Efficacy of *Ipomea pes-caprae* Ointment as an Add-on Therapy in Patient with Jellyfish Dermatitis

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**Background:** Jellyfish dermatitis is a common skin problem among travelers who expose to seawater. In the tropics, the plant *Ipomea pes-caprae* has been known as an effective herbal treatment for jellyfish dermatitis. However, no clinical trial has been done to prove its efficacy.

**Objective:** To prove the efficacy of *Ipomea pes-caprae* ointment as an add-on therapy in patient with jellyfish dermatitis.

**Material and method:** This was an open label, prospective, test of superiority efficacy trial of *Ipomea pes-caprae* ointment in patient with jellyfish dermatitis. Adult patients with the onset of dermatitis less than 7 days were eligible to the study. The investigator divided the dermatitis area of each patient into two parts (Test and Control). Each patient received standard medical treatment depended on the severity of dermatitis in both areas. *Ipomea pes-caprae* ointment was applied as an add-on only to the “test area”.

Patients were asked to come for follow up 6 times in the 28-days study period. Primary outcome was time to non-active skin lesion while the secondary outcomes were the duration of pain and itching due to jellyfish dermatitis.

**Result:** Forty-eight patients (19 males, 29 females) with jellyfish dermatitis were enrolled in this study. Their median age was 31 years, 72.9% of participants exposed to jellyfish on the day of enrollment. Nearly all patients (89%) received topical steroid, 50% received oral antihistamine while 10% received oral prednisolone as standard treatment. All participants applied *Ipomea pes-caprae* ointment for only test area. Time to non-active skin lesion in test and control area were 5.52 days, 5.93 days, respectively (p=0.057). There was no different in duration of pain between test area and control area (4.15 VS 4.37 days, p=0.192). However, duration of itching in test area was significantly less than the control area (3.30 VS 3.77 days, p=0.04). Overall skin outcomes were recovery without scar (59%), hyperpigmentation(35%) and healing with scar (7%). There was no statistical significant in test and control area.

**Conclusion:** The current result could not demonstrate the efficacy of *Ipomea pes-caprae* ointment in the treatment of jellyfish dermatitis. However, this ointment was effective in reducing the duration itching.
Analysis of the Quality of Web-based Pre-travel Health Advice for Prospective Travellers to High Altitude

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Background: Travel to altitude carries health risks, including the development of potentially fatal high altitude illness. A high degree of self reliance is critical in a wilderness environment and this is particularly so at high elevations, where facilities are often rudimentary and the remoteness of the location may hamper any attempts at rescue of an incapacitated traveller. It is important that individuals who engage in adventure travel to high altitude be fully aware of the dangers inherent in this activity, be familiar with the presentation of high altitude illness, and be prepared to take appropriate action if they or a travelling companion become unwell. There is a responsibility on expedition providers to educate trekkers on the health risks they face. Little has been published about the quality of such advice provided.

Objective: This study aimed to evaluate the health advice given to travellers on websites promoting high altitude treks.

Method: Active websites advertising high altitude treks were identified. Each website was interrogated to extract information relating to the specific advice provided about altitude illness and its prevention. Websites were also examined to determine if prospective trekkers would have access to a portable hyperbaric chamber.

Results: Of 74 eligible websites analysed, 81% referred to altitude travel risks. Seventy percent mentioned acute mountain sickness while 30% discussed high altitude cerebral or pulmonary oedema. Sixty-two percent advised gradual acclimatisation to altitude. Over a third discussed the use of a portable hyperbaric chamber while a quarter of sites provided information about drugs used to manage altitude illness. Forty-two percent invited clients to share their medical history, while 39% stated that an expedition doctor would be available. The overall mean score of the websites (maximum 20) was 9.01, based on an aggregate of the 20 variables examined.

Conclusion: This study yields valuable information about the extent of pre-travel health advice provided by trekking companies to prospective clients. Deficiencies are revealed regarding severe high altitude illness, and access to an expedition doctor and hyperbaric chamber. Companies should make every effort to inform and protect these vulnerable travellers.
Air embolism results from vascular occlusion due to a significant amount of air trapped in a patient’s bloodstream, representing a leading cause of death among SCUBA divers, perioperatively and other patients usually undergoing invasive procedures. Arterial Gas embolism (A.G.E.), leads to Cerebral Gas Embolism (C.G.E), when gas bubbles traverse the blood brain barrier resulting in CVA, Cerebral edema, seizures, and multitudes of focal neurological deficits. Venous Gas embolism (V.G.E), involves air or gas bubbles occluding veins, and is usually non-fatal, unless bubbles gain access to systemic circulation. We elucidate the clinical features, dire consequences and preventive measures of air and arterial gas embolism distinguished by whether ambient air vs. a mixture of pressurized gases is utilized by divers and other patients.

The Pathophysiology, Signs & Symptoms, several diagnostic modalities deployed in rapid triage of this life-threatening constellation of syndromes are reviewed. We explore evidence-based preventive measures and therapeutic modalities, effective forms of supplemental oxygen therapy, proper patient positioning, thereby preventing propagation of air bubbles, through a Patent Foramen Ovale (PFO) which may be present in 27-30 % of the population, potentially resulting in coronary vascular occlusion, Myocardial infarction and dangerous dysrhythmias. Additional ominous clinical consequences of vascular occlusion in the CNS, Kidneys or extremities lead to necrosis and eventual organ failure, without timely triage.

Breath-holding during accelerated rapid ascent after a prolonged deep dive, with a paucity of residual gases remaining and dangerous pressure gradients arising from indiscriminate high altitude air travel shortly before or after diving must be avoided. Meticulous adherence to NAVY Dive tables, compliance with Diver Alert Network (DAN) guidelines must be followed thus ensuring maximal survival rates. A rapid triage sequence is imperative limiting long-term disability, expedient diagnosis, prudent use of diagnostic modalities, without delay of the formidable and measurable benefits of Hyperbaric Oxygen Therapy (HBOT) and facilitation of safe transport to tertiary referral centers, equipped for administering HBOT.
**A Placebo Controlled Pilot Study of Dietary Nitrate as Beetroot Juice, in the Prevention of Traveller's Diarrhoea**

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**Background:** Diarrhoea and gastrointestinal disease are frequent causes of morbidity in travellers to developing countries. Dietary nitrate is absorbed into the circulation through the gut, then concentrated and secreted in saliva. Nitric oxide is generated in the mouth and stomach and an 'entero-salivary' circulation of nitrate undergoes sequential reduction to become nitric oxide in the stomach. The presence of gastric acid and nitric oxide has been shown to be a potent bactericidal combination against most enteric pathogens, including viruses and bacteria.

**Objectives:** A placebo controlled study of beetroot juice containing high levels of nitrate versus nitrate depleted juice in the clinical prevention of traveller's diarrhoea in a cohort of individuals visiting Everest base camp in Nepal.

**Methods:** 40 healthy participants (Aged 14-18) were randomised to either 140mls of beetroot juice containing 8.06 - 9.17 mmol of nitrate or a low nitrate appearance similar drink, daily. Stool frequency, consistency and other abdominal and constitutional symptoms were recorded using a study diary. Main outcomes were diarrhoea attack rate, duration of illness and length of incapacitation.

**Results:** A non-significant difference in attack rate of diarrhoea of 33% and 31% (7 intervention and 6 control) OR of 1.056 in the groups. Odds of having loose stools was 3.2 (CI: 1.2 - 8.7) in the intervention group compared with 1.7 (CI: 0.7 - 4.3) OR of 1.9 ($\chi^2 p=0.369$). There was a 53% reduction in the duration of diarrhoea in the intervention group from 86.5 hours to 40.6 hours (p>0.05) and a mean reduction of 46 hours of diarrhoea. A reduction in the mean number of days lost to diarrhoea in the intervention group was 2.43 days compared to 4.5 days in the control. There was no significant difference in the severity of diarrhoea between either group.

**Conclusion:** Dietary nitrates, through the entero-salivary circulation and symbiotic generation of nitric oxide contribute to the body's innate gastrointestinal defence. Despite not having as clear-cut effect as with antibiotic chemoprophylaxis in this pilot study, nitrates could with further research, be a safely taken dietary prophylaxis against traveller’s diarrhoea, reducing the need for antimicrobial agents.
Norovirus Outbreak at a Resort Hotel - United States Virgin Islands, 2012

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**Background:** Norovirus is highly infectious, environmentally persistent, and the leading cause of acute gastroenteritis outbreaks. On April 17, 2012, CDC was requested to assist in investigating an outbreak of gastrointestinal illness among guests and employees of a resort (Hotel A) in St. Thomas, US Virgin Islands.

**Objectives:** To determine the etiology, describe the extent of the outbreak, and identify the likely source.

**Methods:** Cases were defined as ≥3 episodes of loose stools and/or ≥1 episode of vomiting in 24 hours, in an employee or guest of Hotel A, with onset on or after April 1, 2012. Confirmed cases had a stool sample positive for norovirus by real-time reverse transcription-polymerase chain reaction (RT-qPCR). Employees who met the case definition were interviewed and asked to submit stool samples. Hotel guests were contacted and asked to complete an online survey aimed to identify cases, potential exposures and estimate quality adjusted vacation days (QAVD) lost.

**Results:** Of 20 employees that met the case definition, 18 were interviewed. Eighty-six guests responded to the survey, among which 46 (53%) met the case definition. The first reported illness onset occurred in a hotel employee on April 8, while the first reported onset in a guest occurred on April 13 (figure). An employee suffered a public diarrhea event on April 13 in the central kitchen, followed by illness onset in the next day among employees that assisted with the cleanup. We estimated 59 QAVDs were lost by 43 guests (1.37 days/patient). Using an approximate cost of $450 per vacation day, we estimated indirect illness cost at $616.50 per case. Seven (64%) of 11 stool specimens collected from ill employees tested positive for norovirus, subsequently genotyped as GII.4 Den Haag.

**Conclusions:** Norovirus was identified as the cause of this outbreak, affecting at least 53% of guests of Hotel A. Due to timing of events, illness among employees was suspected as the source of the illness among guests. Ill employees, particularly those working in food service, should be excluded from work for ≥48-72 hours after resolution of symptoms.

**Figure:** Date of illness onset for Hotel A employees (blue) and guests (red)—United States Virgin Islands, 2012.

![Figure]
Enteric Fever in 3 Vaccinated Portuguese Travelers Returning from India


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Introduction: Enteric fever (EF), caused by either Salmonella Typhi or S. Paratyphi, is rarely diagnosed among us. In returning travelers from developing countries the estimated incidence is from 3-30 cases/100,000 travelers. Polysaccharide Typhoid Vi Vaccine efficacy on preventing EF is estimated from 50 to 80%.

Aim: To describe 3 EF cases in vaccinated back-pack travelers returning from India.

Methods: We retrospectively accessed to clinical data of the patients admitted with imported EF, from 1984-2014, selecting those who were previously vaccinated with EF Polysaccharide Vi Vaccine. Demographic, laboratory, clinical and treatment features were analyzed.

Results: From the 7 travelers with EF, the 3 vaccinated for the disease were Portuguese healthy young adults (aged 21-27 years-old) who were also vaccinated for Hepatitis A plus B and have done malaria chemoprophylaxis. They have traveled across India, including rural areas. Cases are depicted on the table.

<table>
<thead>
<tr>
<th>Patient ID</th>
<th>Patient A</th>
<th>Patient B</th>
<th>Patient C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trip’s duration (days)</td>
<td>60</td>
<td>52</td>
<td>210</td>
</tr>
<tr>
<td>Days of symptoms before admission</td>
<td>21</td>
<td>11</td>
<td>4</td>
</tr>
<tr>
<td>Symptoms: Malaise, fever, bloody diarrhea</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Signs: Mucosal dehydration, Cervical-axillary lymph nodes, Abdomen diffusely tender/ Rash</td>
<td>Yes/No</td>
<td>Yes/No</td>
<td>Yes/No</td>
</tr>
<tr>
<td>Hepato/ splenomegaly</td>
<td>No/No</td>
<td>Yes/No</td>
<td>No/Yes</td>
</tr>
<tr>
<td>Blood cultures/Stool cultures</td>
<td>S.Paratyphi a/Negative</td>
<td>S.Paratyphi a/Negative</td>
<td>S.Paratyphi a/Negative</td>
</tr>
<tr>
<td>Widal Test</td>
<td>Negative</td>
<td>1/100</td>
<td>Negative</td>
</tr>
<tr>
<td>Resistance to fluoroquinolones</td>
<td>Susceptible</td>
<td>Susceptible</td>
<td>Resistant</td>
</tr>
<tr>
<td>Treatment</td>
<td>Ceftriaxone+Azytromycin</td>
<td>Ceftriaxone+Azytromycin</td>
<td>Co-trimoxazol</td>
</tr>
</tbody>
</table>

Screening tests for malaria, Q fever, toxoplasma acute infection, and syphilis were negative. Despite transitory hepatitis during Patient A’s stay, the outcome was favorable in all patients.

Conclusions:
1. Enteric fever remains a possible cause of fever in returned travelers, even for those who report having been immunized, as vaccine does not confer protection for S. Paratyphi.
2. Pre-travel advice should always include EF precautions, especially when it comes to young back-pack travelers.
3. Widal test was negative in 2 patients.
4. Resistance to fluoroquinolones was found in one patient.
5. Concerning S.Paratyphi, drug resistance and lack of effective vaccination suggests that this infection may become a concern.
Phenotypic Characterization of Enterotoxigenic Escherichia coli (ETEC) Isolates Obtained from International Travelers with Diarrhea to India and Latin America and a Pediatric Population from USA

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Background: Enterotoxigenic Escherichia coli (ETEC) is the most common bacterial cause of diarrheal disease in children in developing countries and the major cause of diarrhea in travelers from North America and Europe visiting developing countries. ETEC strains produce an antigenic heat-labile enterotoxin (LT) and a poorly antigenic heat stable toxin (ST). LT-based vaccines provide protection against LT-producing strains. ST-producing strains which may outnumber LT-positive ETEC strains require an immune response against the antigenic colonization surface colonization factors (CFs) to prevent infection. An ideal ETEC vaccine combines LT antigens with CFs of prevalent ETEC in the area in which the vaccine is being developed.

