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CRYPTOCOCCAL SCREENING: AN UPDATE

Cryptococcal meningitis is a common AIDS-defining opportunistic infection and is the leading cause of laboratory-confirmed meningitis among adults in South Africa [1, 2]. In routine care settings, cryptococcal meningitis is associated with a case-fatality ratio of >50% at 12 weeks post-diagnosis [3]. There are several interventions with the potential to reduce the burden and mortality associated with cryptococcal disease, including earlier diagnosis of HIV infection and initiation of antiretroviral treatment (ART). Targeted screening of patients with a CD4+ T-lymphocyte count <100 cells/ μ l for cryptococcal antigenaemia is a newer intervention that has been suggested for routine implementation as part of the National Strategic Plan on HIV, STIs and TB, 2012-2016 [4]. Screening has the potential to detect patients with early cryptococcal disease (prior to development of meningitis) and thus prevent deaths.

With input and support from implementation partners including the Department of Health, cryptococcal screening was implemented at the NHLS CD4 laboratory at Charlotte Maxeke Johannesburg Academic Hospital on 3 September 2012. Twenty-five health care facilities, (including three regional hospitals) that refer specimens to this laboratory have begun participating in the programme. Blood samples submitted for a CD4+ T-lymphocyte count from these facilities have been tested for cryptococcal antigen (CrAg) using a

cryptococcal lateral flow assay (LFA) if the CD4+ T-lymphocyte count is less than 100 cells/ μ l. The LFA is a simple, quick test with high sensitivity and specificity and has been integrated into the CD4 laboratory workflow with only minor adjustments. Results for patients who test CrAg-positive are communicated by the laboratory to a pre-selected point of contact at the facility. A comment for CrAg-positive results has been added to the CD4 laboratory report to alert the healthcare worker of the CrAg test result. Healthcare workers at participating facilities have been trained to manage patients based on a standard treatment algorithm.

In order to evaluate the impact of the screening programme, a comprehensive monitoring and evaluation plan has been developed. Patients with cryptococcal antigenaemia who provide informed consent are being followed up prospectively by the facility and the NICD surveillance team for up to 12 months. The following data are collected for CrAg-positive patients: lumbar puncture results; antifungal treatment; ART; time from CrAg testing to treatment initiation; adverse events and outcome (i.e. development of cryptococcal meningitis, death or loss to follow-up). In addition, data on other key programme indicators such as number of personnel who are trained and availability of fluconazole at facilities will be collected.

As at 1 November 2012, 1,106 patients have been screened at the first 25 facilities; 56 (5.1%) patients have tested CrAg-positive thus far. Figure 1 shows the number of cases of cryptococcal antigenaemia by healthcare facility. Two other NHLS CD4 laboratories in Gauteng and the Free State, which process CD4 samples from approximately 450 health care facilities, have also been selected for Phase 1. The NHLS CD4

laboratory at Tambo Memorial Hospital is scheduled to begin screening in the first quarter of 2013 once permission has been obtained and healthcare worker training is completed. Additional NHLS laboratories will implement screening beyond Phase 1 to expand coverage of the programme.

Source: Centre for Opportunistic, Tropical and Hospital Infections (NICD-NHLS), on behalf of the South African Cryptococcal Screening Initiative Group.

