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Arenavirus outbreak, South Africa

This updates all previous reports and includes available data as of 24 October 2008.

An outbreak of infection due to an arenavirus was identified in South Africa in early October 2008. A total of 5 cases has been reported for the period 12 September to 24 October 2008.

The primary case (case 1) had onset of illness on 2 September 2008 (Figure 1). An additional 3 secondary cases (case 2, 3 and 4) and 1 tertiary case (case 5) have been confirmed to have an arenavirus infection by laboratory testing. The primary case and 3 secondary cases have died. The tertiary case is currently hospitalized. Ages of cases ranged from 33 to 47 years. Four cases were female and 1 male. The source of infection is, as yet, unknown for the primary case. The other 4 cases all had potential exposure to blood and/or body fluids of a primary or secondary case in the health-care setting.

The primary case was a safari booking agent resident in Zambia. The patient was flown to South Africa for medical care in a critically ill condition on 12 September, and died on 14 September. Case 2 was a paramedic who cared for case 1 during the transfer from Zambia on 12 September and case 3 was a nurse who cared for case 1 in the intensive-care unit from 12-14 September. Case 2 was admitted on 27 September and died on 2 October and case 3 was admitted on 30 September and died on 5 October. On 14 September, case 4 performed terminal cleaning of the room in which case 1 was hospitalized. The fifth patient is a nurse who cared for case 2 from 27 September to 2 October. She became ill on 9 October and is currently critical but stable. Ribavirin has been used for treatment in this case based on good evidence of efficacy in patients with Lassa fever (an arenavirus infection).

The estimated incubation period (interval from exposure to symptom onset) in secondary and tertiary cases ranges from 7 to 13 days. In 4 patients who died, the interval from onset of illness to death ranged from 9 to 12 days (Figure 1).

Only limited clinical data are currently available for case 4, who presented late in the course of illness with bleeding and confusion and died soon thereafter. Clinical features of the remaining 4 cases, for which more clinical data were available, are presented. All patients presented initially with a non-specific flu-like illness with symptoms of fever, headache and myalgia. The illness increased in severity over 7 days with all four patients developing diarrhoea and pharyngitis during the course of illness. A morbiliform rash on the face and trunk was reported in 4 cases on day 6 - 8 of illness. Facial swelling occurred in 3 patients. There appeared to be an initial clinical improvement after hospital admission in 3 patients, followed by clinical deterioration. Sudden and rapid deterioration with respiratory distress, neurological signs and circulatory collapse were terminal features in all patients who died. Bleeding was not a prominent feature. However, one patient had a petechial rash and another had oozing of blood from venepuncture sites. Chest pain was reported in case 1.

At the time of admission all patients had thrombocytopenia (range: 42-104 $X10^9$/L). Liver transaminases (AST and ALT) were available for 4 of 5 cases and were variable at the time of admission, however all four patients had raised AST and ALT during the course of their illness. Leucopenia was present on admission in 2 patients and 3 patients had a normal white blood cell count on admission. Four patients subsequently developed leucocytosis during the course of hospitalisation.

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All contacts (family members, friends and healthcare staff) are being monitored with twice daily temperature measurements for a period of 21 days after the last exposure to a known case. In addition, safe burial of the deceased has been supervised by environmental health officers. Full personal protective equipment (PPE) and isolation precautions as per VHF protocols have been instituted.

The causative agent in this outbreak was initially identified as an Old World arenavirus by immunohistochemical tests performed at the Infectious Diseases Pathology Branch of the Centers for Disease Control and Prevention in Atlanta, USA, and on autopsy liver and skin samples taken with biopsy needles and skin punches in the Special Pathogens Unit of the National Institute for Communicable Diseases, National Health Laboratory Service, Sandringham (SPU-NICD/ NHLS), South Africa, from cases 2 and 3 on 9 October 2008 under biosafety level 4 laboratory conditions. Subsequently, infection with an Old World arenavirus has been confirmed in all 5 cases by positive PCR results and virus isolation by SPU-NICD/NHLS and CDC. Analysis of sequencing data generated at SPU-NICD/NHLS, Columbia University, New York, and CDC, Atlanta appears to indicate that the current outbreak is caused by a unique Old World arenavirus.

