



Brucellosis

In December 2010, the cause of several abortions in a goat herd on a farm in Gauteng Province was confirmed as a *Brucella melitensis* outbreak by the Department of Agriculture, Forestry and Fisheries. The farmer and one of the farmworkers were subsequently diagnosed with brucellosis (on the basis of positive ELISA tests, both with titres of 1:640). The farmer presented with a 6-week history of recurrent fever, polyarthralgia, malaise and anorexia. He had consulted a general practitioner and subsequently a specialist, and despite mentioning the outbreak of brucellosis in his goats the possibility of brucellosis as the cause of his illness was dismissed by both clinicians. The farmworker presented with similar symptoms a few weeks later. Both cases have been treated with the recommended triple-drug regimen, and are at present recovering well. All other family members, farmworkers and residents of the farm (none of whom had developed any symptoms) were tested, and serology was negative for all. Fortunately, the does were never milked for human consumption, so possible infection of further persons was highly unlikely and the outbreak appears to have been contained.

Brucellosis (also known as Malta fever or undulant fever) is estimated to be one of the most common bacterial zoonosis worldwide. It remains grossly underdiagnosed and under-reported in many developing countries where it is endemic, including South Africa. *B. melitensis* causes the vast majority of human brucellosis cases, followed by *B. abortus* and *B. suis*. In South Africa, the prevalence of *B. abortus* in cattle is relatively high and outbreaks are reported from all provinces (Figure); in contrast, outbreaks of *B. melitensis* in animals have been rare but could be on the rise. Human brucellosis (due to any species) is a notifiable disease in South Africa, and a recent outbreak of *B. melitensis* has highlighted the need for increased awareness of this important zoonosis.

The usual reservoirs of *B. melitensis* are goats, sheep or camels; in areas where cattle co-exist with goats or are fed sheep offal, they can also be infected and therefore a source of human disease. Persons working in occupations where contact with animals/animal products frequently occur are at highest risk of brucellosis (farmers/farm workers, abattoir workers, veterinarians and other animal-health workers, etc.).

Humans acquire brucella infection via 3 routes:

- Direct contact with infected animals or their secretions through skin cuts/abrasions or conjunctival splashes,
- Inhalation of contaminated aerosols, and
- Consumption of unpasteurised dairy products (incl. milk, yoghurt, cheese).

It is important to note that pasteurised/adequately boiled milk or milk products and cooked meat from infected animals are safe to consume and do not transmit infection. Human-to-human transmission is extremely rare, but case reports have described vertical transmission, transfusion-transmitted/transplant-associated infection, and sexual transmission of brucellosis.

Owing to its ability to cause a wide spectrum of clinical manifestations with a tendency towards chronicity and persistence, brucellosis is one of the three 'great imitators', along with TB and syphilis. It evolves into a granulomatous disease capable of affecting any organ system. The clinical features depend on the stage of disease as well as the organ/s involved. Fever is the most common feature, followed by osteoarticular involvement, sweating and constitutional symptoms. Hepatosplenomegaly is evident in a third of patients, and lymphadenopathy in 10%. Osteoarticular manifestations (sacroiliitis, spondylitis, peripheral arthritis and osteomyelitis) account for over half of the focal complications. Pulmonary disease (pneumonia, pleural effusion)

may be evident in up to 16% of complicated cases and genitourinary complications (including glomerulonephritis, epididymo-orchitis and renal abscesses) can be found in 10% of patients. Neurological involvement may be evident in about 6% of cases, with protean manifestations including peripheral neuropathy, chorea, meningoencephalitis, transient ischaemic attacks, psychiatric features, or cranial nerve palsies. Less frequent manifestations include mucocutaneous involvement (papular rash, purpura, Stevens-Johnson syndrome) and endocarditis (the most serious complication). Anaemia is the most common haematological abnormality, affecting a quarter of cases. Leucocytosis, leucopenia and thrombocytopenia are seen in similar frequencies ($\pm 10\%$).

Brucellosis in childhood may easily be missed and a high index of suspicion for the disease is important. Children usually present with monoarticular arthritis (usually hips/knees) rather than the sacroiliitis seen in adults.