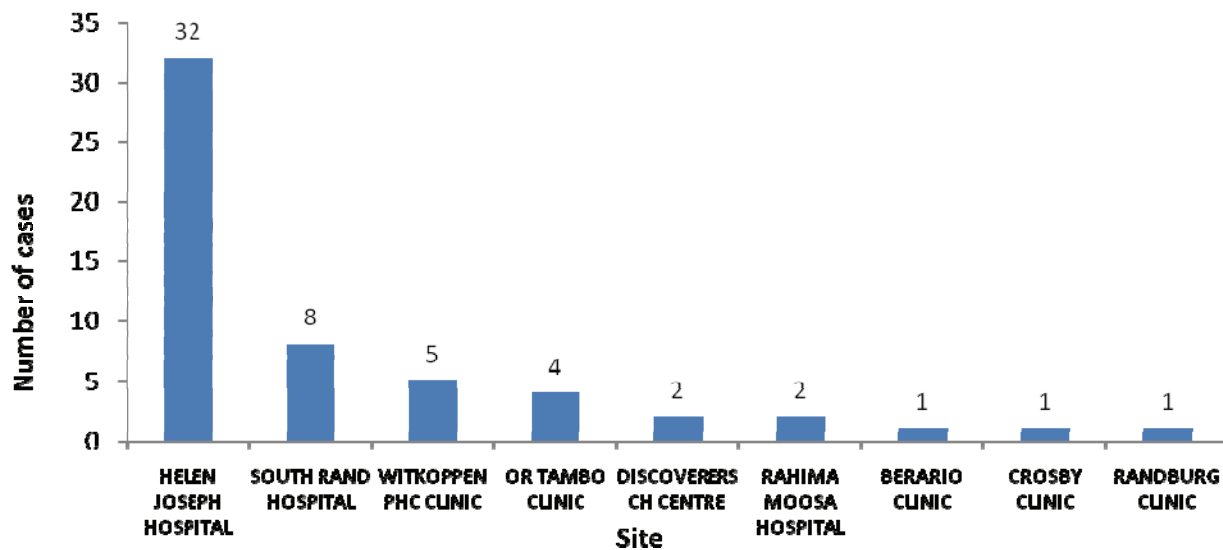


Figure 1: Cases of cryptococcal antigenaemia by healthcare facility, 3 Sep -1 Nov 2012, n = 56

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3. Park BJ, Shetty S, Ahlquist A, et al. Long-term follow-up and survival of antiretroviral-naive patients with cryptococcal meningitis in the pre-antiretroviral therapy era, Gauteng Province, South Africa. *Int J STD AIDS* 2011; 22(4):199-203.
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MENINGOCOCCAL DISEASE

Sporadic cases of meningococcal disease continue to be reported across the country. Numbers of cases generally peak during the months of August to October. The total number of cases reported thus far in 2012 (n=188) decreased as compared to the same period in 2011 (n=295).

By the end of epidemiological week 44, a total of

188 laboratory-confirmed cases was reported to the bacteriology laboratory at the Centre for Respiratory Diseases and Meningitis (CRDM), NICD-NHLS (Table). Forty-nine cases had been reported in the <1 year old age group this year so far, similar to the number of cases for the equivalent time period and age group in 2011 (n=51). Lower case numbers compared to 2011 were seen in older children

(1 to 9 years) and adolescents and young adults (10 to 29 years): from 100 to 56 cases and 81 to 44 cases reported for each year, respectively.

The reported cases have diverse serogroups, which is in keeping with sporadic endemic disease in the country. Serogroup data were available for 144/188 (77%) of cases. Serogroup S B and W135 have been identified most commonly this year (48/144, 33% serogroup B and 55/144, 38% serogroup W135). Other serogroups included C (14%, 20/144) and Y (13%, 19/144). The most notable reductions by serogroup were seen in serogroups W135 (118 to 55) and Y (38 to 19).

There should be a high index of suspicion for meningococcal disease in patients who present with non-specific early signs and symptoms. Disease typically has a rapid progression and should be managed as a medical emergency in order to reduce morbidity and

mortality. All cases of suspected meningococcal disease (meningitis and sepsis) should be notified telephonically to the Department of Health.

Table: Number of laboratory-confirmed meningococcal disease cases reported until end of week 44, 2011 and 2012, by province

| Province | 2011 | 2012 |
|---------------------|------------|------------|
| Eastern Cape | 41 | 34 |
| Free State | 21 | 11 |
| Gauteng | 122 | 70 |
| KwaZulu-Natal | 33 | 20 |
| Limpopo | 8 | 2 |
| Mpumalanga | 16 | 4 |
| Northern Cape | 6 | 1 |
| North West | 5 | 7 |
| Western Cape | 43 | 39 |
| South Africa | 295 | 188 |

Source: Centre for Respiratory Diseases and Meningitis, NICD-NHLS

MALARIA ALERT

The malaria season in southern Africa is from September to May and an increase in both local and imported cases in travellers can be expected over the upcoming holiday season. There should be a high index of suspicion for malaria as the cause of acute febrile illness in all residents of areas with local transmission and in all returning travellers from these areas. Urgent laboratory testing is mandatory. The majority of travel-related malaria is seen in persons returning to South Africa from Mozambique. This is clearly a reflection of the large numbers of visitors to Mozambique, and also of the significant malaria risk in Mozambique (particularly in areas north of Maputo) at this time of the year. In accordance with national guidelines, artemether + lumefantrine (Coartem[®]) is the first choice for treatment of uncomplicated falciparum malaria

