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CONTENTS

1 ZOONOTIC AND VECTOR-BORNE DISEASES

a Crimean-Congo haemorrhagic fever in the Western and Northern Cape provinces

Two cases of Crimean-Congo haemorrhagic fever (CCHF) were confirmed in the first week of January 2017. The first case, a 53-year-old farmer from Mamre, Western Cape Province, became ill on 22 December 2016 with abrupt onset of fever, headache, back pain and gingival bleeding. He was referred to the secondary level referral hospital in Cape Town with a differential diagnosis of severe pancreatitis or thrombotic thrombocytopenic purpura. With progressive gastrointestinal bleeding and ecchymoses, he was transferred to the tertiary referral hospital with supposed severe intra-abdominal sepsis and DIC. He entered the convalescent phase on day 9, and 5 days later, following a review of negative laboratory results, the diagnosis of CCHF was considered and subsequently confirmed by the NICD; CCHF IgG IFA positive (titre of 1000), CCHF IgM IFA positive (titre of 100), CCHF PCR was weakly positive at a cycle threshold of 38. In retrospect, he remembered a small red tick firmly embedded in his leg three days prior to symptom onset. The patient grazes his goats in the communal lands where cattle owned by different farmers are herded and roam amongst his animals. Over 200 HCW and family contacts were monitored for symptoms up to 14 days post-exposure, but no secondary transmission occurred.

The second case involved a 58-year-old male sheep farmer from Van Wyksvlei, a small town near Carnarvon, Northern Cape Province. The patient developed malaise, headache, myalgia and epigastric pain early January 2017. He was treated with doxycycline by his general practitioner but when his clinical condition failed to improve, he was admitted to hospital in Kimberley. Findings included severe thrombocytopenia (platelets=5 x 10^9/L) with bleeding and petechial rash, and significantly raised liver transaminases (ALT=589 IU/L and AST=2616 IU/L). The patient died on 8 January 2017 following a gastrointestinal bleed. The diagnosis was confirmed by CCHF RT PCR and no anti-CCHF serological responses were detected. Monitoring of 17 contacts continues at the time of this report.

Two additional suspected cases of CCHF underwent testing at CEZD, during late December 2016 and early January 2017, each of whom presented with bleeding and hepatitis. However, a diagnosis of staphylococcal septicaemia and disseminated herpes simplex virus was made respectively, and tests for CCHF virus were negative.

Since 1981 202 cases of CCHF have been confirmed in South Africa. Cases are mostly reported from the semi-arid Northern Cape and Free State provinces, although cases have been reported from all nine provinces of South Africa. More than two-thirds of cases diagnosed in South Africa report a definitive tick exposure history. The virus may also be transmitted through contact with infected animal blood or tissues – various livestock and wildlife species may be infected with the virus although they do not develop disease. The virus is transmissable from person to person through contact with virus-containing bodily fluids such as blood and saliva; however strict infection prevention and control procedures can prevent transmission.

For more information on CCHF in South Africa visit www.nicd.ac.za

Source: Centre for Emerging and Zoonotic Diseases, NICD-NHLS; (januszp@nicd.ac.za); Groote Schuur Hospital Infectious Diseases

b Human rabies cases in South Africa, January-December 2016

During 2016 only two cases of human rabies were laboratory-confirmed in South Africa. These cases were reported from KwaZulu-Natal and Free State provinces respectively. This is the lowest annual incidence in South Africa in thirty years. On average 5 - 30 cases of human rabies have been laboratory -confirmed per annum in the country since the 1980s. Possible explanations for this year's low number of cases include: 1) underdiagnosis and missed cases; 2) improved clinical management of animal bites with appropriate provision of rabies post-exposure prophylaxis; and 3) improved control of canine rabies. While each factor may contribute to the low number of cases over the past year, canine rabies is unfortunately still endemic, and particularly prevalent in KwaZulu-Natal, Mpumalanga, Limpopo provinces and in the eastern parts of Free State Province.