The diagnosis of brucellosis can be problematic. Isolation of brucellae from blood, bone marrow or other tissue remains the gold standard. However, isolation rates depend on the method used (varying from 15% - 90%), the stage of disease and previous use of antibiotics. Serology is playing an increasing role in diagnosis, with the traditional Rose Bengal test largely having been replaced by ELISA tests with

higher sensitivity and specificity. However, serology needs to be interpreted cautiously: no single titre is always diagnostic, but most cases of active infection have titres of 1:160 or higher. PCR tests have shown promise, but standardisation remains problematic and their diagnostic value requires further assessment.

Treatment of brucellosis is complicated by treatment failures and relapses. The WHO has not updated its recommended treatment regimes for brucellosis since 1986; these regimes have been found to have treatment failure and relapse rates ranging from 4.6% to 24%. A meta-analysis has shown that dual or triple regimens including an aminoglycoside (doxycycline-streptomycin/gentamicin or doxycycline-rifampicin-streptomycin/gentamicin) significantly reduces treatment failure and relapse rates, and are currently recommended as first-line treatment regimens. Duration of treatment is 6 weeks for doxycycline and rifampicin, and 2 weeks for aminoglycoside therapy (daily intramuscular injections).¹ Patients require prolonged follow-up to monitor for further complications or relapse.

1. Skalsky et al. Treatment of human brucellosis: systematic review and meta-analysis of randomised controlled trials. *BMJ* 2008 Mar 29;336(7646):701-4

Source: Outbreak Response Unit, NICD-NHLS; Department of Agriculture, Forestry and Fisheries; and Department of Health

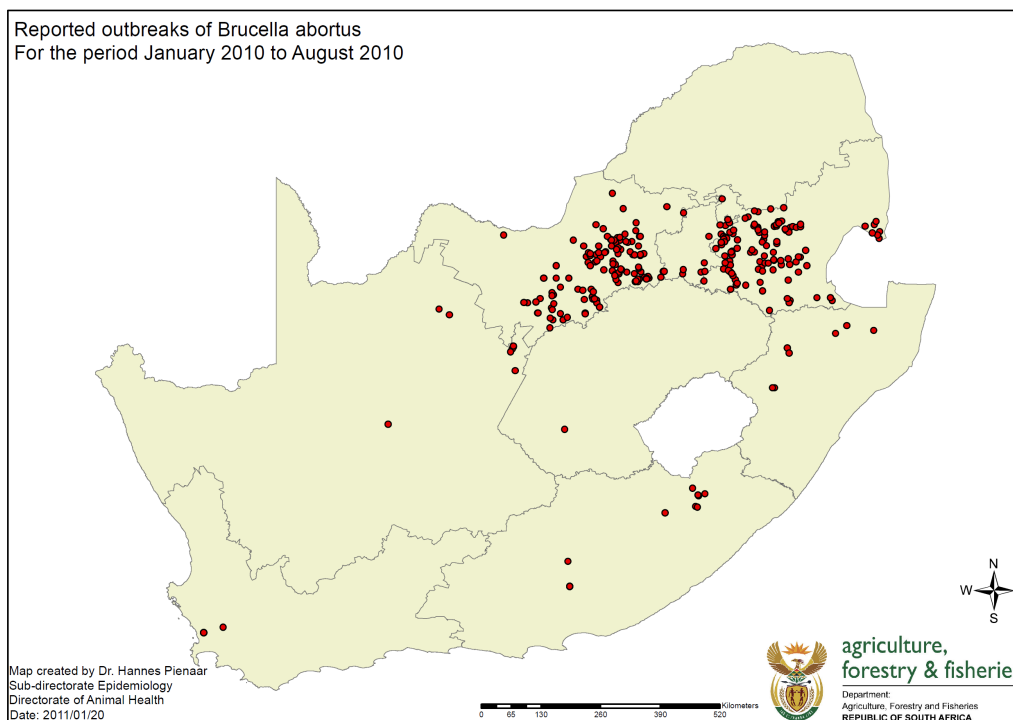


Figure: Reported outbreaks of Brucella abortus in animals, January to August 2010.
Map courtesy of the Department of Agriculture, Forestry and Fisheries

Rift Valley fever alert

Outbreaks of Rift Valley fever (RVF) occur at irregular intervals of years, following heavy rains that favour breeding of the mosquito vectors of the causative virus thus proliferating infection among ruminant animals. These outbreaks can recur over a succession of unduly wet seasons. Human RVF infections typically arise in the context of major outbreaks of RVF in domestic livestock (e.g. sheep, cattle and goats), which may be recognised by abortions and deaths of young animals. Transmission to humans primarily occurs through direct contact with infected animal tissues, blood or other body fluids, and less commonly by mosquito bites, inhalation of aerosolised infected fluids or ingestion of unpasteurised milk from infected animals. Individuals with vocations (e.g. farmers and animal-health workers) where contact with animals frequently occurs are therefore at increased risk.