(except in children <6 months of age and in the first trimester of pregnancy); quinine plus either doxycycline or clindamycin is the alternate option. Artesunate, where available, is the preferred initial treatment for severe malaria; alternatively intravenous quinine can be administered (remember to give an initial loading dose of 20 mg/kg over 4-6 hours). In addition to the use of personal preventive measures to reduce mosquito bites, chemoprophylaxis is recommended for visitors to high-risk areas; mefloquine, doxycycline, or atovaquone + proguanil (Malarone[®]) are recommended agents, with the choice dependent on individual traveller profiles.

Source: Division of Public Health Surveillance and Response, NICD-NHLS.

INFLUENZA

Viral Watch: influenza-like illness (ILI) surveillance programmed

The 2012 influenza season is over. The season started in epidemiological week 21 (ending 27 May)

when the influenza detection rate rose above 10%, peaked in epidemiological week 33 (ending 19 August) with a detection rate of 61.4%, and ended in epidemiological week 40 (ending 7 October). There

have been no positive influenza results since week 41 (Figure 1). As at 11 November, a total of 762 influenza detections has been made from 734 patients. Of the 752 influenza positive samples that have been subtyped, 435/752 (58%) have been

identified as influenza A(H3N2), 313/752 (42%) as influenza B and 4/752 (<1%) as influenza A(H1N1) pdm09. Influenza has been detected in all provinces.

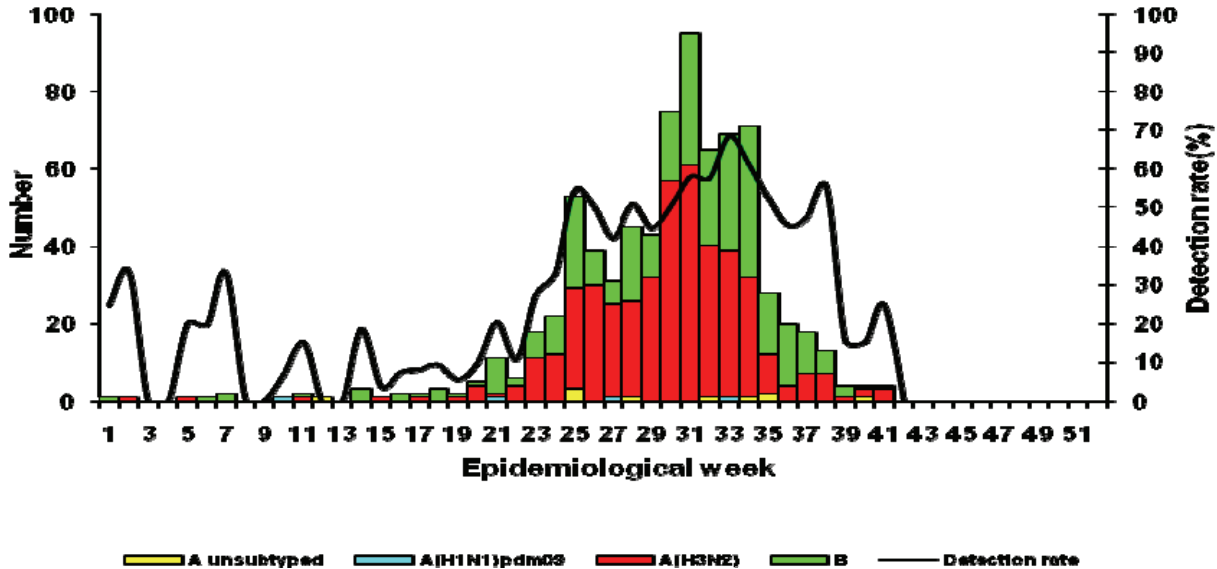


Figure 1. Number of positive samples by influenza types and subtypes, and detection rate by week, Viral Watch surveillance programme 2012

Severe Acute Respiratory Illness (SARI) surveillance programme

For the same period, 4,434 patients admitted with severe respiratory illness at the five SARI sentinel sites were tested for influenza. Of these, 251 (6%) were positive for influenza: 128 (51%) were positive for influenza B, 117 (47%) were positive for influenza A(H3N2), one (<1%) was positive for influenza A(H1N1)pdm09, one (<1%) was positive for

co-infection with influenza A(H3N2) and influenza B and 4 (2%) were positive for influenza A but not subtyped (Figure 2). As at 11 November 2012, the last positive influenza in hospitalized SARI patients was detected in epidemiological week 43 (ending 28 October).

