

FC01 Malaria and Other Parasitic Infections

FC01.01

Does community subsidised malaria chemoprophylaxis reduce imported malaria? A case control study of policy.

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Most imported malaria (64%) in the UK occurs in those who travelled to sub-Saharan Africa whilst visiting friends and relatives (VFRs) with only 7% taking chemoprophylaxis compared to 24% of people traveling for other reasons. In 1995, the UK Health Department changed regulations that malaria chemoprophylaxis, previously available on NHS prescriptions, must be paid for privately. The Public Health Directorate in Lambeth, Southwark and Lewisham boroughs (LSL) decided not to implement this regulation because of fears that imported malaria in their area would increase. This study examines effectiveness of the policy by comparing the number of prescriptions for malaria chemoprophylaxis issued by LSL compared to the neighbouring borough of Hackney, where this policy was followed. The study compared demographics including ethnicity, deprivation, population and cases of imported malaria reported from the two boroughs. Prescription data from Health Authorities, and dispensing from individual pharmacies to capture non-NHS prescribing were collated.

The population parameters were similar, with approximately similar numbers of ethnic African residents (10%). Of these, half were from Nigeria and Ghana. The use of anti-malarials (Mefloquine and Atavaquone and Proguanil) between April 2006 and March 2009 are shown in Table one

Hackney prescriptions for Mefloquine and AP	Prescription rate per 100 000 population Hackney	Lambeth prescriptions for Mefloquine and AP	Prescription rate per 100 000 population Lambeth
1841	877.49	26063	9509.63

[Table one]

The number of case reports from the local hospitals in each borough and rates adjusted to total population for the same period are shown in Table two

Malaria reports Homerton Hospital Hackney	Crude malaria rate per 100,000	Malaria reports St Thomas Hospital Lambeth	Crude malaria rate per 100,000
119	57	201	74

[Table two]

There appears to be little difference in total cases and rates of imported malaria between Lambeth, where malaria prophylaxis is available on the NHS and with higher prescribing rates, compared to Hackney, where prophylaxis is only available for private purchase. However, these data require caution in interpretation. Prophylaxis purchased through private prescriptions is not recorded in the prescribing databases and dispensing data although collected on the private sale may under-represent usage. Private purchase may make a significant contribution to prophylaxis uptake in Hackney.

Other explanations to the lack of effect of this policy may be lack of awareness or problems with access to subsidised prophylaxis in Lambeth. A policy of subsidised chemoprophylaxis for high risk travellers would need to be supported by complimentary strategies to ensure awareness of risk, easy access to services that provide prophylaxis and community-wide education of the benefit of chemoprophylaxis for travelers

FC01.02

Nitroimidazole resistant *Giardia intestinalis* in travellers: Is it more frequent than expected?

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Objectives: Drug resistance is a common cause of symptom persistence after treatment of imported *Giardia intestinalis*. Nitroimidazoles continue to be the drugs of choice but treatment failure might be more frequent than previously described, especially in infections acquired in Asia. This article describes the elevated prevalence of nitroimidazole resistant *G. intestinalis* infection in travellers attended in a travel clinic in Spain, and evaluates differences in drug resistance rates among giardiasis acquired in different continents.

Methods: Retrospective review of medical records of patients with imported *G. intestinalis* infection attended in the Tropical Medicine Unit in Hospital Clínic in Barcelona, Spain, between January 2007 and December 2009. Diagnosis of *G. intestinalis* was done in all cases through microscopy and MIF-concentration. Epidemiological and clinical data were recorded in a database. We defined drug resistant *G. intestinalis* when *Giardia* cysts were found in faeces after antiparasitic treatment.

Results: A total of 95 patients with *G. intestinalis* infection were analyzed. Thirty-seven percent travelled to Asia (34% to India, 3% to South-East Asia), 33% to Sub-Saharan Africa, 24% to Latin-America and 4% to the Mediterranean basin. All patients received nitroimidazoles after diagnosis. In 21 of them *G. intestinalis* was found in the stools by microscopy after treatment, yielding a prevalence of nitroimidazole resistant giardiasis of 22%. The efficacy of a second course of nitroimidazole in those patients with treatment failure was 17%. All 14 patients treated with quinacrine after nitroimidazole failure showed efficacy to eliminate *G. intestinalis* infection. The Mediterranean Basin, Indian Subcontinent and South East Asia were the areas with highest prevalence of nitroimidazole resistant giardiasis in our sample.

Conclusions: There is an elevated prevalence of nitroimidazole resistant *G. intestinalis* in travellers attended in a travel clinic from various areas of the world, especially from Asia. Giving a second course of nitroimidazoles after a first therapeutic failure showed little efficacy in our study. Furthermore, no treatment failure was found in patients treated with quinacrine. We recommend to evaluate the use of quinacrine as a second line drug treatment for drug resistant *G. intestinalis* if available, instead of giving a second course of nitroimidazoles.

FC01.03

Prolonged Prophylactic Efficacy of Atovaquone/Proguanil to Prevent Malaria

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Background: New regimens for malaria prophylaxis that allow weekly dosing might enhance convenience and adherence. Preliminary evidence suggests that atovaquone/proguanil (A/P) may provide prolonged protection from malaria.

Methods: We conducted a partially randomized, placebo controlled, double blind, clinical trial to establish the efficacy of regimens of A/P to prevent malaria with the goal of simulating weekly dosing. 30 volunteers were randomized to receive one of 1) A/P 250/100mg 1 day prior to infectious mosquito challenge, 2) 250/100 mg 4 days after challenge, 3) 250/100mg 7days prior to challenge, 4) 500/200mg 7 days prior to challenge or, 5) 1000/400mg 7 days prior to challenge. All regimens included matching placebo. Six volunteers served as open-label infectivity controls. Volunteers underwent mosquito sporozoite challenge with the 3D7 strain of *Plasmodium falciparum* and were followed for 90 days with close clinical monitoring and serial microscopy to detect parasitemia. Drug levels were determined by liquid chromatography/mass spectrometry.

Results: 6/6 infectivity controls developed parasitemia, confirming the infectivity of the challenge. 1 volunteer withdrew consent prior to challenge. 2 individuals met exclusion criteria during follow-up. 2/5 (40%) evaluable volunteers receiving 250/100mg 7 days prior to challenge, and 1/6 (17%) receiving 1000/400mg 7 days prior to challenge developed malaria during the follow-up period. All other volunteers were protected. Prophylactic failure was correlated with a trend toward lower atovaquone exposure during liver stage (AUC_{0-6.5}) 972.4 (95% CI 0-3,833.7) vs. 1,902.7 (1,139-2,666.2), lower peak atovaquone concentrations during liver development (C_{max 0-6.5}) 279.3 ng/mL (95% CI 0-963.3) vs. 593.6 ng/mL (414.5-772.6), and shorter elimination half-life of atovaquone of 2.57 days (95% CI 0.91-4.22) vs 4.05 days (3.15-4.95).

Conclusions: A/P provides effective malaria prophylaxis in a human malaria challenge model at dosing intervals that are supportive of weekly dosing. Post-exposure prophylaxis up to 4 days after challenge was 100% effective in this model.

FC01.04

Use of malaria imported cases in non endemic countries to assess the return of chloroquine susceptibility of *P. falciparum* strains from Senegal

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Background: Early treatment with effective anti-malarial drugs is the best strategy for those infected by malaria. However, concern is growing about the emergence of resistance to antimalarial treatments. In compliance with WHO recommendations, African countries have discontinued chloroquine, as it becomes ineffective, and now promote artemisin-based combination therapy (ACT), as first-line treatment for uncomplicated malaria. In Senegal, chloroquine was recommended as first line treatment before 2003. But faced with an average chloroquine treatment failure of 25%, Senegal changed its national malaria policy from chloroquine (CQ) to ACT (amodiaquine/artesunate). It is assumed that travelers and immigrants coming from this region and collectively infected by a wide variety of strains of *Plasmodium*, could be an effective tool for detecting the evolution of resistance onsite. The aim of the study is to describe, through imported cases from Senegal, the evolution of chloroquine-resistance in the region after a decrease of drug pressure.

Materials and methods: The study will be conducted by the Malaria National Reference Centre in France in collaboration with the WorldWide Antimalarial Resistance Network (WWARN). The database will collate in vitro response of reference and clinical isolates for CQ. In total, 128 clinical isolates were tested from 1996 to 2003 and 120, from 2004 to 2009.

Results: Mean estimated 50% inhibitory concentration (IC₅₀) for CQ was 133nmol/L (95% confidence interval [CI], 106 to 159) (threshold 100nmol/L) from 1996 to 2003 versus 95nmol/L (95% CI, 78 to 113) from 2004 to 2009 ($p=0.02$). The IC₅₀ isolate/*Pf3D7* ratio was 5.90 (95% CI, 4.63 to 7.17) (threshold =3) versus 2.95 (95% CI, 2.38 to 3.52) ($p< 0.001$), before and after 2003, respectively. The strains showed an increased susceptibility to CQ between these 2 periods.

Conclusions: A reduction in resistance to CQ following official withdrawal in 2003 was observed in imported cases from Senegal. A return of the Chloroquine-susceptible *P.f* is consistent with results observed in Malawi, even if the studied period, after the CQ was withdrawn, was shorter in Senegal than in Malawi (6 years versus 12 years). A confirmation by genotyping *pfcr*, *pfmdr-1*, *dhps* and *dhfr* genes of these samples will be done.

FC01.05

Do they really sleep? Sleeping sickness in Travelers

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Background and Objectives of the study: The numbers of imported Human African Trypanosomiasis (HAT) cases in non-endemic countries increased over the last years. The objective of the analysis is to describe the clinical presentation of Caucasian travelers.

Methods: Literature was screened (Medline, Pubmed) using the terms 'Human African Trypanosomiasis' and 'travelers'; all European languages except Slavic ones were included. Publications without clinical description of patients were not included.

Results: 40 reports on Caucasians with T.b. rhodesiense and 14 with T.b. gambiense infections were included in the analysis. Both species presented with fever (T.b. gambiense: 97.5% and gambiense: 92.8%), headache (50% each) and a trypanosomal chancre (T.b. rhodesiense: 80%, T.b. gambiense 25%). Whereas insomnia and diurnal somnolence dominates the clinical presentation of HAT in endemic regions, there were only rare reports in travelers: insomnia T.b. rhodesiense: 8%, T.b. gambiense 25%; diurnal somnolence T.b. rhodesiense: 5%, T.b. gambiense none). Surprisingly, jaundice was seen in 27.5 % of the Caucasian T.b. rhodesiense patients, but has never been described in HAT patients in endemic regions. These results contrast to the clinical presentation of T.b. gambiense and rhodesiense HAT in Africans in endemic regions, where the presentation of chronic T.b. gambiense and acute T.b. rhodesiense HAT is different. The analysis of 9 reports on T.b. gambiense HAT in Africans living in Europe shows that neurological symptoms such as somnolence (62.5) motor deficit (56%) or reflex anomalies or psychiatric symptoms such as hallucinations (33%) or depression (22%) may dominate the clinical picture. Often the diagnosis was missed initially: some patients were hospitalized in psychiatric clinics.

Conclusions: Sleeping disorders in travelers with sleeping sickness are rarely reported.

T.b. rhodesiense and gambiense present as acute illness in travelers and chancres are frequently seen. The diagnosis of HAT in Africans living outside the endemic region is often missed or delayed, leading to presentation with advanced stages of the disease.

FC01.06

Analysis of 160 cases of LOA LOA.

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Objectives: The aim of the study was to describe the clinical features, laboratory data and diagnostic approach in loiasis. Secondly, we investigated the differences between native people from endemic area (NEA) and expatriates (EXP).

Methods: Cases of loiasis diagnosed in our hospital from January 1993 to June 2009 were selected. We included all cases diagnosed in older than 15 years old. Cases without complete clinical or laboratory information were excluded. The diagnosis was made by the presence of microfilariae in blood, Calabar swellings and / or ocular migration of adult filaria.

Summary of results: 160 cases of loiasis were collected. Mean age (\pm SD) was 42.93 ± 16.77 years. 65% of cases were in female. 90.62% of all cases were acquired in Equatorial Guinea, the country from which most of our patients are. 131 cases were described in NEA and 29 in EXP. Microfilariae were positive in 85.49% of NEA and 34.48% in EXP ($p < 0.001$). Calabar edema was described in 22.90% of NEA and 82.75% in EXP ($p < 0.001$). Ocular migration of adult filaria was reported in 14.50% of NEA and 17.24% in EXP ($p = 0.709$). Subcutaneous migration of filariae was described in 2.29% of NEA and 13.79% in EXP ($p = 0.02$). Laboratory findings include the presence of eosinophilia in 70.99% of NZE and 89.65% of EXP ($p = 0.027$). Eosinophilia was more frequent and intense in patients with Calabar swellings ($p < 0.001$). Serum IgE was elevated in 87.59% of NEA and 57.14% in EXP ($p = 0.001$). 48.12% of patients had one or more associated filariasis: *Mansonella perstans* (43.75%), *Onchocerca volvulus* (14.37%), *Mansonella streptocerca* (2.50%) and *Wuchereria bancrofti* (0.625%).

