International Society of Travel Medicine

Conference Review

Making Education Easy

11th Conference of the International Society of Travel Medicine May 2009, Budapest, Hungary

In this issue:

- > Crossing borders for medical care
- > WHO, CDC & yellow fever issues
- > New Japanese Encephalitis Vaccine
- > Malaria cases in travellers to India
- > Imported malaria in Germany from 1993-2005
- > Imported malaria in the Netherlands: 2000–2007
- > Malaria overdiagnosed in Tanzania
- Hepatitis A vaccination in immunosuppressives
- Vaccine preventable diseases in travellers
- > Sleep deprivation impairs immunity
- Pre-travel education for the VFR
- > Obtaining PPVs in TB screening tests
- > Taking kids to adventurous places

Welcome to the 11th CISTM Conference Review, a locally focused summary of some of the latest scientific developments from worldwide research in travel medicine presented at CISTM11.

The CISTM is held every two years. At this year's conference there was good news about the diagnosis and epidemiology of malaria and data about a new Japanese Encephalitis vaccine. Medical tourism, Safety, those Visiting Friends and Relatives (VFRs) and new yellow fever maps were discussed. Selection and review of the research has been carried out independently by Dr Joan Ingram, an Infectious Diseases Physician with a special interest in Travel Medicine, who attended CISTM11 held in Budapest, Hungary, from May 24–28, 2009.

I hope you find the conference review stimulating and I look forward to your feedback.

Kind regards,

Dr Joan Ingram

ioaningram@researchreview.co.nz

Globalized Health Care: Medical Tourism

Authors: Woodman J and Jaimovich D

Summary/Comment: The opening plenary addressed medical tourism. The first speaker was Josef Woodman author of "Patients Beyond Borders". He outlined the rapid recent growth of patients crossing international borders for medical care. It is estimated that 2 to 3 million people are medical tourists annually and that the number of medical tourists increases by 15% each year. Contributors to this are: rising health care costs, aging affluent populations, rising numbers of un- and underinsured and the growing numbers of hospitals with accreditation around the world. It is not just Americans reducing costs or British escaping waiting lists. For example each year 300,000 Indonesians travel to Malaysia and Singapore for health care.

Fastest growing areas are dentistry in countries such as Mexico, Costa Rica, Thailand and Hungary; cosmetic surgery in Mexico, Brazil, Thailand and Korea and orthopaedics in India, Singapore and Thailand. Cardiac surgery, oncology and fertility are other specialties people travel for. Some travel agents have specialised in arranging travel for medical tourists and certain insurers have medical travel programmes. Hotels are creating hotel rooms equipped with hospital beds, providing wound care and arranging physio visits.

The second speaker, David Jaimovich, outlined the process of accreditation by the Joint Commission of International (JCI) Accreditation. A few years ago, 45 international hospitals had JCI accreditation, currently there are 270 and in a few years 500 are expected to have accreditation. This growth has been driven by medical tourism and in turn increases patient confidence in foreign hospitals and hence numbers travelling for health care.

Abstract Session: Plenary.



Independent commentary by Dr Joan Ingram, an Infectious Diseases Physician with a special interest in Travel Medicine. She was a foundation member of the New Zealand Society of Travel Medicine and one of the first in New Zealand to be awarded a Certificate in Travel Health by the International Society of Travel.

Update: WHO, CDC & yellow fever Issues

Authors: Poumerol G et al

Summary/Comment: Speakers from WHO and CDC described the updated 2009 WHO Green Book and website and the 2010 (available now) CDC Yellow Book and website, respectively. The fact that WHO and CDC yellow fever maps have been different over the years was acknowledged and an international working group has been trying to update and revise the yellow fever maps. These are scheduled for release later this year. Instead of a blanket yellow fever risk for a country the new maps will reflect a range of yellow fever risk. There are going to be four risk categories: endemic (where there is evidence of stable transmission), transitional (where there is periodic transmission), low risk (where the appropriate vectors and hosts are found but there have been no human or primate cases) and finally no risk. It is proposed that travellers to endemic or transitional zones should be vaccinated but that those visiting low risk areas be vaccinated only if they will be spending a long time in the area or if they are going to rural areas. Such recommendations will reduce the need for yellow fever vaccinations for those visiting countries such as Kenya (parts will be low risk) and Tanzania (will probably all be low risk).