Source: Centre for Respiratory Diseases and Meningitis, NICD-NHLS.

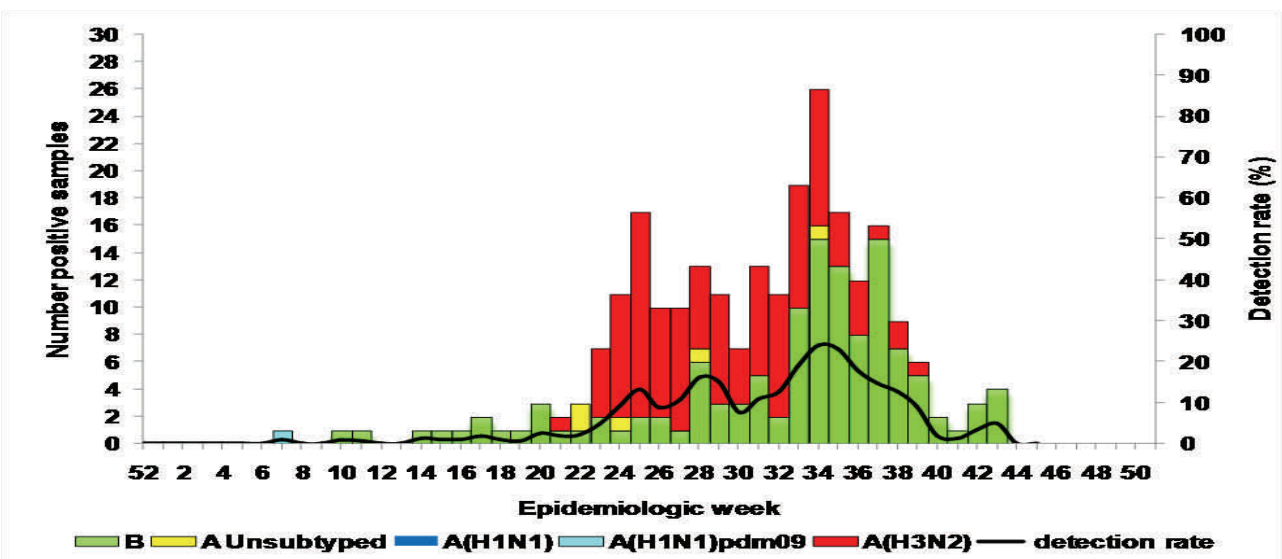


Figure 2. Number of positive samples by influenza types and subtypes and detection rate by week, SARI

COMMUNICABLE DISEASES AND THE AFRICAN CUP OF NATIONS 2013: TRAVEL ADVISORY

The 29th African Cup of Nations will be hosted in South Africa from 19 January to 10 February 2013. Five cities will host the games - Johannesburg, Durban, Port Elizabeth, Nelspruit and Rustenburg. Sixteen African nations will participate in the games.

Communicable diseases pose some risks with both endemic and imported diseases requiring consideration in preparation for the event. The risk of communicable disease spread can be ameliorated through a number of interventions, including pre-travel consultation, enhanced epidemic intelligence to timeously detect incidents, the utilisation of standard operating procedures for epidemic response, and pre-accreditation of food suppliers to reduce the risk of foodborne disease outbreaks. Respiratory and gastrointestinal infections are the most common communicable diseases associated with mass sporting events.

