NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES
Division of the National Health Laboratory Service

Communicable Diseases Communiqué

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CONTENTS

1 ZOONOTIC AND VECTOR-BORNE DISEASES

a An outbreak of animal rabies in north-west Gauteng Province

Since the last week of May 2016, an outbreak of rabies has been reported the north west of Gauteng Province, in the Muldersdrift/Lanseria area (Figure 1). Rabies has been confirmed in the following animals: six jackals, three cows and an unvaccinated domestic dog (a Great-Dane). Rabies post-exposure prophylaxis has been administered to a number of exposed persons. Gauteng Department of Agriculture and Rural Development (GDARD) have been conducting a vaccination campaign for domestic cats and dogs in the affected areas from Monday 10 June, and have vaccinated more than 1 500 pets to date. Dog and cat owners in the area are advised to ensure their animals are up to date with rabies vaccinations.

Residents and visitors to the Kromdraai/ Muldersdrift area are advised to keep away from jackals, and to report all potential exposures (bites, scratches or licks by jackals, dogs, cats or other animals, particularly when these are unprovoked or animals are behaving strangely) to health care providers for assessment.

In an unrelated incident, a domestic dog (a Jack Russel) in Carletonville became ill approximately two weeks after killing a meerkat (mongoose). While the dog was symptomatic, it had scratched and licked its owners. The dog developed seizures and died. Only after being alerted by an astute health care worker was the dog exhumed and a diagnosis of rabies confirmed at Onderstepoort Veterinary Institute. The family members subsequently received post-exposure prophylaxis.

The last major rabies outbreak in domestic dogs in Gauteng was in 2010. There were 47 confirmed rabies cases in animals, and a single human fatality. Since 2010, there have been sporadic cases in Gauteng (see NICD Communique May 2016).

To date in South Africa, there has only been one confirmed case of human rabies – reported in the January 2016 Communiqué. In 2015, there were eight confirmed, four probable and one suspected case of human rabies, and in 2014, there were six confirmed and five probable cases reported.

Rabies virus (Figure 2) is transmissible to humans through exposure to saliva of an infected animal following bites, scratches of skin or licks to mucous membranes. Rabies is 100% preventable by intensive wound cleaning administration of post-exposure prophylaxis consisting of rabies immunoglobulin injected at the site of exposure or bite, and rabies vaccine administered on day 0,3 7 and 14 following exposure.

Source: Department of Agriculture and Rural Development, Gauteng Province; Centre for Emerging and Zoonotic Diseases, NICD-NHLS; Division of Public Health surveillance and Response, NICD-NHLS

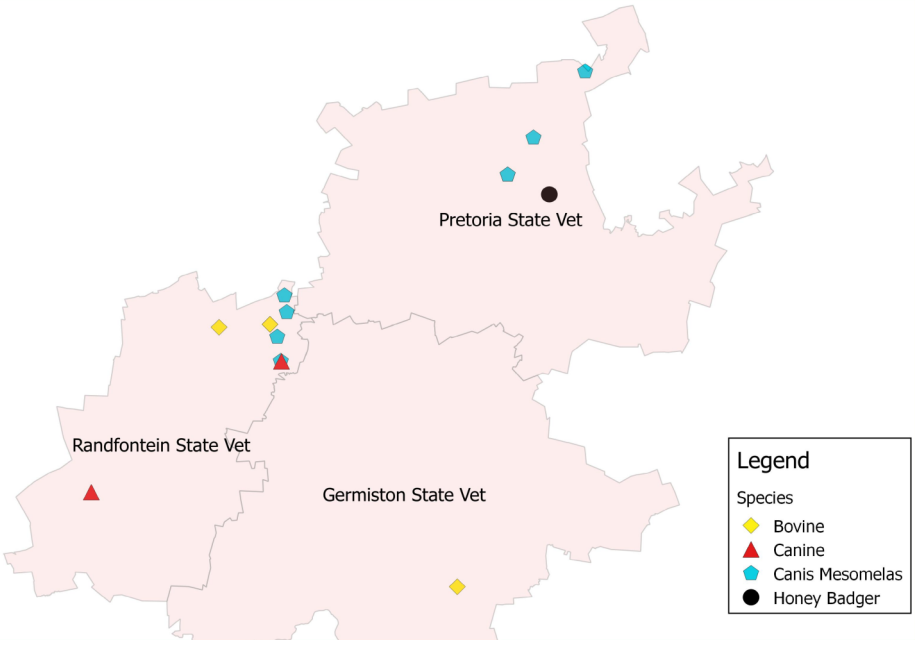


Figure 1 (left). Distribution of rabies cases in animals in Gauteng, 01 May-6 June 2016, courtesy Gauteng Department of Agriculture and Rural Development (Dr Johan Walters)