Abstract Session: Special Symposium.

Six months safety of the Vero-cell culture derived Japanese Encephalitis Vaccine IXIARO[®] across phase III trials

Authors: Dubischar-Kastner KL et al

Summary: Studies of the new Japanese Encephalitis Vaccine, IXIARO from Novartis, were presented. It is an inactivated vaccine prepared in Vero cells given in 2 doses 28 days apart. Seven days after the second dose 97% are protected and at 1 year 83% are still protected. Safety data was presented with 3310 subjects having completed safety follow-up at 6 months after the first dose of IXIARO, 435 after JE-VAX and 657 after a control vaccine consisting of PBS containing 0.1% alum. There were no significant differences in adverse events following immunisation with IXIARO compared to the control vaccination for severe, serious, related or medically attended adverse events. Severe, serious and related adverse events were similar between the IXIARO and JE-Vax but there were fewer medically attended adverse events after JE-VAX (10.7%) than IXIARO (19.4%). A higher rate of severe local reactions was observed in the JE-VAX group (14%) compared to the IXIARO group (3%).

Giving the standard dose ($2x 6\mu g$ on days 0 and 28) was compared to a single dose on day 0 or a double dose on day 0. Although seroconversion rates (SCR) were higher in the double dose group at day 10 (53% vs 21%), at day 56 SCR was 97% for the standard schedule but 25% for the single dose and 41% for the initial double dose.

Comment: IXIARO was approved for use in the States and Europe recently and is available in Australia as JE SPECT (CSL). I hope we will also be able to get it as it would be a welcome arrival in the fridge. Use of IXIARO may lead to a broadening of the recommendations for JE vaccine as it is replacing a vaccine prepared from mouse brain that is associated with significant but uncommon adverse events.

Abstract Session: Poster Presentations.

Imported malaria in Germany 1993 until 2005

Authors: Herbinger K-H et al

Summary: Data of reported imported malaria from 1993–2005 was analysed. No significant change in malaria cases per year occurred with 800 on average per year. The numbers of travellers to malaria endemic countries increased in the same time. The incidence of imported malaria per 100,000 travellers decreased remarkably.

Comment: see below

Abstract Session: Poster Presentations.

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

Authors: van Rijckevorsel GGC et al **Summary:** National surveillance data on all notified cases of imported malaria diagnosed between January 2000 and January 2008 were analysed. The annual number of cases fell from 535 in 2000 to 197 cases in 2007. In the same period, travel to malaria endemic countries increased from 477,000 to 747,000 travellers per year. The incidence of imported malaria fell from 155 to 47 cases per 100,000 travellers.

Comment: In addition to these studies a large amount of evidence was given at a Plenary session showing a true decline in malaria in Tanzania, Kenya, Eritrea, Madagascar, Rwanda, Zambia, Sao Tome and Principe and The Gambia. It is also decreasing in SE Asia and the Americas. This is fantastic news and is resulting in decreasing numbers of cases in travellers from many countries including New Zealand.

Abstract Session: Poster Presentations.

About Research Review

Research Review is an independent medical publishing organisation producing electronic journals in several specialist areas. These journals provide summaries of the 'must see' studies from the most respected medical journals in the world together with a local specialist commentary indicating why they matter.

Research Review publications are intended for New Zealand medical professionals.

