TAISTEAL

Travel Medicine Society of Ireland

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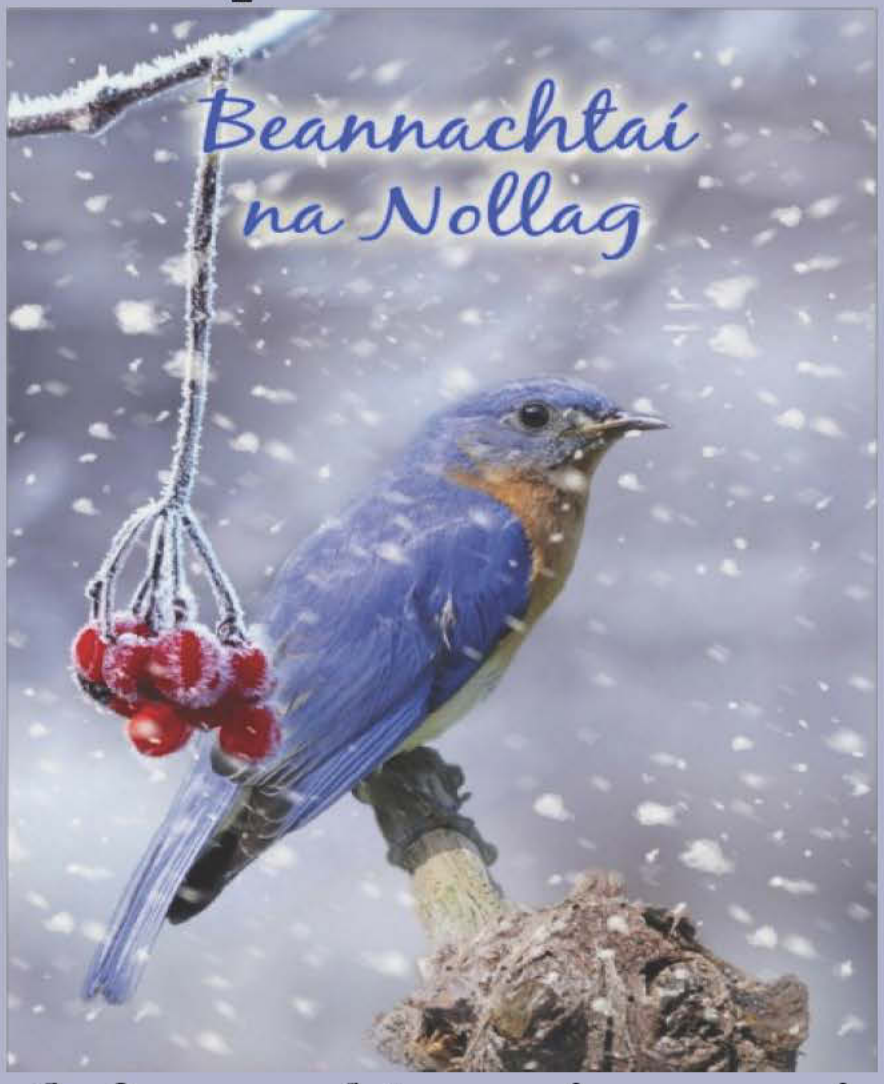
NEWSLETTER

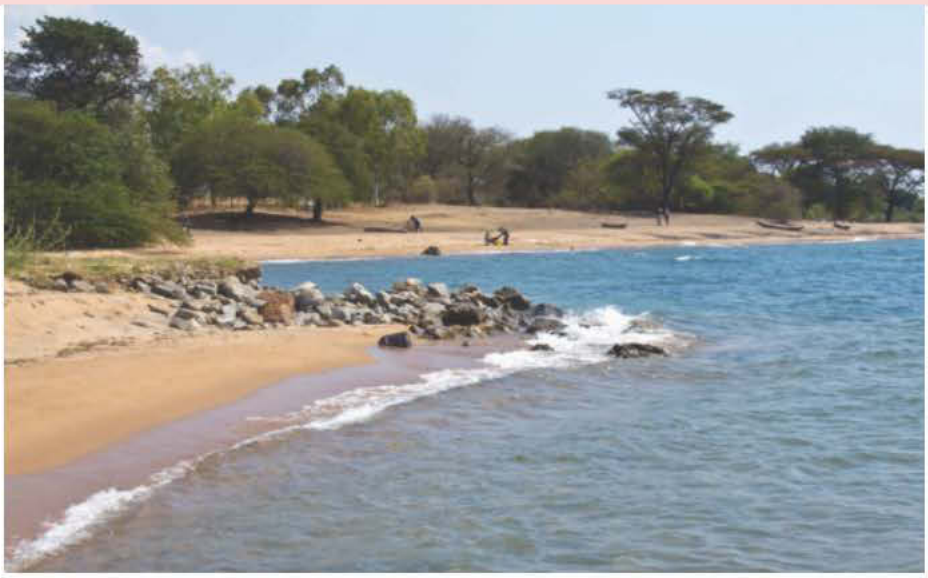
ed. S. Collins

The Travel Medicine Society of Ireland wish all our members a very Happy Christmas and a Prosperous New Year