Methods: 252 ETEC strains isolated between 2009 and 2012 from adult travelers with diarrhea during visits to Latin America (Mexico and Guatemala) (n=146) and India (n=73) and children with diarrhea studied in a hospital clinic in Houston (n=33) were tested for seven of the most frequently occurring and potentially important CFs among ETEC strains causing diarrhea: CS1, CS2, CS3, CS4, CS5, CS6 and CFA-1 using PCR.

Results: We found that ST was the most common toxin type found in the ETEC isolates studied: Latin America (n=81/146 [55%]), India (n=41/73 [56%]), and United States (n=23/33 [70%]). ST/LT-producing ETEC isolates expressed higher number of CFs compared to LT only or ST only producing strains 54/71 (76%) vs. 15/37 (41%) vs. 44/145 (30%) respectively (p< 0.0001). Of the 219 ETEC strains isolated in Latin America and India 110 (50%) had a detectable CF. In the pediatric patients with ETEC diarrhea in Houston only 3 of 33 (9%) were CS-positive. CS6 was the most frequently occurring colonization factor among the ETEC isolates in our study.

Conclusions: ST-producing ETEC predominate in naturally occurring ETEC strains in two diverse regions of the world complicating vaccine development. The most common CFs found in travelers’ diarrhea cases were CS6, CS1, CS2 and CS3 and should be included in future vaccines being developed. ETEC in the U.S. should be studied to determine their virulence and pathogenicity.
Use of a Bioactive Polyphenol Solution to Treat Acute Infectious Diarrhea in Adults

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**Background:** Acute diarrhea is rarely fatal in adults but can impact quality of life and take away from work, resulting in loss of wages. Treatment with rehydration therapy does not reduce duration of diarrhea and repeated use of antibiotic agents can result in resistance in pathogens.

**Objective:** Assess the efficacy of a novel plant extract to reduce the duration of diarrhea and other abdominal problems.

**Methods:** In a randomized controlled study, adults presenting to a community clinic with acute diarrhea (less than 48 hours) were assigned to study arm (polyphenol solution + oral rehydration solution) or control arm (water + oral rehydration solution). After giving informed consent, patients were given one of the mixtures and monitored in the clinic for 2 hours before being released with instructions to note the time diarrhea ceased and to return to the clinic in 5 days for a follow-up visit. At the same time, patients were asked to rank their abdominal pain and bloating levels on a scale from 0 (none) to 10 (worst possible).

**Results:** A total of 78 patients were enrolled in the study, with 54 in the study arm and 24 in the control arm. The median time to resolution of diarrhea was 2 hours in the study arm versus 73 hours for those in the control arm. When patients returned to the clinic 5 days after entering the study, all in the study arm had diarrhea resolved while 17% of those in the control arm continued to have diarrhea. Mean ranking of abdominal pain was less than 1 for those in the study arm at the end of day 1, while those in the control arm had significantly higher ranking of stomach pain and gas/bloating at the end of day 1 and at day 5.

**Conclusion:** In this randomized study, adults with acute diarrhea returned to formed stools sooner when consuming a bioactive polyphenol solution than if they consumed oral rehydration solution alone. This test solution shows promise as a safe, effective supplement to assist in rapidly improving symptoms of acute infectious diarrhea syndromes.
Probe-free, Rapid and Sensitive Detection of Four Diarrhea-causing Pathogens among Travelers Using Quadriplex RT-PCR Combined High Resolution Melting Analysis

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Background: Diarrhea is a common and frequently encountered disease among travelers worldwide. Though spontaneous cure occurs in approximately four days, some patients may develop irritable bowel syndrome if left untreated. Therefore, rapid and sensitive diagnostic method is needed to help physicians make faster and better treatment decision for those patients.

Objective: To establish a probe-free quadriplex RT-PCR combined high resolution melting analysis (HRMA) assay for the rapid and sensitive detection of four major diarrhea-causing pathogens, including rotavirus, norovirus, astrovirus and sapovirus.

Method: Specific primers and amplification parameters of the probe-free quadriplex RT-PCR as well as the range and ramp of melting temperature in the HRMA were optimized to establish the assay. Specificity and sensitivity of the assay were first analyzed using serial diluted RNA templates and then compared with conventional RT-PCR. Clinical stool samples were used to evaluate the efficacy of the assay.

Results: After several rounds of optimization, the quadriplex RT-PCR combined HRMA assay was established successfully with high specificity and sensitivity. Positive signals were only observed when these four viruses were used as templates while no positive result was obtained when other diarrhea causing pathogens, including Enterovirus 71, Coxsackievirus A16, Vibrio cholerae or Salmonella spp were used as targets. Sensitivity analysis indicated that the lower limit of detection was $10^0$, $10^0$, $10^2$, and $10^3$ copies/reaction for rotavirus, norovirus, astrovirus and sapovirus respectively, which was 1000-fold, 1000-fold, 10-fold and 10-fold more sensitive than conventional RT-PCR. Clinical evaluation showed that the assay was 100% concordant to conventional RT-PCR, indicating the high reliability of the new assay.

Conclusion: To the best of our knowledge, this is the first quadriplex RT-PCR combined HRMA assay established for the detection of four major diarrhea-causing viruses. The assay would provide a valuable platform for the probe-free, rapid and sensitive diagnosis of these pathogens among travelers.
Disseminated Strongyloidiasis Successfully Treated with Parenteral Ivermectine

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Background: Disseminated strongyloidiasis is an imported severe parasitosis. There are no official recommendations regarding treatment.

Methods: We report a disseminated strongyloidiasis case successfully treated with parenteral ivermectine and arteriovenous extracorporeal membrane oxygenation (ECMO).

Results: A 36-year-old female from Benin was admitted for a four month-lasting intense abdominal pain associated with vomiting. Clinical examination revealed a severe undernutrition. There was no eosinophilia. Gastroscopy and colonoscopy showed a diffuse congestive mucosa with ulcers at multiple levels. The patient later developed a myocarditis (confirmed on magnetic resonance imaging) followed by multiple organ dysfunction syndrome and was transferred to the intensive care unit. Digestive tube biopsies and bronchoscopic alveolar lavage revealed Strongyloïdes stercoralis larvae. Due to the severe presentation, the patient received arteriovenous ECMO. A 12 µg/day subcutaneous ivermectine treatment (temporary use authorization) was then administered during seven days, followed by seven days of oral treatment due to a favorable course. Shortly after, she developed Enterococcus faecalis meningitis successfully treated by a 14 day-amoxicilline regimen. Immunodepression screening detected HTLV-1-related chronic leukemia with no treatment indication. Patient relapsed eight months later presenting with epigastric pain and weight loss due to a recurrence of digestive strongyloidiasis. Oral ivermectine then albendazole intake amended symptomatology. Due to the recurring characteristic of this parasitosis, an ivermectine monthly regimen was initiated.

Conclusion: This observation confirmed the severity of HTLV1-related strongyloidiasis. As in our case, parenteral ivermectine (available in France only for temporary use authorization) seems efficacious but there are still no official recommendations regarding treatment course. The role of ECMO which successfully helped our patient to recover has not been defined yet.
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A Diarrhea Outbreak Caused by Norovirus at Sea Aboard a Foreign Passenger Cruise Ship

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**Objective:** To investigate the cause of a diarrhea outbreak aboard "Diamond Princess". A foreign passenger cruise ship for the control of the epidemic.

**Methods:** Dejection samples of the diarrheal cases and relevant food samples were collected. Immune colloidal gold technique was adopted for rapid of potential pathogen of the outbreak. Enzyme-linked immunosorbant assay(ELISA), real-time PCR, and virus nucleic acid sequencing were also used to identify the suspected isolates.

**Results:** Norovirus was detected in all dejection samples and in lettuce samples. The results of nucleic acid sequencing demonstrated that the prevalent strain of the epidemic was GI-norovirus without mutation in nucleotide sequence.

**Conclusion:** The pathogen of the diarrhea outbreak is norovirus. Contaminated lettuce is presumed to be the most possible reason of infection.
Safety Analysis of Chinese-produced Quadrivalent Meningococcal Polysaccharide Vaccine

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Background: In recent years, Y and W135 serogroups of meningococcal were under spot light in the United States, Saudi Arabia and countries all over the world. According to WHO statistic data, the global cases of W135 meningococcal infection were up to hundreds of thousands since 2002, causing more than 2,000 deaths in the world. At present, there is no quadrivalent meningococcal conjugate vaccine licensed in China. Only polysaccharide vaccine is available.

Objective: To evaluate the safety of Chinese-produced Quadrivalent Meningococcal Polysaccharide Vaccine (MPVS4, including A, C, Y and W135 serogroups of polysaccharide: each 50 ug, 0.5 ml/dose).

Methods: Two statistically identical groups were enrolled. The test group of 510 recipients aged 12-40 years old received Chinese-produced MPVS4 vaccine injection. The control group of 510 healthy recipients aged 16-55 years old received excellent Chinese-produced bivalent polysaccharide vaccine. A randomized controlled clinical study was conducted to analyze the safety of Chinese-produced MPVS4 vaccine.

Results: No immediate reactions or severe reactions were observed in both groups. Main local reactions including erythema, swelling and pain lasting 1-2 days at the injection site accounted for 0.98% of the recipients. Fever, the main system reaction, accounted for 3.14% of the recipients. No statistical difference of adverse reaction rate was found between the test group and the control group.

Conclusion: The results indicated that the safety of Chinese-produced Quadrivalent Meningococcal Polysaccharide Vaccine (MPVS4) was excellent. MPVS4, instead of bivalent polysaccharide vaccine, can be recommended to travelers of high risk groups: including pilgrims to Saudi Arabia and students planning to study in the United States (In the United States, most schools require freshmen living on campus to complete quadrivalent meningitis vaccine before enrollment).
Background: Diabetic patients are at increased risk for chronic liver disease and hepatocellular carcinoma, and for hepatitis B. Several countries, including the United States, have issued recommendations to vaccinate adults with diabetes against hepatitis B.

Methods: In a prospective controlled study (NCT01627340), adults with type 2 diabetes and non-diabetic controls matched for age and body mass index (BMI) received three doses of recombinant hepatitis B vaccine (Engerix-B™, GlaxoSmithKline, Belgium). The primary endpoint was anti-HBs seroprotection rate one month after the third dose.

Results: 378 diabetic patients and 189 controls were included in the primary analysis. Seroprotection (anti-HBs antibody level ≥ 10mIU/mL) was observed in 75.4% of type 2 diabetes patients and in 82.0% of controls, with a between group difference of 6.61% (95% CI: -0.70, 13.34). The geometric mean antibody concentrations (GMC) were 147.6 mIU/mL in the diabetic group and 384.2 mIU/mL in controls. Age-stratified seroprotection rates in the diabetic group were 88.5% (20-39 years), 81.2% (40-49 years), 83.2% (50-59 years), and 58.2% (≥60 years). Rates of solicited local and general adverse events and overall safety were similar between groups.

Conclusion: Hepatitis B vaccine is immunogenic, with an acceptable reactogenicity and safety profile, in diabetic patients. In this trial, seroprotection rates were above 80% in subjects aged 20 to 59 years. Since age reduces the likelihood to achieve seroprotection, hepatitis B vaccine should be administered as soon as possible after the diagnosis of diabetes mellitus.
Rapid Responses to Two Bivalent Virus-like Particle Norovirus Vaccine Candidate Formulations in Healthy Adults

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Background: Norovirus is the most common cause of acute gastroenteritis (AGE) around the world, posing a significant public health burden, with high morbidity in all age groups and significant mortality in the very young and older adults. Travellers are frequently exposed to outbreaks of norovirus.

Objective: This randomised, double-blind, placebo-controlled phase II study was performed to assess the safety and immunogenicity of two formulations of adjuvanted bivalent norovirus VLP vaccine candidate in healthy adults (clinicaltrials.gov: NCT02142504).

Methods: A cohort of 454 healthy male and female adults, aged 18-49 years, was enrolled and randomized 1:1:1 to three groups to receive one intramuscular injection of placebo (saline) or candidate vaccine formulations containing either 15µg or 50µg GI.1 genotype VLP and 50µg GII.4 VLP (15/50 and 50/50 antigen-formulations), with 50µg monophosphoryl lipid A and 0.5 mg Al(OH)3 as adjuvants. Immune responses to GI.1 and GII.4 were assessed as serum Pan-Ig, IgA and functional histoblood group antigen (HBGA) blocking antibodies at Days 1, 3, 5, once on 7-10, and 28. Safety and reactogenicity were assessed as solicited and unsolicited adverse events, serious adverse events (SAEs), and adverse events of special interest (AESIs).

Results: Immune responses to vaccination were analysed in 442 subjects according to protocol. High levels of immune response were already achieved at Day 7-10 and persisted through Day 28. Higher immune responses to GII.4 were observed in the 15/50 antigen-formulation compared with the 50/50 antigen-formulation. Reactions were mainly mild to moderate. The most frequent injection site reaction was transient pain, reported by 8%, 65% and 73% of placebo, 15/50, and 50/50 groups, respectively, with other local reactions occurring at ≤ 5%. The most frequent solicited systemic reaction was myalgia, reported by 7%, 21%, and 25% of placebo, 15/50, and 50/50 groups, respectively, with 16.2-17.5% of the three groups reporting headache and fatigue. No vaccine-related SAEs or AESIs were reported.

Conclusions: The two candidate VLP vaccine formulations were well tolerated, with acceptable safety profiles, and elicited robust immune responses 7-10 days after vaccination, with persistence through day 28.
Development of Takeda Vaccine's Candidate Norovirus VLP Vaccine

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**Background:** Noroviruses (NoVs) are the leading cause of acute infectious gastroenteritis worldwide. NoV infection is responsible for high morbidity in all age groups, and fatal outcomes may be observed in at-risk populations such as the very young and older adults especially those with underlying diseases. Outbreaks occur globally, in various settings, but those in travellers, notably on cruise ships or in hotels or restaurants, frequently receive extensive publicity. As NoV are highly infectious and highly resistant to environmental conditions they have multiple routes of transmission including fecal-oral, aerosol, person to person, food-borne and surface contamination, which makes physical prevention measures impractical for travellers.