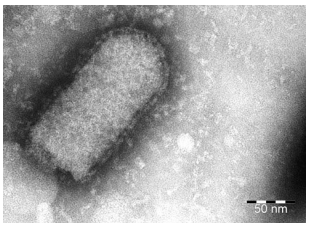


Figure 2 (above). A bullet-shaped enveloped rabies virion (negatively stained with 2% phosphotungstic acid). Photograph courtesy Dr Monica Birkhead, NICD.

b Brucellosis in a child in the Western Cape Province

A 5-year-old HIV-positive girl, formerly resident in an informal settlement in the Western Cape was diagnosed with tuberculosis and brucellosis in May this year. The patient had been put in foster care by social workers, and because she was found to be ill with diarrhea and 'flu' symptoms, the foster parents had taken her to a regional public hospital. Blood cultures taken there yielded growth of an oxidase-positive Gram-negative coccobacillus. The organism was identified by the National Institute for Communicable Diseases using MALDI-TOF (matrix-assisted laser desorption ionization time-of-flight) as a likely *Brucella melitensis*. Several laboratory workers, both in the Western Cape and NICD, were exposed to the organism. Post-exposure prophylaxis (PEP) measures have been implemented (chemoprophylaxis, baseline and 6-weekly serology, and temperature monitoring – see NICD Communiqué August 2015 for PEP regimens).

Investigation by environmental health practitioners showed that the area where the girl stayed prior to being placed in foster-care was surrounded by livestock farms. On interview, the child's mother denied drinking unpasteurised milk, or eating meat from local farmers. The mother reported that she purchased food, including meat and milk from local shops.

Following the notification, veterinary services investigated the area and reported that '*the settlement revealed open spaces frequented by grazing horses and foraging backyard chickens and dogs, but no other livestock. There are, however, several livestock farmers within five kilometres of the settlement, some of whom are known to be speculators. Many dogs in the area are free-roaming, and the possibility that they could spread the infection from livestock to people in the area was considered*' (Epidemiology Report, Western Cape Government, May 2016, Volume 8, Issue 5). Testing of several herds in the area have been done, and results are pending.

The usual reservoirs of brucellosis in South Africa are goats and sheep (*B. melitensis)* and cattle (*Brucella abortus)*. When infected, animals may abort and shed *Brucella* organisms in their milk. Brucellosis has also been previously documented in wildlife in South Africa. *Brucella* infection in animals is a controlled disease through national legislation (Animal Diseases Act, Act 35 of 1984) and any cases must be reported to the Provincial Veterinary Services. Brucellosis in animals is prevented through mandatory vaccination.

In humans brucellosis may be acquired through direct contact with infected animals or their secretions through skin cuts, abrasions or conjunctival splashes, or through inhalation of contaminated aerosols, or through consumption of unpasteurised dairy products. It is possible that the patient in this case acquired the infection through direct contact with infected animals, or indirect contact with animal products in the open veld in the area close to her home.

Brucellosis is treated with a triple regimen of an aminoglycoside, tetracycline and rifampicin. The aminoglycoside is given for two weeks, and the doxycycline and rifampicin are continued for six weeks. Patients require prolonged follow-up to monitor for further complications or relapse.

Source: Directorate Veterinary Services, Department of Agriculture, Western Cape Department of Health; NHLS Microbiology, Groote Schuur Hospital; Division of Public Health Surveillance and Response, NICD-NHLS; Centre for Emerging and Zoonotic Diseases, NICD-NHLS; (preneshni.naicker@nhls.ac.za)

2 RESPIRATORY DISEASES

a Diphtheria in KwaZulu-Natal Province: a reminder to clinicians to be alert for suspected cases, and to laboratories to actively screen all throat swabs for *Corynebacterium diphtheriae*

In the May edition of the NICD Communiqué, two laboratory-confirmed cases of toxigenic *Corynebacterium diphtheriae* infection were reported in adults aged 18 and 44 years respectively from eThekwini, Kwazulu-Natal Province(KZN). Molecular investigations conducted by the Centre for Respiratory Diseases and Meningitis of the NICD have revealed that these

isolates are of the same genotype (sequence type 378) that caused the outbreak from May to June 2015 in the same district of KZN (See NICD Communiqué August 2015). This is suggestive of ongoing and undetected circulation and transmission of *C. diphtheria*e.