Conclusions: Eosinophilia is not always found in loiasis. Clinical manifestations are the key in amicrofilaremic loiasis. In our serie, this situation was more frequent in EXP.

FC02 Travel Advice

FC02.01

Demographics, Travel Destinations and Pre-Travel Health Care among U.S. International Travelers: Analysis of the Global TravEpiNet Surveillance Network

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Objectives: To evaluate demographics, travel destinations, and pre-travel health care of international travelers departing from the United States.

Methods: The Global TravEpiNet surveillance network was established in 2008 to collect data on pre-travel medical care and health advice provided to U.S. international travelers. We analyzed data for 10,564 travelers seen at 15 travel clinics across the continental United States and Hawaii from January 1, 2009, to September 15, 2010.

Results: The median age of travelers was 35 years (range 1 month - 94 years). The median duration of travel was 14 days; 21% of travelers planned trips longer than 28 days. Eighty-two percent of travelers were visiting low- or low- to middle-income (LLMI) countries, as defined by the 2009 World Bank World Development Report. Compared with travelers to upper-middle or high-income countries, travelers to LLMI countries planned more trips >28 days (23% vs. 15%, $p < 0.001$) and stayed more frequently in homes (30% vs. 18%, $p < 0.001$). Among all travelers, leisure was the most commonly reported purpose of travel (62% of travelers), followed by business (17% of travelers). Africa was the most commonly visited geographic region; India, South Africa, and China were the three most common destination countries. Fifty-nine percent of travelers reported a medical condition of some type; 17% of travelers reported a cardiovascular condition and 9% reported a neuropsychiatric condition. Seventy-five percent of travelers were visiting countries with areas endemic for malaria; atovaquone/proguanil was the most commonly prescribed antimalarial. Antibiotics for the presumptive self-treatment of travelers' diarrhea were prescribed to 93% of travelers. Vaccines to prevent typhoid fever (76%) and hepatitis A (53%) were the most commonly administered immunizations.

Conclusions: Global TravEpiNet represents the largest network of providers systematically collecting pre-travel data for U.S. international travelers. Data from Global TravEpiNet provide insight into the types of travelers, travel destinations and duration, and pre-travel health care of this epidemiologically significant population and will facilitate devising risk-reduction strategies for U.S. international travelers.

FC02.02

Introducing the PRE-TRAVEL model

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Objectives: There is no existing model that is specific to the unique requirements of the pre-travel health consultation. A model for pre-travel health care was therefore developed as part of a wider PhD study of the nurse-led pre-travel health consultation in primary care. This presentation describes the new model called PRE-TRAVEL, the evidence upon which it is based and the reasons why it is needed.

Methods: The study employed a mixed methods design. Results from the following methods were synthesised to develop the PRE-TRAVEL model: a literature review and in-depth documentary analysis; an audit of resources available to nurses; audio-visual (AV) recordings of consultations, and follow-up interviews with travellers. The prototype model was piloted in focus group interviews with nurses. The positive evaluations from these confirmed the feasibility of proceeding to field-testing.

Summary of results: PRE-TRAVEL addresses all phases related to the consultation, with particular emphasis on the assessment, intervention and counselling phases.

The model uses Donabedian's quality assurance framework to specify the structures (tangible resources) and processes necessary to achieve intended outputs. Both the structures and processes consist of 18 criteria. These help to break down the consultation process into individual elements which can aid learning and facilitate audits of clinical practice.

The PRE-TRAVEL acronym reflects the values at the heart of the model:

Person-centred Risk assessment and Empowerment; Tailored Risk Advice, Vaccines and malaria prophylaxis, and the need to Enable Learning.

Conclusions: Although the prototype PRE-TRAVEL model was initially envisaged as a guide to consultations with travellers, the model has other potential applications such as to inform an audit of standards, and to organise professional education. Post-doctoral field testing is planned.

FC02.03

Provider Decision-making Regarding Yellow Fever Vaccine Administration

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Objectives: To evaluate: provider attitudes toward sharing yellow fever (YF) vaccine administration decisions with patients, the influence of traveler- and destination-specific variables on provider decisions, and how information about YF disease risk and vaccine adverse events (AE) affect providers' decisions.

Methods: An on-line survey link was e-mailed to U.S. YF vaccine providers (YF stamp owners, International Society of Travel Medicine members, and American Society of Tropical Medicine and Hygiene clinical group members). The survey included 21 questions and 4 case-studies. Vaccine administration decisions were queried before and after presentation of disease risk and vaccine AE rates.

Results: Of 3400 eligible providers, 772 (23%) participated; 514 (67%) completed the survey. Most participants expressed confidence in their ability to tailor explanations of vaccine risks and benefits (95%, 731/772), and indicated a preference for sharing YF vaccine administration decisions with patients (90%, 692/772).

Ten to 26% of participants changed a vaccine administration decision after presentation of YF disease rates and vaccine AE rates for the 4 cases. The largest proportion of changed responses occurred in the case of an elderly man visiting the Amazon; 161/612 (26%) would not give vaccine after explanation of YF risk and vaccine AE's (either vaccine administration decision was considered supportable in this case).

Despite explanations of YF disease risk and vaccine AE rates, 268/627 (43%) would not administer vaccine to a pregnant woman going to West Africa; 78/603 (13%) would administer vaccine to an immunosuppressed man going to Tanzania; and 261/601 (43%) would not administer vaccine to an eight month-old infant going to rural northwest Brazil.

A significant proportion of those who would not administer vaccine when this was insisted upon by a patient had indicated a preference for shared decision-making (88%, 136/155 refused the pregnant traveler; 89%, 104/117 refused the elderly traveler).

Conclusions: Being provided with information about risk of disease and adverse events may be insufficient to alter providers' vaccine administration decisions. Most providers preferred shared decision-making with patients about YF vaccine administration. Preference for shared decision-making did not change a provider's vaccine administration decision when a patient disagreed.

FC02.04

The reliability of pre-travel history to decide on appropriate counseling and vaccinations: a prospective study

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Objectives: Although medical and travel plans gathered from pre-travel interviews are used to decide on the provision of specific pre-travel advice and vaccinations, there has been no evaluation of the relevance of this strategy. In a prospective study, we assessed the agreement between pre-travel plans and post-travel history (real trip made) and the consequence on administration of vaccines and recommendations for malaria prevention.

Methods: We included prospectively all consenting adults who had not planned an organized tour. Travel information were extracted from our travel clinic client electronic files which included questions on destination, itineraries, departure and return dates, access to bottled water as well as plan of bicycle ride, stay in a rural zone and close contact with animals. Post-travel interview was done by phone and included the same questions. The outcomes measured were agreement between pre- and post-travel history and changes in pre-travel recommendations that would have occurred, would the traveler have given the destination he really went and activities he really did.

Results: A total of 365 travelers were included, 188 (52%) were males (median age 38 years). In 81(23%) travelers, there was no difference between pre- and post-travel history. Unlike pre-travel history, 58(16%) travelers changed destination, 52(15%) changed length of stay, 19(5%) had no access to bottled water, 70(20%) rode a bicycle, 142(40%) stayed in a rural zone or with local people and 112(32%) had close contact with animals. According to post-travel history, 125(35%) travelers would have needed rabies vaccine and 9(3%) typhoid fever vaccine. Overuse was < 2% for all vaccines. Change in malaria prescription would have been required in 18(5%) travelers. 3 of them would have needed malaria chemoprophylaxis and 4 standby emergency treatment (SBET). Two received unnecessary chemoprophylaxis and 7 unnecessary SBET.

Conclusions: Pre-travel history does not adequately reflect what travelers do. However, the consequences on preventive measures were only relevant for rabies vaccine that should have been more frequently prescribed. Travel professionals should insist more on the risk of rabies and the need to avoid close contact with animals and to seek care for post-exposure prophylaxis in case of bite.

FC02.05

"Thanks Doctor ! " "Actually, I'm a nurse!" - An evaluation of the satisfaction of clients according to the type of health professional seen

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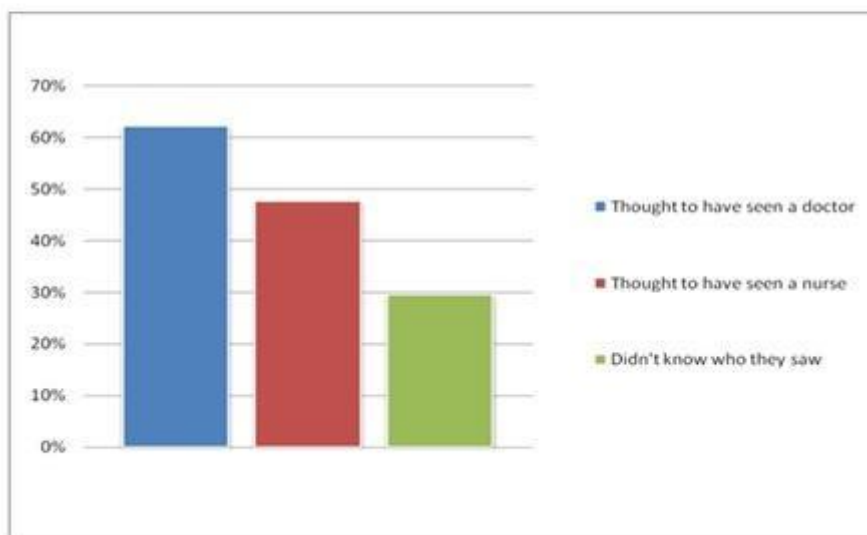
Objectives: In many countries pre-travel consultations are conducted not only by physicians, but also by nurses. The objective of this study was to compare the satisfaction of clients of a travel clinic depending upon the type of medical provider (physician or nurse) seen.

Methods: For a period of two weeks, all clients who consulted the Travel Clinic for a pre-travel consultation were proposed to fill a home-based questionnaire which comprised 9 questions about the general attitude of the medical provider (kindness, respect, professionalism, etc.), 5 questions about the content of the consultation (recommended vaccines, malaria prophylaxis, side-effects, attitude in case of fever) and 2 questions about their general impression. The travelers and health professionals were not informed how the survey would be conducted.

Results: 405 clients consulted during the defined time-period, 223 had come for a first consultation (not follow-up visit) and accepted to take home the questionnaire, 118 clients returned the completed questionnaire (response rate = 53%). Median age was 31 years (range 16-69), 60% were women. 75% of clients were seen by nurses and 25% were seen by physicians.

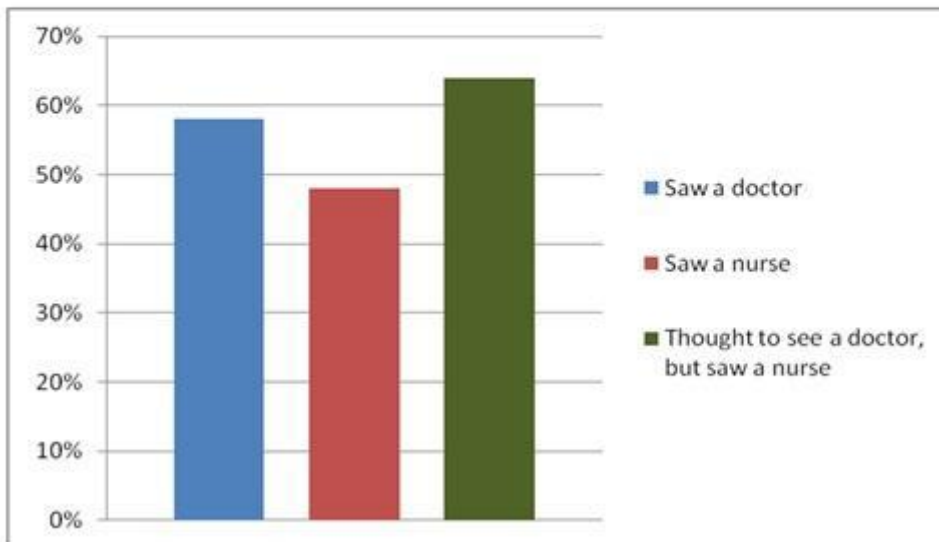
The 45 clients who believed to have seen a physician expressed a higher level of overall satisfaction than the 44 clients who believed to have seen a nurse or the 29 clients who didn't know which professional they had seen (graph 1). However, when investigating satisfaction according to the category of professional the clients had really seen, the highest level of satisfaction was recorded for clients who believed to have seen a doctor, but actually saw a nurse (graph 2).