Therefore, the risk of human rabies is still present and appropriate animal bite wound management and post-exposure prophylaxis should be adminis-

tered when required. This entails flushing of the wound with soap and water for 10 minutes, cleaning with 70% alcohol solution, followed by iodine if available. Rabies immunoglobulin should be injected into the wound with the balance given intramuscularly into the deltoid (only with a category three injury when the skin is broken or scratched or when blood is drawn) and vaccination (four doses administered intramuscularly on days 0, 3, 7 and 14) given intramuscularly into the opposite deltoid.

As human rabies is not treatable, the most important public health intervention to control and ultimately prevent human rabies is vaccination of dogs and cats against rabies (as required by law). Other animals, such as cattle and horses may be vaccinated if necessary.

On 5 December 2016, a family on holiday bought a puppy at the side of the road in the Eastern Cape Province and took it home to KwaZulu-Natal. The puppy fell ill on 23 December 2016 and bit all five family members and licked the face of an unknown two-year-old child while on the beach. The puppy was taken to a private veterinarian who euthanized and tested it for rabies. On 26 December 2016, the diagnosis of rabies was confirmed. The family was administered prophylaxis (PEP) with rabies immunoglobulin and vaccine after the diagnosis was confirmed. Efforts to identify the child who was licked at the beach have been unsuccessful.

Interesting requests for advice regarding rabies post-exposure prophylaxis have been made to the NICD hotline:

- In two separate incidents, children were bitten by vervet monkeys. In both instances, rabies PEP is not indicated. Rabies has not been confirmed in vervet monkeys in South Africa to date and the behaviour of the animals during these incidents is considered normal.
- A holidaymaker was scratched by a hen in the Western Cape Province. Rabies PEP is not indicated following avian exposures as birds are not infected with nor do they transmit rabies virus.
- A person was bitten by a seal. While rabies virus is theoretically transmissible by all mammals, seals have not been known to transmit rabies.

For more information on rabies post-exposure prophylaxis, visit the NICD website (www.nicd.ac.za). Health care workers may contact the NICD hotline on 082 883 9920 when seeking advice on the management of rabies post-exposure prophylaxis in their patients.

Source: Centre for Emerging and Zoonotic Diseases, NICD-NHLS; (januszp@nicd.ac.za)

c Zika virus infection reported from Angola

On 21 November 2016, France notified the WHO of a confirmed case of imported Zika virus disease originating in Angola. The patient, a 41-year-old male who had received yellow fever vaccination, had spent a month in Angola, in Luanda and Benguela districts and returned to France on 5 September. Symptoms of headache, rash, arthralgia and myalgia began on 14 September. PCR tests for Zika virus (ZIKV), dengue, West Nile, Rift valley and chikungunya viruses were negative, but serology demonstrated IgM antibodies and seroconversion with detectable IgG antibodies after 14 days. A confirmatory plaque-reduction neutralisation assay was positive with a titre of 1:320. In addition, French authorities have conducted entomological investigations and failed to find ZIKV vectors (*Aedes* spp) in the city where the patient lives.

In a second incident, a 14-year-old Angolan child who had received yellow fever vaccine in April 2016, and who resided in Luanda-Viana district in Angola, and who had no travel history within the preceding three weeks, presented with fever, headache, muscle pain, vomiting and jaundice. PCR for ZIKV was positive on 26 December 2016 and on 2 January 2017. Specimens have been sent to a reference laboratory for confirmation and sequencing.

The WHO has recommended that Angola determine if ZIKV is circulating in Luanda and Benguela and suggested the following actions:

- To test samples of urine and serum from persons residing in the region for the past four months.
- To conduct an entomological assessment of mosquito vectors in the area including mosquito species identification, mosquito population density assessments, and to test mosquitoes for ZIKV using RT-PCR.