Three isolated animal RVF outbreaks have been confirmed for 2011 to date: two in Western Cape Province and one in Gauteng Province. South Africa has experienced heavy rainfall over a geographically large proportion of the country during December 2010 and January 2011, with flooding in many areas. Consequently, there remains much concern over a possible re-emergence of RVF within previously affected areas. During 2010, a total of 238 laboratory-confirmed human RVF cases was identified across Free State, Northern Cape, North West, Eastern Cape and Western Cape provinces.

Individuals involved in the livestock industry are reminded to use appropriate personal protective equipment, especially when performing high-risk procedures which may include: handling of animal tissue during slaughtering or butchering, assisting with animal births, conducting veterinary procedures and disposal of carcasses or foetuses. In addition, the unsafe consumption of fresh blood, raw milk or animal tissue in epizootic regions must be discouraged; all animal products (blood, meat and milk) should be thoroughly cooked/pasteurised before eating. Protection against mosquito bites by using insect repellents (containing 30-50% DEET), insecticide-treated bed nets, and wearing of light-coloured clothing are extra preventive measures.

Should clinicians identify a suspected RVF case, they are requested to immediately notify the Department of Health and submit specimens to the NICD for laboratory testing. The "2011 Healthcare Workers Guidelines on RVF" is currently under review, and will be available online within the next month; the 2010 guideline should be referred to in the interim (access via the NICD website: http://www.nicd.ac.za/outbreaks/rvf/rvf_outbreak.htm).

Source: Outbreak Response and Special Pathogens Units, NICD-NHLS; Departments of Health, and Agriculture, Forestry and Fisheries.

Crimean-Congo haemorrhagic fever (CCHF)

Crimean-Congo haemorrhagic fever (CCHF) was confirmed in a 64-year-old male from Petrusburg in the Northern Cape Province. The patient is a sheep farmer, and was bitten by a *Hyalomma* tick two days prior to onset of illness. He initially presented with headache, myalgia and fever. Upon admission to Kimberley Hospital, the patient was noted to have marked transaminasaemia and profound thrombocytopenia with subsequent haemorrhagic complications. Platelet counts remained low despite numerous transfusions, and steadily decreased from $44 \times 10^9/\ell$ to $25 \times 10^9/\ell$ within two days. CCHF was confirmed by RT-PCR, virus isolation and detection of CCHF specific IgG and IgM antibodies on a

subsequent specimen. The patient received prompt ribavirin treatment and aggressive supportive management, and fortunately recovered.

This brings to five the number of laboratory-confirmed cases of CCHF diagnosed in South Africa in 2010 (2 cases from Free State and 3 cases from Northern Cape provinces). In addition, two Namibian cases were also confirmed by NICD-NHLS during 2010.

Source: Special Pathogens and Outbreak Response Units, NICD-NHLS

Rabies

A total of 11 human rabies cases has been confirmed in South Africa for 2010. The cases have been reported from Northern Cape (n=1); Mpumalanga (n=1); Gauteng (n=1); KwaZulu-Natal (n=3), Eastern Cape (n=2) and Limpopo provinces (n=3) (Figure 1). However, animal rabies cases were reported from all provinces in 2010 (Figure 2).

outbreak indicate that the virus was initially imported from KwaZulu-Natal Province, where an epizootic has been ongoing since the 1980s. This new outbreak highlights the importance of continued and sustained control efforts - most importantly the prevention of rabies through vaccination of pets and enhanced public awareness. In the past 5 years, rabies has re-emerged in several localities where the disease had been under control for decades, including Limpopo Province in 2005 and Mpumalanga Province in 2008.

