyasis and tungiasis. Risk factors like country of acquisition, age, reason for travel, duration of the travel, gender vary according to the disease. Countries within Latin America with higher risk are Jamaica, Dominican Republic, Brazil, Belize and Bolivia. Some risk groups that have been determined for dermatological conditions include short term travelers, those with tourism as the purpose of travel, male and young travelers. Evaluation of an ill traveler with skin lesions includes very detailed questions to evaluate the history of exposure, prevention measures, immunization, previous treatment and a complete physical examination. Very rarely further diagnostic studies are needed such as blood tests, serology, skin biopsies, cultures and imaging techniques. Many cutaneous diseases related to travel can be prevented wearing closed shoes, avoiding skin contact with some fruit juices and using repellents to avoid insect bites. Use of anti rabies and anti tetanus vaccines is also recommended for some destinies and adventure travels.

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Non-Enteric Helminths Including Cysticercosis

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Segmented tapeworms of clinical importance range in size from a few centimeters (*H. nana* and *H. diminuta*) to several meters (*T. solium* and *T. saginata*) and utilize humans as definitive hosts, intermediate hosts or both. Generally, adult organisms reside and may produce disease in the gastrointestinal tract and larvae can inhabit and produce disease in any human tissue. Teniasis results from ingestion of viable metacestodes of either *T. solium* or *T. saginata*) and is often asymptomatic, but occasionally serious, life threatening illness can result. Cysticercosis is the infection by *Cysticercus cellulosae*, the larval stage of *T. solium*. Neurocysticercosis is the invasion to CNS structures that results in a variety of neurological illness. Echinococcosis is the infection by larvae of *E. granulosus* Cystic), *E. multilocularis* (Alveolar) and related species (*E. vogeli, E. oligarthus*, polycystic). Major epidemiologic and clinical differences exist. Diphyllobotriasis (*D. latum*) is frequent and is transmitted by uncooked freshwater fish. Hymenolepiasis is common in warm climates. Dipylidiasis (*D. caninum*) and sparganosis (*Spirometra*) are much less common. Advances in diagnosis, treatment and prevention of these neglected diseases will be reviewed with emphasis in neurocysticercosis.

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Risks of getting HIV infections and STIs when traveling to Latin America

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Sexually transmitted infections (STIs) including HIV infection are responsible for a variety of acute and chronic medical problems. Travel may interfere with human sexual practices by splitting fixed sexual partnerships and removing social taboos. Increased sexual promiscuity and casual sexual relationships are likely to occur during travel because people have the opportunity to escape from standard behaviors.
In Latin-American countries (LAC) the prevalence of STIs is extremely high. Syphilis has a variable prevalence rate among sex workers in LAC, ranging from 7% in Panama to 29% in Santos, Brazil. The same applies for gonococcal infections and other STIs. Resistance rates of *Neisseria gonorrhoeae* to different antibiotics vary according to different countries. Regarding chronic hepatitis B, seroprevalence for different LAC varies between high-endemicity regions like the Amazon basin, and low and intermediate areas like Argentina and South Brazil, respectively, determining different risks of exposure to travelers. There are no vaccines for STIs, with the exception of those for HBV. It is estimated that in the Latin American area there are 2 million people living with HIV and AIDS. Brazil accounts accounts for more than 40% of total infections. In some Brazilian cities, more than 60% of drug users are HIV positive. The most severe epidemics are found in smaller countries such as Belize, Guyana and Suriname, with HIV prevalence rates of 2.1%, 2.5% and 2.4% respectively. The majority of countries in the region have prevalence rates of less than 1%, but the prevalence among specific groups, such as men who have sex with men and sex workers, is often very high. Primary resistance rates of HIV vary according to the visited area.
Screening of asymptomatic travelers who had casual sex abroad should be encouraged.

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Type: Oral Presentation

The WHO global plan to map and combat neglected tropical diseases

L. Savioli
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Control of neglected tropical diseases has taken on a new dimension.
More than 1 billion people – a sixth of the world's population – suffer from one or more neglected tropical diseases. Success in tackling the situation resides in our ability to create global awareness of these diseases, and the world is increasingly becoming responsive to the plight of the people who live with them. Neglected tropical diseases kill an estimated 534 000 people worldwide every year. Their impact on worker productivity adds up to billions of dollars lost annually and maintains low-income countries in poverty.
During the last five years we have come a long way in convincing the world and particularly political leaders in endemic and non endemic countries to invest in the control of neglected tropical diseases as a means to boost human and economic development towards achieving the Millennium Development Goals. WHO, its international partners, donor agencies and NGOs have set up better channels to support endemic countries to distribute both donated and purchased drugs to needy areas. Convergence of technology is now providing better possibilities of communication and exchange of data with field staff in remote areas. Such collaborative efforts have made interventions against neglected diseases more viable and cost effective.
In addition to efforts made by endemic countries, funds have been pledged by the world community for the promotion of global health. Substantial contribution has come from the United States government, the United Kingdom Department for International Development (DFID), the Bill and Melinda Gates Foundation, The Carter Center, the United States Agency for International Development (USAID) and the private sector.
As the world slowly recovers from one of the worst financial crises, we intend to keep-up the momentum and further motivate the international community to support endemic countries to strengthen existing health infrastructure and service delivery. Investing in the human and social capital of poor people is essential as it enables them to develop the fundamentals they need to renew their own communities through prevention programmes.
Our actions are aimed to promote the common good of every individual and are based on a human rights approach, which requires that interventions and processes are guided by human rights principles of participation, non-discrimination and accountability.
Everyone aspires to live a life free of disease. Our task is to create the conditions to make this happen. Although the task ahead is arduous, we will persevere: this is the only way to go forward.

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Room: Room Jasmine
Type: Invited Presentation

Neglected tropical diseases in Latin America and the Caribbean: Prospects for Control and Elimination

S. Ault
PAHO, Washington, DC,

In Latin America and the Caribbean, 180 million people live in poverty, and carry most of the burden of neglected tropical diseases (NTDs) like soil-transmitted helminthiasis, schistosomiasis, Chagas disease, lymphatic filariasis, onchocerciasis, leishmaniasis, trachoma, rabies, and other infections of poverty like neonatal tetanus and congenital syphilis.
These neglected diseases are often restricted to the rural and urban poor and vulnerable and excluded groups like women and children, and indigenous communities. They adversely affect school attendance, children's physical and cognitive development, pregnancy outcome, labor productivity, and/or income-earning capacity, and create social stigma.
A comprehensive integrated approach with access to diagnostic and treatment tools and an agenda to address their social determinants. Political commitment from multiple sectors is needed to ensure resource availability and international support. To facilitate development of this commitment, the Pan American Health Organization (PAHO)/WHO with its partners have recently taken several major actions. Ten neglected diseases have been mapped by PAHO in 14 countries for "hot spots". PAHO partnered with the Inter-American Development Bank and the Global Network for Neglected Tropical Diseases to develop a new Regional Fund for control and elimination of NTDs and other infectious diseases of poverty. PAHO's Directing Council passed Resolution CD49.R19 (2009) in which Member States committed by 2015 to eliminate or reduce those neglected diseases for which adequate tools and strategies exist, to levels in which they are no longer public health problems.
PAHO and partners will complete mapping of the distribution and overlap of neglected diseases in the Region; develop evidence-based guidelines and demonstration projects for integrated control; develop models to address social determinants; strengthen, scale up and intensify existing programs of control and elimination through technical cooperation; and plan for certification of elimination of diseases like onchocerciasis and lymphatic filariasis which are close to elimination in the Region.

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Chagas disease research: Advances and needs

Z. Yadon
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American trypanosomiasis --a zoonotic disease caused by *Trypanosoma cruzi* (Protozoa, Kinetoplastida) -- is transmitted to humans by blood-sucking triatomine bugs, blood transfusion and congenital transmission. Successful regional vector control programs based on the residual application of insecticide and improved screening of blood donors have achieved important reductions in the incidence of Chagas disease in many Latin American countries. However, this approach has been ineffective in some geographic areas such as the Gran Chaco. As a result, the development of effective new tools in these areas to prevent house reinfestation by triatomine bugs is a high research priority. No less important is the need of innovative approaches including those generated from genomics to improve upon existing diagnostic tests and to develop new parasitological tests for the early diagnosis of congenital infection in the newborn and in immunocompromised patients, as well as for the assessment of treatment response (PCR; antigenemia, recombinant antigens ,synthetic peptides etc.). There is also a pressing need of developing new anti-T. cruzi agents with high activity in both the acute and chronic phases, and epidemiological methods that me may be used to estimate the prevalence of infection, subclinical disease and treatment needs in endemic and non-endemic countries.

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Integrated control of neglected tropical diseases in Africa

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Centre for Neglected Tropical Diseases, Liverpool, United Kingdom

Neglected tropical diseases (NTD) are the 'other diseases' of Millennium Development Goal 6 that have received little attention from policy-makers and politicians who over focus on HIV, tuberculosis and malaria. They include many medically diverse diseases that are strongly associated with poverty. NTDs include bacterial, viral, protozoan and helminth infections that have plagued humanity since antiquity. Globally, over one billion people suffer from one or more NTDs and about 500,000 people die from them every year.
Neglected Tropical Diseases are widespread in Africa due, in part, to the low socio-economic status of rural populations. Many countries are endemic with of 5 or more NTDs including schistosomiasis, soil-transmitted helminths (STH), lymphatic filariasis, onchocerciasis and trachoma, as well as zoonotic disease such as human African trypanosomiasis, rabies, tick borne relapsing fevers, echinococcus (hydatid), taeniosis (cysticercosis), brucellosis and plague, with a large part of the population at risk of co-infection with 2 or more of these diseases.
Fortunately, control strategies as well as diagnostic tools and the availability of safe and effective drugs exist for the NTDs responsible for the greatest burden in Africa: lymphatic filariasis, onchocerciasis, STH and schistosomiasis. The World Health Organization has developed a strategy, Preventive Chemotherapy and Transmission Control (PCT), which is geared towards the implementation of large-scale mass drug administration. The objective of PCT is to provide national programmes with technical guidelines that emphasize a coordinated, cost-effective approach to the implementation of national elimination and control activities where preventive chemotherapy is the main tool, i.e. regular anthelminthic drug administration to all people at risk of morbidity due to helminthic diseases, starting early in life. The availability of rapid diagnostic tools and donations of several drugs from pharmaceutical companies, and the reduced price of other essential antihelminthic drugs has catalysed the rapid expansion of chemotherapy-based control programmes for NTDs. The main challenges to PTC in Africa include poor health service infrastructure in post conflict countries and cost-effective approaches for integrating the individual vertical programmes targeting specific diseases.

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Unusual clinical profile of Dengue Infection in patients attending a tertiary care teaching hospital in north India

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Background: Major outbreaks of dengue virus have been reported from many parts of North India including Lucknow, at regular intervals since 1996. We have carried out a detailed investigation of the Dengue cases occurring in year 2008.
Methods: Clinically suspected patients attending Pediatrics and Medicine outpatient or inpatient Departments and referred to Microbiology Department for serological diagnosis of dengue, were prospectively enrolled after obtaining verbal consent. Detailed clinical history and examination findings were recorded in a pre designed questionnaire from 398 such patients between Jan 2008 to Dec 2008. Dengue specific antibodies were detected using commercial Mac-ELISA kit (IVD, USA). Results of hematological and other investigations were noted from medical records.
Results: Mean age of patients' was10.25±10.9 years and 328/398 were in pediatric age group (≤12 yrs age). A total of 53.26 % **(**212/398) patients were positive for dengue IgM and 93% of these were admitted patients. Male: Female ratio was1.8:1 and ~74% belonged to rural area. Overwhelming majority (92%) of dengue cases were seen between July to November, which are the post monsoon months in this part of world. Frequent clinical features included fever (100 %) with mean duration of 14.07±9.2 days, edema (50%), altered sensorium (39%), rash (31.84%). Mucosal bleeding, hepatomegaly and splenomegaly were present in 31.84%, 57.29% and 56.25% respectively. Thrombocytopenia (58.74%) was common laboratory finding. Liver enzymes SGPT and SGOT were raised in 72.55% and 78.43% of positive cases, respectively. Presentation varied between adults and pediatric populations, while among adults, seizure (p=0.029), skin rash (p=0.029), abdominal pain (p=0.005) and hemoconcentration (PCV>36; p=0.063) were significant findings; however in children, headache (p=0.029), serum sodium and calcium levels (p=0.022 and p=.0006) were significantly raised. Logistic Regression analysis found serum SGOT>40 U/L and presence of splenomegaly as independent predictors for dengue infection. Only 3 cases met the WHO criteria for dengue haemorrhagic fever (DHF), however clinically ~20% of the dengue positive cases were labelled and managed as DHF. Mortality rate amongst dengue IgM positives was 6.02% (5/83).
Conclusion: The unusual clinical profile necessitates continuous sero surveillance and monitoring for changing clinical presentationof dengue infection .

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Type: Oral Presentation

An outbreak of pneumonia associated with emergent human adenovirus serotype 14 - Southeast Alaska, 2008

D. Esposito[1], T. J. Gardner[2], E. Schneider[1], L. J. Stockman[1], J. Tate[1], C. A. Panozzo[1], C. L. Robbins[1], S. A. Jenkerson[2], L. Thomas[3], C. M. Watson[4], A. Curns[1], D. D. Erdman[1], X. Lu[1], T. Cromeans[1], M. Westcott[5], C. Humphries[5], J. Ballantyne[5], G. E. Fischer[1], J. B. McLaughlin[2], G. Armstrong[1], L. J. Anderson[1]
[1]Centers for Disease Control and Prevention, Atlanta, GA, USA, [2]Alaska Department of Health and Social Services, Anchorage, AK, USA, [3]Alicia Roberts Medical Center, Klawock, AK, USA, [4]Craig Public Health Center, Craig, AK, USA, [5]Alaska State Public Health Virology Laboratory, Fairbanks, AK, USA

Background: In September 2008, an outbreak of pneumonia associated with a rare human adenovirus (serotype-14 [HAdV-14]) occurred on a rural island in Southeast Alaska. To determine risk factors for disease and household transmission characteristics, we investigated pneumonia cases in three affected island communities.
Methods: Case-patients were island residents who presented to one of two medical clinics with clinical or radiological evidence of pneumonia between September 1 and October 27, 2008. Controls from the community were matched 1:1 to case-patients based on age, sex, and community of residence. Case-patients, controls, and household contacts were interviewed for information on demographics, recent illnesses, medical history, ill contacts, and other possible exposures. Serum and respiratory specimens were also collected. Risk factors for pneumonia were determined using exact multivariate conditional logistic regression. Household HAdV-14 attack rates were calculated.
Results: Thirty-two pneumonia case-patients and 32 matched controls were interviewed. Among case-patients, the median age was 47.5 (range, 2-95 years), 75% were male, and 74% were Alaska Native. Nine cases resulted in hospitalization and there was one death. Twenty-one (66%) case-patients and no controls were infected with HAdV-14 ($p<0.001$). Independent risk factors for pneumonia were contact with a known HAdV-14 pneumonia case-patient (OR=18.3, 95%CI=2.0-∞), current smoking (OR=6.7, 95%CI=0.9-∞), and having neither traveled off-island nor attended at a large public gathering (OR=14.7, 95%CI=2.0-∞). Fourteen (67%) of the 21 HAdV-14-infected case-patients belonged to a single network of people who socialized and often smoked together and infrequently traveled off-island. HAdV-14 infection occurred in 43% of case- versus 5% of control-household contacts ($p=0.005$).
Conclusion: This is one of the first recognized civilian community outbreaks of HAdV-14 since the virus first appeared in California in 2003. Demographic characteristics and illness patterns in case-patients were similar to those observed in other HAdV-14 outbreaks in Oregon and Washington State in 2007, with disease mostly occurring in adult male smokers. In this setting, HAdV-14 appeared to have spread mostly among close contacts in the home or within a certain social network whose members often reported smoking or sharing smoking materials with other HAdV-14 case-patients. Lack of HAdV-14 infection in controls and their household contacts suggests wide-spread transmission did not occur, either previously or during this pneumonia outbreak.

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Room: Room Orchid B/C/D
Type: Oral Presentation

Uptake and impact of Rotavirus vaccines in US Children

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Background: In 2006 and 2008, two new vaccines were recommended for routine vaccination of US infants against rotavirus. We assessed vaccine uptake and its impact on rotavirus disease in US children.
Methods: To measure vaccine uptake, we examined data from sentinel immunization information system (IIS) sites in eight different US locations. Coverage with at least 1 dose of rotavirus vaccine was measured at age 5 months, and compared with coverage of other established childhood vaccines, DTaP and pneumococcal vaccine, given at the same age. To measure vaccine impact, we examined data from 2000-2009 on laboratory detections of rotavirus from a national network of ~70 laboratories to assess trends and timing of rotavirus activity. Data from a subset of 29 laboratories that consistently reported for >=30 weeks for each season during 2000-2009 were used to measure national and regional changes in rotavirus test results.
Results: By March 2009, coverage with 1 dose of rotavirus at age 5 months has reached about 60%-70% across most of the IIS sites, a level that is about 10%-20% lower than that of DTaP and pneumococcal vaccine. Concurrent with increasing rotavirus vaccine coverage, rotavirus activity during the 2007-2008 and 2008-2009 rotavirus seasons declined by 64% and 60%, respectively, compared with pre-vaccine years during 2000-2006. In addition, compared with pre-vaccine years, the onset of both the 2007-2008 and 2008-2009 rotavirus seasons was delayed by 11 weeks and 6 weeks, respectively, and the seasons were shorter, lasting 14 and 17 weeks, respectively, compared with 26 weeks in 2000-2006. Regional differences in rotavirus activity were observed, with the West census region having a lower reduction and less delayed onset than all other regions in 2007-2008 and a greater reduction and more delayed onset than other regions in 2008-2009.
Conclusion: Uptake of rotavirus vaccine in US children has increased since vaccine implementation. However, rotavirus vaccine coverage remains slightly lower than that of other established childhood vaccines and factors that might account for this difference should be examined. Following rotavirus vaccine introduction, rotavirus activity in US children has declined and disease seasonality has been altered compared with prevaccine years. Factors that might explain the regional differences in changes in rotavirus activity after vaccination should be explored.

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The epidemiology of rotavirus disease among children <5 years of age - Santa Rosa, Guatemala, 2007- 2009

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Background: Diarrhea is the second leading cause of death in Guatemalan children <5 years of age. To evaluate the potential health benefits of new vaccines against rotavirus, we assessed the burden of rotavirus diarrhea in Guatemalan children.
Methods: We examined data from an active population-based surveillance system in Santa Rosa, Guatemala from October 2007 through September 2009 among children <5 years of age presenting to the hospital or ambulatory clinics. Specimens were collected from patients with acute diarrhea (≥3 loose stools in 24 hours during last seven days) and tested for rotavirus via enzyme immunoassay. Genotyping via reverse-transcriptase polymerase chain reaction was performed on rotavirus positive specimens. Results were stratified by age group and setting.
Results: 906 patients identified with diarrhea during the study period provided a fecal specimen for rotavirus testing. Of the specimens tested, 291(35%) were hospitalized and 615 (74%) were ambulatory patients. Rotavirus accounted for 90 (33%) hospitalizations and 57 (9%) ambulatory visits for diarrhea annually. Rotavirus confirmed episodes had a marked seasonality as 80% (N=72) of cases occurred in January and February. During these months, rotavirus accounted for 59% of hospitalizations and 31% of ambulatory visits for diarrhea. More than 85% (N=123) of children with rotavirus were <24 months. During the 2008 rotavirus season, the predominant rotavirus genotype identified in 15 of 27 (56%) samples tested was G1P8. Less common strains including 5 (19%) of the G12 genotype were also observed.
Conclusion: This analysis highlights the prominent role of rotavirus as a cause of severe diarrhea in children <5 years of age in Santa Rosa, Guatemala. Currently available vaccines against rotavirus have demonstrated high effectiveness in preventing severe disease caused by the predominant circulating strain (G1P8) identified in Guatemala during the 2008 season. Although many factors must be considered by a country prior to the decision to introduce vaccine nationally, these data underscore the substantial burden of rotavirus disease on the Guatemalan healthcare system.This active population-based surveillance system will provide a solid platform for the assessment of rotavirus vaccine impact after introduction.

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Time: 10:15-12:15
Room: Room Orchid B/C/D
Type: Oral Presentation

Surveillance for epidemic of enterovirus infections in Taiwan in 2008

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Background: The emergence of enterovirus 71 (EV71) in Taiwan in October, 2007 resulted in a large epidemic of hand-foot-and-mouth disease (HFMD) or herpangina in young children in 2008. EV71 patients may suffer from serious neurological complications or even deaths. The aims of this study were to describe the framework of the surveillance systems for enterovirus infections and to characterize this epidemic in Taiwan in 2008.
Methods: At Taiwan Centers for Disease Control (Taiwan CDC), there were four systems established for the surveillance of enterovirus infections. First, we used the sentinel surveillance with more than 650 clinics for reporting the number of HFMD or herpangina in outpatient weekly. Second, the National Notifiable Disease Surveillance System (NNDSS) was used for reporting the hospitalized cases with severe complications. Third, the laboratory surveillance consisted of 13 contract laboratories and 286 clinics for testing and collecting samples, respectively. Fourth, Taiwan CDC cooperated with the University of Pittsburgh to develop a syndromic surveillance, which is called the Real-time and Outbreak Surveillance (RODS) system, covering 80% of the emergency visits nationally. The Taiwanese RODS system used the ICD-9-CM code of 074.0 and 074.3 to monitor enterovirus infections. A web-based decision support system for this epidemic was also developed for displaying the statistics and epidemic curves of the four systems in real time.
Results: The epidemic started in week 11, peaked in week 25, and was subsiding gradually. The sentinel physicians reported 72,610 visits in one epidemic wave, which represents 18% of the ones nationally. 373 cases of severe complications (including 14 deaths) were reported through the NNDSS. Among those, 347 cases (93%) were EV71. A web-based system with automated updates daily for the public to browse the statistics and epidemic curves of the reported cases in the NNDSS was also released then. There were 11,150 specimens tested and 3,724 (33%) enterovirus isolated in the laboratory surveillance . The three most isolated types were Coxsackie A2 (CA2), EV71 (B5 was the major subtype), and Coxsackie B4 (CB4). The real-time data from the RODS helped us better track the trend of the epidemic.
During the large epidemic of enterovirus infections, our established surveillance systems are helpful for informing decisions about control measures, resource allocation, and risk communication in real time.