Graph 1 : Proportion of very satisfied clients depending on which health professional the clients believed to have seen



[GRAPH 1]

Graph 2 : Proportion of very satisfied clients depending on which health professional the clients had really seen



[GRAPH 2]

Conclusions: Clients attending the Travel Clinic have the feeling that they receive better service if they see a physician instead of a nurse. This feeling is likely to be based on preconceived ideas since the level of satisfaction was highest for those who believed they saw a physician, but actually saw a nurse. Better information on equivalence of training and competences between the different health professionals should be provided to the clients to reassure them on the quality of care they receive whoever attends them.

FC02.06

Immediate recall of health issues discussed during a pre-travel consultation

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Objectives: To assess recall and knowledge level immediately following a pre-travel consultation.

Methods: The study was conducted at a hospital-based pre-travel clinic in Melbourne, Australia. Ten infectious disease physicians rotate through this weekly clinic providing one-on-one 30 minute consultations. All travellers seen in a 3 month period (early Sep to early Dec 2010) were invited to complete an anonymous self-administered questionnaire immediately following the consultation which assessed their knowledge of appropriate preventative measures and (where relevant) presumptive self-treatment strategies for common travel risks. The doctor of each participating traveller also completed a survey so the precise aspects discussed could be ascertained.

Results: 105 participants were recruited (34% male, median age 29 yrs [R:< 1-80]). Most were travelling for vacation (69%) and reported previous travel (90%). Planned travel destinations were: Asia-Pacific region (48%), Central/South America (27%), Africa (16%), other (8%). Planned duration was 6 days to 3 years (median: 29 days). Doctors' and travellers' surveys showed 20% discordance regarding whether or not malaria was discussed. Recall about the importance of screened accommodation/mosquito nets and of using insect repellent was incorrect for 11%, and 6% did not recall that medical advice should be sought if fever developed. For TD, 6% were unable to recall avoidance of undercooked meat/seafood as a prevention strategy, and 4% for drinking only boiled/bottled water. For rabies, 7% did not recall the importance of seeking urgent medical attention following a bite and 24% that wounds should be washed. Preventative measures were often confused: for malaria, 11% selected vaccination, 7% drinking bottled/boiled water, and 6% avoiding high risk foods. For TD, 15% selected using insect repellents, 12% sleeping in screened accommodation or under mosquito nets, and 12% avoiding animal bites. There was 10% discordance between doctors and travellers about whether malaria prophylaxis was prescribed, 12% discordance regarding antibiotics for presumptive self-treatment of TD, and 34% incorrectly recalled prescription of specific vaccines.

Conclusions: Discussion of multiple travel risks can become overwhelming. Immediate recall of information is often incorrect, thereby decreasing the likely effectiveness of preventive advice. Optimal methods for delivering pre-travel information need to be considered.

FC03 Risk Factors and Travel

FC03.01

Acute Mountain Sickness among Travelers to Cusco-Peru (3,310 m)

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Objectives: Describe the epidemiology, pre-travel advice, and impact of acute mountain sickness (AMS) among travelers to Cusco (3,310 m).

Methods: Foreign travelers, \geq 18 years of age that stayed in Cusco \geq 15 days were invited to participate. A convenience sample of departing travelers was obtained at Cusco's International Airport during June 2010. The Lake Louis score (LLS); for self-reported AMS symptoms in the first 48 hours after arrival; was used. Data on demographics, pre-travel advice, preventive behavior, and impact of symptoms were collected.

Results: Of 1153 travelers invited, 991 (85.9%) met the inclusion criteria and agreed to participate. Median age was 32 years (IQR 25 - 49), 55.5% were female, 86.5% had higher education, 86.7% were traveling for tourism, and the main countries of origin were United States (47.7%) and England (8.1%). Most travelers (76.8%) flew from sea level to Cusco and 30.7% visited high altitude destinations in the previous 2 months. Twenty nine percent received professional pre-travel advice on AMS, 19% recalled receiving advice on acetazolamide use, and 16.4% used it. Frequent preventive measures were using coca leaf products (62.3%) and limiting physical activity (39.1%). The most common symptom was fatigue/weakness (68.4%) followed by headache (58.6%) and poor sleep (44.7%). AMS was reported by 47% (LLS \geq 3) and severe AMS by 35.1% (LLS \geq 6). Twenty percent of travelers reporting AMS had to stay in bed, change itinerary, cancel tours, and/or prolonged their trips. Only 11.8% sought advice for their symptoms and a minority (2.1%) sought it from a physician. Three (0.6%) travelers were admitted to a hospital and later evacuated due to AMS. Variables associated with having AMS are shown in table 1 and table 2.

Conclusions: AMS is a common health problem among travelers to Cusco with significant impact on travel plans. Pre-travel preparation and healthcare seeking behavior were alarmingly inadequate. Coca leaf products users were more likely to report AMS.

	AMS	No AMS	OR (95% CI)
Visited cities at lower altitude first	28/463	56/490	0.49(0.31-0.8)
Visited high altitude in the previous 2 months	107/464	182/491	0.5(0.38-0.67)
Age \geq 60 years old	41/466	75/493	0.53(0.35-0.8)
Female gender	278/463	257/493	1.38(1.06-1.78)
Flew from Lima to Cusco	381/466	362/493	1.62(1.19-2.2)
College degree or higher	399/461	419/485	1.01(0.69-1.47)
Prior history of altitude related illnesses	36/448	36/466	1.04(0.64-1.68)
Visited friends/relatives	20/464	11/492	1.97(0.93-4.15)

[Table 1. Travel demographics associated with AMS]

	AMS	No AMS	OR (95% CI)
Used coca leaf products	322/463	275/490	1.78(1.36-2.33)
Used Sorojchi pills (caffeine/NSAID)	32/463	18/490	1.94(1.07-3.51)
Modified diet	99/463	60/490	1.94(1.37-2.76)

Abstracts – Free Communications

Limited physical activity on arrival	227/463	150/490	2.18(1.67-2.84)
Used acetazolamide	65/460	91/490	0.72(0.51-1.02)
Received pre-travel advice on AMS	132/465	144/492	0.95(0.72-1.26)
Used oxygen	26/462	16/490	1.76(0.93-3.33)

[Table 2. Preventive behavior associated to AMS]

FC03.02

5 Years Experience of Aeromedical Evacuation of 4'882 Travelers back to Switzerland: Implications for Pretravel Counseling?

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Objectives: Emergencies occurring abroad for travelers are rarely evoked in pretravel counseling apart from encouraging a travel insurance coverage, foreseeing medical encounters abroad with "in case of" local addresses and prescribing self-treatment strategies. The aim of our study is to identify the scope of the problem on the basis of the nature of the medical reasons needing an aeromedical evacuation.

Methods: REGA founded in 1954 is a private nonprofit organization to whom more than 2 million Swiss are affiliated. Swiss Air-Ambulance is part of REGA and its mission is repatriating patients for medical purposes inside the country by helicopters covering the whole Swiss territory or outside the country by jet ambulance or scheduled aircraft with medical crews. This is a retrospective study of aeromedical evacuation from abroad Switzerland during 5 years (2005-2009) with analysis of the country of destination and the nature of the disease motivating the evacuation.

Results: During 5 years (2005-2009), REGA has dealt with 13'970 medical emergencies occurring abroad (outside of Switzerland). Out of these 13'970 emergencies, REGA repatriated 4'882 (35 % of all emergencies) patients either by jet ambulance (67 % of repatriated cases) or by medical escort on regular aircraft (33 %) towards Switzerland. The other 9'088 medical emergencies were managed either by medical counseling or either on site with local medical means.

Of the 4'882 aeromedical evacuations back to Switzerland, 1'926 (39 %) were linked to trauma and 2'956 (61 %) were linked to diseases. In this last category, cardiovascular and cerebrovascular diseases represented more than a third of the causes of medical repatriation. Infections represented only 6 % of them.

Europe	3311
Africa	645
Near Middle East	352
Asia	291
North, Central and South America	256
Australia / New Zealand	27
Total	4882

[REGA, 2005-2009 : Destinations]

Extremities	804
Head injuries	332
Spine / Pelvis	331
Thorax	163
Para- / Tetraplegia	94
Burns	45
Abdomen	57
Others	100
Total	1926

[REGA, 2005-2009 : Trauma]

Cardio-vascular	621
Gastro-intestinal	401

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Cerebro-vascular	382
Lung diseases	312
Malignancies	265
Psychic diseases	147
Infection / Sepsis	183
Obstetric / Gynecology	88
Nephrology / Others	71 / 486
Total	2956

[REGA, 2005-2009 : Diseases]

Conclusions: The present study puts in evidence that of all medical emergencies signaled to a medical repatriation service, around a third are effectively repatriated. In these cases, more than a half are either trauma related or either cardiovascular or cerebrovascular related. These statistics emphasizes the nature of risks encountered abroad and should be more explained in pretravel counseling. We hope this study will help to offer better preventive advice oriented on these risks and offered to travelers.

FC03.03

Factors of health and well-being associated with international work-related travel

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Background: As working life is becoming increasingly international in nature, the work of ever more people involves frequent travel abroad. However, there is little research data on the strain induced by work-related travel and the effects of this strain on health and well-being.

Objective: The aim of the study was to gain information on the risk factors of international work-related travel from the viewpoints of well-being and the work/life balance.

Method and subjects: E-mailed questionnaires were used to collect data in five internationally operating organizations based in Finland. The study reported here is the first segment of a year-long prospective study during which a questionnaire was sent every six months. A total of 1,513 employees answered the first questionnaire (response rate 56%).

Results: Of the respondents, 91% had traveled abroad for their work at least once during the past 12 months. On average, those who had traveled made 9.6 trips during the last year, the number of trips ranging from one to 100. The number of work-related trips undertaken during the last year was positively associated with long working hours, experienced work demands, negative spillover from work to home, difficulties in recovery, sleep disturbances, and frequent use of alcohol.

Conclusion: The results suggest that international work-related travel may strain the health and well-being of employees through greater work load, difficulties in recovery, and problems in the balance between work and family life as well as through unhealthy lifestyle choices such as excessive alcohol consumption.

Occupational health care practitioners dealing with frequent flyers should be aware of these health-related factors associated with work-related travel, in order to be able to support their clients' well-being.

Organizations, in turn, should give their frequent flyers more consideration and should strive for customization - such as customized work and travel arrangements -that would alleviate the detrimental effects frequent work-related travel abroad may have on health and well-being.

FC03.04

Travel medicine in the face of a crisis

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Objectives: To review the support InterHealth, a specialist travel medicine centre which provides medical and psychological support to international humanitarian aid agencies, provided to humanitarian aid workers (HAWs) who travelled to Haiti following the earthquake on 12 January 2010.

To review the role InterHealth played in minimising illness in this population, to identify areas where support could have been greater and to identify common diagnoses on return.

Methods: Appointment and clinical data (for all returned HAWs who presented for asymptomatic screening or with illness following travel to Haiti) were extracted from InterHealth's patient database and exported into Microsoft Excel[®]. Data from the period 12 January 2010 - 1 December 2010 were extracted.

Results: A total of 180 individuals were seen at InterHealth prior to travel for travel clinic appointments. On return 87 patients were seen for post-assignment medicals. The patient group seen were predominately males (56.3%) with a median age of 39.

On return individuals presented with varying health needs. 37.9% of patients were ill with one or more diagnoses (total diagnoses=44). The most common diagnosis was psychological stress (n=11, 25.0% of total 'ill' diagnoses) of which work-related stress contributed the greatest (n=9, 20.5% of total 'ill' diagnoses). The second most common diagnosis was acute diarrhoea (n=8, 18.2% of total 'ill' diagnoses). One case of dengue was seen but no cases of malaria were reported either on assignment or on return.

Conclusions: Approximately one third of HAWs returned unwell following travel to Haiti. Psychological work-related stress was the most common diagnosis, attributable perhaps to the complete devastation, destruction of infrastructure and cramped living conditions. This illustrates the value of specialist clinics such as InterHealth with in-house expertise in identifying psychological illness which may go undiagnosed at others. It also highlights the need for effective psychological support for those returning from high-scale disasters.

This review highlights the disparity in the number of patients seen pre and post travel, with a small proportion seen post travel, illustrating the disproportionate supportive care offered by sending agencies on return.

FC03.05

Risk perception of travelers to tropical and subtropical countries

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Background: Travelers to subtropical and tropical areas are exposed to special health risks. Better understanding of trends of subjective risk perception of travelers may contribute to adapt and improve pre-travel health consultations.

