ment and defines the spectrum of illness and the relation to place of exposure for the most significant health risks that face travelers.

Founded in 1996, the communications and data collection network currently comprises 50 travel/tropical medicine ISTM (International Society of Travel Medicine) clinics on 6 continents operating in cooperation with the US CDC. Returning travelers seen at relatively few sentinel sites provide a sample of disease agents in over 230 different countries. As of December 1, 2009, over 114,000 patient records increasing by 20,000/yr, track trends against a 12-year long baseline for over 500 diagnoses in order to monitor anomalies that might herald disease emergence.

Real time data entry via internet onto a central server allows monitoring of alarming sentinel events to generate immediate network wide queries and enhanced surveillance during focal or widespread outbreak situations. The GeoSentinel response arm disseminates alerts and advisories through CDC, ProMedMail, ISTM, ASTMH, and other partner networks and agencies.

Examples have included: imported traveler-related cases/outbreaks of SARS, 2009 H1N1 influenza, leptospirosis from Borneo, Hantavirus from Chile, Hajj meningitis from Singapore, firstever dengue from Easter Island, and schistosomiasis from Tanzania.

The presentation will include advances, observations, lessons and limitations from the experience of the global GeoSentinel surveillance network. Data from sentinel travelers upon their return to medically sophisticated environments can also benefit local populations in resource-limited countries.

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## Advances from the laboratory (Oral Presentation)

### 47.001

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

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*Background:* Rickettsia is a worldwide usually rodent-carried tick, flea or lice-borne bacteria. In Colombia, few reports have beed performed, first in the mids thirties causing an outbreak in the population of Tobia Cundinamarca, and from the years 2006 to 2008 in the Northern region of Colombia known as Urabá. Our main goal was to perform an epidemiological description of the infection in the endemic mentioned area in Colombia.

*Methods:* Samples were obtained from the municipalities of Apartadó, Turbo y Necoclí, where 335 rondents were captured and parasites were collected from 33 of them. 220 double-blood human samples were also taken Indirect Immunofluorescence (IFI), was used to detect rickettsial infection in humans and rodents. Additionally, PCR was performed in liver-DNA from rodents searching for specific genetic sequences of Rickettsia genus (Citrate Synthase gene, gltA) and pathogenic Rickettsias (OmpB gene).

*Results:* We obtained 23 rodent DNA samples positive to gltA but only 6 of them, positive for the OmpB gene, resulting on a 6.8% DNA frequency of infection to Rickettsias by PCR. Some PCR products for the gltA gene, were sequenced and showed 98% similarity with the *Rickettsia Prowazekii* species, but the phylogenetic analysis suggests that these sequences form a separated cluster indicating that these Rickettsias could represent a new specie or sub specie. 89 of the 220 human sera were tested by IFI and 11 came up positive in dilution 1:64 (10 of the samples were positive in the convalescence period M2, and one in the acute phase, M1). Most of the ectoparasites collected were identified as hard ticks (*Amblyomma sp,* Ixodidae family,) soft ticks (*Ornithodoros Alectorobius puertoricensis*, Argasidae family) and fleas (*Xenospsilla sp* genus). These samples still remain to be tested for rickettsial infection using both gltA and OmpB.

*Conclusion:* This is the firs of a serie of studies that will allow us to characterize ecologically this endemic site and contribute to recomend the measures to prevent future human cases in this important risk area.

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### 47.002

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

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*Background:* Influenza annual epidemics result in up to 500,000 deaths in human population, and different pandemics occurred over the 20th century, among which the 1918 pandemic was accountable for more than 50 millions deaths. Lethal seasonal or pandemic influenza infections are all associated either to secondary bacterial infections or acute respiratory distress syndrome (ARDS). Since antibiotics will help in treating bacterial pneumonias, it is crucial for public health to understand the pathogenesis of influenza-associated ARDS in order to fight it or to prevent its occurrence. Descriptions of the lung alterations in fatal influenza infections in human and mouse all depict similar lung dysfunctions and lesions. Here we describe the ARDS associated with the inoculation of identical doses of two influenza strains highly pathogenic for mice.

*Methods:* A clade 1 avian H5N1 virus (A/crested_eagle/Belgium/1/2004) and a porcine H1N1 virus (A/swine/Iowa/4/1976) were rendered highly pathogenic for mice by serial lung-to-lung passaging in

mice. Two series of mice were inoculated intranasally with 10 MLD50 of virus. Body and lung weights were monitored daily and several organs were sampled at selected time intervals for histopathological / immunohistochemical evaluation or for viral titration.