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Type: Oral Presentation

Epidemiology of varicella among passengers and crew on international conveyances, United States, 2005-2008

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Background: Although the incidence of varicella in the United States has decreased markedly since a national vaccination program was implemented in 1995, CDC Quarantine Stations continue to receive frequent reports of varicella among international travelers. However, few published reports are available on the the epidemiology of varicella in travelers. Our objective was to describe the epidemiology of varicella on international conveyances and to identify risk factors associated with illness.
Methods: We reviewed reports of varicella captured by the CDC Quarantine Activity Reporting System (QARS) from June 2005 - December 2008. A stepwise backward elimination logistic regresion model (inclusion criterion: alpha <0.05) was used to compare risk factors for varicella with those for all other illnesses in travelers during the same time period, including demographic characteristics, conveyance time (maritime versus air or land [pedestrian, car, bus, train]), season and year of report, and type of traveler (passenger or crew).
Results: Of 3908 illness reports during the study period, 446 (11.4%) met the case definition for varicella. Odds of reported varicella were higher on maritime conveyances (odds ratio [OR]=38.3; 95% confidence interval [CI], 22.0 - 66.5) and in travelers born in tropical countries (OR=2.3; CI, 1.4 - 3.6), males (OR=1.5; CI, 1.02 - 2.3), and younger travelers (for a 1-year decrease in age, OR=1.08; CI, 1.06 - 1.10). Odds of varicella reporting were lower in the fall (OR=0.30; CI, 0.16 - 0.54). There were no statistical differences between varicella and non-varicella illnesses by type of traveler (crew member, passenger), race and ethnicity (Hispanic, non-Hispanic), or year of report.
Conclusion: The higher incidence of varicella reporting by maritime conveyances compared with other conveyances may be due to the large number of unvaccinated crew members originating from tropical countries where varicella commonly occurs in adults. Maritime vessels, compared with other conveyances, may also achieve more complete case finding because of the extended periods of time crew live aboard the vessels. The availability of a vaccine for varicella means that most cases could be prevented, and vaccination should be considered for crew members on maritime conveyances without documented immunity to varicella.

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Dengue fever outbreak in Lima, Peru 2009: Epidemiological changes in urban areas

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Background: Dengue fever is endemic in Peru. The epidemic potential for dengue transmission north of Lima city has spread alarmingly in the last four years. A dengue outbreak occurs during March to June 2009 in three districts of Lima. The 2005 and 2007 outbreaks of dengue fever occurred in these districts only one circulating serotype in each outbreak. Epidemiological investigation was conducted to determine the distribution of cases, serotype circulation, symptoms and signs of dengue fever in order to identify transmission and epidemic control measures.
Methods: Analysis of cases of the outbreak investigation conducted by the network of epidemiology at the Department of Health V Lima City. The information was collected and processed through software NotiSp. Suspected case was considered a person with a history of fever for 2 to 7 days and two or more of the following symptoms: headache, retroocular, myalgia, arthralgia, rash and hemorrhagic manifestations residing in the districts of Carabayllo, Comas and Independence. The cases were registered in epidemiological records, blood samples were taken to determine seroconversion and identification of circulating serotypes
Results: Of 552 cases suspects, 148 (26.8%) were positive for IgM antibody detection of specific dengue indicating primary infection and 99 cases were obtained by PCR serotypes: DEN-3 (74%), DEN-1 (24%) and DEN-4 (2%). Most cases (45%) were adults between 20 and 59 years of age. The median age was 34 years. Women were more affected than men (56% and 44% respectively). The most frequent symptoms were fever (95%), headache (90%), body ache (86%), bone pain (75%) and pain retroocular (70%). The outbreak investigation revealed a cluster of four clusters that could be because they have areas favourable for breeding of the vector, such as presence of disposable plastic containers, clearing rocks, water shortages and the migration of people to Lima from dengue endemic areas
Conclusion: The outbreak investigation confirmed the presence of dengue as an emerging public health problem in Lima, identifying the co-circulation of three serotypes, demonstrating dengue epidemiological changes, so it is important to strengthen surveillance actions epidemiological and vector control in these areas during the coming years.

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Room: Room Orchid B/C/D
Type: Oral Presentation

Risk of being seropositive for multiple HPV types among Finnish and Ugandan women

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Background: Although infections with multiple HPV types have been readily reported, more information is needed for occurrence of the different types at individual or at the population level, e.g., across countries
Objective: We determined the distribution of seroprevalences to multiple HPV types in Finland and Uganda to compare epidemiology of the different HPV types in the two populations.
Methods: Cross-sectional seroprevalence study of antenatal clinic attendants. In Finland serum samples were randomly drawn from a subset of samples collected between 1995 -2007 for the Finnish Maternity cohort and in Uganda, samples were collected (between 2004-2008) from women enrolled after consenting. The serum samples were stored and analysed for HPV antibodies against seven HPV types; 6, 11, 16, 18, 31, 33, and 45 using direct VLP ELISA.
Results: Sera were analysed for 2 784 Finnish and 1 964 Ugandan women (mean ages 22 and 25 years) of whom 44% and 57% had antibodies to at least one of the seven HPV types (6/11/16/18/31/33/45) tested ($p<0.001$). Multiple HPV antibody positivity was common. Finnish women, who were HPV45 seropositive (F-HPV45), had higher adjusted risk estimates of having antibodies to most of the other HPV types (HPV18, 31 and 33) than comparable Ugandan women (U-HPV45): F-HPV45:HPV18 (OR=10.9, 95% CI 5.3-23) vs. U-HPV45:HPV18 (OR=3.4, 95% CI 2.3-5.0), F-HPV45:HPV31 (OR=6.1, 95% CI 2.8-13.4) vs. U-HPV45:HPV31 (OR=2.2, 95% CI 1.6-3.0), and F-HPV45:HPV33 (OR=12.2, 95% CI 5.8-26) vs. U-HPV45:HPV33 (OR=3.3, 95% CI 2.4-4.5). This was true also for antibodies to HPV31 and HPV33 among HPV18 seropositive Finnish women (F-HPV18) vs. HPV18 seropositive Ugandan women (U-HPV18) albeit with somewhat overlapping confidence intervals: F-HPV18:HPV31 (OR=5.2, 95% CI 3.0-9.0) vs. U-HPV18:HPV31 (OR=3.1, 95% CI 2.2-4.4), F-HPV18:HPV33 (OR=6.9, 95% CI 4.1-11.7) vs. U-HPV18:HPV33 (OR=3.3, 95% CI 2.3-4.6). In general, among the HPV16 seropositives increased risk estimates for being seropositive for a second HPV type were observed but major differences were not observed between the Finns and the Ugandans.
Conclusion: We observed remarkably increased risk estimates for being double HPV antibody positive among HPV45 and HPV18 seropositive Finns as compared to the Ugandans .In conclusion, biological, behavioral factors, iatrogenic and societal factors (screening vs no screening) may result in the different occurrence of infections with the high risk HPV types in Finland and Uganda.

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Room: Room Orchid B/C/D
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A phase 3 study of a short, two dose regimen of an investigational Hepatitis B vaccine

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Background: Achieving rapid protection against hepatitis B can be critical for travellers. HBsAg-ISS (HEPLISAV™) is an investigational vaccine containing Hepatitis B surface antigen (HBsAg) and 1018 Immunostimulatory Sequence (ISS), a Toll-like Receptor 9 (TLR9) agonist adjuvant. A Phase 3 study of subjects 18-55 years of age demonstrated non-inferiority of a short, 2 dose regimen of HBsAg-ISS to a 3 dose regimen of a licensed vaccine. This analysis in subjects >40 years of age compares the seroprotection rate (SPR), measured by antibody to HBsAg [anti-HBsAg] ≥10 mIU/mL, and anti-HBsAg geometric mean concentration (GMC) of HBsAg-ISS with licensed vaccine (Engerix-B, 20 mcg). This study demonstrated that the SPR of a short, 2 dose regimen of HBsAg-ISS in subjects 18-55 and in subjects over 40 is superior to the standard regimen of Engerix-B. This vaccine could provide a better solution for clinicians needing rapid, safe and effective protection against hepatitis B disease for travelers.
Methods: A randomized observer-blind study comparing 2 doses of HBsAg-ISS at months 0 and 1 with saline placebo at month 6 to 3 doses of licensed vaccine at months 0, 1, and 6. Anti-HBsAg were measured at months 0, 1, 2, 3, 6, and 7. Safety, including local and systemic reactogenicity and adverse events was assessed.
Results: 2101 subjects, including 1188 subjects over age 40, were included in the per-protocol analysis in a 3:1 randomization of HBsAg-ISS to Engerix-B. The primary endpoint SPR for all subjects was statistically significantly higher for HBsAg-ISS (95% at month 3) vs. Engerix-B (81% at month 7) [$p < 0.0001$]. For subjects over age 40 the primary endpoint SPR was 92% for HBsAg-ISS and 75% for Engerix-B) [$p < 0.0001$]; the GMC (mIU/mL) at month 7 was 236 for HBsAg-ISS and 218 for Engerix-B. HBsAg-ISS was safe, well-tolerated and comparable to Engerix-B with regard to local and systemic adverse events and serious adverse events. Two cases of ANCA-associated vasculitis were observed; one in an HBsAg-ISS subject and one in an Engerix-B subject. A review of AEs potentially associated with autoimmune conditions revealed no difference between groups.
Conclusion: This study demonstrated that the SPR of a short, 2 dose regimen of HBsAg-ISS in subjects 18-55 and in subjects over 40 is superior to the standard regimen of Engerix-B. This vaccine could provide a better solution for clinicians needing rapid and safe protection against hepatitis B disease for travelers.

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Final Abstract Number: 41.001
Session: Carbapenemase-producing bacteria: The threat of 'Panresistance'
Date: Thursday, March 11, 2010
Time: 10:15-12:15
Room: South Hall
Type: Invited Presentation

Detecting Carbapenemase Producers in the Clinic
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Carbapenem resistance among *Klebsiella pneumoniae*, is increasing in many parts of the world, and the treatment options for such strains are very limited. The mechanisms are mainly transferable carbapenemases of K. pneumoniae carbapenemase (KPC) or metallo-beta-lactamase (MBL) type (mainly VIM), but also OXA-48 carbapenemases, as well as extended-spectrum beta-lactamases or AmpC in combination with porin loss. Infection control is of crucial importance for combating such resistance, and depends on adequate detection of carbapenemase-producing isolates. Several authors have reported on problems of detecting such isolates, and the reasons and possible solutions are discussed.
Carbapenem-producers have carbapenem MICs below the current clinical breakpoints of EUCAST and CLSI. However, EUCASTs epidemiological cut-offs (ECOFFs) values, the limit of the wild-type populations, have been found useful to identify such carbapenemase-producers. Disk diffusion correlates to the current MIC ECOFFs are under development, and seem to be working equally well with the tentative zone ECOFFs. In particular meropenem and ertapenem produce a good separation between wild-type isolates and carbapenem-producers. Automated antimicrobial susceptibility testing (AST) systems will in most cases detect all carbapenemase-producers when using ECOFFs actively when reading the quantitative AST results.
Phenotypic tests for confirmation of carbapenemase-production comprise the modified Hodge test (MHT), and in-house combination disks containing carbapenems in combination with boronic acid (for KPC detection) or zinc chelators (for MBL-detection). The MHT has high sensitivity for detection of KPC, but lower for MBL. Also, there are problems with specificity, mainly with AmpC hyperproducers. The combination disk method has recently been updated with the addition of cloxacillin as a third inhibitor, in order to separate AmpC hyperproduction plus porin loss (synergy with cloxacillin and boronic acid) from KPC (synergy with boronic acid only). Further, dipicolinic acid has better specificity for MBL-detection than EDTA.
Although the above mentioned recommendations seem to identify carbapenemase-producers among *K. pneumoniae*, it is still uncertain whether they will be adequate for detection of carbapenemases in other species of Enterobacteriaceae. Further, there are still concerns regarding detection with automated AST-systems. Detection depends on the carbapenems included in the test

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Final Abstract Number: 41.002
Session: Carbapenemase-producing bacteria: The threat of 'Panresistance'
Date: Thursday, March 11, 2010
Time: 10:15-12:15
Room: South Hall
Type: Invited Presentation

Clinical Impact and Current Epidemiology of Carbapenemase producers

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Carbapenemase-producing pathogens have become a major and increasing infectious disease threat. Their most serious impact is the lack effective therapies for the infections they cause. Given that laboratory detection is often poor, our understanding of their epidemiology is incomplete. Some types of carbapenemase producers are already ubiquitous. For other types, there are known hotspots of occurrence. KPC producers are mostly detected in the eastern USA and Israel, but have also been detected in some European and Asian countries. Metallo-β-lactamase (MBL) producers mostly occur in Asia, Europe, Australia and South America. OXA-carbapenemase have been detected worldwide. The most rapidly spreading pathogens are probably *Acinetobacter baumannii* that produce OXA carbapenemases and KPC-producing *Klebsiella pneumoniae*. However, these enzymes also occur in species that are less closely monitored, e.g. OXA-producing Enterobacteriaceae and KPC-producing *A. baumannii* and *P. aeruginosa*. There appears to be less rapid spread of Enterobacteriaceae, *Pseudomonas aeruginosa* and *Acinetobacter* that produce transmissible MBLs, but this observation may be a reflection of suboptimal laboratory testing rather than reality. Prompt and accurate laboratory detection is critical. Outbreaks and therapeutic failures have resulted from testing problems. Another problem is that carbapenemase producers, especially *K. pneumoniae* and *A. baumannii*, are efficient scavengers of additional resistance mechanisms and, as a consequence, are constantly changing. In this sense, they are a “moving target” and contemporary understandings may have reduced relevance to the therapeutic, diagnostic, and infection control challenges of the future. The current needs are for effective therapies, effective infection control based on better detection, education of health care professionals, and for research to provide better understandings of the biology of these pathogens.

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Session: Carbapenemase-producing bacteria: The threat of 'Panresistance'
Date: Thursday, March 11, 2010
Time: 10:15-12:15
Room: South Hall
Type: Invited Presentation

Controlling the Spread of Carbapenemase-Producing Bacteria

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Background: During 2006, Israeli hospitals faced a clonal outbreak of carbapenem-resistant *Klebsiella pneumoniae*, producing the serine carbapenemase KPC-3. Locally-implemented infection control measures in affected hospitals failed to contain spread. A nationwide intervention was launched to contain the outbreak and introduce a strategy to control future dissemination of antibiotic-resistant bacteria in hospitals.
Methods: In March 2007, the Ministry of Health issued guidelines mandating physical separation of hospitalized carriers of carbapenem-resistant Enterobacteriaceae (CRE) and dedicated staffing, and appointed a professional task force charged with containing spread of the epidemic strain. The task force paid site visits at acute care hospitals, evaluated infection control policies and laboratory methods, supervised adherence to the guidelines via daily census reports on carriers and their conditions of isolation, provided regular feedback on performance to hospital directors, and intervened additionally when necessary. During 2008, the intervention was extended to long-term care facilities, and in June 2008 national guidelines for active surveillance were issued. The primary outcome measure was the incidence of clinically diagnosed nosocomial CRE cases in acute care hospitals.
Results: By March 2007, over 1200 patients were affected in acute care hospitals. Prior to the intervention, the monthly incidence of noscomial CRE climbed steadily, peaking at over 180 cases. Crude 30-day mortality was > 30%. With the intervention, the continuous rise in incidence of CRE acquisition was halted, and at the end of the 14-month initial intervention period the number of new monthly cases was 46. Following the introduction of active surveillance guidelines, monthly incidence fell further, reaching a low of 24 as of October 2009. A direct correlation was observed between compliance with isolation guidelines and success in containment of in-hospital CRE transmission.
Conclusions: A centrally-coordinated public health intervention has succeeded in containing a nationwide outbreak of CRE in Israeli hospitals after local measures failed. The intervention demonstrates the importance of strategic planning and national oversight in combating antimicrobial resistance.

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Final Abstract Number: 41.004
Session: Carbapenemase-producing bacteria: The threat of 'Panresistance'
Date: Thursday, March 11, 2010
Time: 10:15-12:15
Room: South Hall
Type: Invited Presentation

Treatment Options for Carbapenenam Resistant Infections

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Carbapenemase producing Gram-negative bacteria (CPGN) become increasingly prevalent and cause serious infections resulting in high fatality. These organisms are resistant, not only to almost all available β-lactam antibiotics but also to other classes of agents, leaving tigecycline and colistin as the only therapeutic options. None of these agents, however, is ideal; tigecycline produces low blood levels and colistin has questionable performance in serious infections owing to poor pharmacokinetics. More worryingly, resistance to both of these compounds has been developed. The newer β-lactamase inhibitors, NXL 104 and BAL 30376, show promises for infections caused by CPGN. A proportion of carbapenemase-producing Enterobacteriacae has MICs of carbapenems within the susceptible range raising the critical question of whether carbapenems might be effective in the treatment of infections caused by such organisms. Anecdotal reports claim microbiological and clinical response in patients infected with MBL-positive carbapenem-susceptible organisms after treatment with a carbapenem. In a prospective study of 67 patients with bloodstream infections caused by VIM-producing *K. pneumoniae*, the lowest mortality was observed in the group of patients who had received combination therapy with two active drugs, one of which was a carbapenem and the other either colistin or an active aminoglycoside, whereas therapy with one active drug resulted in a mortality similar to that observed in patients who had received therapy with no active drug. Based on this experience, it remains doubtful whether monotherapy with a carbapenem would be effective in the treatment of such infections. On the other hand, carbapenems in combination with another active agent may provide some therapeutic benefit against MBL-positive carbapenem-susceptible Enterobacteriaceae. In this respect, the issue of either reporting such isolates as fully resistant to carbapenems or consider the respective MICs at face value should remain open. In conclusion, information about how to treat infections caused by CPGN is surprisingly scarce.

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Final Abstract Number: 42.001
Session: Plenary 6
Date: Thursday, March 11, 2010
Time: 14:30-15:16
Room: Ballroom 1: Brickell
Type: Invited Presentation

Malaria Eradication

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A global campaign to eradicate malaria in the middle of the last century relied chiefly on two powerful tools, insecticide spraying of mosquitoes to interrupt transmission and chloroquine treatment to reduce the human reservoir of infection. While this effort, led by the World Health Organization, did succeed in eliminating malaria from some areas on the edges of the malaria map, it was abandoned as a failure after little more than a decade. The emergence of insecticide-resistant Anopheles mosquitoes and drug-resistant *Plasmodium falciparum* parasites, failure to understand and adapt to local differences in mosquito ecology and malaria epidemiology, and donor fatigue, all contributed to the demise of the campaign, which never included Africa, the region with by far the greatest malaria burden, then and now. In the ensuing decades, the focus shifted from eradication to control, and worldwide malaria deaths increased in the face of chloroquine resistant falciparum malaria and weak health care systems.
The development and deployment of two new tools, long-lasting insecticide-treated nets and artemisinin-based combination drug treatments, have led to dramatic reductions in malaria in several countries, including some in Africa. Malaria has even been completely eliminated recently from some endemic areas with low levels of transmission and relatively good health infrastructure. These success stories have generated such optimism that Bill and Melinda Gates and other donors and, following their lead, malariologists, are talking again about eradication. To achieve a better outcome than the first campaign, malaria eradicators in the 21st century will need to learn and apply lessons from both past and recent failures and successes. If a renewed malaria eradication effort is started with the tools in hand now, it will be essential to keep the pipeline flowing with improved insecticides and drugs to replace those that succumb to resistance, as well as to develop new tools, including safe and effective drugs and vaccines that block malaria transmission. Prospects for malaria eradication may be jeopardized by the apparent recent emergence of artemisinin-resistant falciparum malaria in Southeast Asia.

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Final Abstract Number: 43.002
Session: A rational approach for the treatment and prevention of neonatal sepsis
Date: Thursday, March 11, 2010
Time: 15:45-17:45
Room: Ballroom 1: Brickell
Type: Invited Presentation

Global Burden of Neonatal Sepsis

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As infant and child mortality declines in many developing countries, neonatal mortality becomes the dominant component of all child mortality, now constituting about 40% of child deaths. As attention is focused on this problem, it is becoming clear that, in the high mortality countries, neonatal mortality rates are being systematically underestimated, especially in the poorest, most marginalized communities. Data on the causes of neonatal deaths in the community are seriously inadequate, as deaths occur outside the health service, and post mortem questionnaires are very difficult to interpret in this age group. Studies that examined the incidence and mortality due to neonatal sepsis were reviewed. We sought to determine the relationship between the neonatal mortality rate and the proportion of neonatal deaths due to infection. From a review of 32 community based studies published since 1990, between 8% and 80% of all neonatal deaths in different regions of the developing world are reported as being due to infectious causes. Similar wide variability is seen in the incidence of clinical neonatal sepsis, with reported rates varying from 49 per 1000 live births in rural Guatemala to as high as 170 per 1000 live birthsin rural India. The field of neonatal mortality, and specifically neonatal sepsis, in developing countries is obscured by a lack of credible data. Neonatal sepsis rates are confounded by lack of clear clinical definitions, and even neonatal mortality rates are very unclear. Without any clear means of determining the cause of community neonatal deaths, the contribution of sepsis to overall mortality is equally unclear. The need for new and innovative research in this field is overwhelming.

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Final Abstract Number: 43.003
Session: A rational approach for the treatment and prevention of neonatal sepsis
Date: Thursday, March 11, 2010
Time: 15:45-17:45
Room: Ballroom 1: Brickell
Type: Invited Presentation

Rational Use of Antibiotics in the Critically Ill Neonate and the Premature Infant

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NO ABSTRACT RECEIVED

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Final Abstract Number: 43.004
Session: A rational approach for the treatment and prevention of neonatal sepsis
Date: Thursday, March 11, 2010
Time: 15:45-17:45
Room: Ballroom 1: Brickell
Type: Invited Presentation

Strategies to Limit Infections in the Neonate and to Reduce Infection-related Mortality

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Health-care associated infections remain a major problem in the neonatal intensive care unit (NICU), resulting in significant morbidity and mortality. Specifically, bloodstream infections have been associated with adverse neurodevelopmental outcomes among preterm infants with birth weight <1000 grams. In addition, these infections are associated with prolonged duration of hospitalization among survivors and increased cost of neonatal health care. It is clear that preventive strategies are urgently needed.
Many bloodstream infections in the NICU are associated with the use of central venous catheters, and implementation of evidence-based measures as well as bundles has reduced their occurrence. Nevertheless, much work remains. Candidal infections have become more prevalent in the NICU, and fluconazole prophylaxis is being recommended and used to prevent candidiasis among infants with birth weight <1000 grams. Although fluconazole prophylaxis has reduced invasive candidal infections, the underlying risk factors that result in Candida becoming a more common pathogen remain, namely the overuse of antibiotics especially the third generation cephalosporins. In addition, the use of H2 blocker also has contributed to Candidal colonization and late onset sepsis. Recent results of randomized clinical trials have shown beneficial effects of probiotics for prevention of necrotizing enterocolitis and lactoferrin for prevention of late onset sepsis. Finally, the need to vaccinate not only our preemies but also staff and family members of babies in the NICU will further reduce the likelihood of introducing community-associated pathogens into the NICU.

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Session: Bacterial infections following influenza
Date: Thursday, March 11, 2010
Time: 15:45-17:45
Room: Ballroom 2: Monroe/Flagler
Type: Invited Presentation

Secondary bacterial infections - The other side of influenza pathogenesis

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Secondary bacterial infections are a major cause of morbidity and mortality following influenza. This was especially true during past pandemics, where 50-95% of all deaths were complicated by or attributed to bacterial pathogens. The emergence in 2009 of a new pandemic strain has increased the urgency for us to understand how bacteria work together with influenza viruses to cause pneumonia. Several mechanisms have been postulated to explain this interaction. The viral neuraminidase has been shown to enhance adherence of bacteria and increase the incidence of bacterial pneumonia. The lack of glycosylation of the surface proteins of viruses emerging from the avian reservoir contributes to both primary virulence and secondary bacterial infections by preventing viral clearance. Recent work has implicated the influenza A virus protein PB1-F2 as a virulence factor which enhances secondary bacterial pneumonia. Although the novel H1N1 swine-origin influenza virus has molecular signatures that predict viral virulence in humans including high neuraminidase activity and low glycosyltation, it does not possess a functional PB1-F2 protein. In the context of a pandemic, it is likely that secondary bacterial complications and overall mortality will be lower because of this absence. However, reassortment or mutation to restore PB1-F2 function to this virus could herald greatly expanded virulence.