**Objective:** Of the six NoV genogroups, the most frequent cause of human disease is genogroup II (GII), particularly the GII.4 genotype, followed by genogroup I (GI), which includes the historically first identified Norwalk virus. Takeda Vaccines Inc. is developing a bivalent, adjuvanted candidate norovirus vaccine based on two virus-like particles (VLPs), one from a GI.1 and a second consensus GII.4 sequence derived from three natural GII.4 variants, to potentially induce a broad immune response. NoV vaccine candidates, containing Al(OH)\(_3\) adjuvant, are administered by intramuscular (IM) injection.

**Results:** Investigational vaccine formulations with dosages from 5-150 µg of the two VLPs, with and without monophosphoryl lipid A (MPL), have been evaluated in Phase I and II trials involving over 1100 adults. These trials have shown that candidate vaccine formulations are generally well tolerated with acceptable safety profiles. No vaccine-related SAEs or AESIs have been reported. High and rapid immune responses after one dose have been observed when assessed as total Ig and IgA antibodies, and as functional antibodies with the ability to block histoblood group antigen (HBGA) binding to VLP.

**Conclusions:** The difficulties faced by travellers in avoiding exposure to norovirus infection makes vaccination a practical prophylactic approach. The Takeda Vaccines’ bivalent VLP vaccine candidate formulations are rapidly immunogenic after one dose, with an acceptable safety profile, offering the potential to provide punctual protection for travellers against the leading cause of infectious gastroenteritis.
Background: Vaccination against seasonal influenza (IV) is considered as important measure against related respiratory tract disease, with expected reduction of absence from work. The population of patients in this study consisted of personnel fit for foreign service and travel, with no severe prevailing health conditions, which would exclude an individual from this kind of work. Controversies over mass company immunizations range from proof of benefits to arguments pointing to possible exacerbation of ongoing infections and processes.

Objective: We investigated the overall incidence of acute respiratory tract diseases (RTD) in the following year in a group of vaccinated employees and randomly chosen control group, in respect to other mild chronic health conditions, sex and age in both groups.

Method: A group of employees received inactivated influenza vaccine (IV) types A and B (trivalent, split virion, from the same batch) during the first decade of September 2013 (age range 28 - 70 yrs, mean 50.24, N=100) and were observed and eventually treated for respiratory tract diseases over the following year. The results were compared with control group (age range 28 - 70 yrs, mean 45.61, N=100) of employees remaining under our constant observation.

Results: In the IV group RTD occurred in 15% of healthy pts and in 9% of patients with chronic diseases. Control group developed 22% of RTD in healthy patients and 4% in group with chronic diseases. There was no statistical significance of RTD incidence (binomial regression) in respect to IV (p = 0.987), age (p = 0.014), sex (p = 0.530) nor chronic disease (p = 0.107).

Conclusion: We found no relevant influence of IV on overall incidence of respiratory tract infections, regardless of prevailing health conditions. It is probable though, that population of employees under study is partially resistant due to annual vaccination throughout previous years. The results do not support occupational efficacy of employer-sponsored vaccination against seasonal influenza.
Long Term Immunity 6 Years after Booster Vaccination against Japanese Encephalitis

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Background and Objective: Japanese Encephalitis is a mosquito-borne viral infection. In endemic regions mainly in Southeast Asia, every year about 68,000 clinical cases of Japanese Encephalitis occur. The only internationally available vaccine to prevent from the viral encephalitis is an inactivated whole-cell vaccine containing the strain SA14-14-2. Basic immunization is recommended at day 1 and day 29, followed by a booster vaccination 12 to 24 months later. To date, immunity after the booster dose in adults has been investigated up to 12 months. This study was initiated to assess antibody decline and to predict long-term duration of seroprotection.

Method: A random sample of 70 volunteers from a preceding booster trial (booster given 15 months after the primary series, 45% of originally vaccinated) was invited to the follow up study and 67 (96%) participated approximately 6 years after their booster dose against Japanese Encephalitis. Sera were analyzed using a 50% plaque reduction neutralization test (PRNT50-test). A positive opinion by responsible ethics committees was present and all subjects provided informed consent.

Result: Six years after the last booster dose, geometric mean titer was still 148 (95% CI: 107 to 207), and 96% of the tested subjects had antibody titers above PRNT50 values of 10, the surrogate level of protection according to WHO. Antibody titers generally were lower in subjects aged 50 years and older. Yellow fever vaccination and vaccination against TBE had no significant effects on antibody titers against Japanese Encephalitis.

Conclusion: Long-term protection against Japanese Encephalitis after basic immunization and one booster dose against Japanese Encephalitis up to 6 years could be shown in the majority of subjects. This implies that a second booster may not be necessary for at least 6 years after the first booster.

Conflict of Interest: The study was supported by Valneva, Austria.
PO03.16
Single Visit Intradermal Rabies Vaccination Is Immunogenic

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Background: The current 3-visit intramuscular (IM) rabies pre-exposure vaccination (PrEP) schedule is costly and often hampered by insufficient time between travel clinic visit and departure. Scientific literature provides clues that seroconversion may occur after a single visit rabies vaccination. This dose-finding pilot study provides a proof-of-principle for an ultra-short schedule.

Objective: To determine the optimum dose of purified Vero cell rabies vaccine (PVRV) for inducing seroconversion in all subjects in a single visit. Seroconversion was defined as a rabies virus neutralising antibody (RVNA) titer >0.5 IU/mL determined by Fluorescent Antibody Virus Neutralization test (FAVN).

Methods: 20 healthy rabies-naive volunteers were randomly assigned to 4 study arms for a single visit vaccination: 1x 0.5 mL IM dose (A, control), 1x fractional (0.1 mL) intradermal dose (ID) (B), 2x 0.1 mL ID (C) or 3x 0.1 mL ID (D). Serology was performed 1 month after vaccination.

Interim results: All experimental study arms (B, C, D) reached 100% seroconversion at 1 month after vaccination. In the control arm (A), one subject did not seroconvert (RVNA = 0.5 IU/mL).

<table>
<thead>
<tr>
<th>Study arm description</th>
<th>A 1 dose IM n=5</th>
<th>B 1/5th dose ID n=5</th>
<th>C 2x 1/5th ID n=5</th>
<th>D 3x 1/5th ID n=5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seroprotection (1 month post)</td>
<td>4/5</td>
<td>5/5</td>
<td>5/5</td>
<td>5/5</td>
</tr>
<tr>
<td>Geometric mean titre IU / mL [95% CI]</td>
<td>1.78 [0.88-3.68]</td>
<td>2.95 [1.45-6.00]</td>
<td>6.65 [2.88-15.38]</td>
<td>4.23 [1.38-12.97]</td>
</tr>
</tbody>
</table>

Conclusion: This pilot study provides a strong indication that rabies PrEP can be achieved in a single visit. The intradermal vaccination schedule tested here demonstrated 100% seroconversion 1 month after vaccination. This new schedule should be further investigated in large trials.
Intradermal Meningococcal Vaccination (MEN-ACYW135)

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Background: Vaccination with conjugated purified polysaccharides is generally accepted as the best way to prevent invasive meningococcal disease. But the costs of vaccination are prohibitive in many low-resource settings. Intradermal administration of vaccines has the potential to lower costs through dose reduction without sacrificing efficacy.

Objective: To establish the lowest intradermal dose of conjugated quadrivalent meningococcal vaccine (Menveo® and Nimenrix®) that results in seroprotection for all serotypes in ≥75% of subjects.

Methods: Intradermal dose-escalation study of 12 naïve subjects. Antibody levels were measured using a Luminex multiplex immune assay (MIA) at day 28 after vaccination for all serotypes. Seroprotection was defined as an anti-PS IgG concentration of >2.0 µg/mL, established for serotype C and substituted for the other serotypes. Gold standard serum bactericidal assay (rSBA, protective titer >1:4) will be performed for all serotypes at a later stage.

Preliminary results: Two groups of 4 subjects were vaccinated using a 1/10th dose of either vaccine. Antibody levels (MIA) proved insufficient, so another 4 subjects were enrolled for a 1/5th dose of Nimenrix only because Menveo had become unavailable. After 4-6 months, all 12 subjects were boosted with Nimenrix, using the same fractional dose as received before (Table).

<table>
<thead>
<tr>
<th>Table</th>
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<tbody>
<tr>
<td>Serotype</td>
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<tr>
<td></td>
</tr>
<tr>
<td>A</td>
</tr>
<tr>
<td>C</td>
</tr>
<tr>
<td>Y</td>
</tr>
<tr>
<td>W135</td>
</tr>
</tbody>
</table>

Conclusion: 1/5th ID fractional dose of 4-valent meningococcal vaccine with fractional booster after 4-6 months is effective in inducing protective antibody levels. Initial SBA results for serotype C point to an underestimation of vaccine efficacy in this study.
Immunogenicity of Booster Doses of the Inactivated Polio Vaccine among Japanese Adult Travelers

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Background of the Study: A booster dose(s) of polio vaccine is recommended for adult travelers to polio-endemic or high-risk areas. According to the recommendation by WHO, one dose is given for adults who have previously received three or more doses of OPV or IPV. However, Japanese immunization program has been two doses of OPV, before the IPV introduction in Japan for routine immunization in 2012. Therefore, it is necessary to determine how many booster doses of IPV are required for Japanese adult travelers who have previously received OPV.

Objective: We aimed to evaluate immunogenicity of two booster doses of conventional IPV (cIPV) among Japanese adults previously immunized with OPV.

Method(s): Forty-nine Japanese adults with good general health received two doses of cIPV, 28 days apart. Neutralizing antibody (NT) titers were tested before the first booster dose and on 28 days after each dose. NT titers were Sabin 1, Sabin 2, Sabin 3, Mahoney, MEF-1, Saukett and type 2 vaccine-derived polioviruses (VDPVs; SV3128, SV3130, 11196, and 11198 strains)

Summary of results: Subjects were aged 20-57 years (mean: 36±8.3). Twenty-eight people had twice OPV vaccination history, two people had once, and 19 people were unknown OPV immunization history. The seropositive rates (defined as NT>1:8) were Sabin1(87.8%), Sabin2(93.9%), Sabin3(55.1%), Mahoney(71.4%), MEF-1(91.8%), Saukett(36.7%), and VDPV (SV3128(91.8%), SV3130(91.8%), 11196(91.8%), 11198(89.8%)). The seropositive rates after the first booster dose were Sabin1(96.9%), Sabin2(100%), Sabin3(98.0%), Mahoney(98.0%), MEF-1(100%), Saukett(98.0%), and VDPV (SV3128(100%), SV3130(100%), 11196(100%), 11198(100%). The second booster led to a pronounced increase in NT titers and resulted in 100% of seropositive rates for all poliovirus strains examined.

Conclusions: Two booster doses of cIPV were well tolerated and highly immunogenic among Japanese adult travelers.
We have developed a live attenuated tetravalent dengue vaccine candidate based on an attenuated dengue virus-2 (TDV-2) and three chimeric viruses containing the pre-membrane and envelope genes of DENV-1, -3 and -4 expressed in the context of the attenuated TDV-2 genome (TDV-1, -3, & -4, respectively). This vaccine candidate is currently in phase II clinical trials in humans. Preclinical and clinical characterization of the immune response to this vaccine provides evidence that it stimulates innate immune responses, and elicits a humoral response and T-cell mediated immunity to dengue structural and non-structural proteins. Furthermore, clinical trials in dengue endemic and non-endemic geographic areas demonstrate that the vaccine is generally well-tolerated. A single dose elicits an immune response to all four serotypes, with little improvement when a second dose is given at 90 days. We are currently planning a pivotal phase III study to investigate the efficacy of this vaccine candidate.
PO03.22
Recommendations for Expanded Use of Japanese Encephalitis Vaccine

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No meaningful changes have been made to the ACIP recommendations for JE since 1993. The 1993 recommendations were made while the Mouse Brain (JE-MB) vaccine was the only available option, one which had frequent and often severe side effects. In 2010 when the recommendations were revised, JE-MB was still available for use; however, no JE-MB has been available in the United States since May of 2012. The new Vero Cell culture derived vaccine (JE-VC) was licensed by the FDA in 2009. At the 2010 ACIP meeting only limited safety and efficacy data were available on JE-VC. Five years of data are now available that support the safety and efficacy of JE-VC based on over one million doses being distributed for vaccination in the US. Updated ACIP recommendations for JE-VC vaccine should reflect that the vaccine is safe and effective; it should be considered for all travelers going to known areas of JE virus transmission based on individual exposure risk assessment and a traveler's desire for optimal protection. The 1993 and 2010 recommendations seem precautionary in tone, probably in consideration of the safety profile of the old JE-MB vaccine, and have effectively served to limit use of JE vaccines by suggesting somewhat rigid criteria for vaccine administration. A recent study (Deshpande, et al, 2014) shows that even in the Global TravEpiNet (GTEN) clinics, a sophisticated consortium of expert travel medicine providers (and supported through a cooperative agreement with CDC), only 28% of travelers deemed by current ACIP recommendations to be at high risk received JE vaccination. Approximately 4% of short term travelers in GTEN clinics received JE vaccination. Other studies suggest that among at risk travelers the vaccination rate could be much lower (1% to 11%).

An expert panel met at the 63rd ASTMH Annual Meeting in November 2014 to address the current ACIP recommendations, recent studies and the changes needed. A new set of recommendations will be proposed.
Characterization of an Age-response Relationship to GSK's Recombinant Hepatitis B Vaccine in Healthy Adults: An Integrated Analysis

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¹GSK Vaccines, Wavre, Belgium, ²GSK Pharmaceutical Ltd., Mumbai, India, ³Université Libre de Bruxelles, Brussels, Belgium

Background: Older adults aged 40-80 years demonstrate a reduced response to hepatitis B vaccination. The disease burden is highest in adults aged 25-44 years. However, little is known on when immunogenicity starts to reduce.

Objective: To characterize the age-response relationship to GSK's recombinant hepatitis B vaccine in healthy adults.