About Conference Reviews

Conference Reviews are prepared with independent commentary from relevant specialists. To become a reviewer or to commission a conference review contact admin@researchreview.co.nz



To subscribe to Travel Medicine Research Review and other reviews go to www.researchreview.co.nz

The risk of malaria in travelers to India

Authors: Schmid S et al

Summary: Numbers of malaria cases in travellers to India were collected from January 1992 to December 2005 for 9 countries (UK, United States, France, Germany, Australia, Italy, Singapore, The Netherlands and Sweden). USA and UK contributed 85% of the cases. Denominator data were obtained from the Indian Ministry of Tourism.

The incidence of malaria in travellers to India was 93 cases per 100,000 travellers in 1992, peaked at 110/100,000 in 1996 then fell in 1997. Since 2001 the rate has been 20/100,000. The proportion of *Plasmodium falciparum* was between 10 and 13% with a wide range between countries. There was a total of 16 deaths reported (6 *P.vivax* and 1 mixed) during the study period.

Comment: Data such as this has led to some European countries advising bite avoidance only with standby treatment for travellers to India. British guidelines advise prophylaxis only for those going to the high risk areas (Chhattishgarh, Orissa, Jharkhand, West Bengal, Goa and the states east of Bangla Desh). Travellers to other areas are advised to avoid bites and seek care if unwell.

Abstract Session: Free Communications.

Low quality of routine microscopy for malaria in Dar es Salaam, Tanzania: Implications for the sick traveler

Authors: D'Acremont V et al

Summary: These authors compared the mean positivity rate using routine microscopy for a 15-month period with the mean positivity rate during the following 18 months using rapid diagnostic tests (RDTs) at 3 hospitals, 3 health centres and 3 dispensaries in Dar es Salaam. Mean positivity rates using routine microscopy were 41% in hospitals, 49% in health centres and 65% in dispensaries. Using the RDTs the respective mean positivity rates were 7%, 10% and 9%.

178 of 335 randomly checked blood slides were reported as positive by the nine health facility laboratories while actually only 7 of these (2%) were positive by expert microscopy. When positive, the median parasitaemia was 3 per 200 WBC by routine microscopy and 1193 per 200 WBC by expert microscopy. The sensitivity of routine microscopy versus that of expert microscopy was only 71% and specificity 47%; the sensitivity of expert microscopy was 79% and specificity 99% while both the sensitivity and specificity of RDT was 97%.

Comment: While it has long been recognised that malaria is overdiagnosed in Africa the extent of this at all levels of health care in the capital of Tanzania is surprising. The low level parasitaemia in positive slides show that those performing the slides reported a positive whenever they saw anything at all on the slide. The routine use of RTD will decrease unnecessary use of antimalarials and may improve the care of the many patients with fever due to other causes who previously inappropriately received treatment for malaria. This study shows that travellers should be told not to trust microscopy for the diagnosis of malaria in Tanzania but to try and attend facilities that use RDTs. The same advice probably applies to many parts of Africa.

Abstract Session: Free Communications – malaria and immune response.

A study on the effectiveness of hepatitis A vaccination in travelers with immunosuppressive medication

Authors: ter Waarbeek H et al

Summary: This Dutch study explored the effectiveness of hepatitis A vaccination in 56 travellers with immunosuppression. Their mean age was 42 (9–74) years and 31% were female. Immunocompromising conditions included rheumatoid arthritis (36%), inflammatory bowel disease (21%), organ transplants (9%), psoriasis (9%), malignancies (9%) and other (16%). Steroids were the most frequently taken medications (35%), followed by methotrexate (27%), mercaptopurine derivatives (12%) and TNF-blockers (10%).

Following hepatitis A vaccination, 29% were non-responders with a total anti-HAV titre <20 u/L. Forty-three percent of travellers using methotrexate, 28% of those using steroids and 20% taking TNF-blockers did not develop a protective titre. All travellers who took mercaptopurine derivatives achieved protective titres while both travellers using tacrolimus did not develop adequate titres. **Comment:** Studies have shown that those with HIV have lower rates of seroconversion after both hepatitis A and B vaccinations. This study now shows that almost a third of travellers with other forms of immunocompromising conditions are not protected after a dose of hepatitis A vaccine. It is important to try and vaccinate such travellers well in advance of their trip so there is time to do a blood test and if necessary give a repeat dose of vaccine prior to departure.