Objective: Assessment of the subjective perception of travel-related health risks of travelers to tropical and subtropical countries both before and after travel with a focus on differences in risk perception between experts and travelers.

Methods: We evaluated the risk perception of 314 walk-in clients of the Swiss TPH Travel Clinic seeking pre-travel health advice for subtropical and tropical destinations in 2008 and 2009, and of 30 Swiss experts in travel medicine. The perception of 9 defined travel-related health risks (general risk, mosquitoes, malaria, epidemic outbreaks, rabies, sexually transmitted infections (STI), accidents, terrorist attacks, adverse effects of vaccinations) was assessed before the pre-travel consultation and 2-4 weeks after travel, applying a validated visual measuring instrument, PRISM (pictorial representation of illness and self measure). Travel-related and demographic data was collected by an interview-administered questionnaire.

Results: The return rates were 73% (travelers) and 60% (experts). In general, pre- and post-travel risk perception among travelers was similar with a tendency of a lower risk perception after travel, except for accidents. Contrary to the expert opinion, travelers perceived adverse effects of vaccinations as higher risks and accidents and STI as lower risks both before and after travel. STI showed the biggest difference, ranking third position for experts and last position for travelers on a comparative ranking list of risks. In addition, the results indicate that terrorist attacks were considered as higher and STI as lower risks before travel by travelers older than 40 years.

Conclusions: Based on our results in comparison with available data about the incidence of the respective risks, we strongly suggest adding information about accidents and STI in every pre-travel health consultation.

FC03.06

Innovative community-based initiatives to engage VFR travelers

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Background: VFRs are recognised as a group of travellers who have suboptimal levels of pre-travel care, in part because of low recognition of travel-associated risks. Innovative methods are needed to increase awareness regarding the need for pre-travel visits among impending VFR travelers.

Methods: In Australia (total population 22.5 million) a communications consultancy firm was engaged to convey travel-related public health messages to ethnic groups that contribute high numbers of VFRs. A combination of methods was used involving media outreach, printed materials and attendance at community events.

Results: Over a five month period, five media campaigns were developed mainly targeted at the ethnic media (newspaper, radio, web-based, and television). These cumulatively led to publication of 64 media items on travel health in 4 languages (Chinese, Vietnamese, Hindi and English). All media materials were initially drafted in English before being culturally appropriated and translated by health professionals identified as members of and spokespeople for relevant ethnic groups. Given the estimated audiences of these media outlets, this approach potentially reached a VFR audience of at least 1.1 million. Printed information (posters and tear-sheets) were also developed and distributed by bi-lingual staff to businesses identified as being in areas with high numbers of ethnic residents. Additionally, four multicultural events (two Autumn Moon Festivals and two Diwali Festivals) were chosen as venues for delivery of travel health messages. Stalls were set up and staffed by bilingual personnel to engage the public. Targeted attractions were arranged e.g. Indian sweets (burfi), or artists designing henna tattoos, masseuses giving complimentary Chinese massages. Over 5,000 purposefully designed fold out z-cards were distributed at these festivals.

Conclusions: Community-based opportunistic dissemination of linguistically- and culturally- appropriate information represents a novel way to engage ethnic groups. Simple messages, primarily focusing on the potential for health risks among VFRs and the consequent necessity of seeking pre-travel consultations, can be conveyed.

(Note: These initiatives were supported by an unrestricted educational grant from Sanofi Pasteur).

FC04 Potpourri

FC04.01

Incidence of influenza and respiratory viruses in Australian travellers visiting South and South East Asia

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Respiratory tract infections are among the most common causes of fever in travellers yet data on *attack rates* for respiratory pathogens is limited.

Objective: To estimate the incidence density of influenza in Australian travellers to Asia.

Methods: We performed a prospective cohort study of Australian travellers to South and South East Asia over a 2-year period. Travellers completed validated questionnaires and provided pre and post-travel blood samples for serological testing for Influenza A and B (complement fixation test). Demographic data, destinations and travel patterns, vaccination details and history of influenza infection were obtained. Returned travellers with a respiratory illness had nose and throat swabs taken for respiratory virus multiplex PCR testing for rhinoviruses, influenza A & B, parainfluenza, adenovirus and RSV.

Results: Among 467 travellers enrolled, 387 had returned for follow-up, 59 (12.7%) were lost to follow-up and 22 travellers were not eligible for the study; 58% were female, median age was 37 years and 57% of travellers received influenza vaccination before travel. 72% were short term travellers (< 30 days). The main reasons for travel were vacation/holiday (69%), business (16%) and VFRs (4.9%). India accounted for 30% of traveller days in this cohort followed by 17% in Thailand, 11% Vietnam, 10% China. 65% (n = 254) of travellers experienced an illness episode during or immediately after travel. 39% (n = 153) reported a respiratory illness and 9 of 27 symptomatic returned travellers imported rhinoviruses. The mean number of illness episodes per traveller was 1.52 (min 0, max, 4). Four travellers aged between 21 and 30 years were infected with influenza A during translating to an overall incidence density of influenza of **3.4 per 10,000 days of travel (CI: 1.4 - 8.6)** and for travel to Malaysia (16.3 per 10,000 days of travel, CI:3.9-90.26), Thailand (10.2 per 10,000 days of travel, CI:3.1-13.6) and Cambodia (15.5 per 10,000 days of travel, CI:3.7-85.8). Two were male and 1 out of the 4 cases had received the influenza vaccine in the past.

Conclusion: To our knowledge, this is the largest prospective study estimating the incidence of respiratory viral infections in travellers. These findings have important implications for practitioners advising prospective travellers.

FC04.02

Factors influencing the prescription of malarial chemoprophylaxis and diarrhea self-treatment: findings from the Boston Area Travel Medicine Network (BATMN)

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Objectives: Choice of malaria chemoprophylaxis and traveler's diarrhea (TD) self-treatment is influenced by antimicrobial resistance patterns, trip duration and traveler's age. We assessed the effect of these factors on prescriptions for malaria prevention and TD self-treatment in 5 Boston-area travel clinics.

Methods: We classified chloroquine (CQ) resistance countries using CDC's Health Information for International Travel, and stratified antimalarial prescriptions by age and trip duration. We compared TD antibiotic prescriptions among travelers to Southeast (SE) and South Asia (areas with fluoroquinolone (FQ) resistance) vs other areas.

Results: During March 2008—July 2010, 15,442 travelers were enrolled. Travelers to CQ-resistant malaria countries were prescribed atovaquone-proguanil (AP) (5639/6987, 81%), mefloquine (14%), doxycycline (6%), CQ (0.3%) and primaquine (0.02%); some received >1 prescription. For young travelers (≤ 18 y) to CQ-resistant countries, 413/624 (66%) were prescribed AP, 181 (29%) mefloquine, 31 (5%) doxycycline, and 2 (0.3%) CQ. Among travelers to CQ-sensitive areas, CQ (1118/2241, 50%), AP (40%), doxycycline (30%), mefloquine (8%), and primaquine (2%) were prescribed. Among young travelers to CQ-sensitive countries given antimalarials, 147 (47%) were prescribed CQ, 93 (30%) AP, 68 (22%) mefloquine, and 11 (3%) doxycycline.

Travelers planning trips of ≥ 1 mo to both CQ-sensitive and resistant countries were more likely to be prescribed mefloquine and/or doxycycline than those taking shorter trips (34% vs 11%, $p < 0.001$); 39% traveling for ≥ 1 mo were prescribed AP.

TD self-treatment was prescribed to 84% of travelers, including ciprofloxacin (55%), azithromycin (29%), levofloxacin (2%), and rifaximin (0.2%). Travelers to South/SE Asia were prescribed azithromycin more often than ciprofloxacin (72% vs 20%, $p < 0.001$); the opposite was found for travel to other areas (14% vs 68%; $p < 0.001$). 219/1727 (13%) of young travelers were prescribed FQs and 1048 (61%) azithromycin.

Food/water safety and diarrhea management counseling was provided to 98% and 99% of travelers.

Conclusions: Antimicrobial resistance patterns influence the choice of prescriptions for two common travel-related conditions. AP use was greater for travelers to areas with CQ-sensitive malaria, long-term, and young travelers. Providers need increased awareness of azithromycin as an alternative to FQs for TD self-treatment for children and travelers to South/SE Asia.

FC04.03

The degree to which travelers are inconvenienced by travelers' diarrhea: a prospective follow-up study

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Background: Policy regarding use of preventive and therapeutic agents for travelers' diarrhea (TD) is usually based on the rationale that TD causes significant inconvenience. Limited data exists documenting the degree to which travelers' are actually inconvenienced by TD. We performed a prospective follow-up study to determine the degree of inconvenience.

Methods: Healthy adults who visited our travel clinic and who intended to travel to the (sub)tropics for no more than two months were invited to take part. Participants filled out a web-based questionnaire before departure and after returning home. TD was defined as three or more unformed stools during a 24-hour period, with or without nausea, abdominal cramps, vomiting, fever or faecal urgency.

Results: 776 of 1000 travelers fulfilled the inclusion criteria of whom 406 provided informed consent (response rate 52%); 390 travelers completed both questionnaires (follow-up rate 96%). Participants' median age was 31 years (IQR 24-50 years) and median travel duration 21 days (IQR 14-28 days). Of 160 travelers who contracted TD (attack rate 41%, incidence rate 1.8 cases per 100 person-days of travel) the majority (107/160, 67%) could conduct their activity program as planned despite having diarrhea. However, 21% (33/160) were forced to alter their program and an additional 13% (20/160) were confined to their accommodation for one or more days; 53 travelers (33%) used loperamide and 14 (9%) an antimicrobial agent. Eight travelers (5%) consulted a physician for the diarrheal illness of whom two were admitted to hospital in sub-Saharan Africa with fever and diarrhea. When asked about the degree of inconvenience brought on by the diarrheal illness, 39% categorised it as minor or none at all, 34% as moderate and 27% as large or severe. Severity of symptoms was greater and use of treatment and necessity to alter the activity program were more common in those who regarded the episode of TD a major inconvenience.

Conclusion: Conventional definitions of TD encompass many cases of TD (in our study approximately one-third of all cases) that are so mild that vaccination or treatment is unlikely to provide a significant health benefit. By measuring the degree of inconvenience brought on by TD, researches and policy makers may be able to better distinguish 'significant TD' from mild TD, thus allowing for a more precise definition of the target population for preventive and therapeutic intervention.

FC04.04

Maternal and paternal use of mefloquine chemoprophylaxis prior to and during pregnancy

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Background: Women who are pregnant or who consider becoming pregnant should defer travel to malaria endemic areas with a high risk of *Plasmodium falciparum* malaria. Few effective drugs are approved for malaria chemoprophylaxis in pregnancy and there is a dearth of evidence on the safety of malaria chemoprophylaxis, particularly in the first trimester.

Objectives: The goal of this analysis was to evaluate pregnancy and foetal outcome in infants born to mefloquine exposed women and men based on drug safety records.

Methods: Reports, submitted to the F. Hoffmann-La Roche drug safety database, with a cut-off date of October 26th, 2010, provided information on a large number of outcomes of mefloquine exposure in the peri-conceptual and pregnancy setting. The focus of our analysis was on prospective cases but retrospective cases were also evaluated.

Results: Most reports were submitted spontaneously. A significant proportion of cases were ongoing or lost to follow-up. More than 2,200 maternal prospective cases were evaluated together with maternal and paternal retrospective cases. In a limited number of prospective and retrospective cases there was both maternal and paternal mefloquine exposure. In the maternal prospective cases, most of the exposure occurred prior to conception and/or in the first trimester. In the main collective, the maternal prospective collective, cases were grouped according to outcome: delivery or abortion (spontaneous and therapeutic). In the deliveries, the outcomes evaluated were: normal babies, peri-natal complications and birth defects. No specific pattern of malformations was identified. This ongoing analysis suggests a low prevalence of congenital malformations following peri-conceptual and pregnancy exposure to mefloquine.

Conclusions: Although a large proportion of cases were lost to follow up and we have no denominator data, this evaluation suggests that there is no increased risk of birth defects associated with mefloquine chemoprophylaxis. These data provide an evidence base to assist in decisions regarding the use of mefloquine prior to and during pregnancy. The product label continues to advise women of childbearing potential to practice contraception during malaria prophylaxis with mefloquine and up to 3 months thereafter.