We look forward to seeing you in 2017

SCHISTOSOMIASIS – A BRIEFING

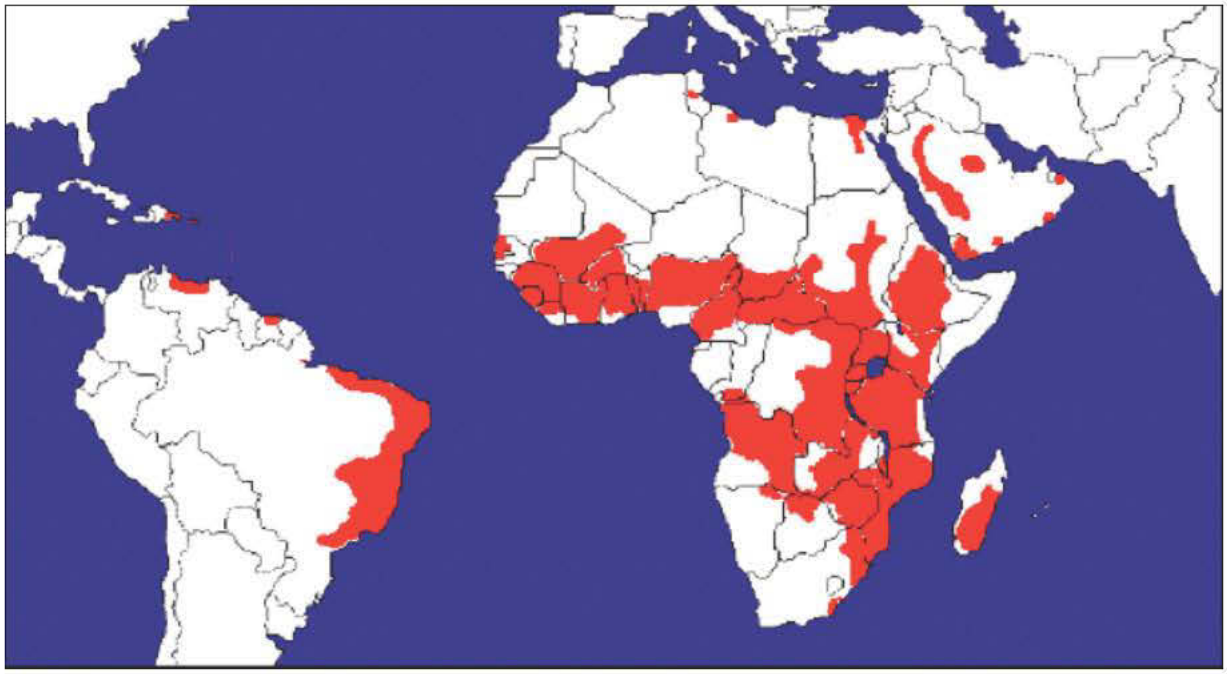


The shoreline at Lake Malawi – freshwater lakes and rivers throughout much of Africa represent a Schistosomiasis risk to travellers.

What is the disease? A microscopic blood fluke parasite found in fresh water (lakes/rivers/shower water drawn from contaminated sources). The intermediate host is a freshwater snail. There are a few variants of the parasite. One type affects the bladder and in this case, infected people pass the parasite in their urine. Urinating into fresh water that is inhabited by the intermediate host snail will continue the cycle of transmission. Another variant of the parasite affects the large bowel and the parasite is shed in the patient's faeces.

How do you become infected? Penetration of your skin by stepping or swimming in fresh water that is contaminated by the parasite.

Where in the world does it occur? In all of the tropical regions. Well over 90% of cases occur in Africa (see map) – classic examples are Lake Malawi, Lake Victoria, Lake Kivu (Rwanda/DRC) and Lake Bunyoni (Uganda). Isolated cases have been reported in travellers visiting the Cambodia/Laos border (Mekong River) and even at Vang Vieng (Laos).



Distribution of Schistosoma Mansoni - Cambridge Schistosomiasis Research Group: (http://www.schisto.path.cam.ac.uk/Schisto2015/helminth_biology.html)

How common is it?
It's common. In the returned traveller, it's a more common finding than other exotic parasites like malaria, Strongyloides or filarial infections. In the case of Lake Malawi, at least one third of one-off swimmers will become infected.

Can you catch Schistosomiasis in swimming pools or by swimming in the sea?
The intermediate host of the parasite is a freshwater snail. This means seawater is not a risk. Swimming pool water is not a risk unless the water with which the pool is filled was drawn from a contaminated source within the preceding 36 hours.

What are the symptoms of Schistosomiasis?

- Often none.
- Cercarial dermatitis (Swimmers' Itch) – this occurs in 10 – 36% of first-time infected patients within the first 48 hours of exposure. It is a skin-based immune reaction. The skin reaction occurs at the site of parasite penetration and manifests as a transient itchy popular rash.
- Acute Schistosomiasis ('Katayama Fever'): 3 weeks – 8 weeks post infection. Again this occurs in a minority. It is an immune-mediated syndrome that is partly accounted for by the migration of the parasite through the lungs of the infected patient:

  Acute Schistosomiasis symptoms (in order of decreasing frequency):
  - Cough (around day 44 – day 66)
  - Fever (around day 30 – day 40)
  - Fatigue (day 27 – day 64)
  - Eosinophilia (transient, acute) occurs in about 70% cases.

- Chronic Schistosomiasis: either no symptoms or painless haematuria or else diarrhoea.

Why should Schistosomiasis be taken seriously?
It's ability to cause unforeseen complications; infection can lead to eosinophilia, haematuria or diarrhoea. Where these occur weeks or months after travel and a travel history is not taken, the link may be missed and the patient might be subjected to unnecessary investigations (including cystoscopies, colonoscopies).

Serious complications are not common but are avoidable. Cases of ectopic migration to the spinal cord (leading to paresis) or fallopian tubes (leading to infertility) are recorded[1,2].

The take-home message is that if you have a patient who attends for a pre-travel consultation prior to going to Africa, particularly if they are likely to be in fresh water while they are there (e.g. swimming in Lake Malawi or rafting elsewhere), then it would be remiss not to alert them to the existence of Schistosomiasis.

How is it diagnosed?
The starting point should be a thorough travel history – particularly travel to Africa. The presence of blood in the urine can occur with the variant of the parasite that affects the bladder. A blood test ('serology') is available – but should not be performed until 3 months or more post exposure to the parasite. Blood tests performed less than 3 months after travel risk not detecting the immature form of the parasite early on in the infective process. The infection can also be diagnosed via microscopy of stool & urine samples but in travellers, microscopy is a less sensitive test than serology. Serology is relatively sensitive but its shortcoming is that it stays positive following treatment. As a result, serology cannot be used post-treatment to gauge how successful a treatment course has been.

Is there any point in testing those who say they have not been exposed to fresh water?
Yes – some positive serologies occur in patients who do not recall fresh water exposure.

How is Schistosomiasis treated?
Oral medication: Praziquantel 40mg/kg/day in two divided doses, for one day – but normally not until at least 3 months post exposure. A course of treatment costs around €50 – €70.

Should patients be treated without having been first tested?
I don't recommend this approach.

What are the key messages to be transmitted to a traveller pre-trip?

- Schistosomiasis is present in fresh water sources, particularly in Africa
- If you are in fresh water while in Africa, come for testing 3 months or more after your last exposure
- Don't rely on local treatment while you are in Africa – it's preferable to test at home and then, if it is indicated by the presence of a positive test, obtain the medication in Ireland, to ensure you are treated with genuine, potent medication.

What are the common errors encountered with Schistosomiasis?

Clinicians failing to test!

Patients saying:

- "I don't need to be tested (I wasn't in fresh water)"
- "The lake I swam in was not infected, according to the locals" (I have encountered plenty of positive test results in such patients)
- "My only fresh water exposure was a shower" (shower water from a protected source like a borehold is fine but in the case of 'bucket showers', cercariae persist for up to 36 hrs in water drawn from an infected source)
- "I have treated myself already" - the pitfalls of this approach include:
  - ➢ premature treatment (not waiting until 3 months post-exposure)
  - ➢ inadequate dosing
  - ➢ fake, expired or sub-potent medication (as a result of prolonged storage at high temperatures) being given to the patient by local pharmacists.