In 2010, the first ever human rabies case and the largest animal rabies outbreak in the greater Johannesburg metropole (Gauteng Province) was reported. Thirty cases of rabies in domestic dogs have been confirmed by the Agriculture Research Council-Onderstepoort Veterinary Institute. Molecular characterisation of virus isolates from this

Source: Special Pathogens and Outbreak Response Units, NICD-NHLS; Department of Agriculture, Forestry and Fisheries

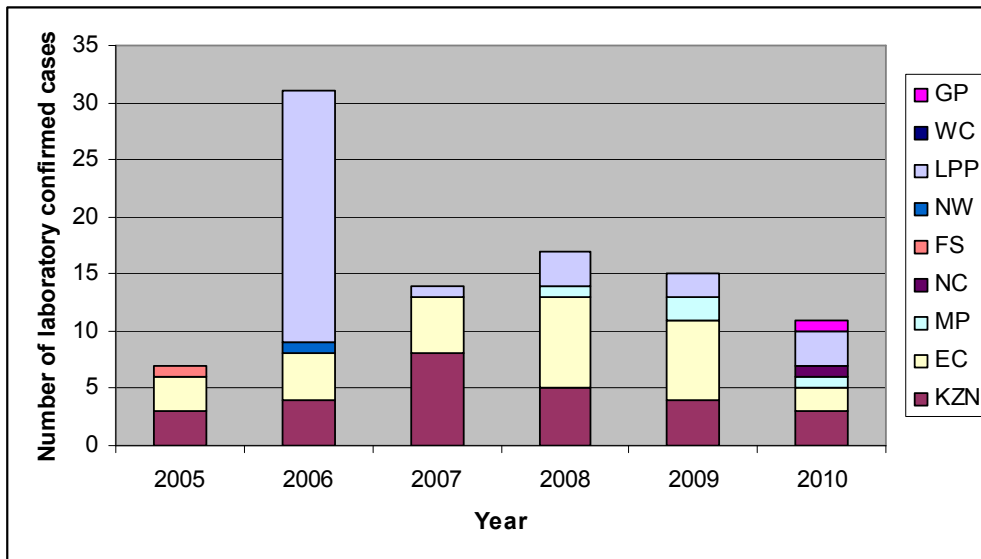


Figure 1: Number of laboratory confirmed human rabies cases by province in South Africa, 2005-2010