*Results:* MLD50 s were similar for both viral strains (3.2 PFUs for the H1N1 and 6.4 TCID50 for the H5N1 strain). The course of the infection was much faster for H5N1 than for H1N1, the endpoint days being days 4 and 8 post-inoculation, respectively. Typically, H1N1-infected lungs were characterised by a progressive extension from the airways to the lung parenchyma, resulting in a massive mononuclear cellular infiltrate. For H5N1, the lung parenchyma was rapidly diffusely involved, the airways being almost unaffected, with a very low density of inflammatory cell infiltrates and, at the end-point day, with massive alveolar edema. Influenza antigens were detected in lungs, brain, liver, spleen, heart, pancreas, kidneys and pervisceral fat of H5N1-infected mice, while H1N1 antigens were only found in the lungs.

*Conclusion:* The clearly distinct histological pictures shown here refute the hypothesis of a single universal pathogenesis beyond all influenza-associated fatal ARDS and suggest that the treatment should be tailored to the influenza pathotype.

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**47.003**

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

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*Background:* Substantial communications between the nervous and the immune systems were well established, but the effect of the nervous system in directing the innate immunity is not known. Accordingly, we hypothesized that opening innate responses to infections are mediated via nervous-to-immune signalling pathway.

*Methods:* To explore the factor(s) involved in this nervous-to-immune signaling pathway, splenicdenervated and non-denervated Sprague-Dawley rats were inoculated with *Trypanosoma brucei brucei* (*T.b.brucei*) followed by immediate dissection of the spleen and culture of splenocytes. ELISPOT and cell proliferation assays were used to assess cellular and biological activities. Using the fluorescent differential display technology the gene involved in this process was identified and further cloned.

*Results:* Supernatants of cultured splenocytes prepared from subcutaneously trypanosomeinoculated rats and mice spleens obtained immediately after inoculation and added to naïve cells significantly stimulate IFN-’ production and cell proliferation compared to PBS-inoculated animals. This action was abrogated by surgical denervation of the spleen. The fluorescent differential display technology depicted the gene involved in this process which was further cloned and its sequence was mapped to chromosome 14 (GenBank accession number: EU552928). Protein expression revealed ∼15 kDa molecule with biological activities similar to the cultured supernatants of splenocytes obtained directly from parasite-inoculated animals. Antibodies raised against the protein blocked the activities of both the protein and the supernatant and also recognized a band in the active supernatant with the same molecular mass as the protein. Furthermore, the protein was able to reactivate experimentally immunosuppressed cells by regaining their ability to proliferate.

*Conclusion:* A nervous system-induced Immune System-Released Activating Agent (ISRAA) was identified and may have a potential therapeutic benefit in immunocompromised situations and in further understanding the mechanism for innate immunity commencement and action.

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**47.004**

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

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*Background:* Considerable controversy exists over the relative importance of alpha haemolysin (Hla), Panton Valentine leucocidin (PVL) and phenol-soluble modulins (PSMs) in the pathogenesis of the different types of infections that can be caused by CA-MRSA and PVL positive MSSA strains. We have investigated factors that affect Hla and PVL expression in *S.aureus* clinical isolates.

*Methods:* Recent isolates of *Staphylococcus aureus* which were confirmed to be positive for PVL by PCR were obtained from diagnostic clinical samples (swabs, pus, blood culture, lung tissue) from Nottingham University Hospitals NHS Trust. 25 strains were grown in CYGP medium for 24 hours at 37 °C with shaking, before exoproteins were prepared from the culture supernatant, separated using SDS-PAGE before Western blotting with anti-LukF and anti-Hla antibodies.

*Results:* A variable level of expression of both the LukF subunit of PVL or HLA was observed between clinical isolates, with some correlation being observed between the level of expression of both in an individual isolate. The level of expression was not related to the *agr* subtype of the clinical isolate. The presence of the type specific auto-inducing peptide (AIP) in supernatants of the clinical isolates was confirmed by bioassays using specific reporter strains. Clinical isolates expressing very low levels of LukF all produced their type specific AIP, however the addition of 100 nM of type specific AIP induced the expression of LukF and Hla (Fig. 1). LukF and Hla expression in clinical isolates was inhibited by the universal *S. aureus agr* inhibitor, ala5-AIP-1 (Fig. 2) [McDowell et al., (2001) Mol Microbiol 41: 503-512]