References:

[1]Hamdy Kamel M et al. Schistosomiasis of the spinal cord presenting as progressive myelopathy. Journal of Neurosurgery: Spine July 2005 (3) 1; 61 – 63.

[2]Katsetos C, Kontoyannis M, Koumousidis A, Petroyannis N, Davies A. Schistosomiasis of the abdominal cavity and infertility: a case report. OA Case Reports 2013 Jul 12;2(6):57.

Further reading: Clernix J, Van Gompel A. Schistosomiasis in travellers and migrants ***Travel Medicine and Infectious Disease*** (2011) 9, 6 – 24.

(This article is based on an OSKE delivered at the TMSI meeting in Cork on 3rd September 2016 and refers to the management of the disease in the occasional visitor to the tropics, not the management of the condition in the indigenous resident of or a migrant from an infected region).

Dr. Simon Collins FFTM RCPS (Glasg) DTM

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Foundation and Diploma Courses in **Travel Medicine**

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TRAVEL VACCINES AND THE PATIENT WHO IS IMMUNOCOMPROMISED DUE TO STEROIDS OR BIOLOGICS

** The information in this article is based mainly on the guidance in chapter 3 of the 'Immunisation Guidelines for Ireland' (available free online at http://www.hse.ie/eng/health/immunisation/hcpinfo/guidelines/chapter3.pdf) – to which you should refer before treating patients **

This topic is important because it embraces in particular a new and rapidly expanding field of pharmacology (immunomodulatory drugs).

Examples of immunomodulatory drugs in common use - clockwise from upper left: Adalimumab (Humira®), Trastuzumab (Herceptin®), Infliximab (Remicade®) and Etanercept (Enbrel®).

These medicines are being used to control what were previously poorly-controlled cases of psoriasis, rheumatoid arthritis, ulcerative colitis and even breast cancer. We now have immunocompromised patients who feel well as a result of their new treatments. They would not previously have been well enough to travel and are presenting to us. They are planning to travel to remote destinations and seeking multiple vaccines, some of which may be live. Although they feel well, these patients are immunosuppressed. This raises questions:

- ➢ Which vaccines can be safely given to the patient?
- ➢ If some of the vaccines are safe to give, to what extent will the protective efficacy of the vaccines be retarded by the patient's lack of normal immune function?
- ➢ Do extra doses of some vaccines need to be given in order to make up for the patient's lack of immune function? If so, when are these doses best given?

Immunosuppression can be due to any of the following causes – in this article the focus by me, out of the following seven categories, are the two that are underlined:

- o Primary immunosuppression
- o HIV
- o Aspelnia
- o Post-transplant
- o Chemotherapy for cancer
- o <u>Steroid treatment</u>
- o <u>Immunomodulatory treatment</u>

Steroid treatment:

Patient is immunosuppressed at following doses:

Prednisolone 20mg or more for 2 weeks or more, in patients weighing >40kg or
Prednisolone 0.5mg/kg/day or more for 2 weeks or more, in patients weighing <40kg,

Main rules to remember with steroid treatment:

- ➢ Avoid live vaccines during and until 3 months after immunosuppressive steroid therapy
- ➢ Inactivated vaccines can be given during immunosuppressive steroid therapy, but the protection conferred by the vaccine(s) will be reduced – consider the option of re-vaccinating the patient 3 months post-completion of steroids
- ➢ Guidance on what steroid therapies are not immunosuppressive can be found in chapter 3 of the 'Immunisation Guidelines for Ireland'.

Immunomodulatory treatment:

The list that follows contains examples and does not include all of the rapidly expanding list of drugs in this class.

I have included examples of minimum time intervals between cessation of therapy and administration of YF vaccine in order to show that the degree of immunosuppression induced by these drugs differs. It is important to check the up-to-date online guidance relating to the relevant drug before vaccinating.

Types:	Subtypes:	Compounds (incomplete list):	Trade name examples:	Examples of time post therapy to admin. of Yellow Fever vaccine:
Alkylating agents:		Cyclophosphamide	Endoxana	(chemo only)
		Chlorambucil	Leukeran	
Antimetabolites:		Methotrexate		
		Azathioprine	Imuran	
T-cell immune suppressants:		Ciclosporin	Neoral	
		Tacrolimus Sirolimus	Rapamune	
Biologic response modifiers:	TNF-inhibitors	Adalimumab	Humira	
		Certolizumab pegol	Cimzia	
		Etanercept	Enbrel	3 months
		Golimumab	Simponi	
		Infliximab	Remicade	
	IL-1 blocker	Anakinra	Kineret	
	IL-6 blocker	Tocilizumab	Roactemra	
	IL-12 & IL-23 antagonist	Ustekinumab	Stelara	
	Complement inhibitor	Eculizimab	Soliris	
	HER2/neu (erbB2) antagonist	Trastuzumab	Herceptin	
	T-cell activation inhibitor	Abatacept	Orencia	6 months
	B-cell depleting agent	Rituximab	Mabthera	6 months
	CD52 antibody	Alemtuzumab	Lemtrada	12 months

Main rules to remember with immunomodulatory treatment:

- ➢ Avoid live vaccines during immunomodulatory therapy
- ➢ How long do you have to wait after immunomodulatory therapy before giving live vaccines? – it depends:
  - o For many of the agents – 3-6 months / for some – 6 months / for one at least – 12 months ("discussion with the treating physician is advised")
  - o For patients on combination therapy (e.g. antimetabolite plus biologic response modifier: then 3 months increases to a 6-month waiting period, because immunosuppression is more pronounced).
- ➢ Inactivated vaccines can be given during immunomodulatory therapy, but the protection conferred by the vaccine(s) will be reduced; current Irish guidelines say:

"[inactivated] vaccines given in the 2 weeks immediately prior to therapy or during therapy should be repeated when off immunosuppressive therapy for at least 6 months and when immune competence is restored."[1]

An example of the extent to which immune response is blunted by immunomodulatory therapy is evident in this study on the effectiveness of Hepatitis A vaccine[2] :

	Proportion of patients on immunomodulatory therapy, who had adequate Hep A immunity post vaccination at the following points it time:	
	Immunosuppressed patients:	Non-immunosuppressed patients:
(1st dose Hep A vaccine given)		
1 month post 1st dose:	29%	95% - 100%
6 months post 1st dose:	45%	95% - 100%
(2nd dose Hep A vaccine given)		
7 months post 1st dose / 1 month post 2nd dose:	84%	95% - 100%
12 months post 1st dose / 6 months post 2nd dose:	77%	95% - 100%

i.e. in an ideal world, it is best to give two doses of Hep A vaccine, six months apart, before the patient goes on their trip.