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Type: Invited Presentation

The role of mucosal antiviral immunity in bacterial secondary lung infections

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Bacterial co-infections are typically a major cause of mortality following influenza infection, including infection with the pandemic H1N1 Cal/04/09 virus, but the reason for this increased susceptibility is only poorly understood. We have found that alveolar macrophages are the first line of defense against pulmonary pneumococcal and MRSA infection, and can very rapidly (within 4 hr) clear almost all bacteria after *in vivo* challenge with a relatively low dose (up to 105 CFU of pneumococci). However, prior influenza virus infection inhibits this clearance mechanism and causes normally sublethal doses of bacteria to be 100% lethal. This is due to production of interferon (IFN)-gamma during pulmonary T cell responses to influenza infection, which inhibits scavenger receptor expression by alveolar macrophages and in turn, leads to decreased bacterial clearance from the lung. Thus, the increased anti-viral immune response causes decreased protection against pulmonary bacterial infection. These results and the potential of vaccination to induce protection against secondary bacterial infections will be discussed in the context of both seasonal and H1N1 influenza infection.

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Room: Ballroom 2: Monroe/Flagler
Type: Invited Presentation

Alteration of the Innate Immune Rheostat and Susceptibility to Secondary Bacterial Super-infections

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Infection of mucosal surfaces culminates in long term modifications that impact on future inflammatory events. These modifications do not necessarily depend on persistence of the original pathogen but on the altered microenvironment which occurs upon resolution. This “imprinting” by the first pathogen involves subtle alterations of epithelial cells, resident mucosal macrophages, production of mediators that recruit immune cells and importantly, an alteration in the local microbial commensal community.
Bacterial super-infections are common following influenza and lead to a worse prognosis often resulting in death. Analysis of post-mortem specimens from the 1918-19 pandemic shows a bacterial prevalence greater than 95%. Control of initial bacterial growth relies on multiple components of innate immunity, many of which are disrupted following influenza virus infection in murine models. One key determinant that limits bacterial growth is the responsiveness of airway macrophages to bacteria in the airspaces. We show that influenza virus limits responsiveness by enhancing an innate immune negative regulator (CD200 receptor) during resolution of adaptive immunity. Removal of this single receptor limits bacterial burden in the airway and lung and completely prevents peripheral dissemination, sepsis and mortality. Adjustment of innate reactivity may therefore provide a novel opportunity to prevent life-threatening consequences of lung influenza virus infection.

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Type: Invited Presentation

Lessons from 1918 and the current H1N1 pandemic on the role of bacterial infections during pandemic influenza

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The current pandemic of H1N1 influenza has features reminiscent of 1918 including infections and excess morbidity in young adults. The impact in terms of mortality has however been far less severe. This is in part due to lesser virulence of the virus, but also to the introduction of antibiotics and most recently to the introduction of conjugate pneumococcal vaccines in some countries that have reduced the morbidity of influenza associated pneumonia. During the 1918 pandemic, post mortem data suggest that the majority of deaths were associated with bacterial superinfection leading to pneumonia following 4 - 6 days after influenza. A re - analysis of contemporary blood culture findings suggest that most of these infections were pneumococcal, followed by hemolytic (probably Group A) streptococcal infections, and a minority of infections were due to *Staphylococcus aureus*. Attempts were made at that time to reduce infection and mortality by killed bacterial vaccines. These trials were poorly controlled, but an analysis restricted to the prevention of pneumonia and mortality among influenza patients who received these vaccines, suggests that vaccines against hemolytic streptococci and pneumococci, but not *Haemophilus influenzae*, may have had some protection against pneumonia and death. In a randomised trial of 9 valent conjugate pneumococcal vaccine in children who subsequently developed seasonal influenza in 1998 - 2000, hospitalization for pneumonia was reduced by 45%. In the current pandemic, postmortem data suggest that staphylococcal infections are more common than in 1918, but pneumococcal infections remain predominant. Where conjugate pneumococcal vaccination of children has led to herd immunity, vaccine serotypes have been largely absent as a cause of fatal pneumonias. The great majority of individuals hospitalized with H1N1 pneumonia have received antibiotics and it is probable that widespread availability of antibiotics has contributed to the reduction in mortality associated with this pandemic, by reducing bacterial superinfections in susceptible individuals.

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Session: Travelers to Latin America with special risks
Date: Thursday, March 11, 2010
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Type: Invited Presentation

High Altitude Itineraries

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Several countries in Latin America double their tourist arrivals in the last 10 years. The Andes Mountains are the common denominator for most countries in South America. Many peaks in this mountain range attract mountaineers and trekkers which may be aware of the risks at high altitude. Of importance are the Andean cities and tourism attractions over 2,400 meters above sea level luring millions every year. Significant numbers of travelers to these destinations are unaware of the health risks of altitude or come unprepared.

The diseases related to high altitude ascend are referred to as high altitude illnesses (HAI). These comprise acute mountain sickness (AMS), high altitude cerebral edema (HACE), and high altitude pulmonary edema (HAPE). AMS affects 20% to 50% of travelers to altitudes up to 4000 meters. HACE and HAPE are less common affecting 0.01% to 2 % of travelers to similar altitudes. The risk factors can be classified as intrinsic (not modifiable), which include age, pre-existing medical conditions, prior history of HAI, and probably genetic factors. Modifiable risk factors include rate of ascend, sleeping altitude, altitude attained, degree of exertion, and medications. The hypoxic ventilatory response is an individual risk factor that can be suppressed or stimulated.

Information is of paramount importance in prevention of HAI. Informed travelers are likely to comply with recommendations, recognize symptoms, and avoid complications. A gradual slow ascent, when possible, is as important for prevention. Other non-pharmacological measures are avoiding exertion, dehydration, or use of respiratory suppressing substances. AMS/HACE pharmacologic prevention consists of acetazolamide or dexamethasone. Nifedipine, tadafil, and inhaled β-agonists are used for HAPE prevention.

Descent is effective to treat all HAI but is not always possible in remote areas or desirable for milder cases. Alternatives like rest, oxygen, medications, positive airway pressure and hyperbarics devices provide support until descent is possible or acclimatization ensues.

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Type: Invited Presentation

Risks on Common Cruise Itineraries

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Cruise travel has become one of the most popular ways to visit different places and is increasing in terms of cruise passengers, voyages and region destinations. Most passengers, voyages and cruises are considered from low to medium health risks. A cruise offers a wide spectrum of services and is oriented to different customers with clearly different life styles risks from children, families up to elderly. Traditionally, about one third of travelers are above 65 years old and other adults have some special conditions. However, during last few years the number of cruises oriented to young adults and visiting different regions and very peculiar environments such as the Amazons may increase the health risk significantly. Although, exposition to a mixture of people from different countries and diverse environments visited tend to change usual lifestyle or behaviors in terms of looking for adventures and new activities during vacations. In terms of travel health risks, the age of the cruise member is extremely related to the chance to suffer an event (sickness or accident) due mainly to underlying chronic health problems. Most common health problems are associated with movement (sea-sickness) and gastrointestinal diseases. Communicable diseases are easily disseminated because a lot of activities for long hours made in semi-enclosed cabins and many times very crowded. And as in crowded places and high interactive communities, cruise passengers are not an exemption for airborne diseases, as flu infections and other acute respiratory illnesses. Injuries account for an important number of infirmary visits. Medical care aboard is important for preventive and caring passengers and crew for health and medical issues. Pre-travel consultation is a great opportunity for advising and providing health education for main risks and preparing passengers for a healthy and safety itinerary.

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Type: Invited Presentation

Immunocompromised Travelers

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In the future, increasing numbers of travelers may have compromised immune systems due to advanced age, medications taken for chronic conditions, infection with human immunodeficiency virus, and immune deficits associated with congenital syndromes, systemic diseases, and/ or treatments. A complete medical history is necessary during the pre-travel health evaluation. Recommendations for travel vaccines, malaria chemoprophylaxis, and care of common travel ailments such as traveler's diarrhea must be tailored to the individual's health status. Required (e.g. yellow fever, meningococcal disease) and recommended (e.g. influenza, hepatitis A and B, typhoid, rabies) travel vaccines may be contraindicated or be less efficacious in the immunocompromised (IC) traveler. In some cases, timing or adjustment of vaccine doses may optimize the immune protection elicited. Drugs for prevention of malaria may interact with medications taken on a regular basis, necessitating additional laboratory testing, dosage changes, and/ or the selection of alternate prevention strategies. Some IC travelers may have increased susceptibility to gastrointestinal pathogens, and may warrant consideration of prophylactic antibiotics as well as specific instruction on food safety at destination. The risk of geographically focal infections such as visceral leishmaniasis, certain fungal infections transmitted through inhalation (*Penicillium marneffei* in Southeast Asia and coccidiomycosis in the Americas) and tuberculosis in some developing countries must be considered because of the increased possibility of severe disease in IC persons.
Travelers with specific needs, such as the IC traveler, should seek travel health advice months in advance of departure, so that the travel health specialist and the primary care provider have adequate time to communicate about and coordinate the medical aspects of the trip preparation. Identification of medical resources at destination, how to obtain special drugs and medical supplies in case of need, and emergency medical evacuation are additional important pre-travel topics for these travelers.

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Pregnant Travelers

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Pregnancy is not an illness, but it is an altered state of health during which many physiologic changes occur. These changes need to be considered when advising a pregnant woman regarding international travel, especially to remote locations.
Some examples are changes in renal and metabolic status that affect pharmacokinetics, cardio-respiratory changes that need to be considered in high altitudes, gastrointestinal changes that predispose to traveler's diarrhea, and immunologic changes that must be considered when giving immunizations. These and related matters are discussed in this presentation on pregnancy and travel. Also discussed are practical comfort and safety measures for the pregnant traveler, insurance issues and assistance in finding medical care.
While immunization and prophylactic medications are the topics that raise the most concern among providers, these are not the most common problems encountered by pregnant travelers. Attention to these few basic principles will greatly reduce the anxiety that patient and provider are both apt to feel when travel is combined with pregnancy.

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Room: Room Jasmine
Type: Invited Presentation

ProMED and HealthMap: Collaboration to improve emerging disease surveillance

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Unofficial or informal sources (also called “rumors” or “unstructured data”) of emerging disease outbreaks such as media reports and firsthand accounts have become an important mechanism for detecting these outbreaks. These sources are disseminated by a variety of human-based and automated biosurveillance networks that are now routinely monitored by public health authorities at all levels. The 2005 revisions to the International Health Regulations recognize that these sources often appear in advance of official notification of disease threats and are important in allowing the timely response to emerging diseases. Early media reports of respiratory illness in Mexico were among the first signs of the H1N1 pandemic and unofficial information sources are a critical mechanism for following the pandemic. ProMED-mail (the Program for Monitoring Emerging Diseases of the International Society for Infectious Diseases) has used largely human-based reporting to detect and report outbreaks of emerging infectious diseases since 1994. HealthMap, based at Boston Children’s Hospital and Harvard Medical School, uses automated mining of open sources in multiple languages to detect emerging disease outbreaks in and place them on a world map. ProMED and HealthMap have begun to collaborate to exploit the strengths of human-based and automated detection and reporting systems. Studies to evaluate the use of informal sources and to improve the detection of emerging disease outbreaks are in progress and have found differences in timeliness of reporting depending on disease type and geographic location. These differences are being used to target the development of new regional and disease specific reporting networks as well as the deployment of new mobile tools for capturing and disseminating news of emerging threats.

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Room: Room Jasmine
Type: Invited Presentation

Google Flu Trends: Mapping Influenza in Near Real Time

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Google.org uses Google's strengths in information and technology to build products that address global challenges. Infectious diseases are responsible for millions of deaths around the world each year. Influenza, in particular, affects 3-5 million people per year, and kills 250-500 thousand. With this in mind, a small group of engineers, working closely with medical professionals at Google.org and externally, began to investigate what innovations Google could bring to this issue. By some estimates, there are more than 1.6 billion people on the planet with access to the Internet and Google receives more than a billion searches daily.

By analyzing influenza-like illness (ILI) data from the U.S. Centers of Disease Control and Prevention, and anonymized, aggregated search query data, we discovered that a rise in the frequency of certain influenza-related search terms in a place corresponds with a rise in actual flu activity for that area. In November 2008, we introduced Google Flu Trends for the United States, an online tool that tracks and analyzes search terms to provide flu activity estimates. Now for 20 countries, Google Flu Trends generates estimates that are automatically updated daily, providing a timely indicator of influenza activity. Our hope is that Google Flu Trends be a complementary surveillance tool for health officials, as well as a source of useful information for the general public.

We continue to receive feedback from health officials worldwide regarding the tool's use, helpfulness and limitations. We have also learned about the positive impact that Google Flu Trends has had on public awareness of the timing and intensity of flu season, as well as preventative measures like hand washing and vaccination. Now entering its second year, Google Flu Trends will continue to adapt in response to a growing body of information regarding its practical application and potential.

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Session: Infectious diseases surveillance systems in practice
Date: Thursday, March 11, 2010
Time: 15:45-17:45
Room: Room Jasmine
Type: Invited Presentation

CaribVET: A Model for Surveillance of Zoonotic Diseases

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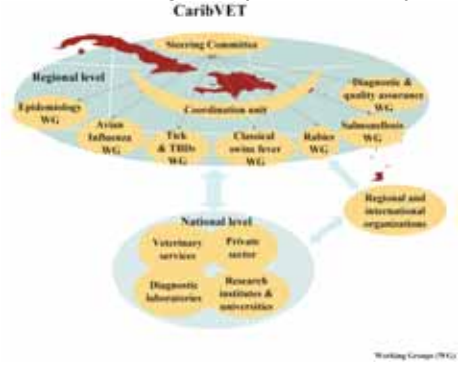
The Caribbean region is considered to be at risk for zoonotic diseases because of widespread backyard breeding system, diverse disease surveillance systems, legal or illegal human and animal movements. Several zoonosis are reported including Influenza, West Nile, Rabies, Leptospirosis.
The Caribbean animal health network (CaribVET) is a collaboration among veterinary services, laboratories, research institutes, and regional/international organizations to improve animal and veterinary public health in the Caribbean. Its specific objectives are to promote a regional approach for emergency preparedness and diseases control especially for emerging and zoonotic diseases, reinforce regional diagnostic capacities, and strengthen national epidemiological surveillance systems.
Meetings, trainings, skills building and development of regional tools for information and data exchange are the main strategies used. The Steering Committee of CaribVET is responsible for the regional strategy while seven Working Groups organize the collaboration on specific diseases (Tick and Tick Borne Diseases, Avian Influenza, Classical Swine Fever, Salmonellosis, Rabies) or activities (Epidemiology, Laboratory quality assurance).
The epidemiology working group has developed criteria for the definition of priority diseases, core surveillance databases, an evaluation of national surveillance systems and risk analysis of regional interest. It participates in the updating of a participatory website (www.caribvet.net), with information and data on surveillance systems, diagnostic laboratories, conferences, and major diseases of the region. The Working Group for avian influenza has developed a regional surveillance protocol, a diagnostic network, surveys of wild birds and on risk posed by fighting cocks trade. Research on West Nile first developed in Guadeloupe, identified risk factors which were used to implement risk based surveillances in the region.
The interaction between surveillance and research within CaribVET facilitates the access to surveillance data and field samples for the development of research studies. Research results are used for emergence prediction, improvement of surveillance and control of diseases.



CaribVET network organisation

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Time: 15:45-17:45
Room: Room Jasmine
Type: Invited Presentation

GeoSentinel: Provider-based Surveillance of International Travelers

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80 million individuals from industrialized nations travel to the developing world each year. Provider-based surveillance of travelers is increasingly sophisticated. One such network, GeoSentinel monitors disease trends among travelers and can inform both pre-travel advice and post-travel management and defines the spectrum of illness and the relation to place of exposure for the most significant health risks that face travelers.
Founded in 1996, the communications and data collection network currently comprises 50 travel/tropical medicine ISTM (International Society of Travel Medicine) clinics on 6 continents operating in cooperation with the US CDC. Returning travelers seen at relatively few sentinel sites provide a sample of disease agents in over 230 different countries. As of December 1, 2009, over 114,000 patient records increasing by 20,000/yr, track trends against a 12-year long baseline for over 500 diagnoses in order to monitor anomalies that might herald disease emergence.
Real time data entry via internet onto a central server allows monitoring of alarming sentinel events to generate immediate network wide queries and enhanced surveillance during focal or widespread outbreak situations. The GeoSentinel response arm disseminates alerts and advisories through CDC, ProMedMail, ISTM, ASTMH, and other partner networks and agencies. Examples have included: imported traveler-related cases/outbreaks of SARS, 2009 H1N1 influenza, leptospirosis from Borneo, Hantavirus from Chile, Hajj meningitis from Singapore, first-ever dengue from Easter Island, and schistosomiasis from Tanzania.
The presentation will include advances, observations, lessons and limitations from the experience of the global GeoSentinel surveillance network. Data from sentinel travelers upon their return to medically sophisticated environments can also benefit local populations in resource-limited countries.

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Final Abstract Number: 47.001
Session: Advances from the laboratory
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Room: Room Orchid B/C/D
Type: Oral Presentation

Epidemiological description of infection with agents of the Rickettsia genus in rodents, ectoparasites and humans in the northern coast of Antioquia, Colombia

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Background: Rickettsia is a worldwide usually rodent-carried tick, flea or lice-borne bacteria. In Colombia, few reports have beed performed, first in the mids thirties causing an outbreak in the population of Tobia Cundinamarca, and from the years 2006 to 2008 in the Northern region of Colombia known as Urabá. Our main goal was to perform an epidemiological description of the infection in the endemic mentioned area in Colombia.
Methods: Samples were obtained from the municipalities of Apartadó, Turbo y Necoclí, where 335 rondents were captured and parasites were collected from 33 of them. 220 double-blood human samples were also taken (acute and convalescent phase) from patients with febrile syndroms negative to malaria by direct blood-smear test. Indirect Immunofluorescence (IFI), was used to detect rickettsial infection in humans and rodents. Additionally, PCR was performed in liver-DNA from rodents searching for specific genetic sequences of Rickettsia genus (Citrate Synthase gene, gltA) and pathogenic Rickettsias (OmpB gene).
Results: We obtained 23 rodent DNA samples positive to gltA but only 6 of them, positive for the OmpB gene, resulting on a 6.8% DNA frequency of infection to Rickettsias by PCR. Some PCR products for the gltA gene, were sequenced and showed 98% similarity with the *Rickettsia Prowazekii* species, but the phylogenetic analysis suggests that these sequences form a separated cluster indicating that these Rickettsias could represent a new specie or sub specie. 89 of the 220 human sera were tested by IFI and 11 came up positive in dilution 1:64 (10 of the samples were positive in the convalescence period M2, and one in the acute phase, M1). Most of the ectoparasites collected were identified as hard ticks (*Amblyomma sp,* Ixodidae family,) soft ticks (*Ornithodoros Alectorobius puertoricensis,* Argasidae family) and fleas (*Xenospsilla sp* genus). These samples still remain to be tested for rickettsial infection using both gltA and OmpB.
Conclusion: This is the firs of a serie of studies that will allow us to characterize ecologically this endemic site and contribute to recomend the measures to prevent future human cases in this important risk area.

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Final Abstract Number: 47.002
Session: Advances from the laboratory
Date: Thursday, March 11, 2010
Time: 15:45-17:45
Room: Room Orchid B/C/D
Type: Oral Presentation

Distinct pathological signatures after lethal avian H5N1 and swine H1N1 influenza infections suggest variable pathogenesis

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Background: Influenza annual epidemics result in up to 500,000 deaths in human population, and different pandemics occurred over the 20th century, among which the 1918 pandemic was accountable for more than 50 millions deaths. Lethal seasonal or pandemic influenza infections are all associated either to secondary bacterial infections or acute respiratory distress syndrome (ARDS). Since antibiotics will help in treating bacterial pneumonias, it is crucial for public health to understand the pathogenesis of influenza-associated ARDS in order to fight it or to prevent its occurrence. Descriptions of the lung alterations in fatal influenza infections in human and mouse all depict similar lung dysfunctions and lesions. Here we describe the ARDS associated with the inoculation of identical doses of two influenza strains highly pathogenic for mice.
Methods: A clade 1 avian H5N1 virus (A/crested_eagle/Belgium/1/2004) and a porcine H1N1 virus (A/swine/Iowa/4/1976) were rendered highly pathogenic for mice by serial lung-to-lung passaging in mice. Two series of mice were inoculated intranasally with 10 MLD50 of virus. Body and lung weights were monitored daily and several organs were sampled at selected time intervals for histopathological / immunohistochemical evaluation or for viral titration.
Results: MLD50s were similar for both viral strains (3.2 PFUs for the H1N1 and 6.4 TCID50 for the H5N1 strain). The course of the infection was much faster for H5N1 than for H1N1, the end-point days being days 4 and 8 post-inoculation, respectively. Typically, H1N1-infected lungs were characterised by a progressive extension from the airways to the lung parenchyma, resulting in a massive mononuclear cellular infiltrate. For H5N1, the lung parenchyma was rapidly diffusely involved, the airways being almost unaffected, with a very low density of inflammatory cell infiltrates and, at the end-point day, with massive alveolar edema. Influenza antigens were detected in lungs, brain, liver, spleen, heart, pancreas, kidneys and pervisceral fat of H5N1-infected mice, while H1N1 antigens were only found in the lungs.
Conclusion: The clearly distinct histological pictures shown here refute the hypothesis of a single universal pathogenesis beyond all influenza-associated fatal ARDS and suggest that the treatment should be tailored to the influenza pathotype.

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Room: Room Orchid B/C/D
Type: Oral Presentation

A novel nervous-to-immune signalling mechanism mediating innate responses to infections

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Background: Substantial communications between the nervous and the immune systems were well established, but the effect of the nervous system in directing the innate immunity is not known. Accordingly, we hypothesized that opening innate responses to infections are mediated via nervous-to-immune signalling pathway.
Methods: To explore the factor(s) involved in this nervous-to-immune signaling pathway, splenic-denervated and non-denervated Sprague-Dawley rats were inoculated with *Trypanosoma brucei brucei* (*T.b.brucei*) followed by immediate dissection of the spleen and culture of splenocytes. ELISPOT and cell proliferation assays were used to assess cellular and biological activities. Using the fluorescent differential display technology the gene involved in this process was identified and further cloned.
Results: Supernatants of cultured splenocytes prepared from subcutaneously trypanosome-inoculated rats and mice spleens obtained immediately after inoculation and added to naïve cells significantly stimulate IFN-γ production and cell proliferation compared to PBS-inoculated animals. This action was abrogated by surgical denervation of the spleen. The fluorescent differential display technology depicted the gene involved in this process which was further cloned and its sequence was mapped to chromosome 14 (GenBank accession number: EU552928). Protein expression revealed ~15 kDa molecule with biological activities similar to the cultured supernatants of splenocytes obtained directly from parasite-inoculated animals. Antibodies raised against the protein blocked the activities of both the protein and the supernatant and also recognized a band in the active supernatant with the same molecular mass as the protein. Furthermore, the protein was able to reactivate experimentally immunosuppressed cells by regaining their ability to proliferate.
Conclusion: A nervous system-induced Immune System-Released Activating Agent (ISRAA) was identified and may have a potential therapeutic benefit in immunocompromised situations and in further understanding the mechanism for innate immunity commencement and action.