There are currently no additional suspected cases. The outbreak appears to be contained and has been confined to individuals with very close contact in a health-care setting. Monitoring of contacts, active case finding and investigation and management of suspected cases will continue as needed. Further characterization of the causative agent is under way and investigation into the source of infection in the primary case is required. Additional studies to determine whether mild/asymptomatic infection occurred amongst close contacts and other exposed individuals would be essential in better characterizing the extent of this outbreak and clinical spectrum of disease.

Arenaviruses are a family of enveloped negative-sense single-stranded RNA viruses. Members of the family are parasites of rodents, in which they establish chronic renal infection. High titres of virus are present in rodent urine, which can contaminate human food or house dust. Exposed humans may become infected as accidental hosts. The prototype of the family is lymphocytic choriomeningitis (LCM) virus and infection of humans with this virus may present as an influenza-like illness, aseptic meningitis or severe meningo-encephalomyelitis. Arenaviruses which cause a haemorrhagic fever syndrome are well documented in South America (New World arenaviruses, including Junin, Machupo, Sabia and Guanarito viruses). The so-called Old World arenaviruses include LCM which in fact has a worldwide distribution, and Lassa fever virus which affects up to 500 000 people annually in West Africa, specifically in Nigeria, Sierra Leone, Liberia and Guinea, but the virus is suspected to be more widely distributed in that region.

The clinical spectrum of Lassa fever virus infection ranges from inapparent, through mild febrile illness to fulminant haemorrhagic disease, and mortality rates vary from 1-2% among cases in the community at large, through 20% among hospitalized patients, to >40% in nosocomial outbreaks. The multimammate mouse (*Mastomys natalensis*), which is the most important host of Lassa fever virus, has a distribu-tion extending from West Africa across to East Africa and from there southwards to the north-eastern corner of South Africa. Its distribution overlaps with that of other *Mastomys* species, and arenaviruses have been found in southern African rodents in the past, but there has been no previous association of these viruses with human disease despite sustained monitoring. Preliminary testing indicates that the virus associated with the present nosocomial disease outbreak is a distinct new member of the family.

Source: Special Pathogens Unit and Epidemiology Division, NICD; Gauteng Provincinal Outbreak Response Team and partners; SA-FELTP residents; Department of Anatomical Pathology, University of the Witwatersrand and the National Health Laboratory Service

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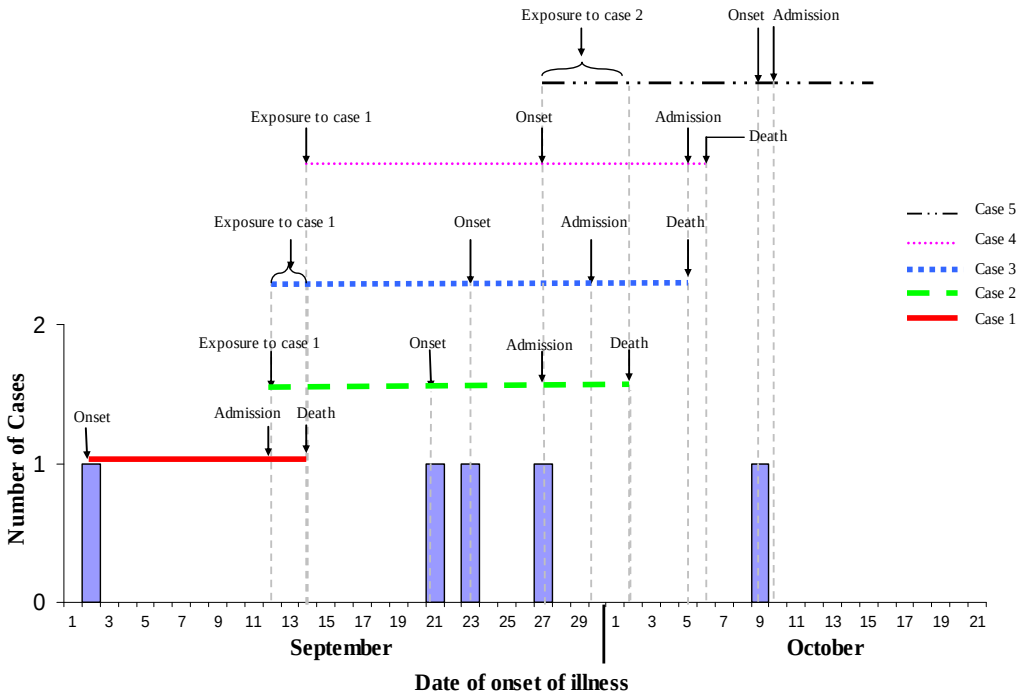

Figure 1: Epidemic curve of cases of infection with an arenavirus, South Africa, September - October 2008

Meningococcal disease

As of 15 October 2008 (including week 41), a total of 346 laboratory-confirmed meningococcal disease cases has been reported to the NICD for 2008, compared to 380 cases reported for the same period in 2007. In 2008, cases have been reported from all 9 provinces, with the majority from Gauteng Province (n=178; compared to 199 cases reported for the same period in 2007).