(This article is based on an OSKE delivered at the TMSI meeting in Dublin on 5th November 2016).

References:

[1]*Immunisation Guidelines for Ireland*, chapter 3.
[2]Askling H et al, Hepatitis A vaccine for immunosuppressed patients with rheumatoid arthritis: A prospective, open-label, multi-centre study *Travel Medicine & Infectious Diseases* (2014) 12, 134 – 142.

Dr. Simon Collins FFTM RCPS (Glasg) DTM

WHERE DO YOU GO....

When did you first catch the travel bug?

I have always travelled since I was young. I was born in Borneo, Malaysia but during my childhood and teenage years, I travelled and lived in different parts of Malaysia and Singapore due to my father's work commitment & my education. After completing my A-Level in Singapore, I opted to enrol in a European college because "I wanted to explore Europe" as I told my dad. I distinctly remember the image I had of Europe – Big Ben, windmills & snow-covered castles. I chose a Dublin college after reading a book on Ireland in the school library (pre-internet days!). The book described Ireland as green and picturesque, full of horses and friendly people. It also described Trinity College Dublin (TCD) as a world renowned institution with amazing architecture located next to Liffey River. I had an image of studying in a beautiful college, fishing & riding horses during my free time. Only on arrival did I realise that TCD is right in the city centre. The book I read also did not touch on the pub culture! I never picked up horse riding or fishing. That was when I first caught the travel bug.

What do you most like about travel?

When I was single, I enjoy travelling alone and travel is a time to learn new cultures and see interesting places. Travel allows me to learn more about myself and develop life skills out of my normal life. Now that I am married with 3 children, travel is a time to relax with my kids and hopefully promote their interest in travelling.

How extensively have you travelled?

I enjoy travelling and have travelled extensively in Europe, Asia & Australia. The different countries in Asia are so diverse and yet so similar in many ways. I never get bored going around Asia. During my days as singleton, I usually visited cities while travelling in Europe. With kids and a sun-loving wife, our recent European travels are mostly sun holidays with sight-seeing trips into nearby cities.

Which country did you most enjoy visiting?

France is my favourite country to visit. I enjoy the smaller towns and villages rather than cities and driving through French countryside, surrounded by beautiful vineyards and magnificent chateaux is a relaxing experience on its own. I don't speak French but I can communicate through hand gestures so I usually manage to get my orders right in restaurants or local patisserie.

What was your favourite city to visit?

My favourite city is Singapore. When I lived there, I did not like what I perceived to be a rather authoritative atmosphere there. In recent years, I find the country much more welcoming. Singapore is a unique melting pot of Western and Eastern cultures: High-rise buildings with colonial shop-houses; Michellin star restaurants with simple "hawker centres" (local food court – my favourite is the Singapore chicken rice) and an Asian country where English is its 1st language and yet Singlish (colloquial Singapore English) is commonly used. It has so many activities for visitors and locals alike: A trip down Singapore River, a visit to the Night Safari, a tour of cultural Little India or Chinatown, shopping on Orchard Road, Formula 1 races, seaside cycling track around the 720 km^2 city state and the island resort of Sentosa. GO NOW.

Are you an adventurous traveller?

No. I prefer the sight-seeing and cultural aspects of visiting a country. Part of my bucket list however is to drive across Borneo with the 5 good friends from my time living in Singapore. I was born in Borneo but apart from the 2 cities which I frequently visit, I have not really travelled in Borneo. I would love to drive across the 3rd largest island in the world and see the real Borneo.

Are there any aspects of travel which you don't enjoy?

Going through airports. While I understand that security checks are essential parts of air travel to keep us travellers safe, the transit through security counters do present me with stress I can do without.

What can travel teach us about ourselves?

In my view travel allows us to learn about our weaknesses and strengths, and to learn to manage our fears, especially when travelling alone. Travelling can be a humbling experience.

Can you give us one useful travel tip?

Travelling with kids requires specific parenting skills. My kids all started travelling from 4 weeks old. I looked back and compared travelling with our 1st child to travelling with our 3rd fellow and I see how much simpler travelling with kids can actually be if the parents are prepared for the trip. I think the one single useful tip is to have adequate distraction for kids on flights, either with toys (electronic games are always handy!) or food.

Have you any interesting trips coming up?

I am due to go to Malaysia and Perth. I visit Malaysia regularly to visit my parents. Such trips are always interesting as I never know what my parents are going to throw at me! My previous trips to Perth were always city based. I am hoping we might get a chance to go out of Perth city and visit places such as Ningaloo Reef, a World Heritage site and Australia's largest fringing coral reef.

Dr. Joseph Sim

WHAT'S IN THE JOURNALS?

In this issue of Taisteal, I will offer a synopsis of the highlights from articles published in the most recent issue of the two leading travel medicine journals. Both journals are published online, with Journal of Travel Medicine (JTM) now having a monthly issue since it migrated to Oxford University Press, and Travel Medicine and Infectious Disease (TMID) a bimonthly publication from Elsevier Publications. Access to TMID is free for Affiliates, Associates, Members and Fellows of the Faculty of Travel Medicine, and ISTM members enjoy free access to JTM, but both journals are available in most Irish university e-libraries. I have recently been appointed as Associate Editor for non-communicable diseases to the Editorial Board of JTM. I already serve on the Editorial Board of TMID. This is a great honour and while the work is of course not remunerated, I enjoy the insight it has given me into the peer review publication process. In this role I am expected to promote the journal and to invite submissions under the category for which I am responsible. I would be very pleased to speak to members by telephone if they have an idea for a manuscript which they would like to submit to either JTM or TMID.

The September-October issue of TMID was very full with 114 pages of interesting content, mostly relating to infectious diseases. A review article reminded us that rickettsial infection is still present in Croatia and should be considered in the differential diagnosis of returning travellers from that country. Mediterranean spotted fever (MSF) and murine typhus are the most common rickettsial infections reported in Croatia. Most cases of MSF, which presents with high fever, headache, a maculopapular rash of the palms and soles and an eschar at the site of the tick bite, occur between July and September on the southern coast between Zadar and Dubrovnik, both popular tourist destinations for Irish travellers. I've been to the beautiful city of Zadar myself as recently as 2014! Travellers who bring their own dogs or cats with them when they travel may unwittingly import ticks capable of transmitting rickettsiae.

An interesting review article from researchers in Colombia and Venezuela described the ocular manifestations of the mosquito-transmitted chikungunya viral infection. Although not frequent, these complications can help the clinician to recognise the possibility of chikungunya in the returned traveller. Ocular manifestations include conjunctivitis, episcleritis, iridocyclitis, retinitis and optic neuritis. There are no randomised controlled trials to guide treatment of chikungunya infection and it is unknown if the disease is self-limiting or if treatment is beneficial. Visual prognosis ranges from full recovery to permanent visual loss despite intervention.