Source: Centre for Emerging and Zoonotic Diseases, NICD-NHLS; (januszp@nicd.ac.za); WHO South Africa Office; Division of Public Health Surveillance and Response, NICD-NHLS

d Dengue infection in returned travellers

Dengue is not endemic in South Africa. However, dengue is occasionally diagnosed amongst travellers returning from dengue endemic regions such as South-East Asia, the Western Pacific, the Americas (Central and the northern parts of South America), Central, West and East Africa and the Eastern Mediterranean. In December 2016, acute dengue infection was confirmed in two travellers returning to South Africa from Singapore and Thailand.

The first case was in a 42-year-old man, who was admitted to a hospital in Gauteng Province. He became ill after travelling to Singapore in mid-December 2016. He presented with a skin rash and influenza-like illness. Malaria infection was unlikely as Singapore is malaria free—however it was excluded on smear microscopy. RT-PCR for Zika virus was negative. Serology (IgM) and RT-PCR for dengue were both positive and the virus was successfully isolated from the patient's serum by tissue culture, confirming an acute dengue infection.

The second case was a 20-year-old female from KwaZulu-Natal Province who returned from Thailand on 22 December 2016 after a 10-day visit. She presented with fever, weakness, headache and vomiting. Malaria smear microscopy was negative. Blood taken on the day of presentation to hospital (22 December 2016) tested positive by RT-PCR for dengue virus and the virus was successfully isolated from the patient's serum by tissue culture, confirming an acute dengue infection.

The typical clinical presentation of uncomplicated dengue includes fever, severe headache, pain behind the eyes, muscle and joint pains, nausea, vomiting, swollen glands and a maculopapular rash. The differential diagnosis includes malaria, hepatitis A, typhoid, invasive bacterial diarrhoea. When a rash is present, the differential includes dengue, Zika, chikungunya or rickettsial infections. RT-PCR is usually positive for dengue virus 1 to 2 days following infection and up to 9 days after disease onset. Antibodies to the dengue virus may be detected by day 3 – 7 after symptom onset. Convalescent sera will demonstrate seroconversion. For further information see the NICD website, www.nicd.ac.za

Source: Centre for Emerging and Zoonotic Diseases, NICD-NHLS; (januszp@nicd.ac.za); Division of Public Health Surveillance and Response, NICD-NHLS.

e Antibiotic prophylaxis after an alligator bite in KwaZulu-Natal Province

A volunteer doing vocational work experience at an crocodile farm in KwaZulu-Natal Province sustained a bite from an alligator on the wrist whilst feeding the animals (Figure 1). Reptilian bites require careful management as the oral flora of reptiles is diverse and that of their prey and wound infections are frequent. In addition, fractures may become complicated by osteomyelitis due to organisms causing wound infections. The following bacteria have been implicated in wound infections following reptilian bites:

- Enterobacteriacae including *Serratia, Citrobacter, Proteus, Salmonella* spp and *Pantoea agglomerans*
- Non-fermenting Gram-negative bacilli including *Burkholderia pseudomallei, Pseudomonas aeruginosa*
- Fermenting, Gram-negative, oxidase-positive bacilli including *Vibrio vulnificus*, and *Aeromonas spp*
- Anaerobes including *Bacteroides* and *Clostridium* spp.
- Normal flora of human skin including *Staphylococcus* and *Streptococcal species.*

Antibiotic therapy with a third-generation cephalosporin with antipseudomonal activity, doxycycline and metronidazole was advised. The clinician was also advised not to suture the wound. The patient has made an uneventful recovery

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

Figure 1. Puncture wounds on the left wrist of a volunteer by an alligator, shown on day 3 following the incident.

e Acute febrile illness with rash amongst Johannesburg residents

A mild acute febrile illness with rash has been reported amongst Johannesburg residents. The rash is characteristically macular with punctate, almost vesicular lesions (Figure 2). The distribution is predominantly on the limbs, hand and feet including soles and palms, and on the trunk. Some patients report intra-oral lesions. Patients have reported mild-to-moderate myalgia, fever, headache and joint pains. No cough, coryza or conjunctivitis have been reported. Laboratory investigations are underway. The differential diagnosis includes arboviruses (sindbis, West Nile virus) or enteroviruses including Coxsackie virus. Tick bite fever may also be considered, especially if an eschar with lymphadenopathy is noted. Please contact outbreak@nicd.ac.za if you are aware of cases with similar symptoms.