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Date: Thursday, March 11, 2010
Time: 15:45-17:45
Room: Room Orchid B/C/D
Type: Oral Presentation

Variable expression of alpha haemolysin and Panton Valentine leucocidin in clinical isolates of *Staphylococcus aureus* are linked to *agr*-dependent quorum sensing

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[1]Nottingham University Hospitals NHS Trust, Nottingham, United Kingdom, [2]University of Nottingham, Nottingham, United Kingdom, [3]University of Notttingham, Nottingham, United Kingdom

Background: Considerable controversy exists over the relative importance of alpha haemolysin (Hla), Panton Valentine leucocidin (PVL) and phenol-soluble modulins (PSMs) in the pathogenesis of the different types of infections that can be caused by CA-MRSA and PVL positive MSSA strains. We have investigated factors that affect Hla and PVL expression in *S.aureus* clinical isolates.
Methods: Recent isolates of *Staphylococcus aureus* which were confirmed to be positive for PVL by PCR were obtained from diagnostic clinical samples (swabs, pus, blood culture, lung tissue) from Nottingham University Hospitals NHS Trust. 25 strains were grown in CYGP medium for 24 hours at 37°C with shaking, before exoproteins were prepared from the culture supernatant, separated using SDS-PAGE before Western blotting with anti-LukF and anti-Hla antibodies.
Results: A variable level of expression of both the LukF subunit of PVL or HLA was observed between clinical isolates, with some correlation being observed between the level of expression of both in an individual isolate. The level of expression was not related to the *agr* subtype of the clinical isolate.
The presence of the type specific auto-inducing peptide (AIP) in supernatants of the clinical isolates was confirmed by bioassays using specific reporter strains. Clinical isolates expressing very low levels of LukF all produced their type specific AIP, however the addition of 100 nM of type specific AIP induced the expression of LukF and Hla (Fig.1). LukF and Hla expression in clinical isolates was inhibited by the universal *S. aureus agr* inhibitor, ala5-AIP-1 (Fig. 2) [McDowell et al., (2001) Mol Microbiol 41: 503-512]

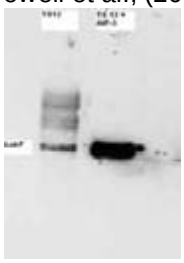

Fig.1. Clinical isolate TS12 +/-AIP-3

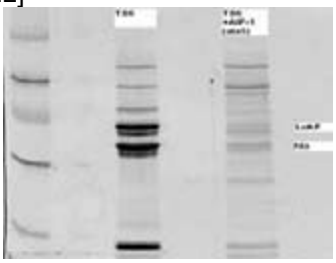

Fig. 2. Clinical isolate TS6 +/- AIP-1 (Ala5)

Conclusion: PVL positive *Staphylococcus aureus* clinical isolates express variable levels of LukF and Hla when cultured *in vitro*. Modification of *agr* activity by the addition of synthetic AIPs suggests that *agr* has a major role in regulating PVL expression in these clinical isolates. Some strains, despite having both *lukS* and *lukF* genes and producing AIP, expressed little LukF unless additional synthetic AIP was added. Upregulation of *agr* could explain the high levels of LukF expression in some isolates.
These findings reveal surprising variation in the *in vitro* expression of PVL in clinical isolates and indicate the potential for attenuating the virulence of *S.aureus*.

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Time: 15:45-17:45
Room: Room Orchid B/C/D
Type: Oral Presentation

HBs mutations related with YMDD mutation induced the expression of hfgl2 gene

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Background: Mutations in the highly conserved tyrosine-methionine-aspartate-aspartate (YMDD) motif are frequently associated with resistance to antiviral treatment and often followed with hepatitis flare, representing a major concern in the treatment of hepatitis B virus (HBV) infection. Previous studies showed that highly expression of hfgl2 gene is related with necrosis of hepatocytes and development of fulminant hepatitis.
Methods: To characterize the interaction between HBs mutations resulted by YMDD mutation and the expression of hfgl2 gene, HBs mutation expression plasmids, I195M and W196S were cotransfected with a hfgl2 promoter luciferase report construct into CHO cells and HepG2 cells respectively.
Results: Cotransfection of I195M or W196S with hfgl2p(-1334)LUC resulted in a significant increase in relative luciferase activity with an average increase of 3.3-fold and 3.7-fold in CHO cells, and 3.5-fold and 4.9-fold increase respectively in HepG2 cells when compared with pcDNA3.1 empty vector cotransfected cells. There was no change in relative luciferase activity when HBs wild plasmid was cotransfected with hfgl2p(-1334)LUC in either CHO or HepG2 cells.
Conclusion: These results suggest that HBs mutations related with YMDD mutation induce hfgl2 promoter activity in both CHO cells and HepG2 cells. It provides new insights in the interaction between HBV mutation and host gene hfgl2 expression and the mechanism of hepatitis flare following YMDD mutation. This work was supported by NSFC No. 30972606 and National Key Basic Research Program of China 2007CB512904.

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Final Abstract Number: 47.006
Session: Advances from the laboratory
Date: Thursday, March 11, 2010
Time: 15:45-17:45
Room: Room Orchid B/C/D
Type: Oral Presentation

Enteric virus detection and identification with a universal virus discovery assay

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[1]FDA Center for Biologics Evaluation and Research, Bethesda, MD, USA, [2]National Institutes of Health, Bethesda, MD, USA, [3]National Institute of Allergy and Infectious Diseases, Bethesda, MD, USA

Background: Detection and identification of known and unknown viruses can be challenging, especially for those with substantial genetic divergence, e.g. caliciviruses. To address this issue, we developed a universal virus detection assay combining virus capsid enrichment with a generic PCR. We analyzed stool and cell culture samples with our degenerate oligonucleotide primer (DOP) PCR.
Caliciviruses are small, non-enveloped (+)ssRNA viruses. The family *Caliciviridae* is comprised of four genera, *Norovirus, Sapovirus, Vesivirus* and *Lagovirus*. Vesiviruses and lagoviruses infect a wide range of animal hosts; noroviruses and sapoviruses are recognized as human pathogens, causing acute gastroenteritis. Human noroviruses and sapoviruses cannot be cultured which impedes the research of these viruses considerably.
Methods: The first step of the assay is the physical and biochemical purification by targeted digestion of contaminating host nucleic acids followed by DOP PCR. The primer population is optimized for the detection of virus-sized genomes. Products can be identified by cloning and sequencing or by high throughput sequencing.
Various DNA viruses (including HSV, VZV, SV40, AAV, EBV, parvoviruses, and hepatitis B) and RNA viruses (including HTLV-1, HTLV-2, several animal retroviruses, poliovirus, hepatitis A, human corona virus, human metapneumovirus, and influenza virus) were detected in previous studies in cell cultures and clinical samples.
Results: Human norovirus (stool) and feline calicivirus (vesivirus, cell culture) were identified with our universal assay. Approximately 35% of the virus genomes were obtained with a single assay. We also identified enterovirus sequences from an asymptomatic individual.
Conclusion: The findings presented here demonstrate the ability of the DOP-PCR assay to not only detect and identify viruses in clinical and cell culture samples but to also provide a large portion of the sequence information with a single assay.
Human diarrheal diseases cause a significant disease burden; an estimated 1.8 million deaths in children under the age of five are caused by gastroenteritis annually. Gastroenteritis is the third leading cause of death due to infection, yet, about 40% of cases are of unknown etiology. Universal detection of viruses with an assay as it was described here could lead to the detection of known yet unsuspected viruses or the discovery of novel viruses.

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Final Abstract Number: 47.007
Session: Advances from the laboratory
Date: Thursday, March 11, 2010
Time: 15:45-17:45
Room: Room Orchid B/C/D
Type: Oral Presentation

Gene expression profilling of mouse host response to *Candida tropicalis* infection

P. P. Chong[1], V.-C. P. Yong[1], H. F. Seow[2], R. Rosli[1]
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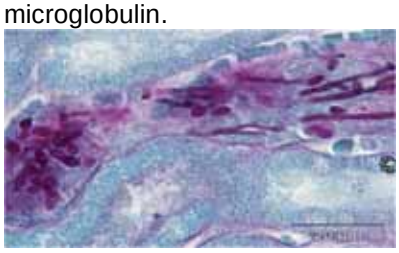
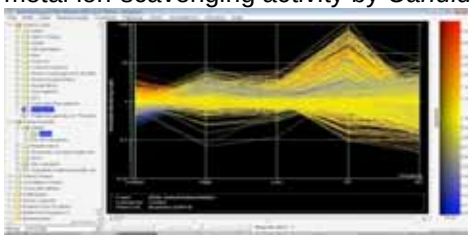
Background: *Candida tropicalis* is an opportunistic pathogen which can cause systemic candidiasis in immunocompromised hosts. Systemic infections caused by non-*albicans Candida* species, especially *C. tropicalis* has seen a rising trend. Nonetheless, studies on the global host immune and serologic responses towards the infection are lacking.
Methods: To further understand the effect of *Candida tropicalis* induced systemic infection on the host gene transcriptional profile, we carried out DNA microarray-based gene expression profiling of lethal infection and sublethal infection in a BALB-C mouse model. Three groups of mice comprising control (non-infected), sublethal or low infection and lethal or high-infection (inoculated with 105 and 107 *C. tropicalis* cells respectively) were sacrificed and total RNA isolated from the sera. The total RNA was reverse-transcribed and hybridized to the Illumina Mouse-Ref8 Microarray BeadChip. The gene expression level was normalized to β2-microglobulin.



Results: The results showed that 1373 genes were differentially expressed in the lethal infection group but lower inoculum size of *Candida tropicalis* in the sublethal infection group had little effect on the host-response gene expression. For microarray data validation, multiplex RT-PCR of 19 selected genes was carried out via GenomeLab GeXP Genetic Analysis System. Confirmed upregulated genes included genes involved in host defense, pathogen recognition, signal transduction, inflammation, chemokines and cytokines, including *Ltf*, *Pglyrp1*, *Ch13l4*, syndecans, *Marco* and *Ngp*. Interestingly, we also observed differential expression of *Actb* and *Gapdh* in the lethal infection group although both are house-keeping genes normally presumed to be expressed at constant levels. From the expected functions of the genes that were upregulated in the infection groups, we speculate that *Candida tropicalis* could possibly cause increment of erythropoiesis in the host as a compensatory mechanism for the haemolysis brought about by the metal ion-scavenging activity by *Candida tropicalis*.



Microarray Data -GeneSpring Analysis

Conclusion: Our results suggest that gene expression profiling of this mouse model may provide new insights into *Candida tropicalis* induced systemic infection particularly in finding molecular mechanisms and early biomarkers.

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Final Abstract Number: 47.008
Session: Advances from the laboratory
Date: Thursday, March 11, 2010
Time: 15:45-17:45
Room: Room Orchid B/C/D
Type: Oral Presentation

Cytokines in experimental leptospirosis: Association with severe disease and postimmunization immune response

A. Chagas-Junior[1], **D. Athanazio**[2], J. Macedo[1], M. Menezes[1], M. Reis[1], F. McBride[2], A. McBride[2]
[1]Oswaldo Cruz Foundation, Salvador, Brazil, [2]Federal University of Bahia, Salvador, BA, Brazil

Background: Leptospirosis shares with bacterial sepsis some clinical features, however, the leptospiral lipopolysaccharide is 10-12 times less toxic than its gram negative counterparts. Severe leptospirosis has been associated with serum levels of proinflammatory markers such as TNF-a, PTX3, IL6, and IL8. In addition, data from bovine whole cell antigen vaccines suggest that induction of strong Th1-type response is associated with protection. The aims of this study were to investigate: 1) gene expression of cytokines by peripheral blood mononuclear cells (PBMCs) in severe disease; and 2) gene expression of cytokines in PBMCs after immunization by whole cell vaccine and homologous challenge.
Methods: Gene expression of IL2, IL4, TNF-a, and IFN-g by Real Time PCR. The virulent strain used in the study was *L.interrogans* serovar Copenhageni strain Cop 4.14. To evaluate gene expression in severe disease, 25 hamsters were infected by 250 leptospires (5x lethal dose 50%) and compared to 4 uninfected controls. Hamsters immunized by whole cell vaccine and controls were evaluated at 8 time points (n=3 in each group) from 0h to 21 days.
Results: All infected hamsters developed lethal disease with typical target organ pathology. Gene expression was higher for all cytokines in infected animals at moribund state (7-8 days after infection) when compared to controls. The difference was statistically significant for IFN-g (p=0.01). Cytokines were not associated with bacterial quantification in tissue or specific target organ lesions. Immunized hamsters survived and expressed higher levels of TNF-a on the eighth day (145 vs 19) and IFN-g on the third day after infection on the third day (32 vs 0.5) after challenge, when compared to the control expression of HPRT.
Conclusion: Severe disease is associated with higher expression of IFN-g in hamsters. The whole cell vaccine used in this study elicited strong IFN-g and TNF-a responses.

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Final Abstract Number: 47.009
Session: Advances from the laboratory
Date: Thursday, March 11, 2010
Time: 15:45-17:45
Room: Room Orchid B/C/D
Type: Oral Presentation

Prevalence of genes responsible for resistance to antimicrobials in surface water *Escherichia coli* isolates

G. Singh, P. Vajpayee, R. Shanker
Indian Institute of Toxicology Research, Lucknow, India

Background: The resistance to antimicrobial agents is an important issue in both human and veterinary medicine. The excessive use of antibiotics is hastening the development of antibiotic resistance in bacteria augment health risks to humans and animals. Lack of access to potable water has forced many inhabitants in developing countries to rely on surface water resources for their daily water needs. Presently, these water resources have emerged as reservoirs of *Escherichia coli* pathotypes harboring virulence as well as multi-drug resistant genes which could play an important role in the diarrheal disease outbreaks. The river Ganga and its tributaries meet 40% of the water requirement for drinking and irrigation in India.
Methods: In this study, *E. coli* isolates (n = 65) retrieved from the river Ganga and Gomti (a major tributary of the river Ganga) were screened using Polymerase Chain Reaction for prevalence of genes (*bla*TEM, *bla*SHV, *aac(3)-IIa, aac(3)-IV* , *aph(3')-Ia, aph(3')-IIa ,ant(3")-Ia* (*aadAI*), *ant(3")-If* (*aadA6*), *tetA, tetB, tetC*, *catI, floR, sul1, sul2)* responsible for resistance to antimicrobial agents of five antimicrobial families (β-lactams, Aminoglycosides, Tetracycline, Phenicols, Sulfonamides).
Results: Our observations indicate that 67.2, 32.3, 55.3, 72.3 76.9, 63.0, 75.3, 43.0, 44.6% *E. coli* isolates exhibit *tetA, tetB, tetC, blaTEM, blaSHV, catI, floR, sul1, sul2* genes, respectively.
Conclusion: The prevalence of *E. coli* isolates harboring multiple antimicrobial resistance genes points to the inherent health risks associated with the use of surface water by inhabitants of the planned and temporary settlements along the banks of these rivers. This will require formulation of strategies for preemptive monitoring of surface water to prevent diarrheal outbreaks.

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Final Abstract Number: 47.010
Session: Advances from the laboratory
Date: Thursday, March 11, 2010
Time: 15:45-17:45
Room: Room Orchid B/C/D
Type: Oral Presentation

E-gene variation with reference to neurovirulence in the Indian clinical isolates of Japanese encephalitis virus

S. K. Pujhari, S. Prabhakar, R. K. Ratho, M. Modi, M. sharma, B. Mishra
Postgraduate Institute of Medical Education and Research, 160012, UT, India

Background: Japanese encephalitis (JE) is an important arboviral infection of public health concern. There is a significant variation in mortality (20-60%) in JE viral infection. It is possibly attributed due to the host genetic makeup or genomic variation in the JE virus. Various approaches have allowed E gene sequences of flaviviruses to be related to virulence in animal models and shows single amino acid substitutions are sufficient to alter neurovirulence and neuroinvasiveness. The present study has looked for the mutational analysis of E gene, in clinical isolates at amino acid positions at 176,177,227,244,264 and 279, which have been shown responsible for neuro-virulence in experimental animals.
Methods: A total of 95 patients with suspected viral encephalitis were enrolled. JEV conformation was done by MAC ELISA and RT-PCR. The RT-PCR positive samples were further subjected to sequencing using ABI PRISM BigDye Terminator cycle sequencing ready reaction kit in ABI PRISM 310 genetic analyzer. The drafting of sequences was performed using BioEdit software. Neighbor joining algorithm was implemented for phylogenetic inference using MEGA 4.0.2.The DNA sequences were translated insilico and mutation analysis was performed. Re-confirmation of mutations was done using BLAST tool in NCBI website
Results: Among confirmed cases 70% belonged to the pediatric age group, with a male to female ratio of 3:1.Patients presented with moderate to high-grade fever (41%); convulsions and rigidity (65%), extra pyramidal features (35%). Convulsion was often the presenting symptom. A mortality of 27% was observed among JE positive cases. JE virus specific RNA was detected in 7 cases. Phylogenetically all our isolates belonged to genotype-III. Interestingly a novel mutation of S227T at amino acid level was detected corresponding to the domain II of E gene in JEV compared to both Indian and overseas isolates.
Conclusion: Genotype III was found to be circulating in this part of India. With the present available limited number of cases no significant correlation was found between E gene mutation and disease severity. However, the observation of novel mutation S227T of E protein in this geographical area has given the impetus to explore its role in JE pathogenesis and vector competency

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Final Abstract Number: 60.001
Session: Plenary 7
Date: Friday, March 12, 2010
Time: 09:00-09:45
Room: Ballroom 1: Brickell
Type: Invited Presentation

Pneumococcal infection and colonization in children and its impact on pneumococcal disease in adults

K. Klugman
Emory University, Atlanta, GA, USA

The introduction of 7 valent pneumococcal conjugate vaccine in children in the USA in the year 2000 has been followed by evidence not only of direct protection from invasive pneumococcal disease, meningitis and pneumonia in immunized infants, but also by a reduction in serotype specific infections in adults, particularly the elderly. The decrease in disease in adults is due to the induction of herd immunity through the vaccine impact on acquisition of vaccine serotypes in the nasopharynx of immunized children. The extent of herd immunity is such that the impact on carriage has been responsible for a greater reduction in morbidity and mortality through herd immunity, than has been the reduction in disease due to direct protection. These data suggest that impact on carriage should be an important component in the evaluation of future pneumococcal vaccines such as 10 and 13 valent conjugates as well as candidate protein vaccines. Replacement disease has occurred, particularly among Alaska natives, HIV infected adults, and adults with underlying chronic diseases. The replacing serotypes are less invasive and therefore the replacement has not eliminated the benefits of vaccination in most groups. Antibiotic resistant infections have diminished, but resistance is emerging among important serotypes such as 19A and 6C. In other countries, there are emerging data suggesting similar protection and herd immunity. In a trial of 9 valent conjugate, including types 1 and 5 in South Africa, HIV infected children have been protected by this vaccine from invasive disease and pneumonia. Temporal shifts in epidemic prone serotypes may mask vaccine impact if these types are increasing at the time of vaccine introduction. Other factors that may mask vaccine effect are increasing submission of strains to reference centers post vaccine introduction, and increasing reliance on molecular methods to detect non-vaccine types from cases of meningitis and empyema.

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Final Abstract Number: 61.001
Session: Antimicrobial stewardship: Challenges and Strategies for the 21st century
Date: Friday, March 12, 2010
Time: 10:15-12:15
Room: Ballroom 1: Brickell
Type: Invited Presentation

Extreme Drug Resistance (XDR) in Nosocomial Pathogens

F. Pasteran
Instituto Nacional de Enfermedades Infecciosas INEI ANLIS Dr. Carlos G. Malbran, Buenos Aires, Argentina

The implacable increase in the prevalence of antimicrobial resistance among gran negative bacilli (BGN) is of great concern. Several highly resistant gram-negative pathogens, namely *Acinetobacter*, *Pseudomonas aeruginosa*, and *Klebsiella pneumoniae* sensitive to a small number of drugs, if not any, are emerging as significant pathogens. The mechanisms of this resistance are often complex but include outer-membrane impermeability, up-regulated efflux pumps, target-site mutation and, not surprisingly, the production of carbapenemases, in addition to several enzymes. Given the frequency of worldwide reports now describing infection with carbapenemase-producing BGN, in addition to the intercontinental spread of hyper-epidemic clones, such as KPC-3-possesing *K*. *pneumoniae* ST258, it is possible that any institution on the globe could be beset by multi-resistant BGNs. Proficient methods are needed for early detection and confirmation in clinical microbiology laboratories of multidrug resistant bacteria, specially those producing carbapenemases, in any attempt aimed for targeting optimal antimicrobial therapy and controlling their spread. Therapeutic options for these pathogens are so extremely limited. Even now, resistance to new “salvage” therapy, such as tigecycline and colistin is being observed. Several new terms definitions have been introduced in the medical literature to describe this complex scenario: pan-resistance, extreme-resistance, extensively-resistant. Although there is no international harmonization of this terminology, their adequately capture the public awareness for the desperate need for attention to this problem. As expected, mortality rates among patients with infections due to these organisms are significantly higher than those caused by sensitive germs. The urgency of the problem is compounded by the recognition that fewer new antimicrobial agents are introduced each year. Thus, clinicians are forced to use older drugs for which there is a lack of robust data about their effectiveness. The complex nature of this scenario requires the coordinated efforts of all sectors involved, in any attempt to curb antimicrobial resistance

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Final Abstract Number: 61.002
Session: Antimicrobial stewardship: Challenges and Strategies for the 21st century
Date: Friday, March 12, 2010
Time: 10:15-12:15
Room: Ballroom 1: Brickell
Type: Invited Presentation

Basic Principles of Implementing an Antibiotic Optimization Program

J. Cortes
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Antimicrobial stewardship is an important and evolving aspect of patient care and safety programs in hospitals around the world. A team of involved specialists, including infectious diseases physicians, clinical microbiologists, hospital epidemiologists and others, is needed to address this complex problem. In United States a clinical pharmacist has been also claimed to collaborate in this kind of program, but in Latin America and other limited-resources areas, lack of appropiate personnel are part of the limitations to implementation. Two strategies, not to be exclusively applied, are proposed. Prospective audit with intervention and feedback is an option, while the use of formulary restriction and pre-authorization might be also used. The first strategy might be time consuming and requires a series of tools to succed. The implementation of the program requires administrative and economic support and the use of education, development of guidelines, antimicrobial order forms, de-escalation therapy (which requires an active participation of the microbiology laboratory), dose optimization, and switch to oral therapy. Effective use of antimicrobials but also prevention of resistance are the goals to achive in the individualised care of patients and new targets are being currently defined (pharmacodynamic objectives). Up to the moment more research is required to find the best ways to achieve these goals.