Methods: We undertook a pooled analysis of GSK sponsored studies evaluating a 3-dose regimen of 20µg of GSK’s recombinant hepatitis B vaccine (HBV) (eTrack-201931). Studies were selected if: they were completed after 1996; had enrolled healthy adults aged ≥20 years; had administered a 3-dose regimen of 20µg HBV according to a 0-1-6-month schedule; had measured anti-hepatitis-B surface antibodies (anti-HBs) seroprotection rate one month post-dose-3 (protection cut-off ≥10 mIU/mL). The impact of age on seroprotection rate one month post-dose-3 was investigated using a logistic model assuming a linear decrease of the log-odd starting from an age cut-off. The seroprotection rate was tabulated with 95% confidence intervals (CI) according to 5-year age sub-groups.

Results: A total of 2,620 subjects from 11 studies were included; 57.7% were female and 91.8% were Caucasian. The overall seroprotection rate was 94.5% among all subjects. The model showed a statistically significant decrease over the full age range, with the highest anti-HBs seroprotection rates in the 20-24 years sub-group (98.6%; 95% CI: 97.5%-99.3%) and the lowest in the ≥65 years sub-group (64.8%; 95% CI: 50.6%-77.3%) (Table 1). The seroprotection rate, estimated from the model was ≥90% in subjects up to 49 years and >80% up to 60 years.

Conclusion: Our study indicates that the immunogenicity to GSK’s recombinant HBV decreases with age according to a log-linear curve. Seroprotection rate remains above 80% of up to 60 years of age, and hence is beneficial in at-risk populations.
Table 1 Seroprotection rates for anti-HBs antibody concentrations measured one month after the third dose of HBV vaccine, stratified by age (in years)

<table>
<thead>
<tr>
<th>Age groups (years)</th>
<th>N</th>
<th>n (%)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>All subjects</td>
<td>2532</td>
<td>2392 (94.5)</td>
<td>93.5-95.3</td>
</tr>
<tr>
<td>20-24</td>
<td>729</td>
<td>719 (98.6)</td>
<td>97.5-99.3</td>
</tr>
<tr>
<td>25-29</td>
<td>415</td>
<td>401 (96.6)</td>
<td>94.4-98.1</td>
</tr>
<tr>
<td>30-34</td>
<td>263</td>
<td>259 (98.5)</td>
<td>96.2-99.6</td>
</tr>
<tr>
<td>35-39</td>
<td>293</td>
<td>274 (93.5)</td>
<td>90.1-96.1</td>
</tr>
<tr>
<td>40-44</td>
<td>287</td>
<td>271 (94.4)</td>
<td>91.1-96.8</td>
</tr>
<tr>
<td>45-49</td>
<td>254</td>
<td>244 (92.4)</td>
<td>88.5-95.3</td>
</tr>
<tr>
<td>50-54</td>
<td>113</td>
<td>98 (86.7)</td>
<td>79.1-92.4</td>
</tr>
<tr>
<td>55-59</td>
<td>60</td>
<td>48 (80.0)</td>
<td>67.7-89.2</td>
</tr>
<tr>
<td>60-64</td>
<td>54</td>
<td>43 (79.6)</td>
<td>66.5-89.4</td>
</tr>
<tr>
<td>&gt;=65</td>
<td>54</td>
<td>35 (64.8)</td>
<td>50.6-77.3</td>
</tr>
</tbody>
</table>

N=Number of subjects in each category  
n (%)=number (percentage) of subjects with anti-HB-antibody concentration >=10 mIU/mL  
95% CI=exact 95% confidence interval  
Seroprotection rate using the best fit model was calculated as Logit (P)=4.2309+(-0.0704)* age, for ages>20
PO03.04
No Evidence that Advancing Age Reduces Response to GSK’s Inactivated Hepatitis A Vaccine in Healthy Adults

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Background: Hepatitis A is a common vaccine-preventable travel-associated infectious disease. It is therefore recommended that in countries with low hepatitis A virus endemicity, individuals at risk of exposure, such as travellers to endemic countries, should be vaccinated. The immunogenicity and field efficacy of GSK’s inactivated hepatitis A vaccine has been demonstrated in clinical trials, population-impact studies as well as in several outbreak settings. However, limited data has been reported on its immunogenicity in adults aged ≥40 years.

Objective: To assess the immunogenicity and safety of the inactivated hepatitis A vaccine in healthy adults ≥40 years by pooling data from completed studies.

Methods: We pooled and analyzed four double-blind randomized studies in which healthy adults aged above 20 years received 2 vaccine doses (1440EU) 6 to 12 months apart. Controls aged 20-30 years from the same studies were matched to subjects aged ≥40 years based on country and, whenever possible, on gender. Immunogenicity was compared in terms of seropositivity rates and geometric mean concentrations (GMCs). Solicited and unsolicited symptoms during the 4-day and 30-day post-vaccination periods, respectively, were also assessed.

Results: Each group consisted of 80 subjects. The mean age was 47 years in the older group and 24 years in the control group. The seropositivity rates 2 weeks and one month after dose 1 in subjects aged ≥40 years were 79.7% and 97.5%, respectively. Corresponding values in the control group were 92.3% and 97.4%, respectively. One month post-dose 2, all subjects were seropositive in both groups (Table 1). Safety profiles were similar in both groups.

Conclusion: The immune response and safety profiles of GSK’s inactivated hepatitis A vaccine in subjects aged ≥40 years were similar to that in younger matched controls. A more rapid seroconversion may be observed in younger subjects.

<table>
<thead>
<tr>
<th>Group</th>
<th>Timing</th>
<th>n/N (% )</th>
<th>95% CI</th>
<th>Value</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥40 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PI (D15)</td>
<td>59/74 (79.7)</td>
<td>68.8-88.2</td>
<td>126.55</td>
<td>88.61-180.74</td>
<td></td>
</tr>
<tr>
<td>PI (M1)</td>
<td>71/79 (91.5)</td>
<td>91.2-99.7</td>
<td>329.12</td>
<td>254.74-425.21</td>
<td></td>
</tr>
<tr>
<td>PI (M6)</td>
<td>71/80 (88.8)</td>
<td>79.7-94.7</td>
<td>144.24</td>
<td>107.39-193.73</td>
<td></td>
</tr>
<tr>
<td>PIi*</td>
<td>78/78 (100)</td>
<td>95.4-100</td>
<td>2378.95</td>
<td>1848.51-3061.59</td>
<td></td>
</tr>
<tr>
<td>20-30 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PI (D15)</td>
<td>72/78 (92.3)</td>
<td>84.0-97.1</td>
<td>219.45</td>
<td>168.05-286.56</td>
<td></td>
</tr>
<tr>
<td>PI (M1)</td>
<td>76/78 (97.4)</td>
<td>91.0-99.7</td>
<td>469.2</td>
<td>365.23-902.75</td>
<td></td>
</tr>
<tr>
<td>PI (M6)</td>
<td>72/78 (92.3)</td>
<td>84.0-97.1</td>
<td>140.54</td>
<td>110.49-178.77</td>
<td></td>
</tr>
<tr>
<td>PIi*</td>
<td>75/76 (95.3)</td>
<td>95.3-100</td>
<td>4370.94</td>
<td>3535.12-5404.37</td>
<td></td>
</tr>
</tbody>
</table>

GMC = geometric mean concentration
n (%) = number (percentage) of subjects with concentration ≥20 mIU/mL
N = number of subjects with available results
95% CI = 95% confidence interval
PI (D15): blood sample 15 days after vaccine dose-1
PIi: blood sample one month after vaccine dose-2
PI (M1): blood sample 1 month after the vaccine dose-1
PI (M6): blood sample 6 months after vaccine dose-1
PIi*: blood sample one month after vaccine dose-2

[Table]
The Pre Travel Consultation and Gained Vaccination Opportunities at a Travel Medicine Center from Buenos Aires, Argentina

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Background: The pre travel consultation offers a dedicated time to prepare travellers for the health concerns that might arise during their trips. The objectives of the pre travel consultation are: to assess their health, analyze their itineraries, select appropriate vaccination and to provide education about the prevention and self treatment of travel related diseases. It can also be useful to update the adult vaccination schedule.

Objective: To analyze the first 6 years of experience in our travel medicine center and describe pre travel consultation and indicated vaccines.

Method(s): From March 2008 to March 2014 a retrospective and observational research was implemented with the travellers who consulted before travelling. Demographical characteristics, purpose of travelling, destinations, style, duration and indicated vaccines was analyzed.

Results: We assisted a total of 1098 travellers before travelling. Demographical characteristics, purpose of travelling, destinations, style, duration and indicated vaccines was analyzed.

Children < 15 years old 8.5%. None pregnant. Older travellers (>60 years) 19%. Immunocompromised 3%. VFR 3.2%. Interview before travel: 33 days (0 - 240). Purpose of travelling: holidays 79%. Style of travelling: urban-rural 65%. The most common destinations were countries in South America (50%), Asia (25%) and Africa (15%). Travelling to malaria and yellow fever endemic countries represented 38% (421/1098) and 33% (365/1098) respectively. Indicated vaccines: Required: yellow fever 31.5% (346/1098) and 33% (365/1098) respectively. Indicated vaccines: Required: yellow fever 31.5% (346/1098). Recommended: hepatitis A 40% (443/1098), thypoid fever 39% (430/1098), polio vaccine 10% (107/1098), meningococcal 2.6% (29/1098), rabies 1.7% (19/1098). Routine vaccines: tetanus/diphetria (Td) 44% (484/1098), hepatitis B 16% (177/1098), measles/rubella (MR) 3% (32/1098); in older travelers or with risk factors also: influenza 42.5% (46/108) and pneumococcal vaccine 16.6% (18/108). Therefore the national vaccination schedule was updated in 49% (539/1098) of our population.

Conclusions: Most of our travellers were young and healthy people who were travelling for holidays to countries in South America. In almost half of the travellers the national vaccination schedule was updated. We emphasize that a visit to a travel clinic should be considered as an opportunity to bring an incompletely vaccination traveller up to date on his/her routine vaccinations.
Persistence of Antibody Response to Tick-borne Encephalitis Vaccine in Adults 7 Years after the First Booster Dose

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Background: Tick-borne encephalitis (TBE) poses a risk to the travelers in TBE endemic areas. Vaccination is the most effective strategy for TBE prevention and is recommended by the World Health Organization for use in individuals of all ages living in highly endemic areas, and in travelers to these areas planning extensive outdoor activities. While the immunogenicity and safety profiles of primary TBE vaccination schedules have been demonstrated in several clinical studies, relatively little long-term persistence data exist. Recently, an extension study evaluated immunogenicity and antibody persistence 5 years after the first booster dose of a licensed TBE vaccine in healthy adults.

Objective: The present study is the second extension study, evaluating antibody persistence from 6 through to 10 years after the administration of the first TBE booster dose, following 3 licensed primary TBE vaccination schedules.

Method: A total of 205 healthy adult subjects who participated in the previous extension study and who received one of three licensed primary vaccination schedules [Conventional (C), Accelerated Conventional (AC) and Rapid (R)] were enrolled in this study. In this extension study, antibody persistence 6-10 years after the administration of the first TBE booster dose were evaluated by neutralizing antibody (NT) assay, with NT ≥10 considered to be a protective titer. To date, data up to 7 years following booster administration are available.

Results: Percentages of subjects with NT ≥10 seven years after the first booster dose were 100% [95% Confidence Interval (CI): 93%-100%] in Group C, 95% (CI: 89%-98%) in Group AC, and 94% (CI: 83%-99%) in Group R. Geometric mean titers remained high (i.e. NT ≥200) across the vaccination groups 7 years after booster administration (Group C: 343, CI: 216-545; Group AC: 254, CI: 183-354 and Group R: 295, CI:170-510).

Conclusion: Seven years following the first booster dose of TBE vaccine, long-term persistence of protective antibody responses were observed for all three licensed vaccination schedules. The results indicate that the current recommendation of a TBE booster dose after 3 to 5 years could be reassessed (NCT01562444).
Determining Immune Responses to Japanese Encephalitis Vaccination - Comparison of Three Different Serological Methods

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Background and objective: Currently, the plaque-reduction neutralization test (PRNT) is regarded as the standard method for studying the immunogenicity of Japanese encephalitis vaccines. This method is considered reliable, yet laborious and time-consuming. In this study, we explored antibody responses elicited by the inactivated, Vero cell-derived Japanese encephalitis vaccine (JE-VC; trade name Ixiaro). The main aim was to compare the results of the PRNT\textsubscript{50} test to those obtained with a rapid neutralization assay, the rapid fluorescent focus inhibition test (RFFIT). In addition, we studied the vaccine-induced IgG responses using an immunofluorescence assay (IFA).

Methods: The study population comprised 31 Finnish and Swedish travelers who received the JE-VC primary series prior to their trip to Asia. Pre- and post-vaccination sera were tested for presence of antibodies against Japanese encephalitis virus (JEV). The results obtained with the standard PRNT\textsubscript{50} method have been published previously [1]. For the purpose of this study, the sera were analyzed using two additional serological methods: RFFIT and IFA. The tests were performed as previously described [2, 3], with minor modifications. The test strain in the assays was Nakayama, which is heterologous to the vaccine strain (SA14-14-2) but belongs to the same JEV genotype.

Summary of results: The response rates varied depending on the serological method used. When determined with PRNT, neutralizing antibodies (titer \geq 10) were detected in 94\% (29/31) of the subjects after immunization. With RFFIT, neutralizing antibodies (titer 5-10) were detected in only 32\% (10/31), and none of the subjects had a RFFIT titer \geq 20. With IFA, anti-JEV antibodies (titer \geq 10) were detected in 84\% (26/31) of the subjects.

Conclusions: With PRNT and IFA, the antibody response to JE-VC could be demonstrated in the majority of subjects. The rapid neutralization test RFFIT was not comparable to the standard PRNT assay in detecting vaccine-elicited neutralizing antibodies.