Source: Centre for Emerging Zoonotic Diseases, NICD-NHLS; Division of Public Health Surveillance and Response, NICD-NHLS; outbreak@nicd.ac.za

Figure 2. A planter rash from a Johannesburg resident with an acute febrile illness

2 SEASONAL DISEASES

a Global influenza update—the northern hemisphere influenza season

Influenza activity in Europe started in November, and peaked early in the week starting 19 December 2016. In comparison the previous season started in the week commencing 8 February 2016. In North America the season also started in November 2016 with influenza activity still increasing. Influenza A (H3N2) is presently dominant in both Europe and North America, as well as in northern Africa, east, south-east, and south Asia, with 98.7% of influenza A isolates subtyped as A(H3N2) by national influenza laboratories from 74 countries. Travellers to the northern hemisphere should receive the influenza vaccine. This season, the 2016 southern hemisphere influenza formulation is identical to the 2016/7 northern hemisphere vaccine, therefore South African travellers to the northern hemisphere may use locally-acquired vaccine prior to travel.

Source: Centre for Respiratory Diseases and Meningitis, NICD-NHLS; (cherylc@nicd.ac.za)

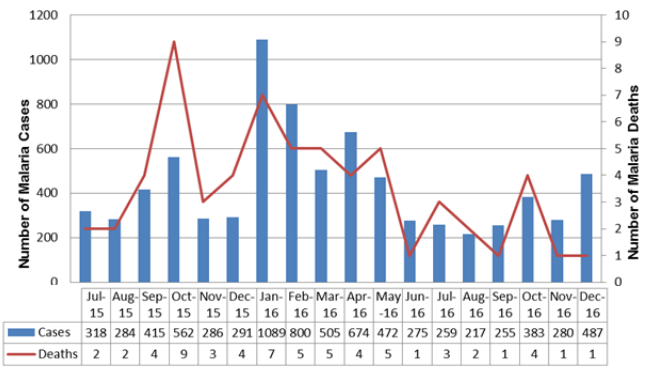
b Seasonal malaria update, December 2016

Malaria Control Programme data indicate an expected increase in notified cases in December 2016 (Figure 3). Malaria in South Africa is highly seasonal and with late rainfall, and warm summer temperatures, the increase is to be expected at this time of year. Fortunately, the malaria fatality rate has remained comparatively low over the past seven months. The majority of cases in the malaria-endemic provinces (Mpumalanga, KwaZulu-Natal and Limpopo) are locally acquired.

Malaria incidence in South Africa is likely to increase further during the coming months owing to increased summer rainfall and high numbers of travellers returning from endemic regions.

Source: Centre for Opportunistic, Tropical and Hospital Infections, NICD-NHLS; (johnf@nicd.ac.za); Malaria Directorate, National Department of Health

Figure 3. Malaria cases and deaths, all provinces, South Africa, July 2015-December 2016



	Jul-15	Aug-15	Sep-15	Oct-15	Nov-15	Dec-15	Jan-16	Feb-16	Mar-16	Apr-16	May-16	Jun-16	Jul-16	Aug-16	Sep-16	Oct-16	Nov-16	Dec-16
Cases	318	284	415	562	286	291	1089	800	505	674	472	275	259	217	255	383	280	487
Deaths	2	2	4	9	3	4	7	5	5	4	5	1	3	2	1	4	1	1

3 ENTERIC DISEASES

a Typhoid fever in South Africa, 2015-2016

South Africa has a low endemicity for typhoid fever, with an estimated annual incidence rate of 0.1 cases per 100,000 general population. Localised clusters of cases occur in vulnerable populations, such as those living in informal settlements or in crowded conditions. Currently, typhoid fever cases are primarily notified through a laboratory-based notification system to the national reference laboratory, the Centre for Enteric Diseases (CED), NICD. Confirmation of *Salmonella enterica* serotype Typhi (*Salmonella* Typhi) and *Salmonella* Paratyphi sourced from clinical laboratories in South Africa, is performed by the CED, followed by further phenotypic and genotypic characterization of the isolates.