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Infection Control Program as an Additional Tool to Control Bacterial Resistance

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The combination of effective antimicrobial stewardship with a comprehensive infection control program has been shown to limit the emergence and transmission of antimicrobial-resistant bacteria, reducing health care costs.
There are multiple mechanisms postulated by which antimicrobial resistance may appear and disseminate within hospital organisms:
1) Introduction of a resistant organism to a previously susceptible population; 2) Acquisition of resistance by a susceptible strain: spontaneous mutation or genetic transfer; 3) Expression of regulated resistance already present in the population; 4) Selection of resistant subpopulations; and, 5) Dissemination or spread of resistant organisms
There have been proposed five strategic goals to optimize antimicrobial use: 1) Optimize antimicrobial prophylaxis for surgery 2) Optimize choice and duration of empirical therapy; 3) Improve prescribing by education; 4) Monitor and feedback information on antimicrobial resistance rates, and, 5) Produce protocols for antibiotic usage. Also the strategies must include optimal selection, dose, and duration of treatment, as well as control of antibiotic use, for prevention or slowing the emergence of resistant among microorganisms.
An effective Antimicrobial Control Program Infection must prevent or reduce antimicrobial resistance. Specific goals related to this program are:
1) A determination of who will be responsible for maintaining control. 2) A determination of which antimicrobial(s) to control. 3) Precise definitions of antimicrobial resistance for antimicrobials and organisms. 4) A system for monitoring the frequency of resistance (clinical and environmental). 4) Education. It is an essential element to influence prescribing behavior. 5) A method to determine antimicrobial use per geographic area per unit time. 6) Ability to distinguish community from nosocomial isolates. 7) A method to assure that clinical care will not be harmed by control measures such as: de-escalation of therapy, dose optimization, and parenteral to oral conversion of antimicrobials with excellent bioavailability can decrease the length of hospital stay and health care costs.

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Type: Invited Presentation

New Antibiotics: Which Role in a Antimicrobial Stewardship Program?

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Infections caused by multidrug-resistant bacteria continue to challenge physicians in the daily practice. We face growing resistance among Gram-positive and Gram-negative pathogens that cause infection in the hospital and in the community. Rice recently reported these as the "ESKAPE" pathogens (*Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumanii, Pseudomonas aeruginosa,* and *Enterobacter* species) to emphasize that they currently cause the majority of world-wide hospital infections and effectively "escape" the effects of antibacterial drugs.
In this context, controlling antibiotic use and bacterial resistance trough an antibiotic stewardship program (ASP) is of major importance to all professionals involved in infectious diseases.
A critical need to develop new antimicrobial compounds and to use the recently approved agents appropriately are components of all ASP. Unfortunately, most of the agents which are in the late stage of develop have activity only against Gram-positives and none is active for treatment of infections caused by the Gram-negative ESKAPE pathogens.
We have analized the body of the literature with the aim to define, within a ASP, the opportunity of use and the potential advantages of new antibiotics in order to reduce the emergence and selection of resistant pathogens.
Related with the role of the new antibiotics in a Asp, it is possible to consider the following points: i-the use of tigecycline instead of carbapenems in clinical settings with high rates of carbapenems-resistant pathogens (ie. in nosocomial peritonitis), ii-the use of doripenem in extended-infusion (ie. in severe infections due to *Pseudomonas aeruginosa*); iii-the use of daptomycin at high doses (ie. in infections due to methicillin-resistant *Staphylococcus aureus*) and iv- the use of ceftobiprole as empiric monotherapy (ie. in some suspected mixed infections).
The use of the new antibiotics in the daily practice based on the individual patient characteristics, causative organism, site of infection, and pharmacokinetic and pharmacodynamic characteristics of the drug is an important part of an ASP.

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Type: Invited Presentation

State of the Art on ARV Therapy: How Many Standards of Care?

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Albeit nobody would support the idea of "first and second class medicine", in real life we confront AIDS with at leat two standards of care. When to start ARV therapy remains a matter of debate. No disagreement exists for symptomatic patients, as well as for asymptomatic individuals with CD4 counts of 350/ mm3 or below. In resource-poor settings, WHO recommended until late 2009 that adolescents and adults should start HAART when they have advanced HIV disease, mildly symptomatic and asymptomatic disease, WHO Stage II or I HIV disease with CD4 counts <200/mm3 .These recommendations were updated in November 2009 and look now closer to those released by other international bodies. Some Western countries guidelines panels, like the DHHS recommends now treatment initiation in asymptomatic patients when the CD4 count falls below 350/mm3 , and have shown a divided opinion regarding the if treatment should be considered in patients with CD4 cell counts <500/mm3, particularly if the patient has high viral load, age above 50 and/or comorbidities like HBV or HCV coinfections, among others. Increasing amount of data suggest that by starting earlier, the so called “non-AIDS” diseases driving to mortality in the HAART era might be dramatically reduced. On top of the benefits at the individual level, ART has been shown as a prevention tool by reducing the median viral load at the community level.Currently available co formulations are the best options for ARV backbone in naive patients. Issues such as childbearing potential and baseline resistance need to be taken into consideration when selecting a regimen. Controversies remain on whether to use a PI or an NNRTI as the third drug in initial therapy, particularly important in the presence of advanced disease. The bottom line is that one size does not fit for all in this challenging field.

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Type: Invited Presentation

Drug Resistance and Other Laboratory Monitoring Assays in HIV infection

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Although CD4 cell counts and plasma viral load assays are the principal laboratory tests used to monitor the progress of HIV-1 infections, several other assays are assuming increasing importance to adequately assess the benefits of antiretroviral therapy (ART) in infected individuals. The accessibility of such assays will vary greatly, depending on the resources available to treat HIV infections.

Where testing capability exists, HIV drug resistance testing is useful when patients enter care prior to initiating therapy and again when considering change of regimens during virologic failure. Genotypic assays are generally preferred because of cost and rapidity, except in situations where multiple ART regimens have been used, when phenotypic assays may be of value.

When abacavir is being considered as part of an ART regimen, genetic screening for HLA-B*5701 is helpful to reduce the risk of severe abacavir hypersensitivity reactions. These reactions, reported in 5-8% of white and 2-3% of black patients occur primarily in individuals with the MHC class I allele HLA-B*5701. Individuals who screen positive for HLA-B*5701 should not receive abacavir.

When a CCR5 antagonist (e.g., maraviroc) is being considered as part of an ART regimen, a coreceptor tropism assay is useful, since an agent of this class will only suppress viruses that utilize this receptor (R5 viruses). CCR5 antagonists should not be used in individuals who carry primarily X4 or dual/mixed tropic viruses. Currently, the principal assay available to measure HIV-1 tropism is phenotypic, though genotypic tests are under study.

Although therapeutic drug monitoring is recommended by some, its use remains controversial, and no clear-cut recommendations can be made regarding its utility.

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Type: Invited Presentation

Opportunistic Infections and IRIS in the Era of HAART

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Despite the important advance that cART represents for the prognosis of the HIV-1 infection, OIs continue to be an important cause of morbidity and mortality in developed countries. This is due to late presentation (up to one-third of new HIV-1 infections), lack of adherence to cART and prophylaxis or virological failure of cART. In addition, OIs are very common in developing countries, being tuberculosis (TB) the most common one. The ACTG A5164 results recommended to start cART during the first 2 weeks after starting antimicrobial treatment for the OI (patients with TB were not included in this RCT). Some of these patients, despite having an excellent viral and immune response to cART, will present a paradoxical worsening of the OI known as the immune reconstitution inflammatory syndrome (IRIS). The microorganisms most commonly associated with IRIS are mycobacteria, fungi, and herpes group viruses. The IRIS has also been reported in tumors, such as Kaposi sarcoma, and causes autoimmune diseases. The percentage of patients who develop IRIS is variable. In cohort studies of patients starting cART, IRIS affects between 15% and 25%. In OIs series like TB the frequency is higher, and can reach 50%. Clinical effects of IRIS range from a mild, self-limiting illness to severe morbidity and mortality. The lack of evidence-based treatment guidelines poses challenges in the management of these patients. Patients are generally recommended to continue with cART and specific treatment against OIs. Adjuvant nonsteroid anti-inflammatory drugs (NSAIDs) and corticosteroids are commonly used. Corticosteroids have demonstrated their usefulness in a recent clinical trial in TB patients. Surgery is necessary to debride abscesses. In life-threatening cases, the possibility of interrupting cART should be considered until the patient's situation has improved. Clinical experience with immunosuppressors or TNF-alpha inhibitors is very limited.

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Session: Current challenges in HIV care
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Type: Invited Presentation

Why are patients dying in the HAART Era?

E. Katabira
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Session: Biomarkers in infectious diseases
Date: Friday, March 12, 2010
Time: 10:15-12:15
Room: Ballroom 3: Tuttle
Type: Invited Presentation

Clinical Use of Biomarkers in the Diagnosis and Management of CAP

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Community-acquired pneumonia (CAP) is a serious health problem worldwide with an annual incidence of 0.3-0.5% in the adult population. Besides, CAP remains the leading cause of death from infectious diseases. This justifies the interest in studying all clinical aspects affecting CAP. A new approach is to evaluate biological markers of infection and inflammation, as an expression of the host´s inflammatory response against the microorganism, in order to achieve diagnosis, aetiology, progonosis and treatment information. The most widely studied biomarkers have been C reactive protein (CRP), procalcitonin (PCT) and cytokines. Other biomarkers are now obtaining promising results. Most authors conclude that biomarkers can help in the diagnosis of CAP. Fewer data analyse the capacity of biomarkers in identifiying the potential causative agent and the best results have been settled down in children. Linked with the above mentioned, biomarkers, mainly PCT, have been used succesfully guiding antibiotic prescription in patients with suspected CAP. Treatment guided by serum PCT was a safe way to avoid antibiotics, although economic savings were overshadowed by PCT analysis costs. Approximately 10-15% of patients hospitalised for CAP develop treatment failure and almost 6% may manifest rapidly progressive pneumonia, it has been demonstrated that serum levels of biomarkers can identify patients at risk of treatment failure and therefore could guide treatment handling. Clinical data scoring systems have been recognized as a useful tool to assess stability and prognosis of patients with CAP. Analysis of systemic biomarkers in adition to clinical scores has shown to improve either the prediction of absence of severe complications and the 30-day mortality prediction by PSI or CURB65/CRB65 scales. Current data from literature seem to support the use of biomarkers in the daily medical practice concerning CAP.

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Type: Invited Presentation

Biomarkers for Sepsis

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Manifestations of the Systemic Inflammatory Response Syndrome (SIRS) (leukocytosis, hyperthermia, tachycardia and tachypnea) can be present in both non-infectious and infectious conditions and do not predict those subjects at high risk for death. Readily available biomarkers can help the practicing ID physician predict the likelihood of infection and a poor outcome. Unexplained hypophosphatemia and eosinopenia are common findings in the setting of bacterial infection. Coagulation abnormalities including elevated D-dimer, unexplained thrombocytopenia, Protein C deficiency and prolonged prothrombin time (PT) are present to a greater extent in patients with a definite focus of infection or bacteremia than in those without. Protein C deficiency occurs early in the setting of infection and the severity predicts outcome. Lactic acidemia is present in the setting of sepsis and the inability to clear it after appropriate antibiotics and aggressive fluid resuscitation predicts a poor outcome.

Newer approved biomarkers for sepsis include serum procalcitonin (PCT) and the Endotoxin Activity Assay (EAA). Serum PCT has been shown to have better sensitivity and specificity than the more commonly ordered C-reactive protein (CRP) in distinguishing SIRS from sepsis. PCT levels have also been used to shorten the duration of antibiotic therapy. The EAA assay is elevated in 85% of patients with severe sepsis and levels >0.6 are associated with the highest mortality.

A number of additional biomarkers for sepsis are actively being investigated. In a clinical trial of a biomarker panel, a score composed of neutrophil-gelatinase –associated lipocalin (NGAL) in concert with IL-1 receptor antagonist (IL-1ra) and Protein C had the highest diagnostic accuracy for severe sepsis. Levels of the biomarkers gelsolin, angiopoietin 2 and inter-alpha inhibitors are associated with sepsis severity and could potentially serve as theragnostics. Sepsis-induced immunosuppression and propensity towards secondary infection may be predicted by decreased monocytic HLA-DR expression and reversed with treatment with GM-CSF.

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Date: Friday, March 12, 2010
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Type: Invited Presentation

Biomarkers for the Diagnosis of TB

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Many patients with tuberculosis are treated empirically and failure to diagnose infection is a cause of morbidity and mortality. Tuberculosis is a great mimic of other infectious and non-infectious medical conditions. It may be difficult to distinguish active disease from latent infection from previous and even treated tuberculosis. There is also a major problem in knowing if prophylactic therapy and new vaccination programmes are effective since the time course of the development of active infection is measured over decades. For all these reasons, there is great interest in the development of novel biomarkers in tuberculosis. To date, the main biomarkers used in infection are skin tests which rely on delayed hypersensitivity reactions and interferon assays. All these tests have limitations in terms of sensitivity and ability to distinguish different forms of infection. Initial interest in biomarkers focused on single markers such as adenosine deaminase. It has become apparent that such markers do not provide sufficient specificity. After briefly reviewing the topic, I shall focus on the current interest in defining multiple biomarkers for the diagnosis of tuberculosis. There has been interest in transciptomics, metabolomics and proteomics to define disease. Proteomics is particularly attractive as there is the potential to develop tools such as dipsticks which are suitable for use in resource-poor areas from such studies. Some data will be presented from our unpublished studies using proteomics to distinguish active and latent infection. An alternative, interesting approach that will be considered is the development of specific immune profiles that reflect either latent or active infection with tuberculosis. The potential and current application of biomarkers for tuberculosis is an exciting area and seems likely to provide a future step-change in the diagnosis of this global infection

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Clinical Utility of Biomarkers in Fungal Infection

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Biomarkers are important means for the diagnosis of invasive mycoses as cultures may not be positive even in the setting of significant infection. Furthermore, invasive procedures which may be necessary to establish definitive evidence of infection are often reluctantly undertaken in severely immunosuppressed patients. For some mycoses, such as *Cryptococcus* and *Histoplasma,* the detection of circulating polysaccharide antigen has proven a very useful target for both diagnosis and response to therapy. More recently biomarkers have been used to diagnose opportunistic pathogens such as *Candida* and *Aspergillus.* A major focus has been on measurement of *Aspergillus* galactomannan from serum and other body fluids to establish a diagnosis of invasive aspergillosis. Serial measurements of galactomannan have been shown to correlate with progressive infection or with successful outcomes of therapy in both pre-clinical models as well as in human infections. A number of factors significantly reduce levels of circulating galactomannan including the use of mould-active antifungal therapy or prophylaxis, immune status of the host and importantly extent of infection. The test may not be positive despite invasive infection, particularly if localized to the lung or if anti-mould agents are administered. PCR based-methods have been developed for *Aspergillus* and *Candida* but the lack of standardization and limited external validation have also hampered utility of that approach. A non-specific fungal biomarker, 1,3-beta, D-glucan, that it detected using a modification of the limulus lysate assay, is present in many fungi, including both yeasts and many moulds (Zygomycetes being a major exception). Detection of 1,3-beta, D-glucan is approved for clinical use though cost and technical issues have limited its clinical acceptance for routine use. These methods are aimed at providing non-invasive and rapid methods for establishing a diagnosis of these often lethal infections.

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Session: Burden of Plasmodium vivax malaria in Latin America
Date: Friday, March 12, 2010
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Room: Room Jasmine
Type: Invited Presentation

Epidemiology of P. vivax Malaria in the World and Latin America
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Morbidity and mortality burden of malaria, particularly in children, represents a public health threat also in those countries from regions such as South East Asia and Latin America with moderate to low levels of transmission. Between them epidemiological patterns are similar, lower malaria inoculation rates sustained with a predominant prevalence of *Plasmodium vivax* infection. Malaria mortality in these areas has been mainly attributed to *P. falciparum*, but its direct and indirect burden has not well defined. These patterns are increasingly causing concern in some countries. Globally, ~250 million clinical episodes occur annually (2.7 in Latin America); most of these are caused by infection with *P. falciparum* and *P. vivax*. Although *P. falciparum* is justifiably regarded as the greater menace because of its high mortality, widespread antimalarial drugs resistance and its dominance on Africa, malaria due to *P. vivax* has also placed significant burdens on health, longevity and general prosperity of large sections of the human population. The debilitating impact of *P. vivax* malaria remains high, unacceptable and preventable for well over one billion inhabitants of the planet. Complicated and even fatal cases of malaria due to *P. vivax* have been increasingly reported in the medical literature. *Plasmodium vivax* can cause both sequestration-related and non-sequestration-related complications of severe malaria, including cerebral malaria, renal failure, circulatory collapse, severe anemia, abnormal bleeding, ARDS and jaundice. In Latin America the burden of mortality due to malaria, although decreasing, is still significant. Powerful antimalarial campaigns in the region directed mainly to *P. falciparum* achieved a significant reduction of mortality in the last century. Evidence suggests that *P. vivax* can imposes a significant burden of mortality that may have resulted from its interaction with other diseases and conditions. These and other epidemiological issues are herein discussed at a global level and focused in Latin America.

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Room: Room Jasmine
Type: Invited Presentation

Molecular Epidemiology of P. vivax: tools for Malaria Control
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Plasmodium vivax is the most prevalent human malarial parasite in several areas of Asia and South-Central America. Although *Plasmodium* genomics is improving our knowledge of the organism's complex biology, population-based investigations are needed to explore the extent of the parasites' genetic variation, how the observed variation is geographically distributed, and how such diversity affects or can be used to assess the success of control measures. Unfortunately, the lack of suitable *in vitro* culturing methods for *P. vivax* imposes the use of field specimens for population studies. Such circumstances have limited molecular epidemiologic and genetic diversity studies to a handful of antigens and few genetic markers that could be considered neutral, that is, that are not expected to be under natural selection by the immune response or antimalarial drugs. First, I will discuss the emerging patterns on the genetic diversity of *P. vivax* using neutral markers and explore the value of comparative approaches to assess potential antigenic regions using closely related *Plasmodium* species found in macaques. I will show an example with genes encoding a well known antigen, AMA-1. Then, I will review the current status of our knowledge on the genetic diversity of this parasite in Latin-America. Overall, *P. vivax* populations in the new world have low levels of genetic diversity and undergo clonal expansions. Such low genetic polymorphism should be considered while using genetic markers in epidemiologic investigations that aim to assess, for example, the frequency of recrudescent infections or the reintroduction/expansion of the parasite in a given geographic area in the context of control efforts.

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Room: Room Jasmine
Type: Invited Presentation

Severe and complicated Malaria due to *P. vivax*

J. Murillo
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Time: 10:15-12:15
Room: Room Jasmine
Type: Invited Presentation

Treatment, Prophylaxis and Resistance in P. vivax Malaria

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The burden of malaria caused by *Plasmodium vivax* remains under-appreciated to a great extent, both in terms of its clinical spectrum and incidence of disease. Control measures are hampered by both the emergence of chloroquine (CQ) resistance and the presence of dormant hypnozoite stages in the liver, which result in relapse infections weeks after the cure of the initial episode. Although CQ remains the first line of treatment for patients with vivax malaria in most of the world, CQ monotherapy is now virtually ineffective in Papua Indonesia with significant clinical resistance apparent throughout the Indonesian archipelago. Sporadic cases have been reported from South America and Asia. Unfortunately, the mechanism of *P. vivax* CQ resistance is largely unknown and as yet no genetic markers have been identified.
Since clinical studies are difficult to carry out in this species due to factors such as individual variations in patient immune status, reinfections and frequent relapses, and in vitro susceptibility assays applicability is limited by lack of culture methods, the global prevalence of CQ resistance to *P. vivax* continues to be poorly defined.
Primaquine, an 8-aminoquinoline compound, is the only commercially available drug with hypnozoitocidal activity against *P. vivax* and is widely used for terminal prophylaxis; yet, little is known about how the drug works, if it works, or how it fails. Reports of true PQ failure and subsequent *P. vivax* relapse are unusual. Most suspected cases can be ascribed to poor patient adherence. The lack of effective alternatives to PQ against hypnozoites represents an important drawback in clinical practice and may be as operationally crippling to control efforts against *P. vivax*, as having no access to insecticides, bed nets, reliable diagnostics, or chemoprophylaxis. *Plasmodium vivax* malaria will linger as a persistent and severe challenge to public health as long as our drug armamentarium remains limited and substantial areas of our knowledge on its biology, epidemiology, genetics, metabolism, and mechanisms of resistance to antimalarials, remain obscure.

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Date: Friday, March 12, 2010
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Room: Room Orchid B/C/D
Type: Oral Presentation

Mixed infection of influenza A viruses is common

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Background: Reassortment, which is the rearrangement of viral gene segments in a host cell infected with two different viruses, is an important mechanism for the evolution of influenza viruses. A mixed infection of more than one virus could lead to reassortment. To better understand the occurrence of quasispecies in one host, we investigated mixed infection in individual isolates for seasonal influenza A viruses using amantadine sensitivity as a marker.
Methods: We cultured viruses with amantadine, and performed sequencing, RFLP, cloning, and quantitative PCR to detect mixed population in clinical samples.
Results: Culturing with amantadine shows evidence of a high number of mixed populations. When sensitive isolates, whose M genes were in a certain lineage, were cultured in medium with amantadine, the viruses with M genes from a different lineage appeared after several passages. In contrast, the other assays can hardly detect mixed populations. The proportion of minor viruses in the mixed population may be too small to be identified by these assays. We showed a considerably higher proportion (at least 6/11) of mixed populations in analyzed samples.
Conclusion: The existence of quasispecies in each isolate is common. However, the proportion of these, which can be less than 1%, is too low to be detected by conventional methods. Such mixed populations, in which reassortment occurs, may have a significant role in the evolution of viruses.