Malaria: The games will be taking place during South Africa's malaria season. While malaria is not transmitted in any of the host cities where matches will take place, visitors may travel to other areas within South Africa where there is a risk. Travellers visiting the north-eastern parts of South Africa, the Kruger National Park and surrounds, and the far northern parts of KwaZulu-Natal Province should take precautions to prevent malaria. Such precautions include personal protection against mosquito bites (which is the mainstay of prevention), as well as appropriate chemoprophylaxis (mefloquine, atovaquone + proguanil (Malanil[®]) or doxycycline). Chloroquine resistance is prevalent in all malaria areas in sub-Saharan Africa and with *Plasmodium falciparum* being the predominant species, artemisinin combination therapy (notably artemether + lumefantrine (Coartem[®])) is effective treatment for uncomplicated disease. Persons who plan on visiting a malaria area must be advised to seek healthcare immediately should they develop flu-like symptoms,

even if they are taking chemoprophylaxis.

African tick bite fever is common, occurs throughout the year and poses a risk for any persons going on hikes in the bush. Tick bites may be prevented by wearing long pants, application of DEET-containing insect repellents to exposed areas, and checking for ticks after hikes and carefully removing them if found. While most disease is mild, complications do occur - especially with delayed treatment. Tick bite fever should be included in the differential diagnosis of persons with febrile illness with compatible exposure history. The finding of a classical eschar and, if present, a maculopapular rash, must prompt early empiric treatment with doxycycline. Chemoprophylaxis is not effective.

The risks of **African haemorrhagic fever** viruses would be expected to be low given the unlikely exposure risk. There have been no human cases of Rift Valley fever since June 2011, and no cases of Crimean-Congo haemorrhagic fever this year to date.

Rabies is endemic in South Africa, with most human cases related to dog exposure. Risks within major cities would be considered low; the 2010/11 outbreak in Gauteng Province has been controlled. However, it is always prudent to emphasise animal avoidance practice. Post-exposure prophylaxis with cell-derived vaccine and human rabies immunoglobulin is widely available in the event of an exposure.

Bilharzia (schistosomiasis) is endemic in the north and east parts of South Africa, and may be present elsewhere. Avoid swimming and paddling in stationary water. Swimming pools which are well-chlorinated and maintained are safe.

TB/STI/HIV: South Africa is classified by the World Health Organization as a country with high TB and high MDR-TB burdens. There is an in-

creased risk of acquiring a sexually transmitted infection (STI) during mass gatherings - this bears particular relevance for visitors to South Africa given the high prevalence of HIV and other STIs. Quinolone-resistant gonorrhoea is widespread in South Africa; also, a cluster of multidrug-resistant gonorrhoea cases (additionally resistant to cephalosporins) was recently described in Gauteng Province.

Visitors who travel from or through **yellow fever** endemic areas, even if in transit, must present proof of vaccination on entry to South Africa. Although there is no risk of yellow fever in South Africa, International Health Regulations requires travellers aged ≥ 9 months arriving from countries where yellow fever is a risk to show proof of yellow fever vaccination, or a waiver certificate. A yellow fever inoculation certificate only becomes valid 10 days after inoculation - after which it remains valid for 10 years. Further information regarding the South African yellow fever vaccination policy, including designated yellow fever risk areas can be accessed at http://www.doh.gov.za/docs/policy/2011/yellowf_policy.pdf.

Hepatitis A is transmitted through contaminated food and water. The risk of infection varies within the country. Travellers should practice strict food, water and personal hygiene precautions. Hepatitis A vaccine may be considered for travellers over one year of age. It should be given at least *two weeks* (preferably *four weeks* or more) prior to departure.

Hepatitis B is transmitted via infected blood or bodily fluids. Travellers may be exposed when receiving medical or dental treatment, via direct contact between open skin lesions, or if participating in risk behaviour such as needle sharing, unprotected sex or contact sports. Hepatitis B vaccine is recommended for all travellers if not previously vaccinated, especially those who might be exposed to blood or body fluids, or have sexual contact with the local population.

Sporadic cases of **meningococcal disease** are reported, with a seasonal increase typically during the period May to October. Currently serogroups B and W135 predominate. Routine vaccination for travellers is not recommended.

The games will be taking place outside of the annual **influenza** season in South Africa. The influenza season in South Africa usually commences in mid-May, peaks during June/July before tapering off and ending by mid- to late August. The 2013 African Cup will therefore be occurring outside the South African influenza season but within the northern hemisphere's influenza season. Visitors from the latter region should be vaccinated to reduce importing infection.

Polio: a booster vaccination is recommended for travellers from polio-endemic countries (Nigeria, Pakistan, and Afghanistan) or where recent circulation of polio has been confirmed.