FC04.05

Calls to a national travel health advice line - Information from the National Travel Health Network and Centre (NaTHNaC)

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Objectives: In 2003 NaTHNaC instituted a national telephone advice line to provide guidance to health professionals with queries regarding either complex itineraries or travellers with special health needs. This study analyses the calls from 1st January 2004 to 30th June 2009, in order to:

- identify the most frequently asked questions
- highlight travel health training needs of health professionals
- determine whether the service provided is necessary

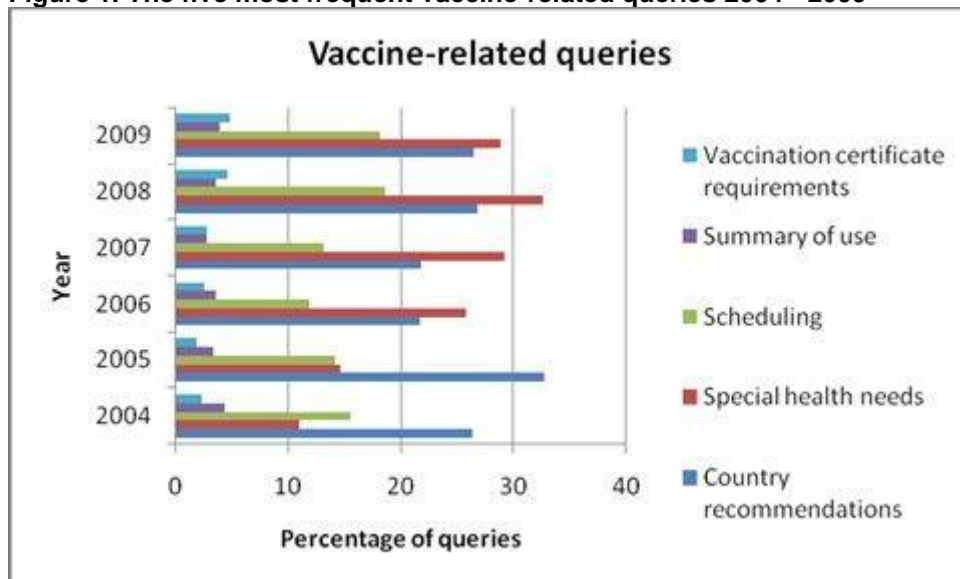
Methods: Every call to the advice line was summarised on a standardised form and voice-recorded. This information was entered into an Access® database. The results were then analysed using Access® and Excel®.

Results: A total of 47,979 calls were analysed. As callers could ask more than question, there were 56,238 separate queries. Practice Nurses (79%), General Practitioners (7%), and Pharmacists (5%) were the most frequent callers. The queries were about vaccines (62.1%), malaria prevention (33.5%) and general travel health topics (4.4%). Of the vaccine-related queries (n=34,933), the most frequent topics were country recommendations (35.0%, 12,240), special health needs (30.6%, 10,698), vaccine scheduling (19.8%, 6,900), summary of use of vaccine (4.4%, 1,542) and yellow fever vaccination requirements (3.6%, 1,273). In 2004 and 5, the most frequent vaccine-related topic query was country recommendations. In 2006-9, the topic of special health needs was the most frequent vaccine-related query (Figure 1).

Of the malaria-related queries (n=18,825), the most frequent topics were country recommendations (60%, 11,101), travellers with special health needs (31%, 5,921), long-term use of malaria chemoprophylaxis (3%, 647) and adverse events to malaria chemoprophylaxis (2%, 333). Country recommendations remained the most frequent malaria-related topic over the six year period (Figure 2).

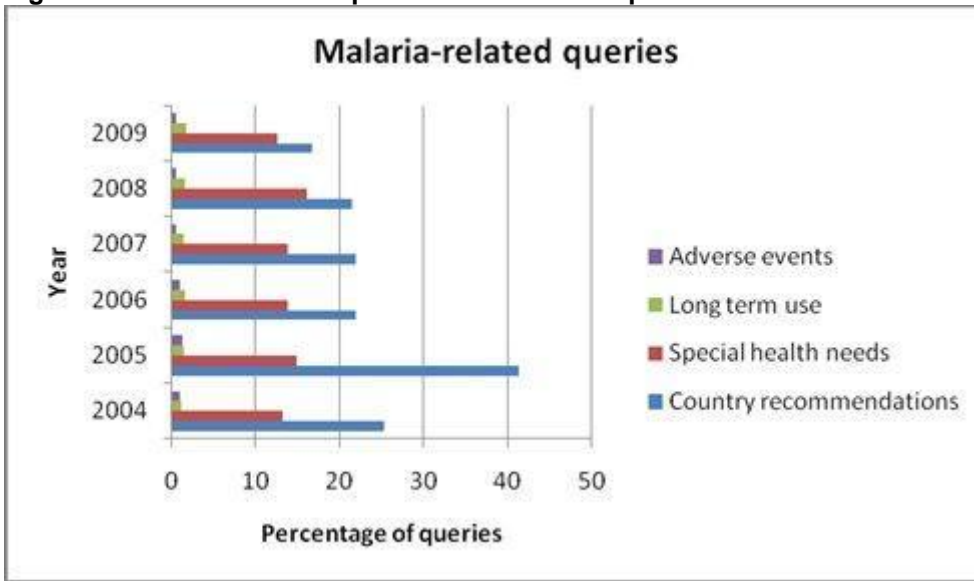
Conclusions: This study analyses the largest known dataset of calls to a national travel health advice line. Health professionals should receive training in the use of available country-specific guidance resources and managing travellers with special health needs. This study illustrates the need for such a service and could be used as a model for other countries.

Figure 1. The five most frequent vaccine-related queries 2004 - 2009



[Vaccinequeries]

Figure 2. The four most frequent malaria-related queries 2004-2009



[malariaqueries]

FC04.06

An Open Label Study of Tadalafil and Acetazolamide versus Acetazolamide for Prevention of Severe Mountain Sickness

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Introduction: Acute mountain sickness (AMS) and its complications high altitude cerebral edema (HACE) and high altitude pulmonary edema (HAPE) occur when acclimatization is insufficient and are aggravated by exhaustion. Acetazolamide is well proven for both prophylaxis and treatment of AMS. Phosphodiesterase-5 inhibitors (PDE-5 inhibitors) are a group of drugs proven to be effective in the treatment of pulmonary hypertension. Recent studies have shown the efficacy of PDE-5 inhibitors in increasing exercise capacity during hypoxia and in reducing the incidence of HAPE in adults with a history of HAPE.

Objectives of the study: To evaluate the efficacy of tadalafil in the prevention of severe AMS, HACE and HAPE in healthy trekkers without a history of severe mountain sickness.

Methods: An open label study comparing tadalafil and acetazolamide versus acetazolamide alone in the prevention of altitude illness. Trekkers participating in group efforts to summit Mt. Kilimanjaro (5895m) were enrolled. The intervention group received tadalafil 20mg qd and acetazolamide 125mg bid, beginning day 2 of the ascent (sleeping altitude 3950m). The control group received acetazolamide 125mg bid beginning the same day. Primary end point was prevention of severe AMS defined as HACE or HAPE. Secondary endpoints included prevention of AMS evaluated using the Lake Louise AMS scoring system and improving exercise capacity measured by successfully summiting Mt. Kilimanjaro.

Results: Fifty one of 55 enrolled participants completed the study protocol. The median age of participants was 50±12.2 years (range 19-68 years) and 9/51 (17%) were females. The intervention and control groups had similar characteristics.

Severe AMS rates were significantly lower in the tadalafil group compared with the control group (4% vs. 26%, P=0.05).

The tadalafil group compared with the control group had lower rates of AMS (50% vs. 59%), lower average AMS score during the summit day (2.9±2.0 vs. 4.1±4.1) and higher rates of summiting the mountain (95% vs. 88%); however, these results were not statistically significant.

Conclusion: Our results suggest that tadalafil was useful in prevention of HAPE and HACE in high altitude.

FC05 Dengue and Yellow Fever

FC05.01

Incidence of dengue virus infection in Australian travellers visiting South and South East Asia.

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Objective: To estimate the incidence density and prevalence of dengue virus infection in Australian travellers to Asia.

Methods: A prospective cohort study of Australian travellers to Asia over a 30-month period was performed. Travellers 16 years of age and over completed validated questionnaires and provided pre and post-travel blood samples for serological testing for dengue IgG by ELISA (Pan-Bio assay) and JE (indirect fluorescence antibody). Demographic data, destinations and travel patterns, vaccination details and history of flavivirus infection were obtained.

Results: Among 467 travellers enrolled, 387 had returned for follow-up, 59 (12.7%) were lost to follow-up and 22 travellers were not eligible for the study; 58% were female, median age was 37 years and 25% were born overseas. 72% were short term travellers (< 30 days) and the median duration of travel was 21 days (7-326). The main reasons for travel were vacation/holiday (69%), business (16%) and VFRs (4.9%). 77% reported prior travel to Asia and only 5.1% had received the JE vaccine in the past 3 years. 6335 days (53.6%) of this cohort were spent in the South East Asian region, mostly in Vietnam and Thailand. 32.8% percent of traveller days were spent in South Asia of which almost all were spent in India. 44.1% (n = 171) reported travel to urban destinations only.

Dengue sero-prevalence: Acute seroconversion for dengue virus infection was demonstrated in 4/387 (1.2%) of travellers tested. This translated to an incidence of 3.4 dengue virus infections per 10,000 days of travel (95% CI: 1.4-8.6). A further 20 travellers (4%) were positive for dengue IgG prior to travel indicating past exposure. All travellers had subclinical dengue infection. Those with acute dengue seroconversion had travelled to China (n=1) and India (n=3), and two of these travellers had received the JE vaccine but had non-reactive JE serology.

Conclusion: For travellers to Asia, the incidence density of acquiring dengue in an inter-epidemic period is 3.4 infections per 10,000 days of travel and the overall seroprevalence of dengue infections in Australian travellers was 5.2%. These findings have important implications for practitioners advising prospective travellers visiting dengue endemic regions.

FC05.02

Dengue fever outbreaks during 2009 - 2010 in Lima, Peru: Epidemiological changes in urban areas

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Objectives: With the increase of national and international travelers the potential transmission of dengue epidemic in the city of Lima has spread alarmingly in the last five years. The 2005 and 2007 outbreaks of dengue fever occurred in these districts only one circulating serotype in each outbreak. Epidemiological investigation was conducted to determine the distribution of cases, serotype circulation, symptoms and signs of dengue fever in order to identify transmission and epidemic control measures.

Methods: All suspected cases of dengue were obtained from the epidemiological forms sent by the health care services to the surveillance epidemiological network. Suspected case was considered a person with a history of fever for 2 to 7 days and two or more of the following symptoms: headache, retroocular, myalgia, arthralgia, rash and bleeding that reside in Lima. All serum samples were tested for anti-dengue IgM and IgG antibodies by ELISA.

Results: Of 878 serum samples tested of suspected cases during 2009-2010, 320 (36.4%) were positive for dengue virus specific IgM antibodies indicating primary infection and 134 (15.3%) were positive for IgG antibodies indicating past infection. Most cases (46%) were adults between 20 and 59 years of age. The median age was 34 years. Women were more affected than men (56% and 44% respectively). The most frequent symptoms were fever (98.5%), headache (94%), body ache (90%), bone pain (74%) and pain retroocular (68%). The outbreak investigation revealed a cluster of four clusters that could be because they have areas favorable for breeding of the vector, such as presence of disposable plastic containers, clearing rocks, water shortages and the migration of people to Lima from dengue endemic areas. In these outbreaks, 156 serum samples were dengue serotypes isolated by PCR: DEN-4 (48,1%), DEN-1 (42,3%) and DEN-3 (9,6%).

Conclusion: The outbreaks investigation, confirmed the circulation of multiple serotypes in Lima that might enhance the probability of development more severe clinical manifestations of dengue in the future. Virus epidemic activity during these 2 years puts the dengue as a major public health problem in Lima. It is important to strengthen surveillance actions epidemiological and vector control in these areas during the coming years.

FC05.03

Dengue Virus Seroconversion in Travelers to Dengue-Endemic Areas

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Objectives: To determine prevalence of dengue virus (DV) antibody seroconversion in travelers and identify travel-related risk factors associated with seroconversion.

Methods: Travelers \geq 2 years of age attending any of 5 Boston-area travel clinics from 1/6/2009-5/18/2010 and who were planning to visit DV-endemic areas for \geq 2 weeks were eligible. Demographic and travel information were obtained. We collected pre-travel sera at enrollment and post-travel questionnaires and sera 2-3 months after return. All post-travel specimens were tested for DV IgG by indirect ELISA and DV IgM by capture ELISA (Focus Diagnostics); pre-travel samples were tested only if corresponding post-travel samples were positive.

Results: Paired sera were available for 412 participants; 56% were female and the age range was 4-78 years. Of 412 post-travel samples, 60 (15%) were IgG positive and 13/412 (3%) were IgM positive, although none were positive for both IgG and IgM.