References:
Background: There is low production of rabies vaccine worldwide, so countries have made efforts to reduce use of this vaccine, for example by administering only 4 intramuscular or 5 intradermal doses for rabies post-exposure prophylaxis (rPEP). However, in Japan, rabies vaccine is administered in 6 doses subcutaneously (days 0, 3, 7, 14, 30, 90), which is not recommended by the World Health Organization.

Objective: We evaluated features and immunogenicity of rPEP in Japan to reduce the number of vaccine doses.

Methods: We conducted a single-institute, prospective, cross-sectional study from September 2013 to December 2014. We included patients who were exposed to animals in foreign countries and received rPEP at our clinic. Patients who previously received rPEP and those who received rPEP with rabies immunoglobulin were excluded. We administered purified chick embryo cultured rabies vaccine (Kaketsuken, 1.0 mL, lot number RB18 to RB20) (PCEC-K) subcutaneously. Blood tests were performed at patients' first visiting and at the fifth and sixth immunization visits. We measured rabies virus neutralizing antibody response by rapid fluorescent focus inhibition test.

Results: Fifty-nine patients were enrolled, and currently 34 patients’ data (16 men; median age 31 years old) are available. Twenty-four patients (70.6%) did not go to the local hospital in the countries where they were exposed to animals, and 26 patients (76.4%) did not receive rPEP at the appropriate time; the median time to rPEP initiation was 2.5 days after exposure (IQR 1-6 days). The geometric mean titers were 1.98 IU/mL and 1.12 IU/mL on days 30 and 90, respectively. The antibody titer on day 30 for patients who started taking rPEP in foreign countries was significantly higher than that of patients who received PCEC-K only (p = 0.016), but there was no significant difference on day 90 (p = 0.11) (Figure). Seroprotection rates (≥ 0.5 IU/mL) were 88.2% and 76.5% on days 30 and 90, respectively.

Conclusions: Based on these data, it is important to educate Japanese travelers on rPEP, and we should reconsider the method of rPEP administration in Japan.
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**Accelerated 1-Week Vaccination Regimens for Rabies Pre-Exposure and Japanese Encephalitis Prophylaxis**


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**Background:** WHO recommends rabies pre-exposure prophylaxis (PrEP) to those at continual, frequent or increased risk of Rabies exposure; and Japanese encephalitis (JE) vaccination for those planning extensive outdoor exposure during transmission season in endemic countries. Both PrEP and primary JE vaccination series take ~1 month to complete, which may not be feasible for individuals requiring vaccination at short notice.

**Objectives:** Report of a phase 3, randomized, controlled, observer-blind, non-inferiority immunogenicity study of accelerated (1-week) regimens for an inactivated Purified Chick-Embryo Cell Rabies vaccine (PCECV, Novartis Vaccines), and a Vero cell-derived, inactivated, adsorbed JE vaccine (JEV, Valneva) conducted in 661 adults.

**Methods:** Participants were randomized to 1 of 4 groups: conventional Rabies (R-Conv: 3 IM PCECV doses: days 0,7,28); conventional JE (JE-Conv: 2 IM JEV doses: days 0,28); conventional Rabies and conventional JE (R/JE-Conv) or accelerated Rabies and accelerated JE (R/JE-Acc: 3 IM PCECV doses: days 0,3,7; and 2 IM JEV doses: days 0,7). For Rabies, the cut-off for adequate immune response after vaccination was defined as Rabies virus neutralizing antibody (RVNA) concentrations ≥0.5 IU/mL. For JE, protective levels of anti-JE antibodies was defined as Plaque Reduction Neutralization Test (PRNT<sub>50</sub>) titers ≥1:10.

**Results:** Non-inferiority of R/JE-Acc to R-Conv at 7 days post final active vaccination was demonstrated as the lower limit of the 95% CI of the difference was -2.8%. At 1-year follow-up, the percentages of subjects with adequate GMCs ranged from 68% (accelerated regimen) to 80% (conventional rabies). Non-inferiority of R/JE-Acc to JE-Conv at 28 days post final active vaccination was demonstrated as the lower limit of the 95% CI of the difference was -4.8%. At 1-year follow-up, 94%, 86% and 88% of subjects in R/JE-Acc, R/JE-Conv and JE-Conv, respectively, had protective titers.

**Conclusions:** No interference of concomitant accelerated Rabies and JE regimens was observed on short- to mid-term immune responses or safety profile of either vaccine. For both vaccines, immunogenicity was sustained for 1 year after the accelerated regimens. Accelerated, 1-week Rabies and JE regimens, if licensed, could potentially be offered as an alternative to the currently recommended regimens, especially for individuals requiring vaccination on short notice.
PO04.01
Comparison of Different Tests for Chlamydia Trachomatis Screening

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Objective: To compare the value of detecting Chlamydia Trachomatis (CT) from cervical swabs by different tests.

Methods: Cervical swabs were collected from 300 asymptomatic cases and the CT was detected by cell culture, polymerase chain reaction (PCR) and two rapid immunological kits (LAB and QUICK). If cell culture is positive or other two or more methods are positive, it is defined as true positive or “expanding gold standard”.

Results: According to the “expanding gold standard”, there were 46 cases diagnosed with CT infection. The Chlamydia positivity was 11.73% (46/392). The sensitivity of cell culture, PCR, LAB and Quick was 58.70%, 91.30%, 95.65% and 54.37% respectively. The specificities were 100%, 98.84%, 63.29% and 96.80% respectively. The positive predicting value of cell culture, PCR, LAB and Quick was 58.70%, 91.30%, 25.73% and 96.15% respectively. The negative predicting value of cell culture, PCR, LAB and Quick was 94.49%, 98.84%, 99.10% and 94.10% respectively.

Conclusion: Clinical diagnosis of female reproductive CT infection has some limitation by only one method.
Measles, Mumps, Rubella, and Varicella: Using Locally Derived Samples to Determine Differences in Seroprevalence by Birth Cohort

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Background: Even after dramatic reductions in the prevalence of measles, mumps, rubella and varicella in the United States, there continue to be outbreaks of these diseases, stressing the need for ongoing immunization and pre-traveling counseling. Most prior studies of seroprevalence for these viral diseases are often based on national surveillance data. It is therefore important to get a clearer understanding on the local level of immunity so that more focused recommendations can be made for our patient population.

Methods: Leftover, non-duplicate outpatient serum samples obtained in Lehigh Valley Pennsylvania were tested for IgG antibodies using commercially available enzyme immunoassays to mumps, measles, rubella, and varicella. Samples were collected sequentially, and de-identified. Five birth cohorts were created and 460 samples were collected as follows: < 1957 (52), 1957-1966 (109), 1967-1976 (117), 1977-1988 (121), and 1989-1995 (61).

Results: Overall seroprevalence (excluding equivocal results) for measles, mumps, rubella, and varicella were (%): 85.8, 82.8, 96.6, and 97.4. There was a significant association between seroprevalence and birth cohort for measles (p=0.010) and mumps (p=0.037) only. Pairwise comparisons of the cohorts found that for measles there was a significant difference between the < 1957 versus 1967-1976 (p=0.005) cohort and the < 1957 versus 1989-1995 (p=0.001) cohort. Additionally, the overall seroprevalence for our study sample was significantly different than national seroprevalence results for rubella, mumps, and measles.

Conclusion: Our study on local seroprevalence showed dramatically lower immunity rates to measles and mumps than prior national seroprevalence studies have shown. The rates in many of the later birth year cohorts were significantly lower than rates reported necessary to sustain herd immunity. The results of this study show the tremendous value in determining seroprevalence on a local basis. We will use these results to alter our approach to assessing travelers and others in our clinics based on their birth year.

[Bar Chart of Percentage of Birth Cohort Immunity]
Figure 2: Line Chart of Percentage of Birth Cohort Immune to Each Disease (Excluding Equivocal)

<table>
<thead>
<tr>
<th>Disease</th>
<th>LVHN % Immune</th>
<th>US % Immune</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rubella</td>
<td>96.1</td>
<td>89.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Mumps</td>
<td>82.4</td>
<td>90</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Measles</td>
<td>87.2</td>
<td>93</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Table 1: LVHN Overall Seroprevalence by Disease Compared to National Seroprevalence (Excluding 1989 – 1995 Cohort)
Epidemiological Characteristics of Treponema pallidum-infected Travelers at Dalian Port

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Background: As one of first coastal opened cities and important ports at Northeast China, Dalian is closely related to more than 160 countries and regions of the world trade, This was accompanied by frequent personnel exchanges. In this background, sex diseases incidence increased by years. Syphilis is a serious infection with potential to cause severe and life threatening disease. Dalian is suffering a growing syphilis epidemic.

Objective: To analyze the epidemiological characteristics of Treponema pallidum (TP) infected cases among entry-exit travelers at Dalian port, so as to provide scientific advice to strengthen syphilis control and surveillance for international travelers at port.

Method: Blood samples of entry-exit traveller were collected at Dalian ports from 2008 to 2013. TP screening was conducted using enzyme-linked immunosorbent assay (ELISA) and positive samples were confirmed by treponema pallidum particle agglutination assay (TPPA). All of positive cases were carried out by epidemiological survey. Data was analyzed using SPSS20.0.

Results: A total of 343 confirmed TP-infected cases were detected, most of which were sexual transmitted. Based on demographic characteristic analysis, 88.63% of infected cases were in the age range from 20 to 49, 78.13% of which is at a middle-school education levels. As to professional characteristic analysis, TP infection ratio of labor and sailor is higher, which is separately 69.06% and 19.22%. According to the classification of nationality, there are 10 in totals, and 89.50% of them are Chinese.

Conclusion: The prevention and publicity of Syphilis should be enhancing in high risk group of exit-entry travelers at Dalian port. Meanwhile, supervision department should Strengthen law enforcement to reduce imported transmit risk of syphilis.
Reasons for Outpatient Visits by Foreign Travellers to an Urban Hospital in Tokyo

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Background: International travel has increased in recent years, which has in turn increased the number of people visiting outpatient clinics in the countries to which they travel. International travellers face unique challenges regarding communication and culture, and it is important to understand both the medical and the cultural needs of international travellers.

Objectives: The problems that people experience during their stay in Japan have not yet been studied, particularly with regard to patients visiting general medicine departments. In this study, we investigated the reasons for these visits.

Method: We retrospectively reviewed the charts of travellers who visited the Department of General Medicine at Juntendo University Hospital between April 2008 and March 2014. The charts of 71 international travellers were screened for symptoms, diagnoses, and number of hospital visits.

Results: The age range of the study population was 3–78 years; the median age was 35 years. The most common symptom was fever, which was noted in 34 patients (47.8%). Sore throat and cough were noted in 18 (25.3%) and 15 (21.1%) patients, respectively. Other symptoms were as follows: headache, 12 patients (16.9%); abdominal pain, 18 patients (25.3%); chest pain, 5 patients (7.0%); and diarrhea, 9 patients (12.6%). Sixteen patients (22.5%) had upper respiratory infections (URIs), 7 (9.8%) had influenza, and 13 (18.3%) had gastrointestinal infection. The diagnoses for the other patients included arrhythmia, herpes zoster, sepsis, pneumonia, hyperventilation, cellulitis, diverticulitis and pyelonephritis.

Summary of Result: The most frequent reason for medical visits was fever, which was predominantly caused by URIs, gastrointestinal infections, and influenza. We also found a large variation in the diagnosed conditions, indicating the absence of a clinical trend regarding hospital visits.

Conclusion: This study describes the reasons for hospital visits by international travellers who fell ill in Japan and their final diagnoses. The small sample population does not enable a definite conclusion. However, we found that fever-related and non-life threatening problems were the most frequent health issue among international travellers in Japan.
PO04.13
Tuberculosis Infection in Travelers: Screening and Serial Testing with an Interferon Gamma Release Assay in 8431 French Travelers

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Background: Very few data exist on risks of Tuberculosis (TB) in travelers. Since 2013, 8431 travelers visiting our clinic have been screened for TB infection using an Interferon gamma release assay (IGRA) which is a laboratory test detecting immune response to tuberculosis infection. Unlike Tuberculin Skin Test, IGRA is unaffected by BCG vaccination, hence convenient in France where BCG is common.

Objective: We investigated incidence and risk factors for TB infection in travelers.

Methods: Screening for tuberculosis infection was performed using QUANTIFERON TB Gold assay (QFT). Study population comprises business travelers and their family. Some of them are expatriates, some other do short but repeated stays (missions or rotations). Residence location was onshore or offshore. 8431 individuals were evaluated at baseline. 590 persons were tested twice or more within an interval of 6 to 15 months. TB acquisition was detected by conversion from a negative QFT to a positive test result. Definition for conversion is transgression above the cut-off (0.35 IU/ml). In QFT positive individuals, advanced medical assessment and chest X rays were performed to distinguish active TB from latent TB infection.

Results:

- At baseline, 587 (6.9%) individuals were found QFT positive
- QFT positivity was more frequent in regular travelers (previous expatriations, repeated missions or rotations) than in individuals traveling for the first time or sporadically (7.3% versus 3.0%)
- In serial testing, conversion rate was 3.8%
- Travel destination appears to be a major determinant for TB acquisition since all individuals with QFT conversion were returning from endemic regions (50% from Africa, 27.5% Asia, 0% Europe/North America/Australia)
- Sex ratio for the conversion group is 2.7 versus 2.3 in the study population. Mean age is 40 years old versus 30 y.o
- No significant difference in conversion incidence was observed respectively between offshore and onshore stays, repeated short stays and expatriations
- No active TB was detected so far

Conclusions: Regular travelers to endemic areas are at increased risk for TB, regardless their conditions of stay (offshore or onshore, missions, rotations or expatriations). They should be screened for TB infection.
PO04.14
Brucellosis in Israeli Travelers

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Background: Brucellosis, a zoonotic infection caused by human exposure to fluids of infected animals, is considered a worldwide health issue. Consumption of infected milk or food products and occupational exposure are the most significant risk factors. Israel is considered endemic for Brucella, however there is also a large number of travelers who visit developing countries and other regions of the world endemic for the disease.

Objective: To explore the role of travel to endemic countries as a risk factor for brucellosis diagnosed in Israel.

Methods: A retrospective study of all Brucellosis cases among the Jewish-Israeli population, reported to the Israeli Ministry of Health and to Sheba Medical Center between the years 2001-2013 was conducted.