Measles: a nationwide outbreak was reported in 2009/2010, but in 2012 only a small number of sporadic cases have been identified. Nevertheless, measles vaccine should be administered to persons considered to be non-immune.

Behaviour modification plays an important role in limiting exposure to many potential pathogens. Hand hygiene and cough etiquette must be encouraged; avoiding close contact with people who have respiratory illnesses is also advised. Avoiding potentially unsafe drinking water, undercooked meats, unwashed fruits and vegetables, and unpasteurised dairy products may reduce the risk of food- or water-borne disease. Practising safe sex is extremely important. Taking appropriate precautions when travelling to malaria areas or the bush must be emphasised. We wish you a happy stay in South Africa, enjoy the games!

Source: Division of Public Health Surveillance and Response, NICD-NHLS; School of Public Health, University of the Witwatersrand

BEYOND OUR BORDERS: INFECTIOUS DISEASE RISKS FOR TRAVELLERS

The 'beyond our borders' column focuses on selected and current international diseases that may affect South Africans travelling abroad.

| Disease & Countries | Comments | Advice to travellers |
|---|---|--|
| <p>Dengue: Portugal (Madeira)</p> <p>South-East and South-Central Asia</p> | <p>As of 11 November 2012, 1 357 cases of dengue fever have been reported from Madeira.</p> <p>Dengue cases continue to be reported in Singapore, Malaysia, Cambodia, Taiwan, the Philippines, Vietnam, India, Sri Lanka, and Thailand.</p> | <p>Dengue fever is a common cause of fever in travellers returning from the Caribbean, Central America, and Asia (South-Central and South-East). The disease is spread through the bites of infected <i>Aedes</i> spp. mosquitoes and cannot be spread from person to person.</p> <p>Symptoms of dengue fever are nonspecific, and include fever, headache, joint and muscle pain, rash, nausea and vomiting. Although uncommon, dengue haemorrhagic fever and dengue shock syndrome are potentially fatal complications. Travellers can reduce their risk of dengue infection by protecting themselves from mosquito bites. Stay in hotels that are well screened or air-conditioned. Use insect repellent on uncovered skin. Wear loose, long-sleeved shirts and long pants when outdoors.</p> |
| <p><i>Plasmodium vivax</i> malaria: Greece</p> | <p>As of 26 October, 76 cases of malaria were reported by the national public health authorities: 60 imported and 16 autochthonous cases. The outbreak is not under control despite increased surveillance and active case detection.</p> | <p>All travellers to Greece should take steps to prevent mosquito bites. Travellers should take preventive measures to reduce mosquito bites, including: wearing long sleeves and trousers during the late afternoon, evening and early morning; use of insect repellents (containing 30-50% DEET); sleeping under insecticide-treated bed nets; keeping windows and doors closed/screened, and use of insecticide aerosol and/or coils. Travellers who have flu-like symptoms should seek healthcare as soon as possible. Physicians should consider malaria in any patient with a febrile illness who has recently returned from a malaria-endemic country.</p> |