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Influenza vaccine delivery to adolescents: Assessment of two multicomponent interventions

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Background: Despite efforts to enhance influenza vaccination among persons at highest risk of complications, influenza remains a health burden in the United States. Evidence indicates that vaccination of elementary school children protects them from influenza, and reduces transmission. However, there are no published intervention trials demonstrating the impact of strategies designed to enhance influenza vaccination rates specifically among adolescents. Objective: Assessing the efficacy of two multi-component interventions designed to enhance influenza vaccination rates among adolescents attending middle- and high-schools in three rural counties in Georgia, U.S.A.
Methods: This study employs a non-randomized, three-armed controlled design across 2 years. The three arms consist of: 1) a multi-component school-based influenza vaccination intervention condition (County 1), 2) a multi-component provider-based influenza vaccination condition (County 2), and 3) a standard of care condition (County 3). The multi-component interventions each consisted of a structural component (school-based or provider-based provision of influenza vaccination) and an educational component (a brochure and a school skit), designed to enhance vaccine education among adolescents and their parents.
Results: During the 2008 to 2009 influenza season in County 1, there were 70 students vaccinated out of 370 students (18.9%). During the same year in County 2, there were 110 out of 736 students vaccinated (14.9%). In the first year, students in County 1 were 25% more likely to be vaccinated than students in County 2 (RR=1.26, 95% CI: 0.96-1.66). During the current 2009-2010 influenza season, in County 1 we have vaccinated 114 out of 375 students (30.4%), a 62.2% increase from the previous influenza vaccination season. Currently, in County 2 we have vaccinated 10.5% of students (70 out of 663). For the current influenza season, students in County 1 are almost 200% more likely to get vaccinated than students in County 2 (RR=2.88, 95% CI: 2.20-3.77).
Conclusion: We have observed a greater percentage of students vaccinated in the school-based intervention than in the provider-based intervention during the previous and current influenza seasons ($p=0.0912$ and $p<0.0001$, respectively). This study has implications for best practices for mass campaigns during an influenza pandemic, such as the current H1N1 influenza pandemic.
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A randomized intervention trial of mask use and hand hygiene to reduce seasonal influenza-like illness and influenza infections among young adults in a university setting

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Background: Early efforts to decrease transmission of pandemic influenza will likely rely on non-pharmaceutical interventions (NPIs), because of delays in availability of suitable vaccines and limited stock of antiviral medications. We conducted a randomized trial to estimate reductions in influenza-like illness (ILI) and laboratory-confirmed influenza infection associated with use of face masks combined with hand hygiene measures and face masks alone in a university setting.
Methods: During the 2007-08 influenza season, 1,111 students residing in university residence halls were cluster-randomized by residence house (N=37) to either face mask and hand hygiene, face mask only, or control arms. Discrete-time survival analysis using generalized models estimated rate ratios, according to study arm, each week and cumulatively over the 6-week intervention period, for clinically verified ILI and laboratory-confirmed influenza A or B.
Results: In the mask and hand hygiene group compared with the control group, adjusting for covariates, we observed significant reductions in ILI incidence during weeks 4 (RR, 52%, [95% CI, 6%-76%]) and 5 (RR, 62%, [CI, 6%-85%]), and a borderline significant reduction during week 6 (RR, 70%, [CI, 2%-91%]). For laboratory-confirmed influenza, both the face mask only and the face mask and hand hygiene groups compared to the control showed a reduction in cumulative incidence, however results did not reach statistical significance; polymerase chain reaction (PCR) confirmed influenza A or B in 11 out of 49 samples (22%) in the face mask and hand hygiene group, 16 out of 58 samples (28%) in the face mask only group, and 18 out of 68 samples (26%) in the control group.
Conclusion: These findings suggest that in shared living environments, the use of face masks and hand hygiene may reduce influenza-like illnesses.
Trial registration: www.clinicaltrials.gov, Identifier: NCT00490633

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Population-based surveillance for 2009 pandemic influenza A H1N1 Virus in Guatemala, 2009

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Background: Worldwide >414,000 cases of pandemic influenza H1N1 2009 (2009 H1N1) and nearly 5000 deaths have been reported. The 2009 H1N1 was first identified in Mexico in April 2009, but spread into neighboring Guatemala occurred weeks later. We describe the clinical and epidemiologic characteristics of patients with 2009 H1N1 infection in two sites in Guatemala.
Methods: We analyzed data from an active population-based surveillance for clinical pneumonia and influenza-like illnesses (ILI) in hospitals and ambulatory clinics, respectively, in the departments of Santa Rosa and Quetzaltenango in Guatemala from February through September 2009. Clinical and epidemiological information, and nasopharyngeal swabs were collected from enrolled patients. Specimens were tested for influenza with real-time reverse transcriptase polymerase chain reaction.
Results: We identified 198 persons with 2009 H1N1 infection between May and September 2009; 61 (31%) were hospitalized with pneumonia and six died (case fatality proportion: 2.7%, 95% confidence interval 0.9%-6.3%). Among influenza cases identified between February and May, the proportion caused by 2009 H1N1 rose from 0% in February to 67% in May. By July in any given week 80% to 100% of influenza A viruses were 2009 H1N1. The median age of persons with 2009 H1N1 infection was nine years, and among patients hospitalized with pneumonia six years. Fever >38°C was documented in 37 (60%) pneumonia patients, 53 (85%) persons self-reported fever. Adjusted hospitalization rates were highest for children <5 years old (154.9 per 100,000) in Santa Rosa. Fourteen (23%) hospitalized patients with 2009 H1N1 were admitted to the intensive care unit (ICU) and five (8%) required mechanical ventilation. Among children <5 years, nine (28%) were admitted to the ICU and three (10%) died. Underlying chronic conditions were noted in <20% of patients hospitalized with 2009 H1N1 infection.
Conclusion: Although seasonal influenza A (H1N1/H3N2) was circulating prior to widespread 2009 H1N1 transmission, it was quickly replaced by the 2009 H1N1 virus. The epidemiology was similar to reports elsewhere except for the low frequency of underlying disease among hospitalized patients. Surveillance for H1N1 requiring documented fever will underestimate burden of disease. Children <5 years old in Guatemala should be prioritized for vaccination.

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Adjuvanted influenza vaccines and their potential role for vaccination of travelers

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Background: Trivalent seasonal influenza vaccine (TIV) adjuvanted with the emulsion adjuvant MF59® (FLUAD®) is licensed in 29 countries worldwide for adults over 65 years of age. Compared with unadjuvanted TIV, the adjuvanted vaccine provides higher hemagglutination inhibition (HI) antibody titers not only against vaccine strains, but also against drift-variant strains. Usually influenza is transmitted in a single epidemic seasonal epidemic in temperate climates, but it may appear in two epidemics during the year or may be transmitted throughout the year, in subtropical and tropical locations. Although persons travelling from the Northern Hemisphere (NH) to the tropics or antipodes may not have access to the TIV made with strains used in the Southern Hemisphere (SH) formulation, they are nevertheless recommended to receive available NH formulation-TIV because one or more of the strains may overlap and because some degree of protection may be elicited, even by an imperfectly matched vaccine.
Methods: The following data from recent clinical trials highlight the cross-protection elicited by the MF59-adjuvanted vaccine. Sera from 222 children, 6-36 months of age, vaccinated with the 2006/07 formulations of FLUAD or unadjuvanted TIV were tested against the H1N1 strain in the 2007/08 formulation (A/Solomon Islands/3/2006 (H1N1)-like). Sera from adults with chronic illnesses and elderly adults (> 65 years) were similarly tested.
Results: In the children geometric mean titer (GMT) HI responses, geometric mean ratios (GMR), and seroprotection (SP) rates were significantly higher in FLUAD recipients. Similar significant differences were seen among 349 adults with chronic illnesses with increased risk for influenza morbidity who were vaccinated with either FLUAD or with an undajuvanted subunit vaccine. Finally, 56 elderly adults who received the 2007/08 FLUAD formulation displayed post-vaccination responses against strains in the 2008/09 formulation which met the European Committee for Human Medicinal Products criteria for GMR, SP and SC for the mismatched H1N1 and H3N2 strains.
Conclusion: Altogether these results suggest that the greater degree of cross-variant immunity elicited by MF59-adjuvanted influenza vaccine may offer an advantage in circumstances where travelers may be exposed to antigenically mismatched viruses.

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Seasonal influenza vaccine may be associated with increased risk of illness due to the 2009 pandemic A/H1N1 virus

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Background: In late spring 2009, concern was raised in Canada that prior receipt of the 2008-09 trivalent inactivated influenza vaccine (TIV) was associated with increased risk of pandemic H1N1 (pH1N1) illness. Several epidemiologic investigations were urgently conducted through the summer to assess this putative association.
Methods: Studies included: (1) test-negative case-control design based on Canada's ongoing sentinel vaccine effectiveness monitoring system in British Columbia, Alberta, Ontario and Quebec; (2) conventional case-control design using population controls in Quebec; (3) test-negative case-control design in Ontario and (4) prospective household transmission (cohort) study in Quebec. Logistic regression estimated odds ratios for TIV effect on community- or hospital-based laboratory-confirmed seasonal or pH1N1 influenza cases compared to controls with restriction, stratification and adjustment for covariates including combinations of age, sex, comorbidity, timeliness of medical visit, prior physician visits, and/or health care worker status. For the prospective study relative risks were computed.
Results: Based on the sentinel study of ~700 cases and 900 controls, 2008-09 TIV provided statistically significant protection against seasonal influenza (OR 0.44;95% CI 0.33-0.59). Conversely, estimates from the sentinel and several other study designs involving ~1200 laboratory-confirmed pH1N1 cases and 1500 controls consistently showed that prior recipients of 2008-09 TIV were at statistically significant 1.5-2.5-fold increased risk of medically-attended pH1N1 illness during the spring/summer 2009 with upper limit of the 95% confidence interval spanning 3-4-fold increase. There was non-significant increase in the strength of the association with more TIV doses received in the prior five years. Risk of pH1N1 hospitalization was not further increased among vaccinated people when comparing hospitalized to community cases.
Conclusion: Prior receipt of 2008-09 TIV was associated with increased risk of medically-attended pH1N1 illness during the spring/summer 2009 in Canada. Possible biological mechanisms and immuno-epidemiologic implications are considered.

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Monitoring for avian influenza in wild birds on the Far East in 2008

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Background: Waterbirds are natural reservoirs for low-pathogenic avian influenza and have been implicated as the primary source of infection in outbreaks of highly pathogenic avian influenza. An understanding of the movements of birds and the ecology of avian influenza viruses within the wild bird population is essential in assessing the risks to human health and production industries. The purpose of this investigation was surveillance for avian influenza in migratory shorebirds at the East Asian-Australasian Flyway. Sample collection was on Kamchatka, on the Kuril islands, at the Amursky region, on Sakhalin and on Chukchi Peninsula.
Methods: Viral RNA was isolated from virus-containing allantoic fluid with the RNeasy Mini kit (QIAGEN, Valencia, CA, USA) as specified by the manufacturer. Uni12 primer was used for reverse transcription. PCR was performed with a set of primers specific for each gene segment of influenza A virus (*18*). PCR products were purified with the QIAquick PCR purification or QIAquick gel extraction kit (QIAGEN). The amplicons were sequenced on an automated Applied Biosystems 3130 system using BigDye terminator cycle sequencing ready reaction kit» (Applied BioSystems).
Results: In the Far East in the 2008 from birds of 127 spices and 32 families were collected 4248 samples and 16 influenza viruses were isolated and analyzed. No highly pathogenic avian influenza viruses were identified. The hemagglutinin genes of stains A/Larus/Kamchatka/521/08(H13N6) isolated in Kamchatka region and A/Teal/Tinda/6114/08(H10N6) (bankit1288867 in genebank) isolated in Amursky region were analyzed genetically. The analysis shows homology with the strains which were isolated in the Astrahansky region and on Hokkaido island.
Conclusion: Surveillance activities for avian influenza in wild birds should be continued to provide further epidemiological information about circulating viruses and to identify any changes in subtype prevalence.
This work was supported by Russian Government and Bio Industry Initiative (BII) USA (ISTC#3436) and was done in collaboration with Novosibirsk State University.

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Influenza surveillance contributions from South and Southeast Asia

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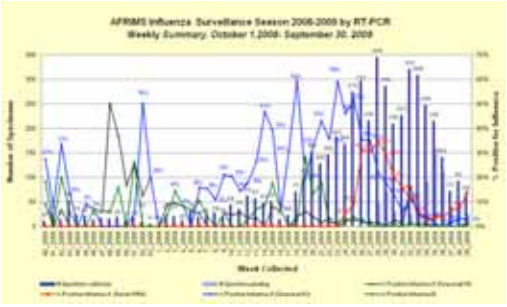
Background: On-going, comprehensive influenza surveillance is critical to detect and monitor influenza outbreaks. The Armed Forces Research Institute of Medical Sciences (AFRIMS) has established 45 influenza sentinel sites in South and Southeast Asia in 4 countries (Thailand, Nepal, Philippines, Bhutan) and an additional 9 countries with participating US Embassies.
Methods: Patients who present with a history of fever and cough or sore throat can participate. Samples are tested with a rapid test for influenza A and B and realtime PCR for influenza A (H1, pH1, H3, H5) and B. Some positive samples undergo virus isolation, characterization and sequencing at AFRIMS or in the US at the Centers for Disease Control and Prevention (WHO Collaborating Center for Surveillance, Epidemiology and Control of Influenza).
Results: From October 2005 through September 2009, AFRIMS sites collected samples from 7,713 patients with 4,239 taken since the H1N1 outbreak started in May 2009. For the entire surveillance period, 42.2% of the samples were positive for influenza A or B by PCR. Since June 2009, 39.1% of the positive influenza samples have been pH1N1 positive. Our surveillance system was the first to detect the presence of pH1N1 in Nepal and Bhutan. Evaluation of influenza rapid tests compared to PCR differed by site but had overall 60% sensitivity and 97% specificity, and pH1N1 had a 68% sensitivity and 98% specificity. Sequences from recent seasonal H1N1 viruses demonstrated greater than 97% homology at the amino acid level with the 08/09 H1N1 vaccine strain. Samples from Bhutan and the Philippines had a very similar strain in circulation with 98.9-99.6% homology at the amino acid level. A/Nepal/NP06C-017/2008 showed the greatest divergence with the other strains (96.6-97.5% homology). Seven pandemic H1N1 HA genes were sequenced and compared to other circulating viruses and were very similar. To date, all seasonal H1N1 and H3N2 viruses that have been screened have genetic markers for M2 blocker resistance and all pH1N1 demonstrate NA inhibitor resistance.



Influenza Strains Circulating from Oct 08-Sep 09

Conclusion: An extensive influenza surveillance program in Asia can document virus movement and genetic changes, and is well positioned to provide assistance during pandemics and prevention efforts.

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H1N1 experience at the Institute for Infectious Diseases Emilio Ribas, Sao Paulo, Brazil. The role of a travel clinic as sentinel for emerging diseases

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Background: According to WHO figures, by November 8 more than 503,536 cases of pandemic influenza had been confirmed and more than 6,260 deaths had been reported. Most cases came from the Americas which also presented the highest number of deaths. South America was severely affected by the transmission of H1N1 and big efforts made to control its dissemination and assist severe cases. Before July 16, when sustained transmission of pandemic influenza H1N1 was recognized in Brazil, most cases were travel related. By late November, 22,565 cases had been reported in the country with a total of 1,528 deaths. The Institute for Infectious Diseases Emilio Ribas (IIDER), a reference hospital for infectious diseases in Sao Paulo city, was responsible for reporting a significant number of the entire state's cases. As H1N1 was initially related to travelers, a number of patients were referred to the clinic to be followed.
Methods: To evaluate the role of the travel clinic during the first months of the pandemic, we analyzed 53 report care forms, broken down by gender, age, symptoms, history of travel, diagnosis and treatment.
Results: Of the 53 patients evaluated, 21 were male (39.6%) and 32 female (60.4%). The mean age was 38.7 and the most common symptoms were cough (90.5%), fever (83%), headache (79%), coryza (64.1%), myalgia (73.5), shortness of breath (49%) and diarrhea (16.9%). Oseltamivir was prescribed to 35 (66%) of all patients. H1N1 was confirmed in 18 patients and Sazonal Influenza was isolated in 6 patients. Out of 17 patients who had traveled internationally, only 3 tested positive for H1N1 and they had come from Argentina (2) and Mexico (1).
Conclusion: Since the begining of the Inluenza pandemic, IIDER had reported a total of 1,924 flu-like cases by October 1, 2009. Because H1N1 transmission was initially associated with travelers, travel clinics were able to provide first warning. In our report, we include the first case of H1N1 infection in Sao Paulo city, a patient returning from Mexico who presented symptoms 2 days before the WHO global alert, which demonstrates the high sensitivity of post-travel evaluations in a pandemic scenario.

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Is a mass immunization program for pandemic (H1N1) 2009 good value for money? Early evidence from the Canadian experience

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Background: Since the H1N1 vaccine approval on October 21, 2009 in Canada, the largest vaccination program in the country's history has been rolled out. This work contributes informed estimates to the current debate about the pandemic (H1N1) 2009 mass immunization program's economic merits.
Methods: We performed a cost-utility analysis of the (H1N1) 2009 mass immunization program in Ontario, Canada's most populous province. We utilize a previously developed model to simulate the current pandemic influenza (H1N1) outbreak in Ontario to compare no intervention to mass immunization of 10% of the population per week, starting 40 days into the pandemic and lasting until 30% vaccine coverage is reached. Data for health care resource use (office visits, emergency department visits, hospitalizations, intensive care unit admissions, use of extracorporeal membrane oxygenation (ECMO)) and deaths were based on pandemic (H1N1) surveillance data in Ontario and Australia, and Ontario administrative data. Program and other costs were drawn from Ontario sources (Ontario Health Insurance Plan (OHIP), Ontario Case Costing Initiative (OCCI)). Utility weights were obtained from the literature and annualized. Years of life lost were calculated using average life expectancy adjusted for quality of life.
Main outcome measures were quality adjusted life-years (QALYs), costs in 2009 Canadian dollars, and cost per QALY gained.
Results: Ontario's H1N1 immunization program is estimated to cost $118 million ($30 per person vaccinated). Immunizing 30% of the population prevents approximately 1.4 million cases, 850 hospitalizations and 35 deaths. This reduces healthcare cost due to illness from $154 million to $77 million and is associated with 24,864 additional quality-adjusted life-years for the population. The incremental cost-effectiveness ratio (ICER) is $1,645 per QALY gained. Results are sensitive to immunization program effectiveness and cost. In all sensitivity analyses the ICER remains well below established thresholds, which determine the cost-effectiveness of a program.
Conclusion: The pandemic (H1N1) 2009 mass immunization program in Ontario is highly cost-effective under conservative assumptions on health care resource use, costs, and mortality. This conclusion is supported by extensive sensitivity analyses and is consistent with the economic attractiveness demonstrated for seasonal influenza programs.

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Rapid real time surveillance and monitoring of pandemic influenza associated pneumonia & risk factors using primary care electronic medical records (EMR)

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Background: The arrival of the influenza pandemic (pH1N1) highlights gaps in surveillance. This pilot project leverages EMR to rapidly detect changes in the severity of influenza-like-illness (ILI) and associated risk factors to support public health actions.
Methods: The sentinel primary care clinics use their EMR with minimal operational disruption to transmit de-identified surveillance information daily to the secure Canadian Network for Public Health Intelligence (CNPHI) server at the Public Health Agency of Canada. The Canadian FluWatch ILI case definition is used :
- fever (T>38 0C) and
- cough and
- myalgia or arthralgia or sore throat or fatigue.
Chi-Square, Fisher Exact and Mann-Whitney tests, with $p < 0.05$ (2-sided) denoting statistical significance are used.
Results: During the initial phase of the 12 month study (Oct 4-Nov 19, 2009), 237 medically-attended ILI (MA-ILI) cases arising from 12,581 patient visits were reported from participating Canadian sentinel sites. Children under 10 years accounted for 33.8% of these cases. Pneumonia was reported in 8.4% of the MA-ILI cases, increasing from none in early October to 22.2% in the second week of November. Comparing ILI cases with pneumonia to those without, the median age was 30 years vs 21 years (p=0.5); 50.0% vs 64.5% were females (p=0.2); 0% vs 0.9% were health care workers (p=1.0); median time from symptom onset to primary care visit was 5 days vs 2 days (p=0.02); 0% vs 2.3% received the current season's influenza vaccine (p=1.0), 5.0% vs 0.5% received the pH1N1 influenza vaccine (p=0.2), 45.0% vs 39.4% received a pneumococcal vaccine (p=0.2); 0% vs 3.3% had diabetes (p=1.0) and 20.0% vs 23.4% had asthma (p=1.0).
Conclusion: Children under 10 years were disproportionately affected but most cases were not life threatening. EMR was able to rapidly detect the shifts in the pandemic severity in real time. The proportion of ILI cases with pneumonia was escalating during the initial phase of this study. Pneumonia was associated with a longer time from symptom onset to primary care visit. With increasing sample size in this ongoing study, statistical power to assess vaccine effectiveness and severity risk factors is anticipated to increase greatly.

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Final Abstract Number: 66.001
Session: MRSA: The clinical challenge
Date: Friday, March 12, 2010
Time: 10:15-12:15
Room: South Hall
Type: Invited Presentation

Systemic MRSA infections

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Systemic Staphylococcal infections were always a dreaded complication of various injuries and for many centuries meant amputation or death for the unfortunate patient. MRSA has become since the 60's a major cause for systemic infections and in various settings are responsible to ~80% of all nosocomial bacteremias. In other settings, MRSA is responsible ~50% and in a recent survey of ICU infections among ~14.000 patients the infection rate had decreased to 47% (Vincent et al JAMA 302;2323:2009). MRSA infections are characterized by various clinical presentations from mild- to rapidly progressing and frequently with involvement of multiple organs includ. heart valvaes, bones, joints and implanted foreign bodies. Those locations, with the particular resistance pattern of MRSA, and only a few effective antibiotics to choose from, make MRSA infections particularly difficult to treat with a frequent need for surgery. The frequent use of foreign bodies in therapy (IV catheters, implants,dialysis catheters, CNS shunts etc') and the biological avidity of this organism to these foreign materials add to the complexity of the infection. Quorum sensing and the ability of the organism to create a biofilm and to detach from the adherent colony add also to the complexity of these infections. Understanding of these biological mechanisms and being able to interfere should allow for some future therapeutic measures. Evidently, meanwhile, hospital infection control and a possible future staphylococcal vaccine are solutions to peruse. CA MRSA can be controlled by hyginic measures as well as vaccine as this organism despite its low potential to cause systemic infections is likely to stay for many years

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Final Abstract Number: 66.002
Session: MRSA: The clinical challenge
Date: Friday, March 12, 2010
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Room: South Hall
Type: Invited Presentation

Treatment of severe MRSA infections: Beyond Vancomycin

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Vancomycin, as the gold standard for therapy of severe MRSA infections, particularly pneumonia, bacteremia, and endocarditis, has been questioned. In recent years reduced vancomycin susceptibility of MRSA has been noted: minimum inhibitory concentrations (MIC) have increased, isolates with intermediate susceptibility (MIC 4 to 16 µg/ml) [VISA] and overtly resistant (MIC ≥ 32 µg/ml) [VRSA] have been noted, and importantly isolates of apparently vancomycin susceptible MRSA with subpopulations exhibiting intermediate susceptibility to vancomycin (survival at vancomycin concentrations ≥ 4 µg/ml) so called heteroVISA [hVISA] have been encountered. VISA and hVISA isolates may emerge when vancomycin therapy is suboptimal. Severe MRSA infections caused by isolates with vancomycin MIC ≥ 1.5-2.0 µg/ml and hVISA have been associated with poor clinical outcome when treated with vancomycin compared with infections caused by more susceptible MRSA. Aggressive vancomycin dosing to achieve trough concentrations 15 to 20 µg/ml has been used to improve outcome when treating infections caused by MRSA. The clinical utility of this strategy has not been established; however, aggressive dosing is associated with nephrotoxicity especially in patients weighing > 101 kg, with reduced renal function and in intensive care settings. Using vancomycin in combination with other antimicrobials has not proven more effective either.
Treatment with other antimicrobials to which MRSA are susceptible is increasingly used to address concerns regarding the inefficacy of vancomycin therapy for severe MRSA infections. Clinical trials suggest that linezolid is at least comparable to vancomycin for treatment of MRSA pneumonia and for pharmacokinetic-pharmacodynamic reasons may be preferable in selected patients. Daptomycin (6 mg/kg/d) was non-inferior to comparator regimens (low-dose gentamicin plus nafcillin or vancomycin) in a clinical trial treating *S. aureus* bacteremia and right sided endocarditis; cure rates were higher with daptomycin compared to vancomycin (not statistically significant) in trial patients with MRSA bacteremia. Doses of daptomycin (10 mg/kg/d) higher than approved by the FDA are preferred by some experts when treating MRSA bacteremia or endocarditis. Linezolid has appeared effective in selected patients with persistent MRSA bacteremia. Televancin, with dual mechanisms of cidality versus MRSA, has recently been approved by the FDA for treatment of complicated skin/soft tissue infection due to MRSA and may offer additional options for treating severe infections. New cephalosporins that bind to PBP2' and to which MRSA are susceptible are under development and fusidic acid is attracting increasing interest as an agent for combination therapy against severe MRSA infections.