Results: Of 123 reported cases, an epidemiological investigation was performed on 53 cases. In 27 of the 53 cases, a risk factor was identified. Six of these cases (22%) were travel related, whereas 21 cases (78%) were acquired in Israel following food or occupational exposure. In 26 (49%) of the 53 cases, no risk factor was identified. However the standard epidemiological questionnaire in these cases did not include travel history inquiry.

Conclusions: Travel to endemic countries appears to be an important risk factor for brucellosis in the Jewish population of Israel, accounting for 22% of cases where risk factor was identified. In about half of the cases no apparent risk factor was identified, but travel to endemic countries was not sought out. Travel history therefore must be an integral part of an epidemiological investigation, even in endemic countries for brucellosis, such as Israel. Pre-travel consultation must include instruction on the prevention of brucellosis, and travelers should know the importance of avoiding unpasteurized milk products, as well as contact with potentially infected animals.
The Efficacy of Three Novel Tetracyclic Iridoids Isolated from *Morinda lucida* against *Leishmania* spp

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*Leishmania* spp. are parasitic protozoans that cause Leishmaniasis which is characterized by disfigurement, morbidity and mortality. Chemotherapy, the main form of control is undermined by toxic effects of available drugs and emerging drug resistance. The use of traditional medicine to treat infections is very common in Africa. *Morinda lucida*, is one of the popular medicinal plants in West Africa. Although several research groups have reported on *Morinda lucida* to have anti-protozoa (e.g. Trypanosome and *Leishmania*) properties, no compound(s) have been assigned the responsibility for this activity. Our research group first identified novel tetracyclic iridoids, ML-2-2, ML-2-3 and ML-F52, active against trypanosome by *in vitro* assay-guided purification from *Morinda lucida* leaves. This study was therefore aimed at finding their anti-*Leishmania* properties. *In vitro* bioassay was performed using FACS and found that ML-2-2 and ML-F52 possessed anti-*Leishmania* activities with IC50 values of 4.24 µM and 3.38 µM respectively while ML-2-3 had no activity. Immunofluorescence study showed that both ML-2-2 and ML-F52 inhibited cytokinesis and caused short stumpy forms of parasites. The mode of action of ML-2-2 and ML-F52 might be associated with parasites cell cycle, and may be good lead compounds for new chemotherapy against Leishmaniasis.
PO04.16
Novel Compounds Isolated from *Morinda lucida* Crude Extract Show Strong Anti-trypanosomal Activity *in vitro*

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Trypanosomiasis, a devastating disease in Africa, is caused by the kinetoplastid parasite; *Trypanosoma brucei* sp. Due to inefficacy of existing drugs against the late stage of infection, toxicity and parasite resistance issues, development of novel chemotherapy is urgently needed. Africa has a long history of the use of traditional medicinal plants and WHO reports about 80% of people relying on traditional medicines as their first-line treatment. *Morinda lucida*, a famous and one of the main medicinal plants in use in West-Africa, has previously been reported to have anti-trypanosomal activity by several research groups, though active compounds are still unknown. This study identified novel compounds responsible for anti-trypanosomal activity in *Morinda lucida*. Bioassay-guided fractionation and purification of *Morinda lucida* crude extract led to the isolation of 3 novel active compounds, “ML-2-2”, “ML-2-3” and “ML-F52”. They share the same side chain and two of them have same functional group. FACS analysis of the Nexin assay revealed that ML-2-3 and ML-F52 induced apoptosis in *T. b. brucei* (GUTat3.1 strain), whereas ML-2-2 did not. Cell cycle assay with FACS revealed an alteration in the G2/M phase in ML-2-3-treated parasites. Further investigation into the phenotypic and morphological changes in ML-2-2- and ML-2-3-treated trypanosomes by immunohistochemistry showed nuclei fragmentation only in ML-2-3- treated trypanosomes, a classical feature of apoptosis, confirming the Nexin assay results. ML-2-3 and ML-F52, as shown by western blot analysis, suppressed the expression of the flagellar protein, PFR-a, in the parasites, while ML-2-2 did not. Time course experiments show PFR-a suppression to precede apoptosis, which suggests that PFR-a suppression could lead to apoptosis via cell cycle arrest. ML-2-3 and ML-F52, so far show very promising prospects for development of new anti-trypanosomal drugs whilst, ML-2-2 may be investigated for its usefulness for other scientific purpose(s).
PO04.17
Ebola; A Migrating Global Disease

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Background: Ebola, a deadly virus with early cases diagnosed since 1976, yet there is no licensed treatment. Subsequent outbreaks indicate a relatively high case fatality rate of up to 90%. The recent outbreak of Ebola disease which started in West Africa in March 2014 has claimed over 8000 lives as per World Health Organization updates of January 2015. The virus has an incubation period of 2-21 days. Evidence from research indicates fruit bats from *pteropodidae* family to be natural Ebola virus host found in the rainforests. An increase in globalization could facilitate an Ebola outbreak in one country imposing threat to other countries. There are many risk factors and behaviors associated with contacting the virus but a direct contact with a symptomatic patient's bodily fluid is needed in its transmission.

Objective: To analyze characteristics between past and current outbreaks and the impact of the current outbreak on globalization.

Method: A literature review was conducted on all relevant articles published on Ebola since 1976, follow-up updates in the News and relevant websites on infectious diseases. Telephone interviews were also conducted for situational analysis in Liberia.

Results: Predominant differences between outbreaks includes the current outbreak occurring in urban setting with densely populated and facilitated border, with more movement of people and strong cultural practices which differ from previous outbreaks. Low literacy rate, lifestyle and lack of trust were identified as negative impacts in this current outbreak.

Conclusion: The initial case of Ebola occurred in Guinea. It is important to note that all the other outbreaks in Liberia, Sierra Leone, Nigeria, USA, Spain, Mali, and United Kingdom, are all traced from mobilization of people from one location to another. This illustrates the very strong role globalization has upon Ebola virus. Thus, risk communication, social and community mobilizations are essential tools for positive management. An understanding of the differences between past and present outbreaks will provide a better platform for intervention and management. Finally, we propose approaches in managing the risk based on the cultural context and perception. Recommendations that can be carried forward will be made to the public, politicians and policy makers.
Analysis on Surveillance Data of Infectious Disease of Entry-exit Population at Dalian Port

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Background: The infectious disease surveillance to the entry-exit population plays an important role in preventing and controlling the infectious disease to spread internationally. The purpose of infectious disease surveillance is to protect public health safety.

Objective: To provide the scientific evidence for future preventing, controlling and surveilling of infectious diseases, by learning about the status of infectious diseases of entry-exit population at Dalian port.

Methods: The infectious surveillance data of entry-exit population at Dalian port between Jul 2009 and Dec 2010 were analyzed statistically.

Results: The general detectable rate is 2.87% (1,674/57,319) for infectious diseases, of which 1,379 cases were HbsAg positive, 118 cases were Anti-HCV positive, 76 cases were treponema pallidum antibody positive, 70 cases were active pulmonary tuberculosis and 4 cases were Anti-HIV positive.

<table>
<thead>
<tr>
<th>Occupation</th>
<th>Surveillance</th>
<th>HbsAg(+)</th>
<th>Anti-HCV(+)</th>
<th>Treponema pallidum antibody(+)</th>
<th>Active pulmonary tuberculosis</th>
<th>Anti-HIV(+)</th>
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</table>

Conclusion: HbsAg positive cases hold great majority in all infectious diseases. The effective mechanism of preventing and surveilling for infectious diseases should be established to strengthen publicity and education, to enhance self-awareness of prevention and contain the spread of infectious diseases at frontier port.
Lack of Convincing Evidence for the Ebola Reservoirs Candidates

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Background: Ebola is a hemorrhagic deadly virus first appeared since 1976 in Democratic Republic of Congo and Sudan. 2014 marked the most badly and complex Ebola epidemics in the history. Fruit-bats were identified as a potential reservoir harbor the live virus, however, there are also several other animal species which tested seropositive for the virus too. Most of these animals unfortunately lack for a convincing evidence for their role as potential reservoirs.

Objectives: Reservoirs, accidental hosts, and hosts are sometimes used as synonymous to describe the transmission dynamics of infectious diseases, however, the three organisms are different and lead to the confusion especially with the lack of evidences regarding several diseases associated with epidemics. This in turn highlight the request for more concise definition for reservoir hosts of Ebola. This will guide the better understanding of Ebola dynamics and control, and provide more evidence to the possible animal-human jumps inside the potential candidate reservoirs.

Methods: We developed a conceptual framework to identify Ebola reservoirs based on several criteria developed by WHO for other disease systems. These criteria were modified to best adapted with the current understanding of Ebola transmission in West Africa. We also surveyed all studies which include at least a single evidence for the association of animals with Ebola transmission to identify if the role of these animals have a sufficient evidence to be Ebola reservoirs or not.

Results: Results of this study revealed the absence of convincing evidence to the role of several candidate animals as an Ebola reservoir based on the number of criteria we used to identify the reservoir harbor and maintain Ebola infection. However, few studies provided strong evidence for the association of animals in the Ebola transmission dynamics in all epidemics since the first outbreak in 1976.

Conclusion: The study highlight the request for strong evidence of identifying the Ebola reservoirs that allow animal-human jumps. WHO should provide several criteria for identifying animals as Ebola reservoirs based on repeated natural infections, experimental infections, and route of infections in animals to improve the control strategies of disease in Africa.
Management of Imported Cutaneous Larva Migrans: A Case Series

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Background: Cutaneous larva migrans (CLM), a zoonotic helminthiasis imported to Canada by travelers to beach destinations in the tropics, causes morbidity due to severe, intractable pruritus. Treatment in Canada is only available through the Special Access Program (SAP) of Health Canada, thus, many patients are prescribed ineffective courses of non-targeted therapy.

Objective: We analyzed the proportion of patients with CLM referred to our specialized Tropical Disease Unit (TDU) having failed non-targeted therapy prior to referral, and characterized the demographic and travel-related factors associated with CLM.

Methods: Patients with CLM seen in the TDU from June 2012 through December 2014 were identified through our SAP application log, and charts were reviewed. Demographic, clinical, and travel-related data were extracted and analyzed following institutional review board approval.

Results: 25 patients with CLM were identified through our SAP log: 12 women, and 13 men. Median age was 35 years (range 4 to 58 years). Patients had primarily acquired their CLM in the Caribbean (80%), with Jamaica being the most well-represented source destination (N=10, 40%). Reported symptoms included intense, function-limiting pruritus (N=25, 100%) and loss of sleep (N=3, 12%). Twelve patients (48%) with CLM had received at least 1 course of non-targeted therapy prior to referral. This included 7 patients who had received topical steroids, 3 patients who had undergone cryotherapy, 2 who had received oral antibiotics, and 11 who had received oral mebendazole. Prior to referral, the median number of physician encounters per CLM patient was 1 (range 1 to 5). Median duration of symptoms was 34 days (range 5 to 226 days). Of the 25 patients with CLM, 23 (92%) were prescribed a single 3-day course of albendazole and responded appropriately, and 2 (8%) required a second 3-day course of albendazole.

Conclusions: Although CLM is non-communicable and of little public health relevance in Canada, it causes significant morbidity. A substantial proportion of patients with CLM referred to our specialized TDU had a prolonged course of illness and were prescribed ineffective and non-targeted therapies. Albendazole or ivermectin are the drugs of choice for CLM, and should be prescribed as first-line therapy.
The Efficacy of Albendazole against Soil Transmitted Helminths and the Impact of Mass Drug Administration of Albendazole and Ivermectin on Health Status of School Children and Pregnant Women

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Background: The lymphatic filariasis (LF) control programme has been on-going in Ghana since 2000 with mass drug administration (MDA) of ivermectin (IVM) and albendazole (ALB). Soil-transmitted helminth (STH) infections control is augmented within this programme. Therefore this study aimed to determine the efficacy of ALB against STH infections and impact of MDA on study participants.

Method: A total of 783 subjects including school children (between the ages of 2-17 years) and pregnant women were randomly selected from four endemic communities in Kpandai district of the Northern region. Coprological assessment for parasites was based on the Kato-Katz technique in both dry and rainy seasons. The body mass index (BMI) and haemoglobin (Hb) levels were assessed using the stadiometer and Hb meter with lancet and blood strip.

Results: Of all the parasites found (Hookworm, Trichuris trichiura, Hymenolepis nana, and Taenia sp.); hookworm was the most prevalent. In the dry season, the overall STHs prevalence at pre-treatment was 29%, while 9% and 13% prevalence was recorded at 21 days, and three months respectively after ALB treatment. However, in the rainy season, the overall STHs prevalence was 8%, while 4% and 12% was recorded at 21 days and three months respectively after ALB treatment. In general, ALB treatment resulted in an overall hookworm egg count reduction rate of 89% in the dry season and 93% in the rainy season, while the T. trichiura egg count reduction rate was 100% in both seasons. We also observed a significant improvement in BMI and Hb levels following two rounds of ALB treatment (p< 0.05) among the study participants.

Conclusion: Hookworm infection seems to respond poorly or sub-optimally to ALB, raising concerns of possible emergence of resistance which may lead to a major setback for the control and elimination of STH infections, especially hookworm infections. Parasitic samples are being analyse to identify polymorphism related to ALB resistance.
A Potential role of *Tetrahymena* Ciliates in the Transmission of Legionnaires' Disease

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**Background:** Legionnaires' disease (LD) is an atypical pneumonia caused by the Gram-negative bacterium, *Legionella pneumophila*. *L. pneumophila* replicates intracellularly in amoebae in freshwater environments, and then accidentally infects susceptible humans. In contrast to most respiratory diseases, LD is not transmitted from person to person. *L. pneumophila* has a developmental cycle that alternates between replicative forms and resilient, metabolically dormant mature infectious forms (MIFs), which are thought to be responsible for the transmission of LD. We have previously shown that MIFs are poorly produced inside human macrophages and that *L. pneumophila* progeny from human macrophages is less fit and infectious than its progeny from amoebae. *Tetrahymena* ciliates also inhabit freshwater environments. They do not support the intracellular replication of *L. pneumophila* but rather package legionellae into pellets. The role of legionellae-laden pellets has not been yet identified.