| Disease & Countries | Comments | Advice to travellers |
|---|--|---|
| <p>Yellow fever: South Sudan (Darfur) and Sudan (Khartoum)</p> | <p>Since 9 November 2012 to date, 266 suspected cases of yellow fever have been reported, including 85 deaths (case-fatality rate of 31.8%). Most (72.9%) of the reported cases are from Central Darfur. Only one case has been reported in Khartoum, the capital city of Sudan.</p> | <p>Yellow fever (YF) is a viral haemorrhagic disease transmitted by infected mosquitoes (<i>Aedes aegypti</i>). Cases have increased globally due to deforestation, urbanization, population movements and climate change. YF illness ranges from mild flu-like illness to a haemorrhagic fever (which carries a 50% case-fatality rate). Following an incubation period of 3 to 6 days, fever, muscle pain with prominent backache, and headache occur. Most patients improve and their symptoms resolve after 3 to 4 days. However, 15% of patients enter a second, more toxic phase within 24 hours of the initial remission. High fever returns and is accompanied by severe multisystem illness (including icteric hepatitis and haemorrhagic diathesis). There is no specific treatment for yellow fever. Travellers to at-risk yellow fever areas need to have proof either of yellow fever vaccination or a medical waiver certificate.</p> |
| <p>Salmonella Stanley: European Union</p> | <p>An outbreak of <i>Salmonella</i> Stanley infection involving 167 confirmed and 254 probable cases is ongoing in several EU countries, namely Austria, Belgium, Germany, Czech Republic, Poland and Hungary.</p> | <p>As control measures have not yet been implemented to remove the source of infection and potential food vehicles from the market, it is likely that additional human cases of <i>S. Stanley</i> infections will be reported in EU Member States. Travellers should be very strict with personal (hand washing) and food hygiene (avoid cross-contamination between ready-to-eat and raw meat) when handling raw turkey meat.</p> |
| <p>West Nile virus: Tunisia</p> | <p>As of 9 November 2012, 41 cases of West Nile virus have been reported, including the two newly affected areas of Tozeur and Sfax, and a possible case originating in Montenegro.</p> | <p>Travellers should take preventive measures to reduce mosquito bites, including: wearing long sleeves and trousers during the late afternoon, evening and early morning; use of insect repellents (containing 30-50% DEET); sleeping under insecticide-treated bed nets; keeping windows and doors closed/screened, and use of insecticide aerosol and/or coils at night.</p> |

| Disease & Countries | Comments | Advice to travellers |
|---|---|--|
| Marburg virus: Uganda | As of 28 October 2012, a total of 18 cases and 9 deaths, including a healthcare worker, have been reported from 5 districts (Kabale district in south-western Uganda; Kampala, Ibanda, Mbarara and Kabarole). Marburg virus has been detected in blood samples from 9 cases so far. | Marburg virus is the causative agent of Marburg haemorrhagic fever, a disease with a case-fatality rate of up to 88%. Transmission is mainly human-to-human, resulting from close contact with the blood, secretions, organs or other bodily fluids of infected persons. The incubation period (interval from infection to onset of symptoms) varies from 2 to 21 days. Treatment requires supportive care. No specific treatment or vaccine is available. |
| Novel coronavirus: Saudi Arabia and Qatar | As of 23 November 2012, a total of 6 laboratory confirmed cases of novel coronavirus infection has been reported: 4 cases (including 2 deaths) from Saudi Arabia and 2 cases from Qatar. | Coronaviruses are a large family of viruses that cause a wide range of illnesses in humans, from the common cold to SARS. Viruses of this family also cause a number of animal diseases. In the cases reported to date, infection with novel coronavirus has manifested as an acute febrile respiratory infection (presenting as a pneumonia or acute respiratory distress syndrome). Investigations are ongoing with regards the likely source of infection, route of exposure, and possibility of human-to-human transmission of the virus. The World Health Organization (WHO) does not recommend any travel/trade restrictions to Saudi Arabia or Qatar. |
| Ebola haemorrhagic fever: Uganda | As of 23 November 2012, the Ugandan Ministry of Health has reported 10 cases (6 confirmed, 4 probable) including 5 deaths in Luweero and Kampala; the last confirmed case was hospitalised on 17 November 2012. All cases originated from Luweero district in Central Uganda, but some travelled to/were transferred for care to Kampala (the capital city), ±75 km away. | The Ebola virus is transmitted by direct contact with the blood, secretions, organs or other body fluids of infected persons. Healthcare workers have frequently been infected while treating patients with Ebola virus infection, through close contact without appropriate infection prevention and control precautions and inadequate barrier nursing procedures. The incubation period is 2 to 21 days, and disease is characterised by the sudden onset of fever, intense weakness, muscle pain, headache and sore throat. This is often followed by vomiting, diarrhoea, rash, impaired kidney and liver function, and in some cases, both internal and external bleeding. Laboratory findings show low counts of white blood cells and platelets as well as elevated liver enzymes. The WHO does not recommend any travel restrictions to Uganda. |

References and additional reading

ProMED-Mail (www.promedmail.org)

World Health Organization (www.who.int)

Centers for Disease Control and Prevention (www.cdc.gov)

European Centre for Disease Prevention and Control (www.ecdc.europa.eu)

Last accessed: 20 November 2012

Source: Division of Public Health Surveillance and Response, NICD-NHLS; School of Health Systems and Public Health, University of Pretoria