Although the Zika epidemic in Latin America seems to be diminishing, it was interesting to learn about the extent of microcephaly in Brazil, based on data compiled by the Brazilian Ministry of Health. Between November 2015 and July 2016, there were 8,301 cases of congenital microcephaly in Brazil, mostly in the north-eastern region, representing a huge burden on families affected. There were 165,241 cases of Zika virus infection reported in Brazil between January and June 2016. The authors call for ongoing monitoring and surveillance of microcephaly and neurological abnormalities resulting from Zika virus infection.

A letter to the editor poses the question – does the Zika virus outbreak provide an educational opportunity for sexually transmitted infection prevention in the pre-travel setting? Each spring, there is a surge in the number of travellers departing from the USA to Latin America for educational, work or mission-related trips. These travellers are mostly adolescents and young adults. The authors cite previous work showing that 45% of high school students are sexually active, with only 57% of those using barrier protection. Given that many of these seasonal travellers will be accompanied by their parents in the travel clinic, the issue of STIs may not routinely be addressed by the travel medicine provider. The risk of sexual transmission of Zika virus provides a useful

opportunity to provide pre-travel STI prevention advice to these younger travellers. Elsewhere in the Journal, Jane Chiodini reviews an excellent Zika app from the World Health Organization. More details of this resource can be found at http://www.who. int/risk-communication/zika-virus/app/en/.

A group of authors from South America provide a helpful reminder of the wide range of conditions which may be diagnosed in the returned traveller using a simple peripheral blood smear, using Wright or Giemsa stain. These include malaria, babesiosis, ehrlichiosis, trypanosomiasis and louse-borne relapsing fever. How many travel health clinics in Ireland have the facilities or the training to perform blood smears I wonder?

Have you ever heard of "airplane headache"? I report the first case in the travel medicine literature in the Diagnostic Challenge section of the Journal but I am certain that most cases go unreported. It can be a very debilitating condition, however, and its pathogenesis is not completely understood. Table 1 summarises its main features according to the international classification of headaches. Look out for it in your travellers or YOUR travelling companions.

Table 1 ICHD-III diagnostic criteria for airplane headache[†]

A	At least **two** episodes of headache fulfilling criterion C
B	The patient is travelling by airplane
C	Evidence of causation demonstrated by at least **two** of the following: 1. Headache has developed exclusively during airplane travel 2. Either or both of the following: a) headache has worsened in temporal relation to ascent after take-off and/or descent prior to landing of the airplane b) headache has spontaneously improved within 30 minutes after the ascent or descent of the airplane is completed 3. Headache is severe, with at least **two** of the following **three** characteristics: a) unilateral location b) orbitofrontal location (parietal spread may occur) c) jabbing or stabbing quality (pulsation may also occur)
D	Not better accounted for by another ICHD-III diagnosis

[†]ICHD-III: International Classification of Headache Disorders

Kling and colleagues report a case of acute strongyloidiasis in a 32-year-old male Swiss traveller who presented with fever, flu-like symptoms, diffuse arthralgia, dry cough, abdominal pain, and erythematous macules. There was a mild eosinophilia, a moderately raised CRP and microhaematuria. The skin rash evolved into a widespread pruritic maculopapular exanthema. The eosinophil count rose significantly and larvae of Strongyloides stercoralis were eventually isolated from the patient's stool. The patient was successfully treated with ivermectin for two days. The authors emphasise the point that the prepatent period (interval between infection and ability to detect a diagnostic stage in samples) for strongyloidiasis is 2-4 weeks. This prepatent period can be as long as 2 months for schistosomiasis, so timing of diagnostic investigations is very important in many parasitic tropical diseases.

The current issue of JTM is labelled as the July issue but it is the seventh monthly issue so far in 2016. It is not yet complete as articles only appear on the journal's website when they have been fully accepted and proofed according to the continuous publication model. Access to recent issues requires a current membership of the ISTM but two articles are designated as open access in each issue at the discretion of the Editor-in-Chief. Of interest in this issue is a report of ten years of recreational diving fatalities in the US and Canada. The deaths mostly occurred in recreational divers who harvest marine animals for personal use. Each year in Florida up to 50,000 divers and snorkelers enter the water during a 2-day sport season in search of the spiny lobster Panulirus argus. Divers who ran 'low-on' or 'out-of' breathing gas were more likely to be harvesters and fatal dives were more likely to occur at night. There were more uncertified divers among the harvester diving group. The authors recommend that public safety information targeting hazards associated with diving for lobster should be distributed ahead of the sport diving season. Sometimes Irish travellers engage in adventure activities to which they are unaccustomed or which their travel insurance may not even cover, so it is good to be aware of some of these more obscure, but very real adventure-related dangers of travel.

Prativa Pandey's group in Kathmandu report two cases of a rare cervical artery dissection occurring at altitude in the Himalayas, one a vertebral artery dissection in a 48-year-old female Australian trekker which occurred at 5000m on Mera Peak, and the other case, also a vertebral artery dissection, affecting a 49-year-old Swiss woman on the final ascent of Island Peak (6189m). This condition usually presents with acute onset of focal neurologic signs and symptoms, including cranial nerve palsies, seizures, migraine and stroke. While cervical artery dissection represents only 2% of all ischaemic strokes, it is more common in the young and middle-aged individual. Fibromuscular dysplasia is often the underlying pathogenic defect. It is thought that the vigorous neck movements associated with technical high altitude mountaineering may have precipitated the two cases of cervical artery dissection reported. Treatment includes antiplatelet therapy, anticoagulants, endovascular stenting and possibly surgical repair.

There has been much focus in the literature on the risk of acquiring multidrug-resistant (MDR) bacteria during travel. A cross-sectional study of 191 individuals attending a travel vaccination clinic in France found that only 10% were aware of the risk of being a carrier of MDR bacteria during travel. The authors acknowledge that the low rate of knowledge about this issue in their group of travellers may be partly the result of a low proportion of travellers to South Asia where there is the greatest risk of acquiring multidrug-resistant Enterobacteriacea.

Cornaglia et al. report a fascinating case of a 67-year-old French Caucasian male who returned from a sport fishing trip on the Brazilian island of Tocantins during which he repeatedly consumed raw freshwater fish marinated with lemon juice. He presented three days following his return to France with a small pruritic inframammary skin nodule. Five days later he reported a large swelling on his abdominal wall. His blood eosinophil and IgE levels were elevated. Cutaneous gnathostomiasis was suspected and he was treated with a 3-week course of albendazole. A single dose of ivermectin was finally effective in this patient. Although typically associated with travel to Asia, gnathostomiasis has become an increasing problem in Central and South America, especially in Mexico, Guatemala, Peru, Ecuador and Colombia. Human gnathostomiasis is a foodborne parasitic zoonosis acquired by consuming raw or undercooked freshwater fish, shrimp or crabs containing third-stage larvae of the nematode (roundworm) *Gnathostoma*. We should remind our travellers never to eat undercooked or raw fish or meat.