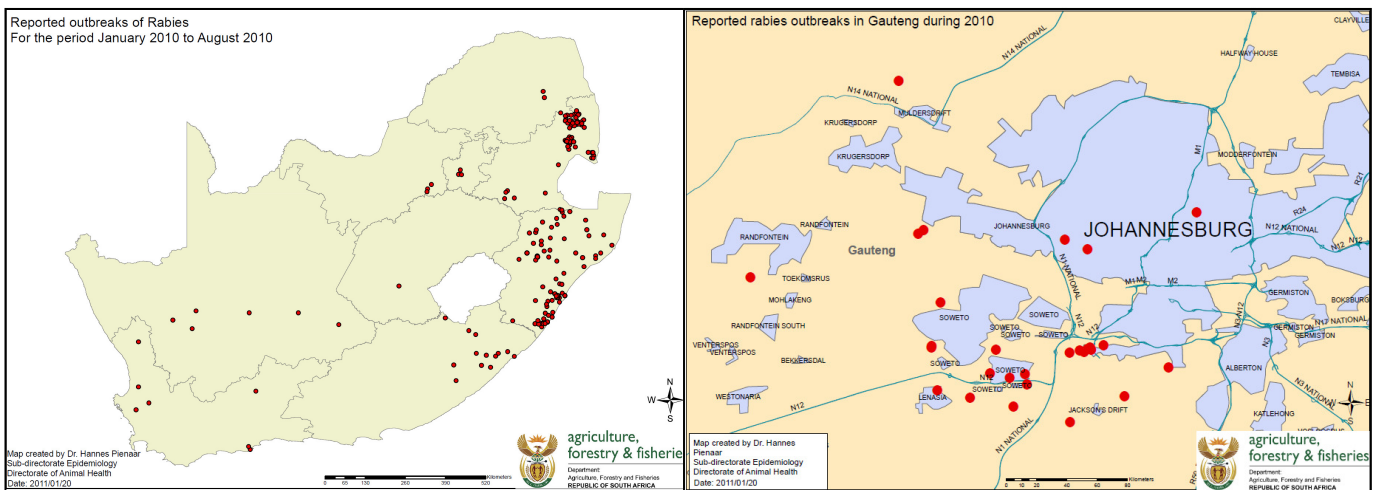


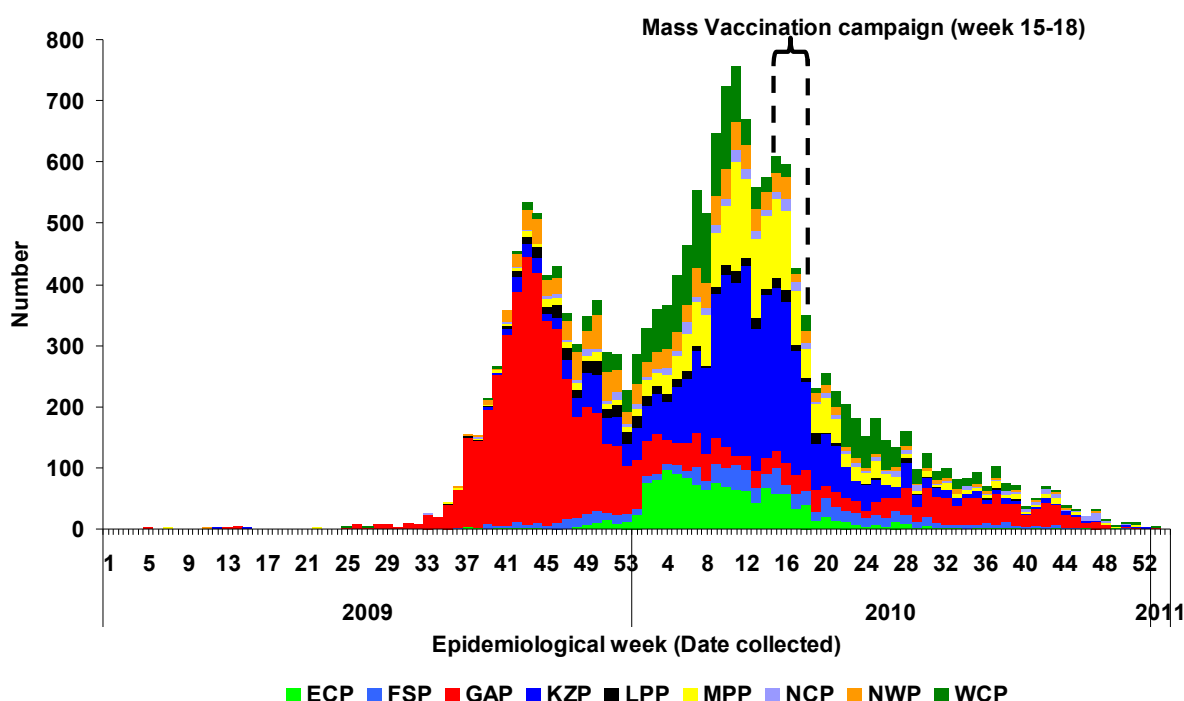
Figure 2: Map showing confirmed animal rabies cases in (left) South Africa during January to August 2010 and in (right) Gauteng Province during 2010. Maps courtesy of the Department of Agriculture, Forestry and Fisheries

Measles update

There have been 52 additional laboratory-confirmed measles cases since the last published Communiqué, bringing the total to 18 363 cases from the beginning of 2009 to 5 January 2011. Cases have been reported from all nine provinces, with Gauteng (31%, 5 733/18 363), KwaZulu-Natal (23%, 4 261/18 363) and Western Cape (11%, 2 061/18 363) provinces accounting for the highest proportions of the total (Figure 1). Of patients with known age (n=17, 470), children < 1 year account for 35% of cases, with 26% occurring in those aged 6-11 months.

Although the measles outbreak is ongoing, there is a trend towards decreasing numbers of new cases reported each week. Measles is currently active in numerous other eastern and southern African countries; healthcare workers and travellers should take cognizance of this.

Source: Divisions of Epidemiology and Virology, NICD – NHLS



Province abbreviations: ECP=Eastern Cape; FSP=Free State; GAP=Gauteng; KZP=KwaZulu-Natal; LPP=Limpopo; MPP=Mpumalanga; NCP=Northern Cape; NWP=North West; WCP=Western Cape

Figure: Measles IgM positive results per province: South Africa, January 2009 - 5 January 2011

Malaria

In southern Africa the malaria season extends from September to May, and many travellers will have been exposed to infection during their recent holidays. There should be a high index of suspicion for malaria in any person who develops a febrile illness post-travel to a malaria-risk area.