**Objective(s):** We set out to test the hypothesis that legionellae-laden pellets could be infectious to protozoa (in natural water environments) and to susceptible humans and therefore may play a role in the transmission of LD.

**Method(s):** Legionellae-laden pellets from the ciliate *Tetrahymena tropicalis* were compared to *L. pneumophila* progenies from the amoeba *Acanthamoeba castellanii* and U937-derived human macrophages with respect to morphology (electron microscopy), resistance to antibiotics, and infectivity (plaque assay and fluorescence-based assays).

**Results:** Pellets of MIFs produced in *Tetrahymena* ciliates demonstrated similar levels of morphological differentiation, higher resistance to ciprofloxacin (used to treat LD) and higher infectivity to L929 cell model when compared to the *L. pneumophila* progeny obtained from amoebae. They both demonstrated comparable infectivity levels to monolayers of amoebae and human macrophages.

**Conclusion:** *L. pneumophila* pellets produced in *Tetrahymena* ciliates provide some fitness and infectivity advantages. *Tetrahymena* ciliates may play an important, and previously unrecognized role, in the life cycle of *L. pneumophila* and in the transmission of LD, acting as ‘packagers’ of MIFs. These findings may further explain, at least in part, why LD is not communicable.
Two Hemorrhagic Viruses Coexist: Ebola and Lassa Fever Case in West Africa

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Background: Ebola and Lassa virus share similar clinical features of hemorrhagic fever in human cases. Ebola was known only in Central African basin and Philippines since 1976; on the other hand, Lassa virus occurred only in West Africa since 1969. The geographic patterns of the two viruses was different; however, the 2013-2014 outbreak raised the concerns for the possibility of the overlap of the two viruses' niches.

Objectives: This report was interested to a more updated version of risk mapping to the potential distribution of two hemorrhagic viruses occurred in Africa. We were also enthusiastic to test the possibility of overlap in the geographic, and environmental dimensions for the two viruses to avoid misdiagnosing the etiological agent when clinical features is the only available diagnostic regime.

Methods: Lassa and Ebola occurrences were reviewed from all outbreaks between 1976-2014. To estimate the grinnellian ecological niche for each of the virus species, we used Land Surface Temperature (LST) and Normalized Difference Vegetation Index, and aridity Index. These data provide high-resolution imagery of $\approx$ 1km spatial resolution for 2000-2014. Principal components analysis (PCA) was carried out for all environmental variables in the SDMtoolbox available for ArcGIS 10.2. We selected the first PCAs that explained 95\% of the cumulative proportion of the variance for the analysis. We finally estimated the ecological niches of both viruses using the maximum entropy approach implemented in Maxent version 3.3.3. Background Similarity test was performed to test the possible overlap of the two viruses' niches.

Results: The models developed in the current study revealed the areas of the higher risk in the African continent including both Central Africa and West Africa. The results of the background test cannot reject the null hypothesis of the niche similarity for both virus species.

Conclusion: The results raised the concerns for the coexistence of two hemorrhagic fever in the same geographic and environmental dimensions. This make the diagnosis of these viruses to be more complex when clinical features is the only implemented diagnostic tool. Development of sensitive tools of diagnosis should be considered in the areas of epidemics where both species coexist.
PO04.23
Imported Systemic Helminthic Infections in a Tertiary Care Centre in the Czech Republic

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Background: The aim of this study was to describe the clinical and epidemiological characteristics of imported systemic helminthic infections diagnosed and treated in a centre for tropical diseases in the Czech Republic.

Methods: Retrospective study analysed schistosomiasis, echinococcosis, filariasis, onchocerciasis and cysticerciasis cases managed at the Department of Infectious Diseases, Hospital Na Bulovce in Prague.

Results: During 2003-2014 there have been investigated at our department 17 patients with schistosomiasis, 10 patients with cystic echinococcosis (CE), 3 patients with strongyloidiasis and one patient with lymphatic filariasis, onchocerciasis and neurocysticerciasis. Schistosomiasis is the most common systemic helminthosis imported to the Czech Republic. All our patients except one (Indonesia) visited or lived in sub-Saharan Africa. Six patients presented with systemic febrile illness (Katayama fever), five with intestinal schistosomiasis, four with urinary schistosomiasis, two with eosinophilia, positive serology and history of contact with freshwater in endemic region. All our patients were treated with praziquantel. Eight of ten CE cases were diagnosed in migrants from endemic countries: Bulgaria (2x), Romania, Russia, Kazakhstan, Montenegro, Tajikistan, and Uzbekistan. The CE cysts have been identified in liver in 7 patients, in lungs only in 1 case. There is one patient in the long-term follow up at our department with prolong hypereosinophilia and probable lymphatic filariasis after visiting West Irian in 2007. Imported onchocerciasis was diagnosed in traveler to Cameroon and neurocysticerciasis in 6-year old boy living with parents in India for 4 years.

Conclusion: Tissue helminthic infections are chronic diseases with low mortality but substantial morbidity and long-term sequel. The acute stage of these infections may be connected with the systemic immune reaction based on immune complex production and presented as fever, rigor, headache, muscle and joint pain, cough, chest pain, rash and high eosinophilia. They represent infrequent infections and need specialized diagnostics and treatment. Systemic helminthic infections are recognized as an important health problem as increasing number of Czech tourists and workers travel to epidemiological risky regions in tropics.
Rapid Differentiation of Filariae in Unstain and Stain-paraffin-embedded Sections by a HRM-PCR Assay

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Background of the Study: Apart from infection with human filariae, zoonotic filariasis also occurs worldwide and the numbers of cases have steadily increased. Diagnosis of some intact filariae in tissue or organ depends on histological identification. The morphology of parasites in tissue embedded section is very impoverished, and shows high levels of homoplasy. Thus the use of morphological characters in taxonomic studies difficult and may not allow a specific diagnosis.

Objectives:
1) to determine whether HRM-PCR can be a useful method for identify and differentiate filarial infection in FFPE specimens;
2) to gain a rapid paraffin removal, we developed a quick paraffin removal technique and compare with standard paraffin removal technique;
3) to test the interference of H&E in DNA extraction by compare with the unstained FFPE specimen.

Methods: This study applied a real-time PCR with high resolution melting analysis (HRM) to detect and identify B. malayi, B. pahangi, D. immitis and W. bancrofti in paraffin embedded sections. Specificity of the assay was studied using other tissue dwelling parasites i.e. Angiostrongylus cantonensis, Gnathostoma spinigerum and Cysticercus cellulosae. We also developed a quick paraffin-removal protocol.

Summary of Results: Both human and animal filarial in formalin-fixed paraffin-embedded sections (FFPES) could be rapidly diagnosed and identified whereas the other parasites show negative result. Tm of amplified products of filarial DNA from the unstained FFPES and the H&E stained sections revealed no difference. It is indicated that the DNA extraction protocols presented in this study could be used for a real time PCR with HRM.

In Conclusion: We report the successful application of a HRM-PCR assay to differentiate 4 filarial parasites in FFPES, thus providing the pathologist with an alternatively effective diagnostic procedure. Further, a quick paraffin removal protocol developed here could shorten time and step of the paraffin removal using standard protocol.
A Comparison of Various Methods on the Detection and Genetic Tracing of *Vibrio cholerae*

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**Background:** Till now, cholera remains a global threat to public health, especially for people living in or travelling to developing countries with poor hygiene. As cholera has the potential to cause death from severe dehydration, rapid and sensitive detection and genetic tracing method is needed to help physicians make faster and better treatment decision for those patients.

**Objective:** To optimize and establish detection and genetic tracing methods for *Vibrio cholerae* and make a head-to-head comparison to find out the best approach.

**Method:** Amplification parameters (including primers' sequences and concentrations, cycling conditions) of the modified inter simple sequence repeat-polymerase chain reaction (MISSR-PCR), enterobacterial repetitive intergenic consensus sequences-based PCR (ERIC-PCR), randomly amplified polymorphic DNA (RAPD) and 16S rRNA evolutionary clock, were optimized for several rounds to establish these methods. Head-to-head comparison study was then conducted between MISSR-PCR and three other methods for the detection and genetic tracing of *Vibrio cholerae* isolated from China.

**Results:** After optimization, these four genotyping methods were established successfully. Comparison study indicated that the MISSR-PCR system could generate the highest polymorphic fingerprinting map in a single round PCR and showed the best discriminatory ability for *Vibrio cholerae* genotyping by clearly separating toxigenic/nontoxigenic strains, local/foreign strains, and O1/O139/non-O1/non-O139 serogroup strains, comparing to ERIC-PCR, RAPD and 16S rRNA evolutionary clock. Moreover, the MISSR-PCR is better than previous described traditional simple sequence repeat based PCR method on genotyping by more clearly separating different clusters.

**Conclusion:** This first head-to-head comparison study of four detection and genotyping methods for *Vibrio cholerae* indicates that the MISSR-PCR system is the superior one. Therefore, the MISSR-PCR system could serve as a simple, quick, reliable and cost-effective tool for genotyping and epidemiological study of *Vibrio cholerae*. 
Background: There are several hundred infectious diseases that are important to travel medicine physicians. A well-designed relational database of this complex information could be useful as a decision-support system. Such a system could help the physician to drill down from the categories and to run queries to find all matching diagnoses.

Objective: The objective is to identify the key requirements of a global infectious disease decision-support system to help physicians find the specific information they need when they need it.

Method: The key requirements were identified as follows:

- Microsoft Access, a relational database, will be used to build the system.
- The database will include four linked tables: diseases, findings, high-risk job tasks, and jobs.
- The diseases in the database will be roughly the same as those in Control of Communicable Diseases Manual (CCDM).
- The sources of all facts in the database will be cited.
- The 12 main sources of information will be CCDM, ABX Guide (Johns Hopkins), The Yellow Book (CDC), Cecil Medicine, Tropical Infectious Diseases (Guerrant), Harrison’s Infectious Diseases, Principles and Practice of Infectious Diseases (Mandell), and five other references.
- Updating will be based mainly on new editions of the 12 sources, but also on new information from CDC and WHO websites.

Results: Physicians can query the database for all diseases matching one or more criteria: signs & symptoms, occupation, region of the world, incubation period, and epidemiological factors such as mode of entry, source, vector, and reservoir. The results of a query become a differential diagnosis list based on the criteria of the query. For example, the user can find that 8 of 249 diseases match the criteria of “jaundice” and “ticks.” The database contains 105 signs & symptoms in ten categories and 249 diseases in 15 categories. The database also includes 94 jobs, 16 regions of the world, 7 incubation periods, and 39 epidemiological factors.

Conclusion: Infectious disease information can be collected and indexed into a relational database to help practitioners quickly build differential diagnoses and find details about specific diseases.
The Rate of HIV-Malaria Co-Infection Depends on the Prevalence of HIV Infection in a Community

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Background: Today, human immunodeficiency virus (HIV) and malaria are the most prevalent diseases, with the highest mortality, in Cameroon and many other developing countries. Very little is known about the rate of malaria infection in HIV patients and the rate among pregnant women and the general population, which compromises proper planning, prevention, resource allocation and control activities.

Objectives: The aim of this study was to determine the rate of malaria infection in HIV patients and its correlation with the rate HIV infection in pregnant women attending antenatal care (ANC) in North Western region of Cameroon. This study hopes to set a platform for better management of these diseases in this patient population.

Methods: All malaria patients and pregnant women attending health institutions for malaria diagnosis and treatment as well as ANC were consecutively enrolled in 2012 - 2013. Malaria diagnosis, treatment and HIV testing were done according to the national guidelines. Blood samples were collected from anonymous HIV testing. We used univariate and multivariate logistic regression analysis to determine the risk factors for HIV infection and linear regression analysis to determine the correlation between HIV infection in malaria patients and pregnant women.

Results: Of the 1308 malaria patients enrolled, 226 (18%) (95%CI:15.8-20.0) were HIV positive. The rate of HIV infection was higher in malaria patients from urban 25% (73/298) than rural areas 16% (149/945) [AOR = 1.78, 95%CI: 1.27-2.48]. Of the 4199 pregnant women attending ANC, 155 (3.8%) [95%CI: 3.2-4.4] were HIV positive. The rate of HIV infection was higher in pregnant women from urban (7.5%) (80/1066) than rural areas (2.5%) (75/3025) [OR = 3.19, 95% CI: 2.31-4.41]. In the study participants attending the same health institutions, the rate of HIV infection in pregnant women correlated with the rate of HIV infection in malaria patients (R² = 0.732).

Conclusion: The rate of HIV infection in malaria patients and pregnant women was higher in study participants from urban areas. The rate of HIV infection in malaria patients was associated with the prevalence of HIV infection in pregnant women attending ANC.
Identification of Leptospiral Low Molecular Weight Membrane Proteins for Early Diagnosis of Leptospirosis

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**Background:** Leptospirosis is one of the most widespread zoonoses worldwide. Laboratory testing of leptospiral infections is important for accurate diagnosis of leptospirosis. Moreover, early diagnosis is particularly important for the clinical management of the patients with undifferentiated febrile illness syndromes.

**Objective:** To identify and characterize low molecular weight membrane proteins from pathogenic *Leptospira* strains for early diagnosis of leptospirosis.

**Method:** Outer membrane (OM) components from pathogenic *Leptospira interrogans* serovar Autumnalis were extracted by alkaline plasmolysis buffer followed by sucrose gradient ultracentrifugation. Each pooled fraction of 5 orderly fractions was prepared. Protein, lipopolysaccharide (LPS) and lipid in pooled fractions were tested by coomassie brilliant blue, LPS staining kit and Sudan Black B staining, respectively. Immunoreactive membrane components were detected by using one dimensional SDS-PAGE coupled with immunoblotting with acute-phase serum samples from leptospirosis patients.