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Session: MRSA: The clinical challenge
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Room: South Hall
Type: Invited Presentation

The potential for a staphylococcal vaccine

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Staphylococcus aureus is a frequent cause of bacteremia, pneumonia, skin and soft tissue infection as well as osteomyelitis and septic arthritis. The remarkable pathogenic potential of this microbe has been demonstrated over the past decade, with the rapid spread of highly virulent, drug (methicillin)-resistant *S. aureus* strains (MRSA). The search for protective immunity against invasive *S. aureus* disease has been a research goal since the discovery of this microbe, however this pursuit has not yet been successful and a staphylococcal vaccine is currently not available. To identify protective antigens for a staphylococcal vaccine, three models systems for *S. aureus* infections in mice were developed - pneumonia, lethal septicemia and persistent abscess model. Using a combination of molecular genetic tools, the genetic requirements of the pathogen for each of the three disease complexes were characterized. Genes encoding secreted products that proved to be necessary for the pathogenesis in any one of three disease models were examined further, subjecting the purified products to vaccine trials for protective immunity. Gene products that generated protection were also tested for cross-protection in other disease models or examined for specific animal or human immune responses following infection. Taken together these studies revealed that staphylococci elicit only moderate host immune responses to infection owing to their expression of several different immune-suppressive molecules, in particular adenosine synthase AdsA. a-hemolysin was the sole protective antigen for staphylococcal lung infection. Antibodies against heme-iron scavenging factors provided protective immunity against staphylococcal abscess formation, whereas combinations of different antibodies generated protection against lethal septicemia in mice. These studies therefore suggest that the generation of a successful vaccine against *S. aureus* infection requires a combination of different antigens, but cannot be accomplished by a single factor.

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Session: MRSA: The clinical challenge
Date: Friday, March 12, 2010
Time: 10:15-12:15
Room: South Hall
Type: Invited Presentation

MRSA in Latin America: special considerations

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Until the year 2000, epidemiological surveillance in Latin America was conducted in only a few countries, including Venezuela and Argentina. Since then, with the support of the Pan American Health Organization (PAHO), a network for surveillance of bacterial resistance has been organized, which includes the majority of Latin American countries: the Monitoring/Surveillance Network for Resistance to Antibiotics. Criteria for admission of surveillance centers to the network include concepts of standardization, quality control, supervision visits and regular data reporting. Results are published each year on the PAHO web site (www.paho.org) .The data are collected during the daily work of selected laboratories in the region, with strong support from national and regional reference laboratories.

The Resistance Group of the Panamerican Infectious Diseases Asociation, under the leadership of Dr. Jose Maria Casellas has kept surveillance on the incidence of MRSA and updated reports are published on the API journal.

The methodology used for definition of a given strain as MRSA is different in each country. Some countries work with the Bauer and Kirby method using the oxacillin or cefoxitin disks, and others use automated methods like VITEK 1 or 2 (bioMérieux) and/or MicroScan (Dade Behring).

Confirmation tests such as the methicillin screen plate test are not widely used. The high cost of E-test strips does not permit their routine use in laboratories in the region, and rapid methods of mecA gene detection are not available for the majority of laboratories. Molecular analysis of MRSA strains is restricted to some centers in Brazil, Argentina, Chile, Mexico and Colombia. In cases of nosocomial outbreaks, the identity of MRSA strains is usually assumed from the phenotypic pattern of antibiotic resistance.

Nosocomial, multidrug-resistant MRSA is a growing problem in Latin America . Information gathered by the PAHO-sponsored program on nosocomial infections demonstrated that for the year 2004, MRSA prevalence was as follows: Argentina, 42% (n=5851 isolates); Bolivia, 36% (n=1167); Chile, 80% (n=246); Colombia, 47% (n=4214); Costa Rica, 58% (n=674); Cuba, 6% (n=80); Ecuador, 25% (n=1363); Guatemala, 64% (n=1483); Honduras, 12% (n=393); Mexico, 52% (n=497); Nicaragua, 20% (n=296); Paraguay, 44% (n=980); Peru, 80% (n=1407); Uruguay, 59% (n=1431) and Venezuela, 25% (n=2114).

Similarly, data submitted to the Pan-American Association of Infectious Diseases for the year 2006 showed the following rates of HA-MRSA: Argentina 51%; Bolivia 55%; Brazil 54%; Chile 29%; Ecuador 25%; Mexico 32%; Panama 28%; Paraguay 30%; Uruguay 24%; and Venezuela 27%

The first published report of CA-MRSA infections in Latin America came from Brazil , where three well-characterized strains, isolated from patients with SSTIs or septic arthritis in 2003, harbored SCCmec type IV, PVL, enterotoxin and α-hemolysin genes. A further report followed of a large outbreak of CA-MRSA infection that affected inmates in jails and people from the community in Montevideo, Uruguay, beginning in January 2002 . At the end of the outbreak, more than 1000 patients had been affected and 12 deaths had occurred. SSTIs accounted for more than 65% of the cases, but severe forms of pneumonia were reported, including 4 deaths. In this outbreak, TMP-SMX was very active in the treatment of skin infections .

Since those first reports, MRSA has been identified as the cause of community-acquired infections in several more countries across South America. In Lima, 27% resistance to methicillin was reported in isolates collected from 30 community-acquired infections in 2002 . Two cases of SSTI caused by CA-MRSA strains were reported from Bogotá in 2006 , and a report from the Colombian network of resistance surveillance showed an increase in CA-MRSA from 1% of S. aureus isolates in 2001 to 5.4% in 2006 [21]. The PAHO program has also included surveillance of community-acquired MRSA infections since 2005, and in Venezuela, 12.4% of 845 isolates of S. aureus from the community were resistant to oxacillin . However, no clinical information is available for these cases. A few isolated cases of CA-MRSA infection have been reported in Chile, but some of these were in people returning from cities in Uruguay or Brazil with a high incidence of MRSA .

MRSA is an increasing problem in Latin America, both in the healthcare environment and in the community. In nosocomial *S. aureus* infections, the frequency of methicillin resistance has surpassed 50% in over half of the Latin American countries for which data were identified . Community-acquired-MRSA has been reported in Latin America and even though large outbreaks such as the one that occurred in Uruguay – causing 12 deaths – have not been reported elsewhere, this example highlights the problem. Surveillance programs are only recently beginning to record CA-MRSA, and the true incidence of MRSA in the community is still largely unknown in the region.

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Final Abstract Number: 67.001
Session: Plenary 8
Date: Friday, March 12, 2010
Time: 14:30-15:15
Room: Ballroom 1: Brickell
Type: Invited Presentation

Microbial chemical ecology and the future of antibiotics

R. Kolter
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When it comes to cell-to-cell communication the predominant language is that of small signaling molecules. The microbial world is no exception - microbes are known to exchange messages both within and across species by secreting and recognizing small molecule natural products. Among such compounds can be found many of the antibiotics that have been extensively used in medicine since the middle of the last century. Concomitant with their use has been the evolution of antibiotic resistance. In order to understand the phenomenon of antibiotic resistance and to devise better strategies for future antibiotic discovery and use it is useful to consider this topic from an ecological perspective. In this sense, it is important that to recognize that we remain largely ignorant of the role that antibiotic substances play in environmental settings. Work that I will discuss in this lecture supports the idea that antibiotics can serve non-lethal signaling functions in bacteria - both within and across species. In addition, I will discuss instances in which interspecies interactions mediated by small molecule natural products lead to narrow spectrum action of antibiotics in ecological settings. These results suggest new ways to look for and use antibiotics in the future.

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Final Abstract Number: 68.001
Session: Tuberculosis: Tools for the Future
Date: Friday, March 12, 2010
Time: 15:45-17:45
Room: Ballroom 1: Brickell
Type: Invited Presentation

Unlocking the Mycobacterial Cell Wall: Insights into Virulence, Biosynthetic Pathways and systems-based approach to drug discovery

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Biosynthetic machinery of complex lipids in *Mycobacterium tuberculosis* (Mtb) includes a family of FadD proteins, which are otherwise universally involved in fatty acid degradation. Mtb produce several exotic lipids, many of which are important for its virulence as well as survival in the host. By combination of structural, genetic and biochemical studies, we have identified several novel mechanisms and pathways that generates complex cell envelope lipids. We show that polyketide synthase in conjunction with a new family of fatty acyl AMP ligases (FAALs) in Mtb are involved in biosynthesis of lipids. Based on the structure of a FAAL homologue and by generating loss- as well as gain-of-function mutants, we show that an insertion motif dictates the synthesis of acyl-adenylates or acyl-CoA, and thus bifurcates metabolic fate of fatty acids. Since FAALs are focal nodes in biosynthetic network of virulent lipids, inhibitors directed against these proteins provide a unique multi-pronged approach of simultaneously disrupting several pathways in lipid metabolism. Our study illustrate how obligate pathogens like Mtb have evolved such novel themes of functional versatility to generate unusual metabolites. We also reveal possible evolutionary path traced by FAALs from omnipresent fatty acyl CoA ligases. Furthermore, our study also provide credence to the ‘systems pharmacology’ approach for drug discovery.

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Session: Tuberculosis: Tools for the Future
Date: Friday, March 12, 2010
Time: 15:45-17:45
Room: Ballroom 1: Brickell
Type: Invited Presentation

Diagnosing Drug Resistance in Low-Resource Settings: Practical Approaches

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Tuberculosis (TB) remains one of the major causes of death from a single infectious agent worldwide. Of great concern for TB control is the emergence of drug resistance. Since there is no cure for some multidrug-resistant strains of *Mycobacterium tuberculosis*, there is concern that they may spread around the world, stressing the need for additional control measures, such as new diagnostics, better drugs for treatment, and a more effective vaccine. Pulmonary TB can be diagnosed by its symptoms, chest radiography, sputum smear microscopy and by cultivation of *M. tuberculosis*, which is considered as the gold standard. Recent advances in molecular biology and molecular epidemiology, and a better understanding of the molecular basis of drug resistance in TB, have provided new tools for rapid diagnosis; however, the high cost of most of these techniques, and their requirement for sophisticated equipment and skilled personnel have precluded their implementation on a routine basis, especially in low-income countries. Other nonconventional diagnostic approaches proposed include the search for biochemical markers, detection of immunological response and early detection of *M. tuberculosis* by methods other than colony counting. In the present mini review, some of these approaches will be reviewed and the feasibility for their implementation in diagnostic laboratories will be discussed. However, with the resurgence of interest in the development of new tools for TB control, and the recent influx of funding and political support, it is likely that the next few years will see the introduction of new diagnostic tools into routine TB control programs and particularly in high disease burden, and resource-poor countries.

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Session: Tuberculosis: Tools for the Future
Date: Friday, March 12, 2010
Time: 15:45-17:45
Room: Ballroom 1: Brickell
Type: Invited Presentation

Applicable Insights from Pharmacokinetic and Pharmacodynamic Modeling of Antituberculosis Chemotherapy

E. Nuermberger
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Current chemotherapy for tuberculosis leaves considerable room for improvement. Major objectives include shortening the duration of therapy necessary for cure, improving the efficacy of intermittent treatment regimens, and preventing the development of drug resistance. Better understanding of the pharmacodynamic relationship between drug exposure and drug effect will identify strategies for optimizing drug effect in order to achieve these objectives, thereby informing pre-clinical drug development, clinical trial design and clinical practice. Recent work in *in vitro* and animal models involving both new and existing anti-tuberculosis drugs will be reviewed and discussed in this context.

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Session: Tuberculosis: Tools for the Future
Date: Friday, March 12, 2010
Time: 15:45-17:45
Room: Ballroom 1: Brickell
Type: Invited Presentation

Addressing Latent TB in Areas with High TB Burden: Implications for Control

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Brazil is a country in South America with a total population of 191 million of people (81% urban; 19% rural) with an estimated incidence of 92,000 new cases of tuberculosis (TB) yearly (data from 2007). Treatment of latent TB infection (LTBI) in Brazil is currently recommended only in the case of contacts of pulmonary smear-positive TB patients aged ≤ 15 years with a tuberculin skin test (TST) ≥ 10 mm and no previous bacilli Calmette-Guérin (BCG) vaccination or with a TST ≥ 15 mm regardless of previous BCG vaccination. However, a recent retrospective cohort study evaluating contacts aged ≥ 15 years who did not meet the Brazilian criteria for LTBI treatment shown a TB incidence of 3.2% (22/667), with an estimated TB rate of 1,649 per 100 000 population. The risk of TB was greater among the 349 contacts with TST ≥ 5 mm (5.4%) compared to the 318 contacts with TST < 5 mm (0.9%; RR 6.04, 95%CI 1.7–20.6). The high incidence of TB among contacts who did not meet the Brazilian criteria for LTBI treatment strongly suggests that a change on these criteria could have a direct impact on TB control

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Final Abstract Number: 69.001
Session: Update on infections in transplant recipients
Date: Friday, March 12, 2010
Time: 15:45-17:45
Room: Ballroom 2: Monroe/Flagler
Type: Invited Presentation

Tropical Infections in Solid Organ Transplant Recipients

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Tropical infections in solid organ transplant recipients are an increasing problem worldwide. This increase is the result of several factors. Firstly, the number of countries with transplantation programs is increasing and now includes countries in the tropics. Secondly, there has been an increase in immigration and international travel worldwide. And finally, commercial transplantation is a growing emergent problem. Chagas disease, strongyloidiasis and less so tuberculosis, are only a few of the infections that have traditionally been considered to be limited to tropical regions, but that are common enough to pose a challenge in the management of transplant recipients or candidates worldwide. Evidence based recommendations on the prevention and treatment of these diseases in the transplant population is scarce, and usually the result of small retrospective studies.

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Final Abstract Number: 69.002
Session: Update on infections in transplant recipients
Date: Friday, March 12, 2010
Time: 15:45-17:45
Room: Ballroom 2: Monroe/Flagler
Type: Invited Presentation

Polyoma Virus Infection, Replication, and Disease after Kidney Transplantation

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Six polyomaviruses (PyV) infect humans, but show different seroprevalence rates i.e. BK 82%, JC 58%, KI 69%, WU 55%, MC 42% and SV40 <5%. BK and JC PyV are known to persist in the renourinary tract with asymptomatic urinary shedding in 7% and 19% of healthy adults, respectively. KI and WU PyV can be detected in less than 2% of respiratory secretions, but may cause bronchitis/pneumonia in immuno-compromized patients. MC PyV integration has been linked to Merkel carcinoma in immunocompromized, but MC genomes can also be detected in 38% of healthy skin swabs. BK PyV is linked to two major complications in transplant recipients, polyomavirus-associated nephropathy (PyVAN) and polyomavirus-associated hemorrhagic cystitis (PyVHC). PyVAN and PyVHC have been encountered in a variety of immunodeficient patients, but most cases of PyVAN arise in kidney transplant patients at rates of 1-10%, while PyVHC preferentially affects allogeneic hematopoietic stem cell transplant patients at rates of 5-15%. BKV has been less frequently associated with other pathologies such as ureteric stenosis, pneumonitis, hemophagocytic syndrome, encephalitis, retinitis, and polyomavirus-associated multifocal leukoencephalopathy (PyVML), a complication of the central nervous system mostly caused by the closely related JC PyV. PyVAN is rare in non-kidney transplant recipients, despite similar or even higher intensity of immunosuppression. The objective of this presentation is to provide an update on PyV in kidney transplantation and highlight the current recommendations of the AST-ID and KDIGO focussing BK and PyVAN regarding screening, diagnosis and management.

Hirsch HH, Randhawa P and AST-ID CPG. Am J Transplant 2009; 9 (Suppl 4): S136-S146
Kasiske BL et al. and the Kidney Disease: Improving Global Outcomes (KDIGO) Transplant Work Group. Am J Transplant 2009; 9 (Suppl 3):S1-155

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Final Abstract Number: 69.003
Session: Update on infections in transplant recipients
Date: Friday, March 12, 2010
Time: 15:45-17:45
Room: Ballroom 2: Monroe/Flagler
Type: Invited Presentation

Respiratory Viral Infections in Hematopoietic Stem Cell Transplant Recipents

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Influenza, parainfluenza, respiratory syncytial virus and picornavirus infections are common causes of upper respiratory infection. For many years these viral infections were considered to be of minimal concern in patients with cancer. However, during the past 20 years, these viruses have been recognized as a possible cause of serious infections in patients undergoing hematopoietic stem cell transplantation (HSCT) or therapy for hematologic malignancies, especially acute leukemia. Some of these patients have only URIs from which they recover uneventfully, but others have infections that progress to pneumonia, which can be fatal. Important advances have been made in recent years in the management of these infections, including the development of rapid diagnostic tests and the discovery of therapeutic agents for some of these infections. Many studies from different institutions, including ours, looked at their experience with these infections to determine their impact on this group of patients, most of who were immunocompromised and acquired their infections in the community. Several important predisposing factors for these infections have been identified in HSCT recipients and patients with hematological malignancies. These include age >65 years, severe neutropenia, severe lymphopenia, allogeneic transplantation, transplant conditioning regimen, graft versus host disease and adrenal corticosteroid therapy. HSCT recipients are at greatest risk within the first 100 days post-transplant. Several studies have suggested that aerosolized ribavirin is effective for the therapy of RSV pneumonia in HSCT recipients, especially when administered with immunoglobulins, although the number of cases has been small. In summary, there is some evidence to suggest that it may be beneficial to administer therapy routinely to HSCT recipients and patients with hematologic malignancies who have known predisposing factors for pneumonias (i.e. age>65 years, ALC <200 cells/ml) when they are diagnosed with a URI caused by influenza or RSV to prevent progression to pneumonia and possible death.

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Final Abstract Number: 69.004
Session: Update on infections in transplant recipients
Date: Friday, March 12, 2010
Time: 15:45-17:45
Room: Ballroom 2: Monroe/Flagler
Type: Invited Presentation

Prevention of Cytomegalovirus Infection after Hematopoietic Stem Cell Transplantation: Preemptive Therapy Vs Universal Prophylaxis

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Blood products administered to all HSCT recipients; particularly those who are CMV seronegative, should be leukocyte depleted, or obtained from CMV seronegative donors.

Allogeneic HSCT recipients should be managed under a CMV prevention strategy; either universal prophylaxis or preemptive therapy for the first 100 days. There are advantages & disadvantages to both strategies. Intravenous ganciclovir (GCV) or oral valganciclovir (VGCV) are the most commonly used agents. Foscarnet & cidofovir are alternatives, but both require prehydration & may be nephrotoxic. Acyclovir & valacyclovir are much less active against CMV. Universal prophylaxis with IV GCV or VGCV may cause neutropenia, which can usually be managed with G-CSF and temporary suspension of drug. Preemptive therapy requires the ready availability of a sensitive test for early detection of asymptomatic CMV replication, such as antigenemia or PCR. Such test should be done at least once weekly, and treatment promptly initiated when test is positive, and continued for at least for 2 weeks; longer if test is still positive. Weekly surveillance testing should be continued to detect recurrence. Patients who are CMV seropositive, whose donors are CMV seronegative, or whose donors are unrelated, haploidentical, cord blood, or T cell depleted, or who develop CMV viremia < 100 days after HSCT, or steroid-requiring chronic GVHD, or with CD4 counts < 50/mm3 are at a higher risk for late CMV viremia occurring > 100 days after HSCT. Such patients should be monitored with CMV antigenemia or PCR for preemptive therapy.
Autologous HSCT who are CMV seropositive, and who are at a higher risk for CMV reactivation due to total body irradiation, CD34+ selected T cell depleted grafts, or receipt of alemtuzumab, fludarabine, or 2-chlorodeoxyadenosine in the 6 months preceding HSCT, should be monitored by weekly CMV antigenemia or PCR for preemptive therapy for 60 days after HSCT.

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Final Abstract Number: 70.001
Session: International perspectives on infection control
Date: Friday, March 12, 2010
Time: 15:45-17:45
Room: Ballroom 3: Tuttle
Type: Invited Presentation

Engaging Nations in a Commitment to Infection Control

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Health care-associated infection is a major, global issue for patient safety and its prevention was chosen by WHO Patient Safety as the theme of its First Global Patient Safety Challenge “Clean Care is Safer Care” launched in October 2005. Since then, a formal statement has been signed by over 120 ministries of health as a pledge of support to implement actions to reduce health care-associated infection, corresponding to more than 85% coverage of the world population. The Challenge has focused on raising global awareness of the importance of health care-associated infection as a priority patient safety issue with the promotion of hand hygiene as the cornerstone.

The main output of the Challenge has been the development of the WHO Guidelines on Hand Hygiene in Health Care and the design of an implementation strategy to translate the guidelines into practice. These have been tested in eight pilot sites and used in over 350 healthcare settings worldwide with very promising results. Over 40 countries have also established hand hygiene promotion campaigns at national level. In August 2009, around 50 participants of the “campaigning nations” network met in Geneva to share knowledge, experiences and concerns, including approaches to take account of cultural diversity.

The *SAVE LIVES: Clean Your Hands* initiative was also launched by WHO Patient Safety on 5 May 2009 to encourage health-care workers to be part of a global movement to improve and, importantly, sustain hand hygiene. More than 5500 health-care facilities have already registered their commitment to the initiative with a target to achieve 10,000 registrations by 5 May 2010. The ultimate aim of *SAVE LIVES: Clean Your Hands* is to demonstrate that hand hygiene is the essential basis for the reduction of health care-associated infection and to engage nations in a firm and ongoing commitment to infection prevention.

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Final Abstract Number: 70.002
Session: International perspectives on infection control
Date: Friday, March 12, 2010
Time: 15:45-17:45
Room: Ballroom 3: Tuttle
Type: Invited Presentation

International Controversies: Bare Below the Elbow and the Incremental Value of MRSA Screening

M. Edmond
Medical College of Virginia Campus, Richmond, VA, USA

This presentation will summarize the relevant data for two of the most controversial interventions to reduce healthcare associated infections. The first half of the presentation will lay out the arguments for why elimination of white coats and adoption of a bare below the elbows approach should be considered for implementation. The second half of the presentation will review problems associated with a MRSA search and destroy strategy and demonstrate that horizontal strategies for infection prevention are cheaper, pose less risks to patients, and offer greater benefit by reducing infections due to many pathogens, not just those due to MRSA.

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With Limited Resources: How to begin and How to Sustain an Infection Control Program

S. Wey
University of Sao Paulo, Sao Paulo, Brazil

Infection control (IC) efforts may encounter greater obstacles in developing countries. However, progress appears to have been made composed of designated and trained doctors, nurses, and others. E-learning is an important tool to bring health care professionals updated information, especially where teaching resources are limited. It allows the exchange of experiences between professionals, promotes simultaneous knowledge acquisition, and reaches some remote areas. Trained IC personnel are a scarce resource and their job is to prevent and control infection; their time and expertise must not be disproportionately utilized in counting infection only. Basic surveillance is an essential component of IC Programs and should be tailored for each institution. The data should be used to identify preventable infections so that resources are targeted in high priority areas requiring minimum resources. In addition, surveillance data can be used to compare infection rates between healthcare facilities, convince administrators, clinical teams and health care professionals to adopt recommended practices and help evaluate IC measures. For this last purpose one can easily find Guidelines issued by international health institutions or professional societies that indicate the basic requirements for an effective IC. The IC team should take into account to implement measures that are more cost-effective, and use all effort and creativity to adopt tools that could improve compliance. Positive Deviance method that is a social and behavioral change process based on the premise that in most organizations and communities there are people or groups of people who solve problems better than colleagues who have exactly the same resources. Another important concern in developing countries is integrating epidemiology and microbiology. Despite its relevance, knowledge about the status of antibiotic resistance in the developing world remains on the whole lacking. Regional special laboratories could provide a good amount of information about resistance and help in outbreak control.