The National and Provincial Malaria Control Programmes have been very successful in reducing the

malaria risk in South Africa with numbers of reported cases steadily decreasing from 62 700 in the 1999/2000 season to 6 600 in the 2009/2010 season. In the 2010/2011 season thus far (July 2010 to date), 3 470 cases have been reported in South Africa with Limpopo Province contributing 2 099/3 470 (61%) of the cases, followed by Mpumalanga Province with 937/3 470 (27%) of the cases. Limpopo Province reported an increase in

cases in the Mopani and Vhembe districts (Masisi, Malamulele, Giyani and Ba-Phalaborwa) during the second half of December 2010 as compared to the same period in 2009, while numbers of cases in far north KwaZulu-Natal Province and the lowveld areas of Mpumalanga Province (including the Kruger National Park) have shown the expected seasonal increases. However, although malaria is a notifiable disease many cases are not reported, especially in returning travellers.

The majority of travel-related malaria is seen in persons returning from Mozambique. This is clearly a reflection of the large numbers of visitors from South Africa to Mozambique, and also of the significant malaria risk in this neighbouring country (particularly in areas north of Maputo) at this time of the year.

In accordance with the 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), or quinine plus

either doxycycline or clindamycin. 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 20mg/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 are recommended agents, with the choice dependent on individual traveller profiles.

Reference:

National Guidelines for Malaria Treatment, and Prevention of Malaria: www.doh.gov.za/docs/factsheets/guidelines/malaria/treatment/guidelines2010.pdf

Source: Travel Medicine and Parasitology Reference Units, NICD; Department of Health (including the Malaria Information Systems and the DHIS).

Yellow fever

The Ugandan Ministry of Health recently reported a confirmed outbreak of yellow fever in the northern regions of the country. As of 3 January 2011, the outbreak had affected 190 people with 48 deaths. A mass vaccination campaign is planned for this month, targeting 2.5 million people across 26 districts. In Cote d' Ivoire during the month of December 2010, 2 confirmed cases and a further 21 suspected cases (some of which may be dengue fever), with 11 deaths were reported from the central-north regions of the county. Civil unrest following Cote d' Ivoire's presidential election is blocking a nationwide vaccination drive that was initially planned for the end of November 2010.

Yellow fever is an acute viral haemorrhagic disease transmitted by infected mosquitoes, and can present in one or two phases. After a 3-6 day incubation period infection typically presents as an acute illness (the 'acute phase') characterised by fever with rigors, myalgia, prominent backache, headache, loss of appetite, and nausea or vomiting. Fifteen percent of patients then develop a second, severe phase of illness (the 'toxic phase') within 24 hours of apparent remission, marked by recurrence of high fever and evidence of multi-organ involvement including: jaun-

dice, abdominal pain with vomiting, renal failure and/or haemorrhage. This second phase carries a case fatality rate of 20% to 50%.

The virus is endemic in tropical areas of Africa and Latin America (Figure). Vaccination is the single most important preventive measure. Under the International Health Regulations, South Africans travelling to endemic countries (Figure) must receive yellow fever vaccine at least 10 days prior to departure. Yellow fever vaccination certificates are valid for 10 years. Vaccine is contraindicated in pregnant women, infants <9 months, individuals with egg allergies, and certain immunosuppressed individuals (including HIV-infected persons with CD4<200/mm³). These individuals still require a health certificate indicating the reason for non-receipt of vaccine. Vaccinated travellers should still take precautionary measures to avoid being bitten by mosquitoes due to the many other communicable disease risks transmitted by these vectors (e.g. malaria, dengue).