Abstract Session: Free Communications.

Vaccine preventable diseases in returned international travelers: Results from the GeoSentinel Surveillance Network

Authors: Boggild AK et al

Summary: These authors analysed records of 37,542 ill returned travellers entered into the global GeoSentinel Surveillance network data base between April 1997 and December 2007 to investigate the epidemiology of vaccine preventable diseases. Only 580 (1.5%) of the travellers were diagnosed with a vaccine preventable disease. The most common was enteric fever (n=276) followed by acute viral hepatitis (A= 97, B= 51), influenza (n=70) and varicella (n=37). Factors associated with acquisition of a vaccine preventable disease included younger age, male sex, absence of a pre-travel encounter, travelling to visit friends and relatives and travel to South Central Asia (all p<0.001). At least 55% of those with a vaccine preventable disease were managed as inpatients compared to only 9.5% of those with a non-vaccine preventable disease.

Comment: We all know how many travellers think that a couple of vaccines will ensure they have a healthy trip. This study shows how infrequent vaccine preventable diseases are in a cohort of ill travellers. The high rate of hospitalisation for these illnesses confirms that they are worth trying to prevent.

Abstract Session: Free Communications.

Privacy Policy: Research Review will record your email details on a secure database and will not release it to anyone without your prior approval. Research Review and you have the right to inspect, update or delete your details at any time.

The views expressed in this Publication are personal to the authors, and do not necessarily represent the views or policy of the Ministry of Health on the issues dealt with in the publication.

Disclaimer: This publication is not intended as a replacement for regular medical education but to assist in the process. The reviews are a summarised interpretation of the published study and reflect the opinion of the writer rather than those of the research group or scientific journal. It is suggested readers review the full trial data before forming a final conclusion on its merits.

The effect of air travel on stress and immunological markers

Authors: Wilder-Smith A et al

Summary: This study explored the effect of altitude and sleep deprivation on immune markers. Healthy adult volunteers underwent 3 experiments: 10-hour simulation chamber at a flying altitude of 8,000 feet plus sleep deprivation; 10 hours simulation chamber at sea level plus sleep deprivation, and the control was sleeping at normal conditions. Immunological and stress markers were measured before the experiment, the day after and on days 4 and 7 after the experiment.

Forty-seven subjects aged 21 to 65 years completed the study. Significant differences were seen for CD4, CD8, CD14, CD16, CD19, and CD69, HLA DR and the PHA mitogen assay. These differences were most marked on days 1 and 4 after the experiment and normalised by day 7, except for CD69. There were no differences between the altitude plus sleep deprivation versus sleep deprivation only.

Comment: The transient immunological impairment seen after 10 hours in a flight simulation chamber at sea level as well as hypobarbic and hypoxic conditions suggest that sleep deprivation may be the explanation for the impaired immunity seen rather than the altitude. As I write this conference report during my 33-hour trip home from the conference I feel slightly anxious!

Abstract Session: Free Communications.

Pre-travel education for the VFR

Authors: Stauffer W, Shingadia D

Summary: A working group of the ISTM has recently developed a new definition of VFRs. It is that (1) the main intent of travel is to visit friends and relatives AND (2) there is a risk gradient between their place of departure and the place of destination. This definition means that more travellers will be considered VFRs. For example, miners returning home from South Africa to families in Mozambique and migrant workers in Kuwait returning to families in Asia are VFRs under the new definition.