Forty-nine of 60 IgG positive and 7/13 IgM positive samples were also positive pre-travel and were excluded from the seroconversion incidence calculation. Eleven of 60 post-travel IgG positive and 6/13 post-travel IgM positive samples were negative pre-travel for IgG and IgM, respectively; therefore, 17/356 (4.8%) susceptible participants seroconverted to DV during travel.

Seroconversion occurred in 10/226 (4.4%) of travelers reporting no symptoms and in 1/99 (1.0%) of those reporting dengue-like symptoms ($p=0.18$). Travel to rural areas (RR 1.60; 95% CI 0.37-6.90), insect repellent use (1.69; 0.61-4.71), air conditioning (0.44; 0.17-1.18), and accommodations near standing water (1.95; 0.72-5.25) were not significantly associated with DV seroconversion.

Conclusions: DV antibody seroconversion occurred in 4.8% of susceptible travelers that were surveyed. An additional 49 travelers had elevated pre-travel anti-DV IgG and were at risk for complications of subsequent DV infection. Insect repellent use was not associated with DV protection, which may reflect travel to high mosquito density areas and higher risk of DV infection, or variability in frequency and quality of insect repellent application. Travelers may need more specific counseling on the appropriate use of DEET-containing insect repellent and preventing bites from daytime-biting mosquitoes.

FC05.04

Yellow Fever: Information for Healthcare Professionals Advising Travelers — The First Web-based Yellow Fever Vaccine Training Course by US CDC

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Objectives: To develop a web-based yellow fever (YF) vaccine training course as a tool to establish core competency among current and prospective YF vaccine providers in the United States (US). The course is intended to 1) address the knowledge gaps and practice deficiencies identified in previous surveys of YF vaccine providers and clinics and 2) provide information on the 2010 Advisory Committee on Immunization Practices (ACIP) YF Vaccine Recommendations.

Methods: We identified essential YF and travel medicine topics and developed content based on guidance from YF disease experts, CDC's Health Information for International Travel 2010, ACIP YF vaccine recommendations, and other published references. We used Lectora[®] software to convert the content into an interactive, web-based learning design that integrated multimedia formats (e.g., text, audio, video, maps, photographs, case scenarios, and knowledge assessment questions). Prior to release, we conducted two pilot tests with a sample of 40 healthcare professionals, incorporated changes, and publicized the course to state health departments and professional organizations.

Results: *Yellow Fever: Information for Healthcare Professionals Advising Travelers*, which was released on September 30, 2010, contains two parts. Lesson 1 discusses YF history, epidemiology, vaccine precautions and contraindications, and serious adverse events. Lesson 2 discusses pre-travel consultation; the YF vaccine provider designation process; best practices, requirements and recommendations for YF vaccine; the International Certificate of Vaccination and Prophylaxis; and medical waivers. The course is open access, free, and takes approximately 2 hours to complete. Continuing education credits for healthcare professionals are offered upon completion of the course evaluation and posttest. As of January 7, 2011, 426 professionals have completed the course for credit, including physicians, nurses, pharmacists, and health educators from 41 US states and 10 countries.

Conclusions: This comprehensive YF vaccine course provides an engaging way for healthcare professionals to increase their overall knowledge of YF disease, vaccine, and vaccine recommendations. The web-based system provides data on providers who accesses the course, posttest answer frequencies, and archives comments. Evaluation is planned regarding the extent to which US state health departments incorporate the course into their YF vaccine provider registration processes.

FC05.05

Evaluation of the impact of a national training programme on yellow fever vaccination practice in England, Wales and Northern Ireland

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Objectives: In 2005 the National Travel Health Network and Centre (NaTHNaC) introduced a programme of registration, training and standards for yellow fever vaccination centres (YFVCs) in England, Wales and Northern Ireland (EWNI). This study evaluated the impact of training by assessing confidence levels of those administering yellow fever (YF) vaccine, and adherence to standards.

Methods: In 2009 all YFVCs in EWNI (n=3,465) were requested to complete an on-line questionnaire (Survey Monkey®). Respondents evaluated the influence of training on practice, and answered questions on YFVC demographics, vaccine storage, record keeping and resources accessed. Responses were then analysed.

Results: 1,438 centres completed the questionnaire (response rate 41.5%). Almost all YFVCs were based in General Practice (87.4%); the Practice Nurse (43.0%) or nurse responsible for the YFVC (41.8%) usually completed the survey. 92.2% of respondents had attended NaTHNaC YF training. Nearly all respondents (95.8%) indicated that training improved confidence on YF vaccine issues.

After training, 68.5% of YFVCs made changes to their practice: in risk assessment (61.9%), record keeping (61.6%) and use of internet resources (48.1%). GP surgeries were most likely to make changes compared with other centre types ($p < 0.000$); the size of the YFVC (based on annual number of travel patients) did not affect whether changes were made. Adherence to NaTHNaC core standards also improved. In comparison with a baseline study prior to NaTHNaC's programme for YFVCs (*J Travel Med* 15:287, 2008), only 0.5% (n=7) of centres stored vaccines in a domestic refrigerator (c/w 11%), 0.6% (n=8) did not record refrigerator temperatures (c/w 2%), and 5.5% (n=75) kept vaccine records for less than the required 10-year period (c/w 20%).

Following training confidence levels about YF vaccine were high (76.4%-97.8%). Of those not attending training, 47.3% expressed low confidence about global epidemiology and transmission of YF compared with 15.7% of those trained, and 50.0% expressed low confidence about International Health Regulations compared with 19.8%.

Conclusions: NaTHNaC training for YFVCs has made a positive impact on both the practice and confidence levels of healthcare personnel administering YF vaccine in EWNI. This programme can be a model for improving practice in travel medicine.

FC05.06

Delayed antibody response to yellow fever vaccination in elderly coincides with prolonged viraemia

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Background: The live attenuated 17D yellow fever vaccine is regarded as one of the safest vaccines. However, it can cause vaccine-associated disease that resembles wild type yellow fever (yellow fever vaccine associated viscerotropic disease, YEL-AVD) The risk of YEL-AVD increases with a history of thymectomy, male gender and higher age. For vaccinees of 60-69 years, this risk is estimated to be 1.1:100.000 doses and for vaccinees of \geq 70 years it is 3.2:100.000, a 4.4 and 13.4 fold higher risk than for young adults. We investigated the humoral immune response against YF-17D in elderly subjects, to investigate the mechanism of YEL-AVD.

Method: Young volunteers (age range 18-28 yrs, N=30) and elderly travelers (age range 60-81 yrs, N=28) were vaccinated with YF-17D from the same vaccine batch. Neutralizing antibody titers and plasma YF-17D RNA copy numbers were measured at day 3, 5, 10, 14 and 28 after vaccination. Following vaccination, adverse events were documented in a diary during 3 weeks.

Results: Ten days after vaccination seroprotection (80% virus neutralization in plaque assay by minimally diluted serum) was attained by 77% (23/30) of the young participants and by 50% (14/28) of the elderly ($p = 0.03$, χ^2 test). At day 10, the younger participants had a GMT of 0.18 IU/ml, ten-fold higher than the GMT in the elderly (0.017 IU/ml) ($p = 0.004$). At day 14 the GMT also differed (respectively 4.8 IU/ml and 2.7 IU/ml, $p = 0.035$). Seroprotection was attained by all participants (young and elderly) by day 14. Viraemia was more common in the elderly (86%, 24/28) than in the younger participants (60%, 14/30) ($p=0.03$). In addition viral levels were higher in the elderly than in younger participants and correlated with the occurrence of systemic adverse events.

Conclusion: We found that elderly subjects (age \geq 60 yrs) had a delayed antibody response and higher viraemia following yellow fever vaccine after primo vaccination. We hypothesize that this allows attenuated virus to cause higher viraemia levels that may result in severe disease.

FC06 Clinical Issues/Post Travel

FC06.01

Diagnostic trends over 10 years among travelers returning to GeoSentinel sites

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Aims: To examine trends in diagnoses and characteristics of travelers presenting to GeoSentinel sites over a 10 year period.

Methods: Of the 49 current GeoSentinel sites, 18 have been consistently reporting throughout the 10 year period of interest (2000-2009). Post-travel data from these sites were included in this longitudinal analysis. Trends in the reason for travel and in proportionate morbidity for certain key diagnoses were examined by linear regression.

Results: There were 40,136 patient records from the 18 sites. For each year between 2000 to 2009, the most common destinations of travel (in decreasing order) were Sub-Saharan Africa, South East Asia, South Central Asia, and then South America. The proportion of tourist travelers presenting at GeoSentinel sites decreased by 0.77% per year ($p=0.051$), and the proportion of VFRs increased by 0.84% per year ($p=0.012$). Examination of total GeoSentinel presentations among patients returning from malaria-endemic regions showed that proportionate morbidities for both *Plasmodium falciparum* and *P. vivax* malaria decreased (-0.14% per year, $p=.005$; and -0.14% per year, $p=.001$, respectively); this trend was most marked in travelers returning from sub Saharan Africa (*P. falciparum*: -0.41% per year, $p=0.004$; non falciparum malaria: -0.23% per year, $p=0.003$). The proportionate morbidity for enteric fever rose significantly (+0.1% per year, $p=0.015$), particularly among travelers returning from south central Asia (+0.31% per year, $p=0.035$). The proportionate morbidity of animal bites among returned travelers also rose (+0.069% per year, $p=0.017$). For dengue, no significant overall trend was seen but a clear peak occurred in 2001 (corresponding with a known outbreak in South East Asia).

Conclusions: This study of GeoSentinel surveillance data is the first longitudinal analysis of travel data over a 10 year period. For the diagnoses examined, the annual proportionate morbidity changes, although small, showed statistically significant trends. Caution is required in the interpretation of the data as site specific factors can impact results and changes in proportionate morbidity may not mean a change in absolute risk of disease acquisition at a particular destination. However, as these data accumulate, it may be possible to compare travel-related trends seen in GeoSentinel clinics with global patterns of disease.

FC06.02

Travel-Related Morbidity in Children: a Prospective Observational Study

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Objective: Increasingly, children travel with their parents to tropical destinations. Scarce data is available on the occurrence of ailments and diseases in children during travel. We studied the characteristics and frequencies of ailments in children from 0-18 years old and adults during traveling.

Methods: A prospective observational study, on ailments reported by children and adults traveling to tropical countries, was conducted. All families were given a questionnaire for a weekly report of their health. The ailments were rated with a, previously validated, semi-quantitative scale as mild, moderate or severe.

Results: 154 (69%) children and 49 (49%) adults kept track of their ailments for a total of 501 and 158 weeks, respectively. The children reported a total of 823 ailments of which 146 (17.7%) were graded as moderate and 9 (1.1%) as severe. The adults reported 171 ailments of which 17 (9.9%) were graded as moderate and 9 (5.3%) as severe. Insect bites were the most common ailment in both children and adults. Children between 12-18 years reported more ailments than younger children and adults. Destination is a risk factor for specific ailments.

Conclusions: Skin problems and abdominal problems were the most reported ailments in children and adults, as well as the most recurring problems, occasionally leading to a visit to a doctor or hospital. As children from the age group 12-18 years experienced more ailments than other children, they should be actively informed about the risks of traveling to a tropical country.

FC06.03

Travel-associated illness in older adults (> 60 years)

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Background: The epidemiology of travel-associated in older adults is not poorly known.

Methods: Medical data were prospectively collected on international ill travelers presenting to GeoSentinel sites from 1997 to 2008. The Fisher exact test for categorical variables and the Kruskal-Wallis test for continuous variables were used to compare demographic characteristics and proportionate morbidities (defined as the number of cases of a specific diagnosis or syndromic grouping of diagnoses per 1,000 ill returning travelers) between older adults (≥60 years of age) and a referent group of younger adults (18-45 years of age).

Results: 7014 patients aged 60 years and over were identified as older travelers and compared to 56042 patients aged 18-45 years, as a young adult reference population. Compared to younger, older patients were more likely to be male, had a greater proportion of tourist travelers and were less likely to seek travel advice. Travel region differed among age groups, with Europe, Middle East and North America being more frequent among older individuals. Several etiologic diagnoses were significantly more frequently observed in older patients compared to younger including lower respiratory tract infections, high altitude pulmonary edema, arthropod-bites, rickettsiosis, severe falciparum malaria, gastritis, peptic ulcer, esophagitis and gastro-esophageal reflux disease, trauma and injuries, urinary tract infections, heart disease and death. By contrast, acute bacterial and parasitic diarrhea, upper respiratory tract infections, flu/flu-like illnesses, malaria, dengue, genital infections and sexually transmitted diseases and schistosomiasis were less frequently observed among the older group.