Source: Outbreak Response and Travel Health Medicine Units, NICD-NHLS

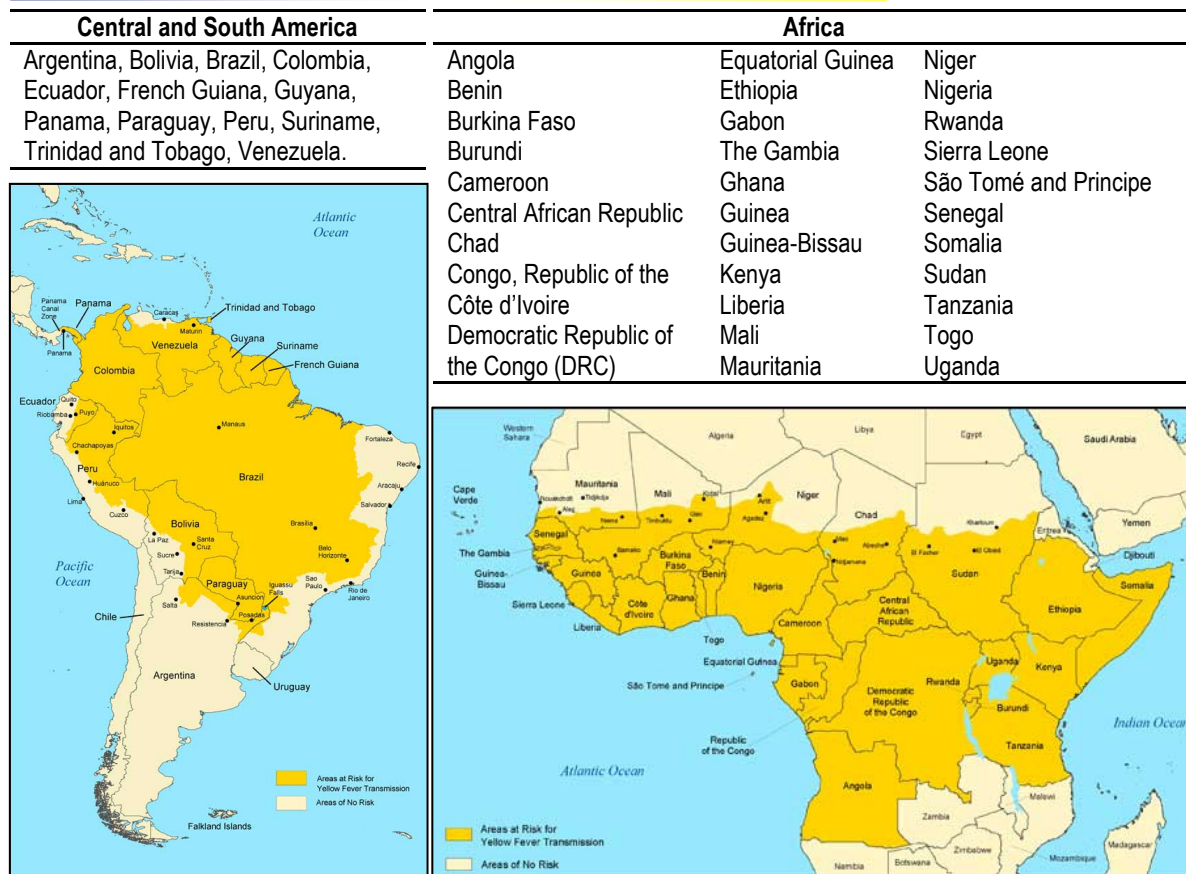


Figure: List and map of yellow fever endemic zones in (left) South and Central America and (right) Africa, 2009. Courtesy of: the Centers for Disease Control and Prevention, Available online: <http://wwwnc.cdc.gov/travel/yellowbook/2010/chapter-2/yellow-fever.aspx>

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
Legionnaires' disease: Australia ex Indonesia (Bali)	A total of 10 laboratory confirmed <i>Legionella pneumophila</i> serogroup 1 cases has been diagnosed among Australian travellers returning from Bali, Indonesia. Nine of the 10 travellers stayed at the same hotel in the central area of Kuta in Bali. Nearly all cases have been severely ill with pneumonia, requiring ICU treatment. Investigations are ongoing.	Legionnaires' disease is caused by infection with <i>Legionella</i> spp. (usually <i>L. pneumophila</i>), which is transmitted by the airborne route. Infectious aerosols can be generated from contaminated water systems by air conditioning systems, shower heads, misters, and whirlpool spas. Person-to-person transmission does not occur. Symptoms include high fever, chills and cough. Up to 15% of cases are fatal. Travellers should avoid staying in hotels currently reporting outbreaks and that have poorly-maintained air conditioning/plumbing systems. If travellers to the area develop symptoms, they should seek immediate medical attention and inform the doctor of the outbreak. Clinicians should include Legionnaires' disease within their differential diagnosis of patients presenting with atypical pneumonia and obtain a thorough travel history to identify possible travel-associated infections.