Finally, I collaborated with colleagues, including Prof. Denis Cusack from University College Dublin, in writing the first review article on the distressing subject of repatriation of the human remains of deceased international travellers. The approved article galley proofs have been uploaded so I expect that, by the time you read this, it will have appeared in the current online issue of the journal. This is a very important topic which all travel

medicine practitioners should be familiar with. I will do my best to secure open access to the article so that we can make it available to our members as a learning resource. Optional open access charges are high for journals (€2275 at time of press for JTM) but publishing with open access increases the reach of one's paper and the number of citations it receives. Universities have discretionary funds for open access publications which generally take account of the impact factor of the journal. That's all for this issue of *What's in the Journals*. I will do another round up for the spring issue of Taisteal.

Prof. Gerard Flaherty

HEPATITIS A – A CASE STUDY:

*[**Editor's note**: the following is a case study submitted by a TMSI member who is currently working in Qatar].*

A 31-year-old male, presented to our out-patient department who has had intermittent fever, abdominal discomfort, fatigue, diarrhea, nausea and vomiting for the past 48 hours. He also reports dark urine. He has previously been healthy and no past medical history, his only surgical history was appendicectomy when he was 11-year old. He smokes 10 cigarettes per day and drinks alcohol occasionally. The patient travel history was remarkable; he returned 4-week prior to presentation from his 2-week holiday in Rio De Janeiro, Brazil during FIFA World Cup tournaments 2014. He stayed in the budget hotel with his two friends, he drank only bottled water but ate both cooked and uncooked foods at numerous restaurants while in Rio de Janeiro and nearby areas. He drank alcohol few times but denies used of illicit drugs and denies sexual activity during his holiday. He has not gone camping or hiking and had no recent tick exposures. The patient was consulted to local clinic 5 weeks prior to travel but did not receive any vaccination as the physician assured him that there was no threat of infection in Rio de Janeiro.

On presentation his vital signs as follows: Temp. 37.6ºC; heart rate- 71/min; respiratory rate -19/min; O2 Saturation 99% on room air; BP- 109/61. On physical examination, lungs were bilaterally clear, with tenderness in the right abdomen, no palpable mass in the abdomen, HEENT noted icteric sclerae. FOB negative on rectal examination. Notable laboratory findings were as follows:

TEST NAME	RESULTS	NORMAL VALUES
LDH	352 U/L*	100-225 U/L
AlkPhosphatase	160 U/L*	30-120 U/L
AST	400 U/L*	0-55 U/L
ALT	770 U/L*	0-50 U/L
Total Bilirubin	3.6 mg/dl*	0-1.5 mg/dl
Direct Bilirubin	2.5 mg/dl*	0.1-0.4mg/dl

* Indicates abnormal results

Patient's Hepatitis Screening

Anti-HAV IgM antibody	POSITIVE
HBVs antigen	Negative
Anti-HBVs antibody	Negative
Anti HCV	Negative

The rest of the blood tests were normal. Abdominal ultrasound reported hepatomegaly.

The patient admitted for observation and needed treatment for dehydration due to vomiting and diarrhea with intravenous fluid and antiemetic drugs. Since the patient diagnosis of hepatitis A was confirmed by his immune response to the presence of the virus, we agreed that treatment for dehydration was the most appropriate course of action. The patient was given intravenous fluids for 2 days and discharged from the hospital. He was prescribed bed rest. Follow up laboratory tests showed steady and eventual full recovery.

DISCUSSION

Yellow fever and typhoid fever were very unlikely for the above patient with no history of travel to rural endemic areas. Hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis C virus (HCV), and hepatitis E virus (HEV) infection were all possible diagnosis. The above patient has presented with classic signs and symptoms of acute hepatitis. Laboratory results confirm diagnosis of acute hepatitis A infection. Exposure probably resulted from contaminated water or food while he was in Brazil.

Approximately 1.5 million clinical cases of hepatitis A occur worldwide annually but the rate of infection is probably as much as ten times higher [1]. The incidence rate is strongly related to socio-economic indicators and access to safe drinking water. The epidemiological pattern is typical in Africa and in the Middle East, as well as in several nations in Latin America and Asia. Studies conducted in the northernmost regions of Brazil have indicated that, although improved hygiene has led to a reduction in childhood exposure to HAV, the greatest exposure still occurs early in life [2], a total of five outbreaks have been reported, four of which occurred in closed communities in the state of Rio De Janeiro and all of these outbreaks involved individuals who, although of low socioeconomic status, were living in houses with adequate sanitation [2]. However, found that, despite adequate sanitation, these individuals are at risk for hepatitis A virus infection due to the overcrowding that is typically seen in such communities. Epidemiological studies indicate that the morbidity and mortality rate of hepatitis A among travelers is 500 times higher than those of cholera, 10 times those of typhoid fever and 3 times higher than hepatitis B [3].

Hepatitis A is a liver disease caused by the hepatitis A virus. The virus is primarily spread when an uninfected and unvaccinated person ingest food or water that is contaminated with the faeces of an infected person. The disease is closely associated with unsafe water, inadequate sanitation and poor personal hygiene [4]. The time between infection and symptoms, in those who develop them, is between 2 and 6 weeks [5].

Although HAV is excreted in the feces towards the end of the incubation period, specific diagnosis is made by the detection of HAV-specific IgM antibodies in the blood. IgM antibody is present in the blood following an acute hepatitis A infection [6]. It is detectable from 1 to 2 weeks after the initial infection and persists for up to 14 weeks. The presence of IgG antibody in the blood means that the acute stage of the illness is past and the person is immune to further infection. IgG antibody to HAV is also found in the blood following vaccination and tests for immunity to the virus are based on the detection of this antibody [6].

During the acute stage of the infection, the liver enzyme alaninetransferase (ALT) is present in the blood at levels much higher than is normal. The enzyme comes from the liver cells that have been damaged by the virus .The above patient elevated AST and ALT levels indicate liver damage through the invasion of the liver cells by the hepatitis viruses. Lacticedehydrogenase (LDH) and alkaline phospatase are also produced in smaller amounts in the liver and are reflected by the slightly elevated serum levels. In addition, patient's elevated bilirubin is an indicator of loss of liver function, since the liver is the key organ for elimination of wastes. The results are key findings for us looking for damaging processes to the liver such as hepatitis.