Conclusions: While typical tropical infections were less frequent in elderly travellers, travel-associated health problems were more often related to concomitant diseases. In addition, older ill travelers are more likely to suffer certain life-threatening diseases (lower respiratory tract infections, high altitude pulmonary edema, severe falciparum malaria, heart disease) and would benefit from reinforced specific preventive measures. Therefore, besides general recommendation they should be advised to contact for travel health insurance that covers chronic stable medical conditions, acute illnesses, accident, medical evacuation and death.

FC06.04

Importation and spread of Pantone-Valentine leukocidin positive *Staphylococcus aureus* through nasal carriage and skin infections in travelers to the tropics and subtropics

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Objectives: Analysis of risk factors for skin and soft tissue infections (SSTI) caused by *S.aureus* in travelers to the tropics and subtropics and assessment of the role of PVL in the pathogenesis of travel associated SSTI.

Methods: (i) comparison of case patients suffering from *S. aureus*-positive SSTI (n=37) and control subjects (n=125) consulting our travel clinic after returning from the tropics and subtropics and (ii) comparison of case patients by PVL-status.

Results: 27 of 37 cases were PVL+, 8 were MRSA+ and 7 were both. The predominant manifestations were abscesses (56%) and furuncles (15%). A history of recurrences (73%), surgical drainage (49%) and SSTI in close contacts (38%) was frequent. Most controls consulted the clinic with gastrointestinal (61%) and respiratory (23%) complaints. 31 control subjects (25%) had nasal swabs positive for *S.aureus* all of which were PVL-.

Cases versus controls: Cases were more often exposed in Africa (OR 4.9, 95% CI1.6-17.0), Central America (OR 13.9, 2.0-105.9) and Australia/Oceania (OR 8.3, 1.2-56.0) while or shortly before onset of SSTI. Volunteering abroad, longer duration of travel, working in childcare and nasal carriage of *S.aureus* was associated with *S.aureus*-positive SSTI.

PVL and virulence: Presence of PVL in lesions of cases was strongly associated with recurrent disease (OR 18.7, 1.9-180.4), surgical drainage (OR 16.0, 1.2-211.7) and with presentation as abscess or furuncle (OR 32.0, 2.2-464.1). Nasal carriage of PVL+ strains could be detected in 52% of case patients with PVL+ lesions but not in case patients with PVL- lesions. PVL was more often found in the nares of cases suffering from recurrent lesions. Antibiotic resistance in particular against trimethoprim-sulfamethoxazole was more prevalent in PVL+ MSSA compared to PVL- MSSA (p< 0.002). Spread to close contacts as revealed by spa-typing and PFGE was more frequently reported by case patients with PVL+ *S.aureus* (OR 8.4, 0.8-90.3). PVL+ lesional isolates were assigned to genotypes considered endemic at respective travel destinations.

Discussion and Conclusions: Detection of PVL+ *S.aureus* indicates complicated and transmissible disease and is thus a useful marker for the clinical management of SSTI in returnees from the tropics and subtropics. The increased risk of SSTI and import of more virulent, antibiotic resistant *S.aureus* highlights the need for pre-travel counseling and surveillance of risk groups such as volunteers.

FC06.05

Update of practice guidelines for fever in returning travelers and migrants on the basis of a systematic review and a validation study

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Objectives: Practice guidelines represent a powerful tool to improve quality of care and rational use of diagnostic tests and drugs. In 2001, we developed guidelines for the management of fever in returning travelers that were targeted to primary care physicians and made available as a computerized algorithm on the website www.fevertravel.ch. Objectives were to revise and adapt the guidelines according to an update of the literature and a computerized validation study that assessed their feasibility and safety.

Methods: In the validation study, we investigated physicians' adherence to recommendations, reasons for non-adherence, safety and users' satisfaction. For the systematic review (SR) of the literature, papers in all languages, published from 1st January 2001 up to 25th May 2010, were extracted from a Medline search using the Medical Subject Headings terms and keywords 'fever+travel+guidelines (or synonyms)', 'fever+travel or migrant' and 'travel or migrant+name of the disease'. The research strategy was adapted for the Cochrane Database of Systematic Reviews, Embase and Web of Science.

Results: 539 patient/physician pairs from 116 different internet users were included in the validation study. Overall adherence to the guidelines per case was 40%, whereas adherence to a specific attitude corresponding to a specific symptom, sign or laboratory result was 62%. Half of the reasons for non-adherence were not repeating malaria test after a first negative result, not giving presumptive antibiotics in case of febrile diarrhea or abdominal pain. All complications observed could be attributed to an underlying disease rather than use of the guidelines; all patients recovered except one with lymphoma. For the systematic review, from the 5717 identified articles, 477 were retained and 105 added after cross-referencing. We found new evidence on predictors of tropical diseases which led us to add total hyperbilirubinemia as predictor of malaria and enlarged spleen as predictor of typhoid fever. Evidence for the use of rapid diagnostic test for malaria and Dengue fever was included, as well as information on how to retrieve and take into account ongoing epidemics.

Conclusions: We present a new web-based version of clinical practice guidelines for fever in returning travelers, based on up-to-date and evidence-based information and developed to fully comply with the needs of the end-users.

FC06.06

Post-travel screening of long-term travelers to the tropics for intestinal parasites using molecular diagnostics

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Background: Asymptomatic infection with protozoa or helminths can cause morbidity long after the primary infection. Early detection and eradication is beneficial. We aimed to determine the utility of routine post-travel screening of asymptomatic long-term travelers to the tropics for *Entamoeba histolytica*, *Giardia lamblia*, *Cryptosporidium hominis/parvum* and *Strongyloides stercoralis* using multiplex real-time PCR on stool samples. We also determined the utility of routine serological screening for *Schistosoma spp.* in travelers to sub-Saharan Africa.

Methods: Adults who visited the travel clinic at LUMC or WUR and who intended to travel to the tropics for >1 month were invited to take part. Participants submitted stool- and serum samples and filled out web-based questionnaires before departure and 2 and 12 weeks after returning home. Stool samples were sent by regular mail.

Results: 679 travelers provided informed consent of whom 123 submitted less than 2 stool samples and were excluded from analyses (follow-up rate 556/679, 82%). Participants' median age was 25 years (IQR 23-30), median travel duration 12 weeks (IQR 6-20) and the main mode of travel was qualified as 'backpacking' (47%). The attack rate for travelers' diarrhea was 74%. Two weeks after returning home 542 participants (97%) submitted a stool sample; 437 (79%) also submitted a sample after 12 weeks. Based on the multiplex-PCR, 4 were diagnosed with *Cryptosporidium* (1%) and 1 with *S. stercoralis* (0.2%). There were no infections with *E. histolytica*; 29 travelers were diagnosed with *G. lamblia* (5%), 5 of whom also had a positive pre-travel sample. Abdominal complaints were more common in infected than in uninfected travelers (RR 2.2, 95% CI 1.1-4.7). Half of all infected travelers were asymptomatic at the time of diagnosis. Of 175 participants who traveled to sub-Saharan Africa, 132 (75%) submitted serum samples, 9 of whom (7%) showed seroconversion to schistosome antigens; 7 were asymptomatic and 2 had Katayama syndrome.

Conclusion: Based on the low incidence of asymptomatic infection, routine screening of long-term travelers to the tropics for *E. histolytica*, *S. stercoralis*, *C. hominis/parvum* and *G. lamblia* was not useful. Asymptomatic infection with *Schistosoma* was more common and screening should be offered to all travelers with fresh-water contact in (highly) endemic regions.

FC07 Challenges and Controversies in Rabies, JE and Hepatitis B

FC07.01

Risk of Possible Exposure to Rabies among Travelers from Developed Countries in Southeast Asia
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Objectives of the study: Each year millions of travelers from developed countries visit Southeast Asia where rabies is still prevalent. This study aimed to assess the risk of rabies exposure, i.e. by being bitten or licked by an animal among travelers in Southeast Asia. The secondary objective was to assess their attitudes and practices related to the risk of exposure to rabies.

Methods: Travelers from developed countries were invited to fill out the study questionnaire in the departure hall of Bangkok International Airport. Only travelers who had completed their trip and were departing to the destination outside Southeast Asia were eligible to participate. They were asked about their demographic profile, travel characteristics, pre-travel health preparations, and their possible exposure to rabies and their practices related to rabies during this trip.

Summary of Results: In May 2010-Jan 2011, 3213 completed questionnaires were collected and analyzed. Sixty percent of travelers were male, and the median age was 30 years old. The majority (70.5%) of the participants were European, while 17.9% were Australian-New Zealander and 11.6% were American and Canadian. Up to 75.4% had sought health information before this trip however only 37.1% had received information about rabies. Only 15.2% of the participants had completed their rabies pre-exposure prophylaxis, 11.5% received only 1-2 shots, while 73.2 had not been vaccinated at all. In this study, the risk of being bitten was 0.56% (18/3,213) and the risk of being licked was 3.01% (97/3,213) on the average stay of 28.3 days. Among those who were bitten, only 20% went to the hospital to get rabies post exposure treatment. Younger age and longer duration of stay were significantly related to higher risk of rabies exposure.

Conclusions: Travelers from developed countries were at risk of being bitten or licked by animal while traveling in Southeast Asia. They were inadequately informed and prepared for this life-threatening risk. Rabies prevention advice should be included in every pre-travel visit.

FC07.02

Do travelers receive timely and adequate rabies post-exposure prophylaxis ?

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Objective: Potential rabies exposure happens at a rate of 16 - 200 per 100'000 travelers and occurs mainly in less developed countries. We aimed at investigating the adequacy of rabies post-exposure prophylaxis (PEP) in travelers consulting our travel clinic after they had returned from abroad.

Methodology: A retrospective analysis of the files of all travelers consulting our centre for rabies PEP between 2005 and 2010 was conducted. Besides demographic characteristics, we extracted from the files the information about exposure, medical management on site and after returning to Switzerland.

Results: 72 patients were identified who had consulted for rabies prophylaxis after potential exposure abroad. 58% were women; median age was 37 years (range 2-74). 8 patients (11%) had received pre-exposure prophylaxis with 3 doses of vaccine. 40 travelers had potential rabies exposure in Asia, 10 in Africa, 10 in South and Central America and 12 in Europe. The animals responsible for exposure were dogs (40), cats (6), monkeys (18), bats (3) and others (5). The 42 patients who sought care abroad started PEP within a median of 0 days (range 0-14 days). For the 30 patients who started PEP once back in Switzerland, the median delay from the date of bite was 10 days (range = 0-327 days). Only 5 of the 38 patients (13%) without pre-departure rabies vaccination and who consulted abroad received immunoglobulins. Of the 66 patients for whom antibody titers were available on day 21 after start of PEP, 4 (6%) did not have a protective antibody titer ($\geq 0,5$ IU/ml).

Conclusions: Travelers should be advised to seek medical care on site for potential rabies exposure abroad, as vaccination appears to be widely available which ensures a prompt start of rabies PEP. Availability of immunoglobulins is however scarce in most developing countries. Serological testing to check antibody response after 4 doses identified 4 individuals (6%) who were not adequately protected according to the accepted threshold. This challenges the recent CDC recommendation that serological testing after 4 doses of vaccine is not necessary.

FC07.03

The immunogenicity of a modified intradermal pre-exposure rabies vaccination schedule - A case series of 420 travellers

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Background: Current Australian recommendations for rabies pre-exposure vaccination involve the use of cell-culture-based rabies vaccines, which are administered via intramuscular or intradermal routes. Intradermal vaccination is cheaper and more affordable for travellers, but is only recommended if there is sufficient time to perform serology 2 to 3 weeks post vaccination and confirm immunity prior to travel. We report the immunogenicity of a modified intradermal schedule which was called TRID 2 (Travellers Rabies ID 2), that can be completed in a shorter time compared to the standard intradermal schedule, and potentially allow more travellers to be protected prior to departure.

Methods: Travellers were offered a modified schedule if they were unable to afford standard intramuscular vaccinations, and did not have time to complete a standard intradermal course. The modified schedule consisted of two intradermal injections of 0.1ml of human diploid cell rabies vaccine administered on days 0 and 7, and serology was performed to determine immune status at day 21 to 28.

Results: A total of 420 travellers aged between 10 and 65 years were vaccinated using the modified intradermal course. The overall seroconversion rate was 94.3%, with 397 travellers developing antibody levels of >0.5 IU/ml when tested at approximately 21 days post-vaccination. Antibody levels were significantly lower in the older age groups ($p=0.003$).

Conclusion: The modified intradermal schedule used in this case series was highly effective, has similar immunogenicity to the standard intradermal schedule, and could be considered in travellers who are unable to complete standard intramuscular or standard intradermal courses of rabies vaccines.