In 2016, 125 cases of *Salmonella* Typhi were reported from multiple provinces in South Africa (Figure 4). Of the 125 cases, 113 viable isolates were received by the CED and confirmed as *Salmonella* Typhi. Antimicrobial susceptibility data suggest that resistance to ciprofloxacin and azithromycin is emerging. In 2016, 12% of isolates were resistant to ciprofloxacin and 0.9% to azithromycin. Molecular subtyping using PFGE analysis is routinely performed on all *Salmonella* Typhi; a database of diverse PFGE patterns has been established, which has proved invaluable in relating isolates and monitoring for emergence of new strains and clusters. PFGE analysis has assisted to show importation of typhoid cases from neighbouring countries and overseas countries, and also to demonstrate person-to-person transmission in localised clusters, and help in local outbreak investigations. Going forward, PFGE analysis will be augmented by whole-genome sequencing analysis of selected isolates, as required for investigation of clusters and outbreaks.

As there have been reports of typhoid fever outbreaks in neighbouring countries, all provinces in South Africa are on high alert for identification, notification and reporting of cases of typhoid fever.

Source: Centre for Enteric Diseases, NICD-NHLS; Division of Public Health Surveillance and Response, NICD-NHLS; outbreak@nicd.ac.za

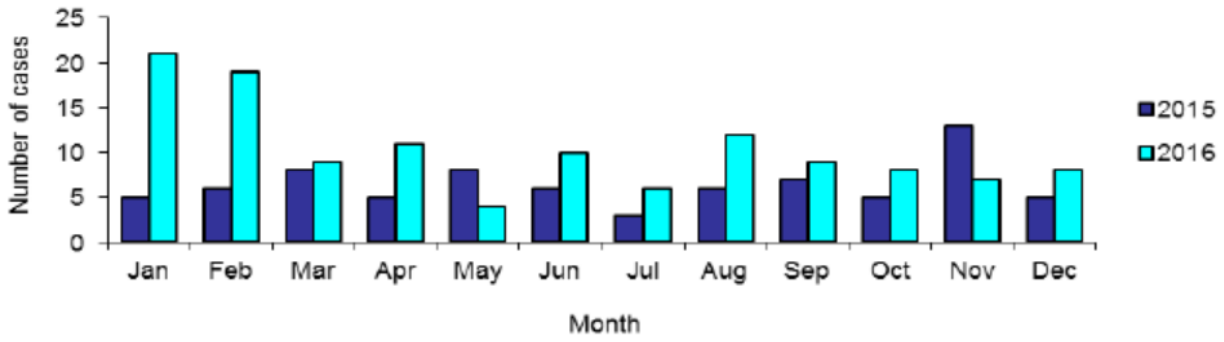


Figure 4. Number of *Salmonella* Typhi cases by month in South Africa, January to December 2015 & 2016

4 SURVEILLANCE FOR ANTIMICROBIAL RESISTANCE

a Update on carbapenemase-producing Enterobacteriaceae

The Antimicrobial Resistance Laboratory and Culture Collection (AMRL-CC) of the Centre for Opportunistic, Tropical and Hospital Infections (COTHI) at the NICD has been testing referred isolates of suspected carbapenemase-producing Enterobacteriaceae (CPE) for the presence of selected carbapenemases. CPE have become a threat to healthcare and patient safety worldwide by compromising empiric antibiotic therapeutic choices and increasing morbidity, hospital costs and the risk of death. We are receiving clinically significant isolates from all specimen types, based on antimicrobial susceptibility testing criteria, for molecular confirmation. For December 2016, a total of 124 Enterobacteriaceae isolates was received. One hundred and one isolates were screened, 90 of which expressed the carbapenemases that were screened for. Five isolate expressed two carbapenemases (NDM and OXA-48 & variants, n=3 and NDM and GES, n=2) (Table 1). The majority of the screened isolates were *Klebsiella pneumoniae* (70) followed by *Enterobacter cloacae* (16).