**Results:** Protein bands in pooled fractions 1, 2, 5, 6, 7, and 8 were detectable. The protein bands were observed at MW of 11, 16, 17, 18, 20, 25, 35, 41, 59, 69 and 75 kDa. LPS bands were MW of 9, 13, 18, 22 and 65 kDa, Lipid band could not be detected. Interestingly, specific immunoreactive bands were detected in only pooled fraction 2 (fractions 6 to 10). The pooled fraction 2 from 6 *Leptospira interrogans* serovars Autumnalis, Bataviae, Bratislava, Copenhegeni, Australis and Patoc were characterized for immunoreactive activity by immunoblotting with rabbit polyclonal antibody against serovar Autumnalis. The results showed that the low-MW antigens showing strong immunoreaction were the 18 kDa bands found in two types, a discrete protein band and a diffuse LPS band, 20 kDa protein and 25 kDa protein. In pooled fraction 2, IgM immunoreactivity with the serum samples at early phase from leptospirosis patients were tested. IgM antibody could react with the low-MW antigens at the 18 kDa LPS/protein, the 20 kDa protein and 25 kDa protein. However, the results clearly indicated that the reacted antigens in all serum samples were proteins at MW of 25 kDa.

**Conclusion:** The identified 25 kDa immunogenic protein can be used as antigen for early serodiagnosis of leptospirosis.
Correlation Analysis and Epidemiological Surveillance of Anti-HCV, ALT and HCV-RNA of Entry Foreigners in China

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Objective: To monitor the prevalence and epidemic of HCV (Hepatitis C virus) among the entry foreigners, and also to investigate the relationship between Anti-HCV, HCV-RNA (Ribonucleic Acid) loads and the levels of ALT (Alanine aminotransferase), detect the HCV infections more effectively.

Methods: The epidemiological surveillance of the HCV infection who were monitored through Sichuan ITHC in entry foreigners were analyzed. From 2010 to 2012, 235 positive Anti-HCV samples were collected from Guangdong, Shenzhen, Yunnan, Sichuan and Liaoning International Travel Healthcare Center (ITHC). Anti-HCV were retested by ELISA in Sichuan ITHC, the loads of HCV-RNA were detected by PCR (Polymerase Chain Reaction) and the datas of ALT value were collected from these ITHC. The datas were analyzed by SAS 9.13 (Statistics Analysis System).

Results: Anti-HCV positive rate was 2.8‰ at Sichuan port in entry foreigners, 51～60 age group, overseas students were on the highest risk. 131 samples showed HCV-RNA positive (56.7%) in 231 samples which were anti-HCV positive. 89 samples showed the level of ALT was abnormal in HCV-RNA positive cases. Both the abnormal rate of ALT and the average of ALT value increased with the HCV-RNA load increased.

Conclusion: The methodological sensitivity, the period of HCV infection and the application of antiviral drugs affected the positive rate of HCV-RNA significantly. HCV-RNA loads and ALT levels showed significantly correlation. The HCV surveillance should focus on 51～60 age group and overseas students.
Genotype Study on Hepatitis C among Entry Foreigners in China

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Objective: To monitor the genotype and subgenotype of hepatitis C among the entry foreigners. To identify the new genotype and trace the transmission.

Methods: From 2009 to 2013, 235 positive Anti-HCV (Hepatitis C virus) samples were collected from Sichuan, Liaoning, Guangdong, Shenzhen and Yunnan ITHC (International travel healthcare center). Using specific PCR (Polymerase Chain Reaction) primers to amplify the HCVCore, then PCR products were sequenced by genetic analyzer. The genotypes were identified by alignment to the Genbank reference sequences and construction of the phylogenetic tree of Core.

Results: 129 samples showed HCV-RNA (Ribonucleic Acid) positive (54.9%) in 235 samples which were anti-HCV positive. We detected six kinds of genotypes in 115 sequencing successfully. Genotype 1 (G1) accounted for 62.6% of all HCV infections among entry foreigners making it the most common, followed by G3 (18.2%), G2 (9.6%), G4 (6%), G6 (2.6%) and G5 (0.9%). Genotype 1b was the most common sub-type, accounting for 47% of all infections. The phylogenetic tree indicate the HCV 4 strains in entry foreigners closed with that in Egypt and Europe, while HCV 6 strains closed with that in China.

Conclusion: HCV 1b was the advantage of popular genotype in HCV carriers. Subtype 4 will be the possible new genotype transmitted into China. The entry foreigners might be the sources of new genotype of HCV.
Background: A company which has globalized their business has to pay attention to the health condition of the employees overseas especially in developing and rising countries because of increased risk of diseases.

Objective: Many employees overseas in developing and rising countries will face the difficulty to handle the issue regarding the work and daily life. Some of them might develop diseases in mentally or physically. We take care of our company's employees overseas to reduce the incidence of various diseases through pre, during and post travel.

Method: On pre-travel clinic, we administer the appropriate vaccines to the employees and provide updated medical information on their destination. During their stay overseas, we accept electric mail and a call regarding health problems from them and treat those. The company doctor who is in charge of travel clinic for them has regular visit to India once a year.

Result: More than 60% of the visitors in our travel clinic are our company's employees. India to which our company sends many employees occupied 52% of visitors' destination. We have administered vaccines against hepatitis A, hepatitis B, tetanus, Japanese encephalitis, rabies and typhoid fever to the employees leaving for India. The company doctor who is in charge of travel clinic has visited various places in India including 19 medical facilities, 7 thermal power plants and 8 residences to support the employees in medical aspect. As the post travel clinic we have experienced traveler's diarrhea, dengue fever and surgical diseases.

Conclusion: A company has the responsibility for the health management for the employees overseas and has to provide considerable information on daily life, security, medical situation and so on to the employees overseas especially in developing and rising countries. Not only pre-travel care, but also during travel care as regular visit by medical staff and strengthening post travel clinic are needed to maintain employees’ health. First of all, we initiated medical support for the employees overseas in India three years ago. We expect to continue these support for the employees overseas in India and also in other countries.
Travel-associated Infectious Diseases in Long-term Expatriates to Africa: Surveillance Analysis from Sichuan International Travel Healthcare Center in 2014

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Background: Each year, almost 20,000 expatriates are dispatched to underdeveloped countries from Sichuan Province located in southwest China, and 90% of the destinations are in Africa. Since 2008, imported malaria has posed a real challenge to local public health safety as the indigenous cases are under elimination.

Methods: To investigate the spectrum of travel-related infectious diseases in long-term expatriates to Africa, we conducted a retrospective study in returned expatriates who came to our center spontaneously, symptomatic or asymptomatic. Between January and December in 2014, through a series of questionnaires and specific laboratory tests, a general situation concerning demographic, clinical characteristics was gained.

Results: During the study period, 192 returned expatriates presented to our center, 31 (16.1%) of whom were symptomatic on site. The duration of stay in destination countries ranged from 7 to 81 months with the average time of 27 months. 81 (42.2%) expatriates were diagnosed as travel-related infectious diseases when they were in destination countries, and the spectrum of diseases included malaria (n=75[92.5%]), dengue fever (n=3[3.7%]), typhoid fever (n=2[2.5%]), filariasis (n=1[1.2%]) and unknown insect-bite induced skin lesions (n=2[2.5%]). Among 75 cases of malaria, 53.3% were confirmed by laboratory tests but without evidence of plasmodium type. The number of malaria attacks varied from 1 time to 5 times but could not distinguish relapse from recrudescence. 3 (3.7%) expatriates suffered from two kinds of diseases, which were malaria with dengue fever, malaria with typhoid fever and malaria with filariasis. Among 31 symptomatic returned expatriates, 18 (58.1%) expatriates had a diagnosis of infectious disease abroad, and 4 (12.9%) expatriates showed positive when using rapid diagnostic test for plasmodium. Another 3 cases showing positive in rapid diagnostic test for plasmodium were asymptomatic, and 1 case had been diagnosed abroad before.

Interpretation: The long-term expatriates to Africa are considered at the highest risk of travel-associated infectious diseases. It is encouraging that 147 (76.6%) expatriates in this study had sought pre-travel advice, completed required vaccinations and got antimalarial drugs (artemisinin-based compound). As more and more long-term expatriates raised the awareness of travel health, malaria was still the most concerned. One case of filariasis was confirmed and two cases of skin lesions were undiagnosed in the study, which indicated that skin lesions as the initial symptom should be recognized.
Mexican Expatriates: Monitoring Mental Health during their Stay Abroad

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In Mexico, expatriates' health is unknown during their stay abroad. (Expatriates= No pleasure trip, stay >30 days). CAPV has a voluntary monitoring program for this travelers.

Identify anxiety problems, depression, social phobia, alcohol and sexual behavior determinants caused during traveling.

All travelers that came to pre-travel consultation during February 2013 to October 2014, were included in this study. Procedure was explained and they were asked for previous consent. Web based questionnaire was sent through e-mail every 30 days while abroad following the first month of stay.

Data was analyzed in PAWS Statistics program.

2,050 travelers had pre-travel consultation during the 20 months study period, 656 expatriates were included. The response rate for the first questionnaire was 34% (222/656). The average age is 24 ± 6 years old, 52% were female and principal residence was located inside metropolitan area.

International students and teaching were the main reasons for travel (78%) with average stay of 31 to 180 days. Psychiatric relevant background was documented in 9% of expatriates, only 36 (16%) had chronic diseases during the medical consultation (endocrine 25%, dermatological 22%, gynecological-obstetric 17%, gastrointestinal 17%, psychiatric 14% and HIV 1%). 222 expatriates were included and 388 questionnaires were received (90 expatriates answered at least 2 questionnaires), obtaining the main health problem is generalized anxiety 171 (44%), depression 46 (12%) and seasonal flu 16 (4%), ultimately, social phobia (12) and traveler’s diarrhea (12) were reported. Condom use between heterosexual (93%) and homosexual (7%) expatriates were collected, only 58% of heterosexuals and 60% of homosexuals reported always using condom during sexual relation. 13% reported increased rates of alcohol consumption.

Common health problems observed in this study were depression, generalized anxiety and sexual behaviour. Elevated rates of the present diseases may be associated with cultural shock adaptation.

Alarming rates of non-use condom relationships, and alcohol consumption increased rates are shown. Expatriates directed programs are necessary to implement this need to cover pre-consult issues, abroad contact and post-travel attention. More studies in the student community need to be done in order to prevent health deterioration.
Concurrent Dengue and Malaria: To Alert the Domestic Traveler. A Case Report

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Introduction: Malaria and dengue are two major public health concerns in tropical areas and concurrent infections are rare. We report a case of dengue fever with acute malaria due to Plasmodium vivax.

Objective: To describe and to alert health professionals about co-infections malaria and dengue in travelers returning from or living in endemics areas.

Case report: A 63-year-old female presented to the Malaria Clinical Trial, in Evandro Chagas Institute, Pará, Brazil, on 17 September 2012 with vivax malaria confirmed with blood cells in thick (2000 forms asexual parasites/mm³) in use chloroquine and primaquine. She travelled to Brazilian Amazon (Acre State) to work, where she has been for seven days. In the fifth day of treatment the patient persisted with headache, severe myalgia, fever, chills, sweating, back pain and anorexia. There was no vomiting and bleeding. Two days later the patient was reevaluated and showed little improvement, persistent anorexia, headache, insomnia and isolated episodes of diarrhea. Physical examination: she was conscious, febrile (38°C), dehydrated, hypotensive (BP: 100x70 mm Hg), diffuse rash. After physical examination was formulated the hypothesis of concurrent dengue fever and malaria due to the persistence of symptoms. Laboratory tests: Blood hemoglobin 13.2 g/dl, total leucocyte count 13,500/mm³; differential leukocyte count, 87% neutrophils, 10% lymphocytes, 1% monocytes, platelet count 229,000/mm³. Biochemical tests were normal. Blood serology positive for dengue virus on the six day after onset of symptoms. Laboratory tests after 1 week presented leucocyte count 6400/mm³; platelet count 421,000/mm³ and absence of malaria parasites in the blood film. The patient was monitored daily and clinically oriented to increase fluid intake daily and to rest. She relapsed three months after the follow-up, when a new treatment with chloroquine and primaquine (30 mg daily for 17 days) was established for radical cure of P. vivax. After the new treatment, she evaluate asymptomatically with normal hematological and biochemical parameters during six months.

Conclusions: Malaria and dengue must be in suspected febrile patients living in or returning from areas endemic for these infections.
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CXCL10 Gene Promoter Polymorphism -1447A>G is Associated with Susceptibility to Malaria in Ghanaian Children

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Plasmodium falciparum malaria kills nearly a million people annually. Over 90% of these deaths occur in children under five years of age in sub-Saharan Africa. In Ghana, malaria accounts for about 60% of all outpatient visits in public health facilities, with 40% of the affected being children under age 5 years. The disease accounts for 13.2% of all mortalities in Ghana and ranks fifth as the commonest cause of death in children under 5 years of age. The risk factors for severity of malaria pathogenesis and the wide variation in clinical manifestations of malaria are poorly understood. The influence of host genetics on susceptibility to P. falciparum malaria has been extensively studied over the past twenty years. Recent studies indicate that interferon gamma inducible chemokine, CXCL10, is a predictor of both human and experimental cerebral malaria severity. In addition, polymorphisms in the CXCL10 gene promoter has been associated with increased CXCL10 production, which is linked to severity of malaria in Indian malaria patients. In the present study, we hypothesized that in a subset of Ghanaian malaria patients, susceptibility to malaria is associated with different variants of the CXCL10 gene. We determined whether polymorphisms in the CXCL10 gene are associated with the clinical status of malaria patients. We identified one reported single nucleotide polymorphism in the CXCL10 promoter (-1447A>G [rs4508917]) and compared 43 malaria and 111 non-malaria cases using PCR-restriction fragment length polymorphism assay. The median age for malaria patients was 6 years and that for non-malaria patients was 4 years. There was no significant difference with regards to hemoglobin level between malaria patients (9.5g/dL) and non-malaria patients (10.0g/dL), p=0.588. The -1447A>G genotype of the CXCL10 gene was significantly associated with malaria (adjusted odds ratio =2.55, 95% CI=1.13-5.74, p=0.024). These results suggest that the -1447A>G polymorphism in CXCL10 gene promoter could be partly responsible for malaria outcomes in Ghanaian malaria children.