Of those cases with isolates for serogrouping (n=229), the majority (132/229, 58%) of isolates were serogroup W135, while serogroup B (50/229, 22%) and serogroup C (33/229, 14%) are also being identified. These data represent only those cases reported through an active laboratory-based surveillance system and do not reflect the true burden of meningococcal disease in South Africa.

Although the majority of cases of meningococcal disease occur during the winter season, sporadic cases continue to occur throughout the year. Symptoms and signs may be non-specific initially with rapid progression. Healthcare workers should maintain a high index of suspicion for meningococcal disease (both meningitis and/or septicaemia) as early, appropriate treatment can be life-saving.

Source: Respiratory and Meningeal Pathogens Reference Unit and Epidemiology Division, NICD

Rubella

The number of specimens submitted for case-based measles surveillance started to increase from the last week of July as did the number of positive rubella IgM results (Table 1). This year to date, rubella IgM antibodies have been detected in the blood specimens of 1239 patients. Age and sex was known for 1149 of these patients. Ages ranged from 3 months to 64 years with a median of 7 years. Amongst these patients were 55 (4.8%) females of child-bearing age (12-49 years).

Table 1. Positive rubella IgM results per province by date specimen collected, January to October 2008*

	ECP	FSP	GAP	KZP	LPP	MPP	NCP	NWP	WCP	Total
Jan-Jun	63	1	48	33	13	22	4	17	18	219
May	9	0	9	24	19	8	0	5	3	77
Jun	26	0	18	22	3	3	0	1	4	77
Jul	34	0	9	22	15	10	1	1	0	92
Aug	63	0	26	69	15	30	4	15	1	223
Sep	89	0	59	96	48	59	3	28	9	391
Oct*	56	0	43	92	25	27	7	30	4	284

*Up to week beginning 13 October

Source: Epidemiology Division and Viral Diagnostics Unit, NICD

Diarrhoeal disease outbreak—school trip

During August 2008, an outbreak of diarrhoeal disease occurred amongst participants in a river rafting school trip. A total of 99 people (students = 85, staff = 7 and parents = 7) participated in the 7 day excursion, 4 days of which consisted of white river rafting on the Zambezi River starting on day 2. Potable water was provided in bottles and boiled river water was also used. All participants were male. The age range was 16 to 44, with a median age of 17 years.

In order to investigate the outbreak, initial interviews were conducted on a limited number of cases, followed by a cohort study to determine possible risk factors for illness amongst exposed participants. A self-administered questionnaire was distributed to all the trip participants (n=99) and completed under supervision where possible. Of those who responded (79/99, 80%), 75 reported diarrhoeal illness in relation to the trip (estimated attack amongst respondents=95%, 75/79). The first cases of diarrhoea started on day 3 of the trip and the number affected increased over the following 2 days (Figure 1). The most common symptoms reported were watery diarrhoea (n=75/75, 100%), fatigue (n=60/75, 80%), nausea (n=51/75,68%) and abdominal pains (n=48/75, 64%). Although mostly self-limiting, the duration of illness exceeded 7 days in 29% of the cases (22/75). A total of 55 cases (73%) visited a doctor upon return and 14 of these had various specimens taken (8 blood tests for pathogens such as malaria or TMX serology, 1 blood culture and 7 stool cultures). Four students

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were hospitalized. *Salmonella* Typhi infection was confirmed in 2 of these (one from blood culture and one from stool). They received treatment with fluoroquinolones and have recovered. A household contact of one the cases, developed similar symptoms and was treated empirically with a fluororquinolone prior to specimen collection. A causative agent could not be confirmed and the contact has since recovered. *Salmonella enterica serovar* Enteritidis was cultured in a further 4 students (all from stool), one of whom had a mixed infection with *Campylobacter* species. All 75 affected participants have recovered.