There is no specific treatment for hepatitis A. Sufferers are advised to rest, avoid fatty foods and alcohol, eat well-balanced diet and stay hydrated [5]. Hepatitis A can be prevented by vaccination, good hygiene and sanitation. There are two types of vaccines: one containing inactivated hepatitis A virus, and another containing live but attenuated virus, both provide active immunity against a future infection. The vaccine protects against HAV in more than 95% of cases for longer than 25 years [8]

Hepatitis A virus is one of the most common travel-associated infectious diseases and can be effectively prevented by vaccination [9]. Individuals traveling to high risks areas should take the initiative to be vaccinated. In addition to vaccination, travelers need to be aware of the importance of drinking water and eating foods safely in abroad. Cases of hepatitis A should be reported to the local health department immediately.

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STEM CELL TOURISM – PROTECTING INTERNATIONAL TRAVELLERS

This article is based on an OSKE delivered at the TMSI meeting in Cork on 3rd September 2016

- Subset of medical tourism
- Online, direct-to-consumer advertised industry involving patients travelling to receive unproven stem-cell based therapies
- True extent unknown, but probably involves tens of thousands of patients
- Flourishing industry in many countries, prominent among them India, China, Thailand and Mexico
- Risks are often underplayed and warnings are not given to prospective stem cell tourists.
- The International Society for Stem Cell Research has published a useful handbook for patients. Available at: http://www.closerlookatstemcells.org/docs/default-source/patient-resources/patient-handbook---english.pdf?sfvrsn=4.
- Currently over 2000 stem cell clinical trials in progress globally – clinical outcomes awaited
- Unaccredited stem cell clinics entice patients to avail of unlicensed stem cell therapies in order to avoid delays imposed by clinical trials in their own countries.
- Study by Connolly, O'Brien and Flaherty (Travel Medicine and Infectious Disease, 2014) highlighted lack of travel health preparation of stem cell tourists and dubious methods used to induce these vulnerable patients to travel for stem cell therapy.
- Most common type of stem cells reported in this study of stem cell clinics was adult autologous, derived from bone marrow or adipose tissue, and delivered intravenously.
- Top 5 indications for stem cell tourism were:
    1. Multiple sclerosis
    2. Anti-ageing
    3. Parkinson's disease
    4. Stroke
    5. Spinal cord injury
- Other indications include cerebral palsy, autism, motor neurone disease and ageing.
- Apart from severe treatment complications, risks include endemic diseases, multi-drug resistant bacteria, and poor medical follow-up.
- The public and many healthcare professionals are confused about the regulation and efficacy of clinical stem cell research and greater public education is required in order to distinguish legitimate research from fraudulent therapies.
- Ultimately patients will exercise autonomy in deciding to undergo stem cell treatment abroad but travel medicine providers should anticipate stem cell tourism as a reason for travel and advise against obtaining such treatment in an unregulated environment.

Prof. Gerard Flaherty

TICK-BORNE ENCEPHALITIS [TBE]

Tick-borne Encephalitis - it is an important human pathogen involving central nervous system that could cause long term neurological symptoms even death.

- It is a growing public health challenge. The number of human cases in all endemic region of Europe has increased by almost 400% in the last 30 years. Risk areas have spread and new foci have been discovered.

- Caused by TBE virus. Member of the family ***Flaviviridae***.

- Belongs to ***flavivirus genus*** in the *flaviviridae* family of RNA viruses,which comprises 70 different viruses.

- Flaviviridae family also comprises different genotypes of ***hepatitis viruses***.

- Most of Flaviviruses are transmitted through the bite of an infected arthropod , i.e mainly ticks or mosquitoes [i.e, Arboviruses]. e.g. yellow fever, Japanes Encephalitis, Dengue & west nile viruses.

Discovery Of TBE Virus

- The disease first described in 1931 by Austrian physician H. Schenider who reported seasonal disease which was called Epidemischea aKute meningitis serosa.

- Initially isolates in Russian far east in 1937, as the new disease called Taiga encepalitis. A new virus was isolated from the patients, rodents and ticks. E.N Pavlovskyj defined a theory of natural foci of TBE.

- Czechoslovakia ,1948: Krejci [and Gallia]: Rampas and Gallia- First isolated of TBEV in Europe. Dr Galli died from TBEV at the age of 38 years.

Geographical Distributaion of TBE Virus

- Occurs in many European counteries and large parts of Northern Asia, including counteries of the Russian federation, Northerns china, Northern Japan and korea.

- Genetic analysis of strains from different regions show that there are 3 subtypes of TBEV, based on their geographical distribution:

A- European or west TBEV: transmitted by Ixodes ricinus tick in rural and forested areas of central, eastern and northern Europe milder form with mortality up to 1%.

B- Siberian TBEV: transmitted by *I.persulcatus*, in siberria, far eastern russia, and in some areas of north-eastern Europe. This form is more severe than European.

C- Far eastern: transmitted by *I.persulcatus*, endemic in far eastern russia , Northern China & Japan.

-Formerly known as Russian spring summer encephalitis virus. Most severe with mortality over 20%.

- Some of the viruses that closely related to TBEV include Omsk hemorrhagic fever virus in seberia, Kyasanur forest disease virus in india and its close relative, Alkurma virus in Saudi Arabia.

- Louping ill virus [United Kingdom] is also a member of this family. It causes disease primarily in sheep with TBE like illness in laboratory workers & persons with contact to sick sheep [veterinarian,butchers].

- In the USA and Russia,another Tick-borne Flavi

Transmission of TBE Virus

A- Reservoir: Ticks,specially hard ticks ,act as both the vector and reservoir for TBEV. The main host for TBEV are small rodents[voles, mice]. Indicator hosts supporting virus circulation indirectly by enabling tick multiplication includes different species of wild and domestic mammals [e.g,foxes, bats,deer,dogs, sheep,cattle,goats]. Humans are incidental and dead -end hosts.

B- Transmission mode: TBEV transmitted by the bite of infected ticks.Humans may acquire infection by consumption of infected unpasteurised dairy prodcuct. TBEV not directly transmitted from human to human, apart from vertical transmission.

Laboratory accidents from needle stick injuries or aerosol infection has been reported. When infected ticks can transmit the virus throughout their life both transtadially [from larva to nymph to adult ticks] and transovarially [from adult female to eggs. Tick activity and life cycle depends on climate factors [temp,soil moisture & relative humidity]. Wet summer and mild winters tend to increase tick population density. In cental Europe, two peaks activity has been observed in April/May and in september/October. A single summer peak has been detected in colder regions of northern Europe and the moutain regions.

Risk Group

- In endemic areas, people with recreational or occupational outdoor activities [e.g,hunting, fishing, camping, farming,forestry and military training].