It is important to note that these figures do not represent the current burden of CPEs in South Africa. However our data reveal the presence of carbapenemases in Enterobacteriaceae isolates from all specimen types, nationally. As a first step CPE surveillance is required to determine the extent of the problem in order to restrain the emergence and spread of resistance. The AMRL-CC is currently running a surveillance programme at national sentinel sites for CPE infections in patients with bacteraemia which provides representative data. This significant data will inform public health policy and highlight priorities for action. Controlling the spread and limiting the impact of CPEs in South Africa requires intensive efforts in both the public and private healthcare sectors going forward. NHLS and private laboratories are encouraged to submit suspected CPE isolates based on antimicrobial susceptibility testing (AST) criteria to AMRL-CC, NICD/NHLS. Please telephone (011) 555 0342/44 or email: olgap@nicd.ac.za; for queries or further information.

Source: Centre for Opportunistic, Tropical and Hospital Infections, NICD-NHLS; olgap@nicd.ac.za

Table 1. Enterobacteriaceae by CPE enzyme type for December 2016 and January-November 2016 at AMRL-CC, COTHI, NICD.

Organism	NDM		OXA-48 & Variants		GES	
	Jan-Nov 2016	Dec 2016	Jan-Nov 2016	Dec 2016	Jan-Nov 2016	Dec 2016
Citrobacter freundii	9	-	7	1	-	-
Citrobacter koseri	-	-	-	1	-	-
Enterobacter aerogenes	1	-	7	1	-	-
Enterobacter cloacae	29	3	45	11	-	1
Escherichia coli	11	-	84	5	-	-
Klebsiella oxytoca	2	1	5	1	1	-
Klebsiella pneumoniae	267	15	480	49	10	2
Providencia rettgeri	16	1	1	-	-	-
Salmonella spp.	-	1	-	-	-	-
Serratia marcescens	29	1	24	1	3	-
Total	**364**	**23**	**653**	**70**	**14**	**3**

NDM: New Delhi metallo-beta-lactamase; **OXA**: oxacillinase; **GES**: *Guiana* extended spectrum *beta lactamase*.

5 BEYOND OUR BORDERS

The 'Beyond our Borders' column focuses on selected and current international diseases that may affect South Africans travelling abroad. Numbers correspond to Figure 5 on page 9.

1. Anthrax: Zambia
Cases of animal and human anthrax have been reported in five districts in the Western Province. At least 40 animal deaths and 17 hospitalisations of persons who ate meat from affected cattle were reported in from Kalabo district in Western Province. Health authorities have intervened with massive animal vaccination campaigns, and quarantining of cattle in affected areas.

2. Plague: Madagascar
On 6 December 2016, the Ministry of Health in Madagascar alerted WHO of a suspected plague outbreak in Befotaka district, Atsimo Atsinanana region in the southeastern part of the country. The district is outside the area previously affected by plague, the Lakora district in Ihorombe Region. As of 27 December 2016, 62 cases (6 confirmed, 5 probable, 51 suspected) including 26 deaths have been reported.

3. Ebola: West Africa
No new cases have been reported from West Africa.

4. Typhoid: Zimbabwe
Since late October 2016, there has been an increase in cases of typhoid fever centred in Harare but apparently in many towns across Zimbabwe. Exact numbers of cases are unknown. MSF has set up a treatment centre in Harare, where at least 126 cases of typhoid have been confirmed since the start of the rainy season about 2 months ago.