Contact tracing was performed but no further cases were reported. To date, preliminary analysis of available data has not identified specific risk factors for illness amongst participants.

When travelling, access to safe food and water is essential in preventing transmission of enteric pathogens. If self-catering, proper refrigeration of foods and adequate cooking temperatures must be achieved. Boiling of untreated water for at least 3 minutes is required to render it safe for drinking. Exposure to potentially contaminated recreational water also poses a risk for transmission of infection in such travellers.

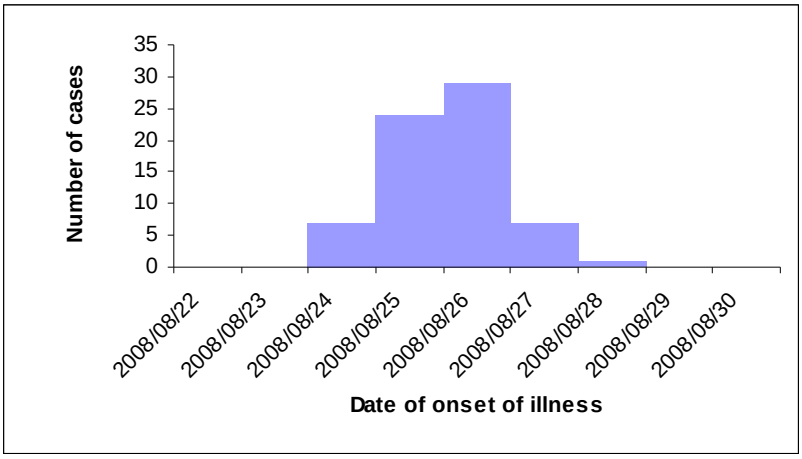

Figure 1: Epidemic Curve of reported cases of diarrhoea amongst participants in school trip, Zambezi River, August 2008

Source: SA-FELTP residents; Epidemiology Division and Enteric Disease Reference Unit, NICD

Rabies update

Rabies was confirmed by PCR on ante-mortem saliva specimens in an 8-year-old boy from Kabokweni, Mpumalanga Province in early October 2008. The patient presented with a clinical illness compatible with rabies approximately three weeks after being scratched by a dog. Although he presented to a healthcare facility at the time of the incident, post-exposure prophylaxis (PEP) was not administered. The scratch apparently did draw blood and therefore would be classified as a category 3 exposure. Since about April 2008, there has been a major increase in rabies in dogs in Mpumalanga, particularly in the White River area. An intensive dog vaccination programme is in operation.

Scratches from infected animals pose a rabies risk as animals typically lick their paws and saliva con-

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tains virus. A scratch without bleeding would constitute a category 2 exposure and would require cleaning of the skin and a course of rabies vaccine. A scratch that draws blood constitutes a category 3 exposure and therefore skin cleaning, a course of rabies vaccines and rabies immunoglobulin is mandatory.

A total of 15 human rabies cases have been confirmed during 2008. These include cases from Limpopo (n=3); KwaZulu Natal (n=5), Eastern Cape (n=6) and Mpumalanga (n=1) provinces.

Source: Special Pathogens Unit and Epidemiology Division, NICD

Gnathostomiasis

A married couple, resident in Maun, Botswana, presented with recurrent episodes of painful migratory skin nodules and transient urticaria since 2007. One of them also complained of malaise and a general feeling of being unwell. The most recent episode began a few weeks after a visit to the Okavango Delta, where as usual they ate raw bream marinated in lemon juice. Some of the migratory swellings localised to form superficial skin lesions from which they extracted several small worms that were referred to the NICD for identification.

Microscopic examination showed third stage larvae of a *Gnathostoma* species. These nematode parasites have a complicated life cycle involving carnivorous mammals as definitive hosts, and a variety of intermediate and paratenic hosts, including snakes, birds, frogs, eels, crustaceans and freshwater fish. Humans become infected when they eat raw or undercooked fish, crabs, or crayfish. The larvae migrate through skin and subcutaneous tissues (the most common presentation), but also sometimes the internal organs, including the central nervous system in the most serious form of the disease.

Gnathostomiasis is well known in Southeast Asia, and Central and South America, and is regarded as an emerging imported disease resulting from increasing international travel and adventurous eating.[1] This is only the 3rd cluster of cases described in Africa; previous cases seen locally acquired the infection via raw bream from the Zambezi River in western Zambia.[2] We recommend that freshwater fish caught in southern Africa should not be eaten raw.