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Type: Invited Presentation

The Future Hospital Epidemiologist's Portfolio for Success

R. Wenzel
VCU Medical Center, Richmond, VA, USA

It is understood that a successful Hospital Epidemiologist will need skills in clinical medicine, especially infectious diseases, and in microbiology, epidemiology and informatics. Yet that is only the beginning. Success builds on a platform of skill sets that include Becoming Articulate and Persuasive and Becoming Inspiring. These skills can be taught. In addition a still more successful Hospital Epidemiologist will need to know more: How to Manage Something New; How to Manage Intimidation; and How to be Creative.
The presentation will be accompanied by examples from the experiences of the speaker as well as examples from leaders in other fields.

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Final Abstract Number: 71.001
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Room: Room Jasmine
Type: Invited Presentation

The Global Impact of Bacterial Meningitis

P. Heath
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Background: Bacterial meningitis is an important cause of mortality and morbidity in neonates, infants, children and adults worldwide.
Methods.
Review of published literature.
Results: *Streptococcus pneumoniae*, *Haemophilus influenzae* type b, and *Neisseria meningitidis* are the most important causes of acute bacterial meningitis worldwide. A number of other bacteria are capable of causing meningitis, often associated with specific population groups; for example, *Streptococcus suis* is a common cause of acute bacterial meningitis in southeast Asia but occurs rarely elsewhere, Group B streptococcus is the leading cause of neonatal meningitis in developed countries but less frequent in developing countries where Gram negative bacteria are more commonly implicated, while in HIV-infected patients, *S pneumoniae* is the commonest cause of acute bacterial meningitis but meningitis caused by *Mycobacterium tuberculosis* and *Cryptococcus neoformans* is also common. However, surveillance, especially in high mortality developing countries usually under ascertains bacterial meningitis and sepsis due to the low sensitivity of diagnostic tests and limited access to care. Furthermore the long term sequelae of meningitis, a particular concern following neonatal meningitis, is poorly described. Finally, most reported estimates of meningitis incidence and case fatality ratios come from hospital-based surveillance studies only.
Conclusion: The global burden of bacterial meningitis is substantial. Better standardisation and reporting of methods and limitations for surveillance studies are needed and more research is required. Expanded use of established and new vaccines could significantly reduce both bacterial meningitis and overall mortality, especially in children.

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Type: Invited Presentation

Pathophysiology of bacterial meningitis

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Bacterial meningitis is characterized by the entry of bacteria into the cerebrospinal fluid (CSF) and bacterial growth in this compartment leading to inflammation within the CSF and the adjacent brain tissue. Long-term neurological sequelae and death are caused jointly by the following factors: (1) The systemic inflammatory response of the host leads to leukocyte extravasation into the subarachnoid space, an increased CSF outflow resistance, and brain edema . The resulting elevated intracranial pressure is an important cause of death in the acute phase and of long-term sequelae. Systemic inflammation can also cause vasculitis, cerebral venous thrombosis and secondary ischemia. (2) Immune cells within the brain parenchyma, in particular microglia, can be stimulated by proinflammatory bacterial compounds, which can directly lead to neuronal injury. (3) Some bacterial compounds, e.g., pneumolysin, possess direct toxicity on neurons. Neuronal injury is mediated by the release of reactive oxygen intermediates, proteases, cytokines and excitatory amino acids, the activation of transcription factors, caspases, matrix metalloproteases and other proteases.
Rapid initiation of effective antibiotic therapy sterilizes the CSF and reduces mortality of bacterial meningitis. In industrialized countries, dexamethasone as an adjunctive therapy to antibiotic treatment, improves outcome of bacterial meningitis, particularly of *Streptococcus pneumoniae* meningitis. In experimental meningitis, dexamethasone as an adjunct to antibiotic treatment causes an increase of neuronal injury in the dentate gyrus of the hippocampal formation, suggesting that corticosteroids might not be the ideal adjunctive therapy. Several approaches that interfere selectively with the mechanisms of neuronal injury, including the use of non-bacteriolytic bactericidal protein synthesis-inhibiting antibiotics, antioxidants and inhibitors of transcription factors, matrix metalloproteinases, and caspases, are effective in animal models. However, adequate clinical studies are lacking. A recent randomized clinical study points to a beneficial effect of adjunctive oral glycerol.

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Date: Friday, March 12, 2010
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Room: Room Jasmine
Type: Invited Presentation

Vaccination Against Bacterial Meningitis

H. Peltola
Helsinki, Finland

Thanks to conjugate vaccines specially against Haemophilus influenzae (Hib) and Streptococcus pneumoniae (Pnc), bacterial meningitis has become disease whose global importance is no more realized in the affluent countries. However, more than 1 MI individuals a year, proportionally more often children than adults, fall down; one-third succumb, and one-third of survivors are left with moderate-to-severe sequelae. In the world where the meningitis problem is greatest, only a fraction of people are vaccinated. The main (though not only) reason is the too high cost of conjugates for those populations.

Years ago, inexpensive polysaccharide vaccines were developed against Hib, Pnc, and Neisseria meningitidis (Mnc). The Hib, polysaccharide is rightly gone, but all potential of polysaccharides against Pnc and Mnc has not been used. The reasoning is that polysaccharides are not sufficiently immunogenic in small children (in greatest risk). However, convincing clinical efficacy data are lacking to prove this statement. It is unlikely that those data will ever be produced, because people are too convinced of the superiority of conjugates to support any major field trial with a Pnc or Mnc polysaccharide.

At present, variable conjugate vaccines are available against Hib, 7-13 serotypes of Pnc, and up to 4 serogroups of Mnc. Hib vaccination is indicated in all countries. So is also Pnc conjugate, albeit its effect specifically against meningitis depends on local epidemiology (serotype distribution). In case of Mnc meningitis, the main problem is the lack of sufficiently good vaccine against serogroup B, the most common group in many countries. Fortunately, encouraging results have been obtained recently regarding a new-type of vaccine.

Group A Mnc is a special problem of Africa. Monovalent conjugate has been used there, and luckily, its price is tolerable because of its manufacturing outside Big Farma. This approach would be welcome to cover other causative agents of meningits as well.

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Room: Room Jasmine
Type: Invited Presentation

Effective Adjuvant Therapies for Meningitis

S. Singhi
Post-graduate Institute of Medical Education and Research, Chandigarh, India

Objective: To review advances in adjuvant therapy of bacterial meningitis.
Data Sources: Work published within past 5 years retrieved from personal knowledge and the U.S. National Library of Medicine for terms: central nervous system infections, meningitis-bacterial; therapy; corticosteroids; fluids; anti-inflammatory; glycerol, and pediatrics.
Study Selection, Data Extraction and Synthesis: Promising articles were reviewed and data used based on clinical relevance and significance.
Results: *Corticosteroid therapy:* Results from clinical trials of adjuvant steroid therapy are conflicting. What emerges from meta-analysis is that in high-income countries steroids reduce the risk of hearing loss in immunocompetent patients with *H. influenzae-b* or pneumococcal meningitis; there is no survival benefit. In low-income countries utility of corticosteroids is unclear.
Fluids: Evidence supports normal maintenance intravenous fluids rather than restricted fluids in the first 48 hours in settings; it reduces risk of spasticity and severe neurologic sequelae.
Oral glycerol therapy during first 48 hours of treatment can prevent severe neurologic sequelae. Within 6 hours of administration oral glycerol increased plasma osmolality by 3%, which is known to reduce secretion of CSF and enhance movement of water back to plasma, and thus improve cerebral blood flow.
Management of raised ICP is not easy because a variety of mechanisms. Neuroimaging may be helpful in selection of appropriate treatment. Cerebral perfusion pressure targeted therapy to maintain CPP >50 mmHg is likely to improve the outcome.
New Adjunct Therapies: Endogenous inflammatory mediators, chemokines and chemo attractant cytokines are believed to contribute to neurologic injury. Agents aimed at blocking these mediators offer future therapeutic hopes: these have been shown to reduce brain edema, postmeningitic hearing loss and cochlear and brain cell injury in experimental meningitis. and
Conclusions: In acute bacterial meningitis use of glycerol and maintenance instead of restricted fluids improve the outcomes; however, role of dexamethasone in prevention of hearing loss needs re-evaluation.

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Room: Room Orchid B/C/D
Type: Oral Presentation

One year impact of a single dose of Praziquantel in five schistosomiasis endemic districts in Rwanda

M. Denise[1], R. Eugene[1], S. Jackson[2], K. Blaise[3], M. Odette[2], K. Michee[3], K. Michael[2], R. Josh[4]
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Background: Schistosomiasis is one of the most prevalent parasitic diseases in developing countries and has a negative impact on the health of the population and consequently the economics of those countries. In Rwanda, the mapping survey of schistosomiasis (and soil-transmitted helminths) conducted in 2007 by the Neglected Tropical Disease (NTD) control program have shown that only *S. mansoni* was prevalent at 2.7% in the whole country with a variation per district from 0 to 69.5%. The disease was more localized near lakes Burera, Ruhondo, Muhazi and Kivu. In total, height endemic districts were identified and a mass drug administration with praziquantel and albendazole was implemented.
Methods: The impact of the treatment programme was monitored through a cohort of 2,166 school children aged 7-16 years in five most infected districts. Their infection status with *S. mansoni* was determined by clinical and parasitological examination at baseline and at year one after treatment. The prevalence and intensity of *S. mansoni* before and after the treatment were analyzed.
Results: After one round of treatment, the prevalence of *S. mansoni* infection have been reduced significantly in all 5 districts from 11.2% [95% CI 9.8%-12.5%] at baseline to 2.0% [95% CI 1.4%-2.6%] at year one follow up. On the intensity, the median number of eggs in the 5 districts decreased by two from 72 eggs per gram (epg) of stool to 36 epg. The proportion of children with heavy *S. mansoni* infection was significantly reduced as well. Signs of early clinical morbidity of *S. mansoni* infection like bloody diarrhea, abdominal pain decreased significantly.The rate of hepatomegaly, which is a late clinical sign for S.mansoni was very low in that cohort.
Conclusion: One single dose of praziquantel in school age children in schistosomiasis endemic districts can decrease significantly the prevalence and intensity of the infection and can contribute to the reduction of the morbidity due to *S. mansoni* in Rwanda.

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Room: Room Orchid B/C/D
Type: Oral Presentation

A comparative study of Arco and Coartem in the treatment of uncomplicated malaria in patients aged 4 months to 16 years attending Mulago hospital, Kampala, Uganda

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[1]Makerere University College of Health Sciences, Kampala, Uganda, [2] Mulago National Referral Hospital , kampala, Uganda, [3]Ministry of Health, Kampala, Uganda, [4]Mulago Hospital, kampala, Uganda

Background: Malaria is a major cause of child morbidity and mortality in Uganda. It accounts for 24-45% of outpatient visits in Uganda. The situation is worsened by the development of drug resistance and lengthy anti-malaria drug treatment which pose problems of compliance to medication. Both Arco and Coartem are Artemisinin Combination Therapies (ACTs). We conducted a study to compare the efficacy and safety of Arco a single dose drug and Coartem in the treatment of uncomplicated malaria in children aged 4 months – 16 years attending Mulago Hospital, Kampala Uganda.
Methods: A phase II single blinded randomized clinical trial was carried out between November 2007 and June 2008. We screened 3344 patients with fever for malaria of whom 353 had positive blood smear, 225 fulfilled the inclusion criteria and were randomized into the two study arms i.e. Arco and Coartem arms. The study patients were followed up for 42 days.
Results: There was 100% parasite clearance by day 2 in both the ARCO and Coartem arms of the study. The overall cure rate on day 42 of follow up was 98% for both Arco and Coartem. Recrudescence occurred in 2 patients in the Arco arm of the study by day 42 and in 2 patients on Coartem by day 21 of follow up. No statistically significant difference in resolution of fever, vomiting, dizziness and back pain was observed throughout the follow up period of the study. No difference was observed in the clinical presentation between the two treatment arms. No serious adverse events were reported/observed in either of the study arms.
Conclusion: Arco and Coartem are equally effective and safe in the treatment of uncomplicated malaria in children aged 4 months to 16 years. Arco is a suitable ACT in the treatment of uncomplicated malaria in children.

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Room: Room Orchid B/C/D
Type: Oral Presentation

The effect of malaria on the outcome of Lassa Fever

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Background: Lassa fever (LF) and malaria can co-exist in patients in countries endemic for both infections and thus lead to delay in diagnosis of LF, with consequent adverse effect on outcome. This study was aimed at addressing the paucity of data on the prevalence of malaria as a co-morbidity in patients with LF and the effect on outcome.
Methods: The clinical presentation and outcome of patients with RT-PCR confirmed LF seen at the Irrua Specialist Teaching Hospital, Nigeria between January 2008 and August 2009 were reviewed. RT-PCR for Lassa virus and blood smear for malaria parasites were done using standard techniques. Treatment was with ribavirin.
Results: 102 patients with RT-PCR confirmed LF were managed during the period. 27 (37%) of 73 patients were LF and malaria smear positive while 46 (63%) were LF positive and malaria smear negative; malaria parasite smear was not examined in 29 (28.4%) of the 102 patients. Malaria positive LF patients had a significantly shorter duration of fever (7.6 + 4.93 versus 10.2 + 5.96 days; p <0.05) but a significantly lower mean temperature (37.54 + 1.09 versus 38.04 + 1.2 oC; p <0.05) on admission. Central nervous system (CNS) features were significantly more frequent in malaria positive patients (51.9% versus 26.8%; p< 0.01), but there was no significant difference in case fatality rates (36.4% versus 54.5%; p >0.1). Overall, patients with CNS manifestations had a significantly higher CFR than those without (54.8% versus 9.4%; p<0.001), irrespective of the presence or absence of malaria parasites. The mortality rate among patients with severe CNS manifestations (coma and/or seizure) was also significantly higher than among those with milder CNS features (80% versus 31.8%; p<0.001).
Conclusion: There is a high prevalence (37%) of co-infection with malaria in patients with LF, thus emphasizing a high index of suspicion for diagnosis and testing for LF even in the presence of malaria parasitaemia in endemic areas. Our study could not demonstrate a major effect of malaria on outcome. Severe CNS manifestations such as coma and/or seizures were associated with excess mortality.

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Room: Room Orchid B/C/D
Type: Oral Presentation

Clinical analysis and eco-epidemiology data of pediatric visceral leishmaniasis (VL) in Argentina

S. Ruvinsky[1], O. Salomon[2], L. Arce[3], D. Jozami[4], J. Altcheh[5], R. Cappellini[6], S. Lopez Papucci[7], A. Riarte[8], S. Gomez[9], L. Borchichi[3], R. Bologna[1], P. Paulin[1], R. Pividori[9], G. Moscatelli[10], H. Freilij[5], R. Chiabrando[6], A. Gentile[6], A. Aletti[7], A. Gajo Gane[11], T. Orduna[12]
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Background: The first Argentinian human VL autochthonous case, with concurrent canine VL, *Lu. longipalpis*, and *L.infantum* typified from human and dogs, was reported from Posadas (Misiones 5/2006)
Methods: The objective was to describe clinical characteristics and eco-epidemiological data of VL in pediatric patients in Argentina
Following method was used: Retrospective multicentre study. Data from children with VL confirmed (2006-2009) were collected by a surveillance database and review of medical records. Data from eco-epidemiology study from Argentina were included.
Results: The screening of vectors in Posadas (3/2007) found *Lu.longipalpis* in 42% of 314 sites, but only 5.2% with > 31 vector/trap, with spatial auto-correlation. The highest captures were associated with peridomestic chicken habitats, and dog closeness to humans. Posadas up to 9/2008 reported more than 5000 infected dogs. La Banda (Santiago del Estero) reported 8 dogs with VL from 10/2007 to 5/2008 within an area of 1.5 km2. This focus was sampled in 11/2007 and 4/2008, and none *Lu. longipalpis* was found but *Lu. migonei* were concurrent with the cases (10 m). *Lu. longipalpis* and canine VL was reported in Corrientes province since 12/2008 Eighteen pediatric patients with confirmed VL were included, median age was 12.5 months (IQR: 8-68 m.), 78% was from Misiones province, 16.6% from Santiago del Estero province, whereas 5.6% was from Corrientes province. Male-female ratio: 3.5:1Clinical features included fever and hepato-splenomegaly (100%), weight loss (66.6%), diarrhea (44.4%), and bleeding disorders (27.7%).VL children were positive by parasitological and/or rk39 studies. Laboratory findings were hypoalbuminemia (83.3%), leucopenia (80%), anemia (83.3%) and thrombocytopenia (72%). Three patients had congenital co-infections (2 Chagas disease and 1 HIV infection) Five children (27.7%) developed secondary bacterial infections. Twelve patients were treated with amphotericin B (10 lipid complex and 2 deoxicolate) and 6 with antimony. One child with severe bleeding and hepatic failure died. No relapse was observed in the survivors.
Conclusion: In Argentina *Lu. longipalpis* colonized recently urban environments showing high spatial heterogeneity (hot spots), and a dispersion trend to southern latitudes.VL should be considered in patients with prolonged fever that live or visit an endemic region. Early diagnosis is essential to avoid severe complication and mortality in children.

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Type: Oral Presentation

Novel molecular detection of drug resistance markers in *Plasmodium falciparum* from Papua New Guinean children with uncomplicated malaria

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Background: Parasite drug resistance is a major obstacle to effective malaria control. Surveillance for parasite drug resistance mutations is becoming an established tool in assessing treatment effectiveness, especially as it overcomes challenges associated with *in vivo* testing. In Madang Province, Papua New Guinea (PNG), conventional treatments such as chloroquine (CQ) and sulfadoxine-pyrimethamine (SP) are associated with increasing failure rates.
Methods: To investigate underlying molecular mechanisms, we used a post-PCR, multiplexed ligase detection reaction-fluorescent microsphere assay (LDR-FMA) to detect single nucleotide polymorphisms (SNPs) in *Plasmodium falciparum* drug resistance genes in 402 field isolates from children with falciparum malaria. This technique enables simultaneous identification of 18 SNPs in *pfcrt*, *pfdhfr*, *pfdhps* and 10 allelic variants in *pfmdr1*. We also assessed associations between drug resistance genotypes and *in vivo* treatment failure rates (PCR-corrected at Day 42) for CQ-SP, artesunate-SP, piperaquine-dihydroartemisinin and artemether-lumefantrine.
Results: There was a high prevalence of multiple mutations across these genes. Eighty-eight percent of the isolates with complete haplotypes were characterised by the quintuple mutation SVMNT+NRNI+KAA+YYSND in the codons 72-76 for *pfcrt*, 51, 59, 108, 164 for *pfdhfr,* 540, 581, 613 for *pfdhps,* and 86, 184, 1034, 1042, 1246 for *pfmdr1*. The presence of the *pfmdr1* 1246Y mutation was associated with treatment failure in all groups combined and in the piperaquine-dihydroartemisinin group (Fisher's exact test, *P*=0.006 and 0.004, respectively). Four isolates also carried the 540E *pfdhps* allele in addition to the quintuple mutation. Of other minor haplotypes, NFSDD was found in four isolates but has been associated with artemether-lumefantrine treatment failure in Africa.
Conclusion: We found fixation of *pfcrt* 76T, *pfdhfr* 59R and 108N and *pfmdr1* mutations (at 92%, 93%, 95% and 91%, respectively), consistent with previous PNG studies. LDR-FMA is cost-effective, enables high-throughput suitable for large-scale epidemiological studies and extends current PCR-based methods. Our findings are consistent with the previous widespread use of 4-aminoquinolines and SP in PNG and support a change to alternative first-line treatment for uncomplicated falciparum malaria. Since introduction of artemether-lumefantrine treatment in PNG is imminent, monitoring changes in the *pfmdr1* gene and the NFSDD haplotype appears a high priority.

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Identification of intestinal parasites from naturally contaminated hands of people living in low socio-economic areas of Dhaka, Bangladesh

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Background: Intestinal parasitic infections are global problem with more than an estimated one billion infected persons mostly in underdeveloped countries. Children are most effected by these infections. This is predominantly due to poor hygienic conditions, low parenteral health education, and absence of safe drinking water. The scientific evidence describing intestinal parasite and bacterial contamination on paper currency from a developing country highlight the role of poor hand hygiene practices promoting dissemination of infectious diseases including intestinal parasitic egg / (oo)cysts. As a part of parasitological survey to assess the intestinal parasites amongst low socio-economic communities of Indian sub-continent stool and hands were analyzed for evidence of parasite eggs / (oo)cysts from children living in slums of Dhaka, Bangladesh.
Methods: A total of 215 stool samples have been analyzed for intestinal parasitic eggs / (oo)cysts using conventional microscopic assay.
Results: The general prevalence in this part of the survey of intestinal parasitic egg / (oo)cysts were 37% (79 positive out of 215 stool samples). Of these 79 stool-positive children, to date hands of 65 were sampled in order to screen for any intestinal parasitic egg / (oo)cyst. Three different types of parasitic egg / cysts were recovered from hands of these children. Amongst the helminths, Ascaris 11%, and Trichuris 1.5% were recovered where as the protozoan parasite, Giardia recovery was 5% of hand samples. Over all, ≥ 17% of the children examined carried intestinal parasitic egg / cysts on their hands and 37% in their stool samples, indicating the perpetuation of fecal-hand-mouth cycle of helminths and protozoan infections in these children. To our knowledge this the first report where intestinal parasites have been recovered from naturally-contaminated hand samples of children.
Conclusion: Our study highlights the need to include proper hand hygiene practices (washing hands with soap and water) including health hygiene educational promotion programs in order to sustain any chemotherapeutic programs. The data being generated in this survey will be presented and its implications on public health will be discussed.

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Training in fever case management and use of malaria rapid diagnostic testing kits improved fever case management in Uganda

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Background: In Africa, there is poor access to diagnostic tests; malaria is typically diagnosed clinically, though presumptive treatment results in significant overuse of antimalarials and delayed treatment of actual causes of fever. The WHO currently recommends antimaralial treatment for only laboratory confirmed malaria. Malaria rapid diagnostic tests (RDTs) may offer a reliable alternative, but effective training for health workers is a key challenge in RDT implementation. We tested the effectiveness of the training on use of RDTS in fever case management.
Methods: Clinicians at peripheral health centers without microscopy in two districts in a low endemic zone in Uganda were trained for two days and immediately followed up in their health facilities to observe performance and offer additional targeted on site training. Training covered clinical evaluation, selection of patients for RDT testing, performing and interpretation of RDT tests and treatment of patients with negative and positive RDT results.
Data on practices in management of patients with suspected malaria before and after the training were collected and compared.Data on out patient consultations for 10 consecutive days in the pre and post training period was compared.
Results: Data revealed appropriate use of RDTs and improved fever case management; there was a reduction in proportion of patients; diagnosed as Malaria [61% to 26% (p=0.000)] amongst the under fives and from 52.3% to 14.5% (p=0.000)amongst adults above 5yrs, prescribed antimalarials from 97% to 80% (p=0.000) among the under fives and from 94% to 86% (p=0.000) among the above 5yrs, with malaria treated with antibiotics among those above 5yrs from 55% to 40% (p=0.000), with malaria given both antimalarials and antibiotics from 63% to 47% (p=0.000) amongst the under fives and from 46% to 29% (p=0.000) amongst those above 5yrs. The training contributed to rational use of antimalarials; the proportion of patients with a negative RDT who received antimalarials in the two facilities 12% compared to 50-70% who receive antimalarials despite a negative blood smear in sites with microscopy.
Conclusion: The training in use of Malaria RDTs in fever case management substantially lead to rational use of antimalarials and antibiotics.