Many factors contribute to VFRs' increased risks at their destination. They often visit rural areas, stay in local housing, eat like locals and stay for prolonged periods. This increased risk is combined with a lower rate of pre-travel care. VFRs may not be aware of health risks at their destination or may think they are immune from previous exposure. They may not realize there are preventive measures and may be unable to afford vaccines etc or may not have time to access them if their trip is hurried for something like a funeral.

Comment: We need to reach VFRs and overseas attempts to do this have been made through schools, community groups, mosques and temples as well as ethnic radio stations and publications. Doctors with those who may be VFRs should try to explain the need for pre-travel care to their patients when seeing them for other reasons. The website <u>www.tropical.umn.edu</u> has patient travel handouts on various topics such as vaccines, diarrhoea, malaria, accidents and travelling with children translated into 20 languages (Arabic, Burmese, Cambodian [Khmer], Chinese, Eritrean, French, German, Hindi, Hmong, Indonesian, Nigerian [Ibo, Yoruba], Oromo, Portuguese, Russian, Somali, Spanish, Swahili, Thai, Urdu and Vietnamese). Although some details are not relevant to us most of the information is.

We should also be alert to the possibility that travel may be for the purpose of female circumcision.

Abstract Session: Workshop.

Positive TB screening test results in asymptomatic individuals: what to do?

Authors: Keep L

Summary/Comment: Lisa Keep from the US military spoke on this topic. She reminded us that both the Mantoux skin test and interferon- γ release assays (IGRAs) (such as Quantiferon TB Gold available at LabPlus) are diagnostic aids not diagnostic tests. Even if the tests are highly sensitive and specific in low risk populations there will be false positives. For example:

Prevalance	PPV	Sensitivity	Specificity
0.1	1.8	90	95
1	15.4	90	95
5	48.6	90	95
50	94.7	90	95
1	31	90	98

The Positive Predictive Value (PPV) indicates the likelihood of a positive result being a true positive. This table illustrates how important it is only to do these tests in those with a high pretest probability to increase the PPV or likelihood that a positive result is a true positive. Lisa suggested doing testing for latent TB in: VFRs and their children, missionaries, health care workers, those with a high likelihood of progression to active TB (e.g. HIV infected, children) and those who have visited certain high risk destinations. Those such as VFRs who may have pre-existing latent TB infection should have a baseline test prior to travel. IGRAs have the advantage of a single blood draw rather than the four trips to a lab required for two-step Mantoux testing.

Practical tips are to ensure the same IGRA is used pre- and post travel and that a skin test done just prior to an IGRA may boost it.

Abstract Session: Symposium.

Adventurous travel for adventurous kids

Authors: Shlim D

Summary: Travel with children to high altitudes and other adventurous destinations has been discouraged by travel medicine authorities such as the International Society of Mountain Medicine. There is actually very little morbidity and mortality data on travelling children but anecdotal experience and informal surveys suggest that deaths of children while travelling are rare. Motor vehicle accidents and drownings are the main cause of deaths.

A number of factors should be considered before travelling with children: the chances of injury or illness and the access to medical care should it be needed. For example, if trekking in Nepal the likelihood of severe injury or illness is low and helicopter evacuation to Katmandu can get someone to reasonably good care in 4 to 24 hours. While the likelihood of injury or illness while trekking in Tibet is similar, evacuation to Lhasa may take 3 to 7 days and medical care there may be problematic. The parents' competence to obtain pre-travel advice and vaccinations, knowing how to solve problems and obtaining help should problems arise should also be considered.

Comment: David Shlim spoke in his usual thoughtful and balanced way about adventure travel with children. Although adventure travel may involve uncertainty, isolation and risk he made the case that the benefits of carefully planned and considered adventure travel probably outweigh the risks.

Abstract Session: Plenary.



Publication of this Conference Review was supported by an educational grant from Sanofi-Aventis New Zealand. The content and opinions expressed in this publication do not reflect the views of Sanofi-Aventis New Zealand Limited unless so specified.

www.researchreview.co.nz