FC07.04

What is known about the protective efficacy of rabies vaccine in humans? An unexpected result from an immunogenicity study of pre-exposure rabies vaccination of healthy volunteers.

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Virus neutralization is viewed as the major correlate of protection from rabies virus (RABV) infection; however, this process is extremely complex *in vivo*. Protection is defined through the relationship between live rabies virus inoculation and animal survival. There has been notable progress made in characterizing the protective efficacy of RABV vaccines in small animal models where challenge experiments can be undertaken. Whether similar human immune responses to RABV vaccines achieve protection against a fatal outcome from an equivalent immunological response is unknown. This correlate is impossible to test rigorously as the standard of care in humans potentially exposed to RABV involves 4 vaccine doses together with exogenous rabies immunoglobulin (RIG). RABV neutralizing antibodies are used as a correlate of disease protection, when titre of 0.5 IU/ml or above are present, but how can we be certain that these titres of neutralizing antibodies alone, provide a sufficient degree of protection? We conducted a study based on 29 healthy UK adults, whereby Rabipur (Novartis; Flury LEP strain) vaccine was administered in 3 doses at baseline day 0, day 7 and day 21. Plasma was extracted from venous blood immediately before baseline and Day 21 timepoints and 1 month following the third dose and RABV neutralizing antibodies were measured by the fluorescent antibody virus neutralization (FAVN) assay. While the mean titres at days 21 and 50 were significantly higher than baseline ($p < 0.0001$), 2 out of the 29 subjects (6.9%) did not respond to the vaccine. A recent study, measuring efficacy of RABV vaccine in stray dogs, demonstrated that in 5 out of 9 vaccinated dogs, RABV neutralizing antibody titres were < 0.5 IU/ml, yet all 9 dogs were protected when challenged with live RABV. Animal studies have described fatal outcomes in fully immunised animals when the challenge lyssavirus was significantly distant phylogenetically from the vaccine strain with which they were immunised.

Current knowledge and practice, based on the use of neutralising antibody titres for determining protection from disease may not accurately reflect true protection.

FC07.05

Safety, Immunogenicity and Dose Confirmation for the Inactivated Japanese Encephalitis Vaccine IXIARO®, IC51, in Filipino Children aged 3 to 12 years

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Introduction: IXIARO, a Vero cell-derived, inactivated Japanese encephalitis (JE) vaccine manufactured by Intercell AG, is licensed for adults as 6 mcg/0.5 ml dose. IXIARO is investigational for pediatric use. A Phase II study in 1- < 3 year old Indian children supports using a half dose 3 mcg/0.25 ml in this age group. The dose for children aged 3 to < 12 years had not been confirmed.

Objectives: To confirm the appropriate dose of IXIARO in children aged 3 to < 12 years.

Methods: Randomized, controlled open-label Phase III study in a JEV endemic country (Philippines) with a dose-finding run-in phase. In the run-in phase, 200 children aged 3 to < 12 years were randomized to receive a full (6 mcg/0.5 ml) or half (3 mcg/0.25 ml) dose of IXIARO at Days 0 and 28. NT titers were assessed by PRNT at Day 56. Systemic and local adverse events (AEs) were solicited for 7 days, unsolicited AEs were collected up to Day 56.

Summary of Results: 100 children were randomized to the 0.5 ml and 101 to the 0.25 ml dose group. Demographic data (mean age 7.6 years) and baseline Flavivirus immunity (JE virus antibodies (PRNT) in 14%, DEN1-4 IgG (ELISA) in 51%) were well balanced among the study groups. Seroconversion rates (SCR) at Day 56 did not differ significantly between the 0.25ml (95.9%) and 0.5ml dose (100.0%, p =0.058). The 0.5ml dose resulted in a statistically significantly higher GMT (214) than the 0.25ml dose (111, GMT ratio 1.92) at Day 56. No related, serious AE was reported. 22.8% in the 0.5 ml and 16.0% in the 0.25 ml group reported local symptoms, and 20.8% and 25.0% reported solicited systemic symptoms, respectively. The most common solicited systemic symptom was fever (14% in the 0.5 ml and 21% in the 0.25 ml dose group). The majority of AEs was mild.

Conclusions: Both tested doses of IXIARO appeared to have a comparable safety profile. Due to higher SCR and significantly higher GMTs, the full adult dose will be pursued for further development in this age group.

FC07.06

High response rate in previous non-responders after revaccination with high potent hepatitis B vaccines

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Background: Hepatitis B vaccination plays a key role in preventing hepatitis B infection and its complications. However, some vaccinees do not develop a protective titer (10IU/L) after a standard 3-dose regime and administration of three additional doses with one month interval is frequently recommended but non-response still often occurs. Therefore, alternative vaccination strategies are necessary. Newly available high dose hepatitis B vaccinations registered for renal insufficiency might be more effective in non-responders. The study's aim is to determine which of four different revaccination interventions will induce best protective anti-HBs titres in healthy non-responders.

Methods: 388 healthy employees known to be non-responders were enrolled. We assessed the effect of a second hepatitis B vaccination series (after the standard 3 dose regime) using four different regimes: group 1. (n=211). three revaccinations with Engerix-B® (one month interval), group 2. (n=30). one revaccination with Engerix-B®, group 3. (n=108) one revaccination with HBVaxPro-40® (40µg HBsAg in 1ml, Sanofi-Pasteur MSD, Lyon, France), and group 4. (n=39) one revaccination with Fendrix® (20µg HBsAg in 0.5ml, GlaxoSmithKline, Rixensart, Belgium). Predictors for non-response after revaccination were assessed using univariate and multivariate regression analysis.

Results: The two independent predictors for protection after revaccination were low non-response titer after vaccination (titer 0: 94% versus titer 1-9: 64%) and booster type: group 1 and 2 showed less protection after revaccination of 75% (158/211) and 76% (23/30) than group 3 and 4 with 91% (98/108) and 100% (39/39). Sex and age were not significantly associated.

Discussion: Fendrix® and HBVaxPro® both showed higher revaccination response than the standard three additional revaccinations scheme, suggesting these vaccines to be the first choice for non-responders.

FC08 Late Breaking Free Communications

FC08.01

Characteristics and spectrum of disease among ill travelers returning from post-earthquake Haiti: the GeoSentinel experience

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Objectives: On January 12, 2010, a destructive earthquake struck near Port au Prince, Haiti, prompting a massive multinational relief and recovery effort. We examined surveillance data collected from ill international travelers to describe the characteristics and spectrum of disease among ill persons returning from post-earthquake Haiti.

Methods: GeoSentinel Global Surveillance Network data were used to determine characteristics and frequencies of diagnoses (specific and syndromic groupings) for ill travelers returning from Haiti. One year post-earthquake versus three years pre-earthquake were compared by using chi-square and Wilcoxon rank sum tests. Persons emigrating from Haiti were excluded.

Results: There were 117 pre- and 147 post-earthquake ill travelers returning from Haiti reported to GeoSentinel. Median age for the pre- and post-earthquake groups differed by 7 years (44 versus 37, $p=0.004$). Of the ill Haiti travelers, 188 (71%) were from the United States and Canada; there was a proportionate increase among United States travelers (from 26 [22%] to 70 [48%], $p<0.001$) post-earthquake. Volunteerism (aid workers, missionaries, and researchers) increased markedly from pre- to post-earthquake (33 [28%] versus 108 [73%], $p<0.001$); however, visiting friends and relatives decreased markedly from pre- to post-earthquake (46 [40%] versus 11 [7%], $p<0.001$). An increase in post-earthquake pre-travel medical encounters (from 30 [34%] to 99 [74%], $p<0.001$) was observed and linked to shifts in travel-purpose. Rank-ordered top-five post-earthquake syndromic diagnoses were acute diarrhea, febrile/systemic illness, respiratory illness, psychological conditions, and dermatologic conditions; three were significantly higher during the post-earthquake period: acute diarrhea (from 17 [12%] to 24 [43%], $p=0.007$), respiratory illness (from 6 [4%] to 23 [13%], $p=0.008$), and psychological condition (from 3 [2%] to 19 [11%], $p=0.03$). The top five reported post-earthquake specific diagnoses were upper respiratory tract infection, acute unspecified diarrhea, acute bacterial diarrhea, dengue, and *Plasmodium falciparum* malaria.

Discussion: These results suggest that post-earthquake, a greater proportion of Haiti travelers who returned ill were volunteers and of these, a higher proportion returned with acute diarrhea, respiratory illness, and psychological conditions. Along with the standing health recommendations for travel to Haiti, these findings may help identify target populations for pre-travel advice and health hazards that are amenable to focused health educational strategies.

FC08.03

Yellow Fever Outbreak — Uganda, 2010

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Objectives: In December 2010, the first outbreak of yellow fever (YF) in Uganda since 1975 was identified in several remote, northern districts. Initially, the cause of the outbreak was unknown. CDC provided testing support to define the etiology and scope of the outbreak and conducted a survey to describe the incidence, clinical features, and risk factors for infection.

Methods: A standardized system of specimen collection was developed. Several CDC laboratories performed testing for agents such as viral hemorrhagic fevers, enteric pathogens, and plague. A population-based community survey was conducted in two villages. We screened all households for residents with a history of febrile illness from October 2010-January 2011. Information on demographics, symptoms, YF vaccination history, and possible risk factors was obtained. A blood sample was collected to test for evidence of YF.

Results: From 114 specimens tested from the outbreak for YF, 14 laboratory-confirmed cases were identified; all other tests were negative. Patients positive for YF resided in five districts and the majority (80%) had illness onset dates in November and December. Viral RNA with 97%-98% nucleotide identity with an East Africa YF genotype was sequenced. Among 1,100 village residents screened as part of the community survey, 357 (32%) persons with a recent febrile illness were enrolled. Among 349 persons tested, 9 (3%) had confirmed evidence of YF virus infection for an attack rate of 8 per 1,000 residents. The median age of confirmed cases was 19 years (range: 12-82), 5 (56%) were male, and 5 (56%) had illness onset in the 2 weeks between November 7-21 (range: October 18-December 12). Seven (78%) case-patients resided in Golgota (15 per 1,000); two resided in the same homestead with illness onset 21 days apart. Among the 9 case-patients, 3 (33%) reported having jaundice and 2 (22%) reported hematemesis; one fatal case had both hematemesis and jaundice. Risk factor analyses are ongoing.

Conclusions: These findings help define the incidence and epidemiology of the first YF outbreak in Uganda in 35 years, and support the need for YF vaccination to prevent future cases and outbreaks.

FC08.04

Quadrivalent Meningitis Vaccination in Children

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The incidence of meningococcal disease is highest among children < 2 years of age, adolescents, and the elderly, with the highest mortality occurring among infants and teens. Risk factors for invasive disease include crowded living conditions, respiratory tract infection and close contact to with an individual with meningococcal disease. For the usual traveler, the risk of infection abroad seems not to exceed the one home, but vaccination of certain groups and for certain destinations such as the African meningitis belt may be indicated.

Conjugated vaccines are - in comparison to polysaccharide vaccines - immunogenic in young children, induce long-term protection and reduce nasopharyngeal carriage. For travel to endemic countries, broad coverage with quadrivalent vaccines is indicated. A quadrivalent conjugate vaccine (conjugated to chemically detoxified diphtheria toxoid = MenACWY-D) was licensed in 2005 in the US (Menactra[®], Sanofi Pasteur), it is approved for individuals aged 2 to 55 years, however, it is not very immunogenic in infants. In the EU another conjugate vaccine (Meningococcal Oligosaccharide Diphtheria CRM₁₉₇ Conjugate Vaccine = MenACWY-CRM₁₉₇) has been licensed for individuals aged >11 years. (Menveo[®], Novartis). Menveo received initial FDA approval in 2010 for use in adolescents and adults from 11 to 55 years of age. In January 2011, Menveo[®] received approval also for use in children 2 to 10 years of age by FDA, up to now there is now approval for Menveo[®] in children in the EU. A third quadrivalent conjugate vaccine (Meningococcal tetanus toxoid conjugate vaccine = MenACWY-TT) is in clinical trials in children and adults (Nimenrix[®], GlaxoSmithKline). GSK has announced in March 2011 that it has submitted a Marketing Authorisation Application (MAA) to the European Medicines Agency (EMA) for this vaccine, however is not currently approved or licensed anywhere in the world.

Thus, quadrivalent conjugate vaccines are available now for children and should be used for children travelling to endemic areas. Indications for children on travel could be:

- Travel into regions with actual outbreaks
- Travel into African meningitis belt and underlying health problems like functional or anatomic asplenia, terminal complement deficiency, hypogammaglobulinemia, chronic renal insufficiency
- Travel into African meningitis belt and high transmission risk: longer stays, visit of schools etc.