5. H7N9: China
More than 125 cases (including 29 deaths) of human infection with avian influenza A (H7N9) have been reported primarily in Guangdong, Anhui, and Jiangsu provinces since November 2016 with sporadic cases in five other provinces. H7N9 is reported exclusively in the winter months and the November onset and unprecedented number of early season cases may herald an especially large outbreak.

6. Lassa Fever: Nigeria
On Friday, 23 December 2016, the Nigerian Centre for Disease Control stated that they had recorded the largest outbreaks of Lassa fever in its history between 2015 and 2016, with 273 reported cases resulting in 149 deaths. Cases have been recorded in 23 of the 36 states. As of 19 January, 4 deaths and 16 suspected cases have been reported from Nasarawa state, and 36 persons who had contact with cases are undergoing follow-up.

7. Yellow Fever: Angola and Democratic Republic of Congo (DRC)
Angola declared the end of the yellow fever epidemic affecting the country on Friday, 23 December 2016, after a vaccination campaign reaching 25 million people.

8. Zika virus disease: Angola
See article on p3

9. Cholera: Tanzania
The Karema Division, located on the eastern shores of Lake Tanganyika has recorded 91 cases of cholera with three fatalities since the beginning of December. Adjacent Kenya has also issued a cholera health alert due to the porous borders between the two countries.

10. Legionellosis: United Arab Emirates:
More than 30 confirmed cases of legionellosis in returning travelers have been identified and reported from the European Centre for Disease Prevention and Control. No common source has been identified as affected travelers have stayed in at least 25 different locations in Deira, Bur Dubai, Downtown, Meydan, and Marina Emirates living districts. Legionellosis should be considered in returning travelers from UAE who presenting with fever and pneumonia within 2 weeks of travel.

11. Yellow fever: Brazil
An outbreak of yellow fever is under investigation in the east-central state of Minas Gerais where 47 cases have been confirmed with 25 deaths. Over 160 suspected cases are known to authorities. In 2016, Brazil reported only 7 cases of yellow fever. Vaccination campaigns are underway. It is presently unclear if these cases represent sylvatic or urban cycle disease.

Source: Division of Public Health Surveillance and Response, NICD-NHLS, from Promed (www.promed.org)

Figure 5. Current outbreaks that may have implications for travellers. Number correspond to text on the previous page. The red dot (solid=cases; open=zero report/no cases) is the approximate location of the outbreak or event

6 PHOTOQUIZ

January photoquiz (above, right): A 53-year-old man who had returned from holiday in Mozambique on 22 December presented with fever, body pains, sparse punctate lesions on the trunk and serpiginous ulcers in the mouth, mainly on the tongue. His family reported that the patient had sustained an insect bite while on holiday in Mozambique due to a mosquito or tick (it was uncertain) that formed a large pustule and resolved spontaneously. The patient was prescribed doxycycline and levofloxacin but his clinical condition deteriorated. His liver enzymes were grossly elevated (ALT 1889 IU/L, AST 4423 IU/L). His full blood count revealed a white cell count of 1.89 x $10^{9/l}$, haemoglobin of 12.3 g/dl and platelet count of 83 x 10^9 /l. On examination, there was no eschar, no lymph nodes, no organomegaly, nor jaundice.

What is your differential diagnosis and what investigations would you request? Please send an email to kerriganm@nicd.ac.za with the words 'January Photoquiz' in the subject line.

December photoquiz (below left). A 32-year-old sheep farmer in Northern Cape Province presented with fever, lower back pain, epistaxis and bruising. His white cell count was 2 x 10^3/µl and platelets were 15 x 10^9/l. This patient was diagnosed with Crimean-Congo haemorrhagic fever by RT-PCR. CCHF is transmitted by the *Hyalomma rupfes* tick, also known as the 'bontpoot' tick (right). Photographs courtesy Professor Lucille Blumberg.