Signs and symptoms

- Incubation period is 7 days on average, but incubation period up to 28 days has been described. Incubation period is usually shorter after food born infection, around 4 days.

- Two-thirds of patients with European TBEV, only an early viraemic phase is experienced. The first viraemic phase lasts aproximately 5 [2 -10] days, and associated with -specific symptoms [fever, fatigue, headache, mayalgia, nausea].

- The first viraemic phase is followed by an asymptomatic interval lasting 5 days [range 1 - 33] days that preceeds the second phase, when the central nervous system is involved in 20% to 30% of patients. Patients may experience a clinical illness that involves the central nervous system with symptoms of meningitis [fever, headaches, neck stiffness], encephalitis [drowsiness, confusion, sensory disturbance and even paralysis] or meningoencephalitis

- European subtype is associated with milder disease, with 20-30% patients experiencing the second phase, and severe neurological squelae in up to10% of patients. In children, the second phase of illness is usually limited to meningitis, whereas adults older than 40 years are increased risk of encephalitis,with higher mortality and long lasting sequelae in those over the age of 60.

- Biphasic symptomatology is frequent after infections with European subtype with up to 1% fatality.occuring 5 to 7 days after the onset of neurological signs.

- Infections by fareastern subtype are generelly more severe, monophasic illness with no asymptomatic interval preceding the onset ofthe neulological disease and higher rates of severe neurological sequelae. Fatality up to 20%.

- The siberian Subtype associted with a less severe disease wth a tendency to develop chronic or prolonged infections.fatality rates 1- 3%. In children could cause enecepahalitis.

Diagnosis

- First phase of the disease: Leucopenia and Tharombocytopenia. Liver enzyme may be mildly raised.

- Diagnosis of TBE is based on the detection of specific IgM antibodies in the cerebrospinal fluid and/or blood mainly during the second phase.Specific IgM antibody could persist up to 10months in Vacinees or individuals who aquire infection naturally. IgG antibody cross reaction is possibly observed with other Flaviviruses. Detection by PCR method could be valuable for an early differential diagnosis of TBE. In the second phase, an increase in the number of white blood cells in the CSF and bloods are observed.

Treatment

- There is no specific antiviral therapy for TBE

- Meningitis,Encephalitis or meningomyelitis require hospitalisation and supportive care based on yndrom severity.

- Anti-inflammatory drugs, such as corticosteroids, may be considered under specific circumstances for ymptomatic relief.

- Intubation and ventilator support may be necessary.

Prevention

- Inactivated vaccine is considered to be the most effective means of preventing TBE in endemic counteries.

- Tick repellents and protective clothing to prevent tick bite. Use appropriate insecticides.

- Inspecting body for ticks after outdoor activities and removing ticks with appropriate tweezers and forceps.

-Avoiding consumption of unpasteurised dairy products in risk areas.

Dr. Hakha Nikookam

Dates for the Diary

Travel Medicine Society of Ireland - half-day meeting Date: 4 February 2017
Location: Sheraton Athlone Hotel, Gleeson Street, Athlone, Co. Westmeath.
Time: 9:00am - 1:00pm. Places limited
For further information, please contact Anne at 045 890 127 or annehredmond@eircom.net

Travel Medicine Society of Ireland - A.G.M. & Lecture and workshop Date: 29 April 2017
Location: Talbot Hotel, Stillorgan Road, Stillorgan, Co. Dublin.
Time: 9:00am - 1:00pm. A.G.M. Members only. Lecture and workshop open to non-members.
Places limited.
For further information, please contact Anne at 045 890 127 or annehredmond@eircom.net

The 15th Conference of the International Society of Travel Medicine. Date: 14-18 May 2017
Venue: Barcelona, Spain
For further information contact: www.istm.org

GLOBAL ROUND-UP

MERS-COV:

On 8 December 2016, the World Health Organisation (WHO) reported one additional case of Middle East Respiratory Syndrome Coronavirus (MERS-CoV).
The case was a 67 year old male from Dakhlia Governorate was admitted to hospital on 20 November 2016 and tested positive for MERS-CoV on 29 November 2016. He was exposed to camels, goats and cows in the 14 days prior to the onset of symptoms. The patient is in stable condition and has been discharged from hospital.
Contact tracing of the cases household contacts is ongoing and investigations of camels is also ongoing.

Advice for Travellers: The risk associated with MERS-CoV to the general population remains extremely low and the risk to travellers to the Arabian Peninsula and surrounding countries remains very low.
Although the source of the virus and the mechanism of transmission is unknown, it would be prudent to try to reduce the general risk of infection while travelling by:

- Avoiding close contact with people suffering from acute respiratory infections.
- Frequent hand-washing, especially after direct contact with ill people or their environment.
- Adhering to food safety and hygiene rules such as avoiding undercooked meats, raw fruits and vegetables unless they have been peeled, or unsafe water.
- Avoiding close contact with live farm or wild animals.
- Avoiding contact with camels, consumption of raw camel milk or camel products, eating undercooked camel meat.
- Travellers to the Middle East who develop symptoms either during travel or after their return are encouraged to seek medical attention and to share their history of travel.
- People with symptoms of acute respiratory infection should practice cough etiquette (maintain distance, cover coughs and sneezes with disposable tissues or clothing, and wash hands) and to delay travel until they are no longer symptomatic.

Based on the information available, WHO does not advise special screening at points of entry with regard to this event nor does it currently recommend the application of any travel or trade restrictions.

Note: Some countries have however, introduced special screening at points of entry with regard to this event.

Source: WHO

AVIAN INFLUENZA

World Health Organisation (WHO) reported that The National Health and Family Planning Commission of China has notified WHO of two laboratory confirmed cases of human infection with avian influenza A(H5N6) virus. The first laboratory confirmed case of avian influenza A(H5N6) was reported on 21 November 2016 in a 47 year old female living in Wugang Prefecture, Hunan Province. The second laboratory confirmed case of avian influenza A(H5N6) was reported on 1 December 2016 in a 30 year old female in Guangxi Province. The epidemiological investigations into both cases are ongoing. Travellers experiencing severe flu like symptoms within 10 days of returning from travel should contact their GP and inform them of their recent travel.

Source: WHO

DENGUE FEVER:

The dengue fever situation in the Western Pacific Region. China has reported 1840 cases of dengue in 2016. Malaysia reorted 91879 for 2016. Philippines have reported a total of 101401, including 422 deaths, in 2016. Singapore reported 12525 in 2016. Cambodia, January to May 2016 reported 1771 cases and 4 deaths. Lao reported 4658 cases and 10 deaths in 2016. Vietnam reported 63504 cases and 20 deaths. Australia reported 1930 cases in 2016.

Source: WHOWestern Pacific Region