Disease & Countries	Comments	Advice to travellers
<p><u>Cholera:</u> Haiti, Dominican Republic and the United States of America (USA)</p>	<p>The number of newly reported cholera cases in Haiti is gradually declining since the outbreak peaked in November 2010. As of 1 January 2011, PAHO reported a total of 171 304 cumulative cholera cases with 3 651 deaths (CFR 2%). An estimated 55.5% of cases were hospitalised. The outbreak has spread to affect border towns within the neighbouring Dominican Republic. As of 31 December 2010, 139 cases were reported. In addition, cholera has been confirmed among relief workers returning to the USA from Haiti.</p>	<p>Cholera is transmitted through the faecal-oral route, and primarily through contaminated water. Travellers are urged to take precautions when consuming food and water, utilise water purification tablets where needed, and practice good hand hygiene. Vaccine is not routinely recommended for travellers.¹</p>
<p><u>Avian Influenza (H5N1):</u> Egypt, Indonesia, Vietnam, and Nepal</p>	<p>During December 2010 numerous suspected and confirmed human cases, as well as confirmed infection of poultry, were reported from Egypt, Indonesia, Vietnam and Nepal. Since the initiation of surveillance in 2003 up to 13 January 2011, the WHO has reported a global total of 517 confirmed cases, of which 308 (60%) were fatal infections. The most affected countries include Egypt (120 cases, 40 deaths); Indonesia (171 cases, 141 deaths) and Vietnam (119 cases, 59 deaths).</p>	<p>Most of these cases have resulted from people having direct or close contact with H5N1-infected poultry or H5N1-contaminated surfaces. Travellers are advised to avoid contact with live poultry markets, poultry farms and dead wild birds when visiting these areas.</p>
<p><u>Influenza (seasonal):</u> Northern hemisphere</p>	<p>The Northern hemisphere's winter influenza season is now underway. As of 30 December 2010, the WHO reports increasing transmission across temperate countries within North America, the United Kingdom, Europe, the Middle East and northern Asia. Influenza A(H3N2) and B strains are predominating in North America, whereas higher rates of influenza A(H1N1) 2009 infections are being reported across the United Kingdom. The large majority of viruses that have been characterised to date have been antigenically similar to those contained in the current trivalent influenza vaccine.</p>	<p>Travellers are advised to avoid close contact with people suffering from acute respiratory infections and, where possible, crowded enclosed spaces. Frequent hand-washing, especially after direct contact with ill persons or their environment may reduce the risk of infection. Ill persons are encouraged to practice cough etiquette (maintain distance, cover coughs and sneezes with disposable tissues or clothing, wash hands). There are currently limited stocks of influenza vaccine in South Africa; however, if travellers are visiting affected countries for an extended period, they may opt to obtain the current trivalent vaccine upon arrival. They should, however, take note that a period of up to 14 days post-vaccination is required to infer immunity, during which time the person may be infected.</p>

1. Prevention of food and waterborne diseases: drink water that is bottled or bring it to a rolling boil for 1 min. Bottled carbonated water is safer than uncarbonated water. Avoid ice and food products (e.g. ice cream) that are potentially made with contaminated water. Eat foods that have been thoroughly cooked and that are hot and steaming. Avoid raw vegetables and fruits that cannot be peeled. Peel the fruit and vegetables yourself after washing your hands with soap. Do not eat the peelings. Avoid foods and beverages from street vendors.

References: ProMED-Mail (www.promedmail.org), World Health Organization (www.who.int), Centers for Disease Control and Prevention (www.cdc.gov), Europe Media Monitor (<http://medusa.jrc.it/medisys/helsinkiedition/en/home.html>); last accessed 2011/01/17

Source: Outbreak Response and Travel Health Units, NICD

This communiqué is published by the National Institute for Communicable Diseases (NICD), a division of the National Health Laboratory Service (NHLS), on a monthly basis for the purpose of providing up-to-date information on communicable diseases in South Africa. Much of the information is therefore preliminary and should not be cited or utilised for publication. Questions and comments may be addressed to: The Outbreak Response Unit: outbreak@nicd.ac.za; Private Bag X4, Sandringham, 2131, South Africa