References:

1. Moore DAJ, McCroddan J, Dekumyoy P, Chiodini PL. Gnathostomiasis: an emerging imported disease. Emerg Infect Dis 2003; 9: 647-650.
2. Hale DC, Blumberg L, Frean J. Case report: gnathostomiasis in two travelers to Zambia. Am J Trop Med Hyg 2003; 68: 707-709.

Source: Parasitology Reference Unit, NICD

Crimean-Congo haemorrhagic fever

Crimean-Congo haemorrhagic fever (CCHF) was confirmed in two new patients in October 2008. The first patient was a 44-year-old man from the Northern Cape Province in whom CCHF was confirmed by RT-PCR and the demonstration of IgM and IgG antibodies on 6 October 2008. He is employed at an abattoir in Calvinia and developed a febrile illness with myalgia and headache, followed by bleeding. The occupational exposure, clinical presentation and presence of a leucopenia (WCC 2.15×10^9/L), thrombocytopenia (platelets 7×10^9/L) and raised transaminases (AST 603 IU/L and ALT 206 IU/L) was highly suggestive of CCHF. He was isolated, oral ribavirin was administered, and contacts were monitored for 14 days post-exposure.

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The patient made an uneventful recovery and no secondary cases have been reported to date.

The second patient is a 53-year-old man who had worked on farms in Calvinia, Northern Cape Province and in Aberdeen in the Eastern Cape Province. He presented with fever (40°C) and a lower back pain, followed by haematemesis and haematuria 5 days later. Although no specific tick exposure was noted, *Hyalommas* are common in these areas. Possible exposures related to his occupation and residence as well as the clinical history and laboratory findings of a profound thrombocytopenia (platelets $7x10^9$/L), leucopenia (WCC $2.3x10^9$/) and raised transaminases (AST 230 IU/L and ALT 150 IU/L) were highly suggestive of CCHF. He was isolated immediately, and ribavirin was started. CCHF was confirmed by RT-PCR and the presence of IgM and IgG antibodies on 24 October 2008. The patient's condition is improving. He is hospitalized in Mossel Bay, Western Cape Province.

The majority of cases of CCHF have been in farm workers exposed to ticks or infected animals. CCHF must always be considered in the differential diagnosis of fever and any bleeding in abattoir workers even outside of endemic areas because of potential exposure to animals from these areas.

To date in 2008, there have been 8 laboratory-confirmed cases of CCHF in South Africa including cases from the Northern Cape (n=3), Mpumalanga (n=1), Free State (n=2) and Eastern Cape (n=2) provinces.

Source: Special Pathogens Unit and Epidemiology Division, NICD; Kimberley NHLS, Northern Cape, Western Cape and Eastern Cape Communicable Disease Directorates

Ross River virus

A traveller returning to South Africa from Queensland, Australia presented with a febrile illness, myalgia and arthralgia. The patient reported exposure to Ross River virus (RRV) while in Australia. Seroconversion was demonstrated by the presence of RRV-specific IgG. Unfortunately, a follow-up serum sample could not be obtained to demonstrate a rise in titre. A second traveller, who had visited New South Wales in Australia presented with similar symptoms plus a maculopapular rash on arrival in South Africa in mid-September 2008. A blood sample taken before her departure from Australia tested positive for anti-RRV IgM .

Infection with Ross River virus, also known as epidemic polyarthritis is a major public health problem in Australia (especially New South Wales and Queensland) and Papua New Guinea. The virus, a member of the genus Alphavirus in the family Togaviridae, is transmitted by several species of mosquito. The incubation period is 3 days to 3 weeks (usually 1 to 2 weeks) and, although most infections are asymptomatic, typical disease manifestations include self-limiting fever, headache, myalgia, arthralgia/arthritis and a macular or maculopapular rash occurring in two thirds of cases. Arthralgia may persist for up to a year.

Arboviral infections are important in the differential diagnosis of travellers with febrile illness, myalgia and arthralgia. The history of travel to a specific geographical area is critical. Dengue fever is another important arboviral infection in travellers returning from Oceania, South East Asia and Central and South America.

Source: Special Pathogens Unit and Travel Health Unit, Epidemiology Division, NICD

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