In view of this, we urge clinicians throughout the country to have a high index of suspicion for cases of diphtheria, to be aware of the diphtheria case definition (see below) and to submit specimens from suspected cases for laboratory testing. Dacron, Rayon or nylon-flocked swabs should be used to collect throat swabs. These should be placed in Amies or Stuart's transport media, and labelled '*throat swab, ?diphtheria*' When cases of suspected diphtheria are identified, it is appropriate for clinicians (including facility infection control practitioners) to inform the District or Provincial Communicable Diseases Co-ordinator who will then be prepared to initiate contact tracing and post-exposure prophylactic measures should the case be confirmed.

Diphtheria case definitions (from NICD diphtheria guidelines, www.nicd.ac.za)

A diphtheria 'case under investigation':

- A person who presents with an upper-respiratory tract illness characterised by sore throat, low-grade fever AND an adherent membrane of the nose, pharynx, tonsils, or larynx.

A confirmed case of diphtheria:

- A person presenting with an upper respiratory tract symptoms with or without an adherent membrane AND culture or detection by PCR of *C. diphtheriae* or *C. ulcerans* or *C. pseudotuberculosis* from a clinical specimen which is confirmed to be toxin producing by ELEK testing or *tox* gene-positive by PCR.

In addition, we remind all NHLS and private laboratories nationally to continue actively screening for *C. diphtheriae* by plating all throat/ tonsillar swabs onto Hoyle's (tellurite-containing) medium. *C. diphtheriae* reduces potassium tellurite to tellurium to produce grey-black coloured colonies. On blood agar, *C. diphtheriae* is easily overlooked as glistening, creamy white colonies resembling *Staphylococcus* species. Alternately, please submit throat swabs directly to the Centre for Respiratory Diseases and Meningitis (CRDM) of the NICD for culture and PCR. NHLS and private laboratories are asked to submit Hoyle's plates with suspected *C. diphtheriae* colonies to the NICD for confirmation and/or detection of toxin by PCR.

Guidelines for diphtheria management and laboratory detection can be accessed at http://nicd.ac.za/assets/files/Guidelines_diphtheria_20160322_v2_3.pdf. Additionally, please contact CRDM to assist with identification of suspected organisms or supply of Hoyle's plates (Linda de Gouveia 011 555 0327, lindad@nicd.ac.za or Mignon du Plessis 011 555 0387, mignond@nicd.ac.za).

Source: Centre for Respiratory Disease and Meningitis, NICD-NHLS; KwaZulu-Natal Provincial Department of Health; Ethekwini Metro CDC team; Division of Public Health Surveillance and Response, NICD-NHLS (annev@nicd.ac.za; outbreak@nicd.ac.za)

b The 2016 influenza season, South Africa

The 2016 influenza season in South Africa has begun. The season is considered to have started when the detection rate of 'Viral Watch' specimens tested at the NICD has risen above 10% and remains there for ≥2 weeks. The influenza detection rate for the Viral Watch rose to 19.2% in week 19 (week starting 9 May) and continued to rise, and currently is 47.2% for week 23 (week ending 12 June) (Figure 3).

To date (week 23, the week ending 12 June), influenza has been detected in 182/2543 individuals tested from 3 surveillance programmes carried out by the NICD. Influenza B accounted for the majority of these detections i.e. 161/182 (88.5%); influenza A(H1N1)pdm09 for 8/182 (4.4%), and influenza A(H3N2) for 13/182 (7.1%).

Influenza vaccination, which provides protection against at least three strains of influenza each season, remains the most effective measure to prevent influenza and influenza-related complications. Individuals at risk of severe disease due to influenza and influenza-related complications, especially pregnant women and those who are vulnerable due to pre-existing illnesses or risk factors, are advised to obtain vaccination as soon as possible.

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

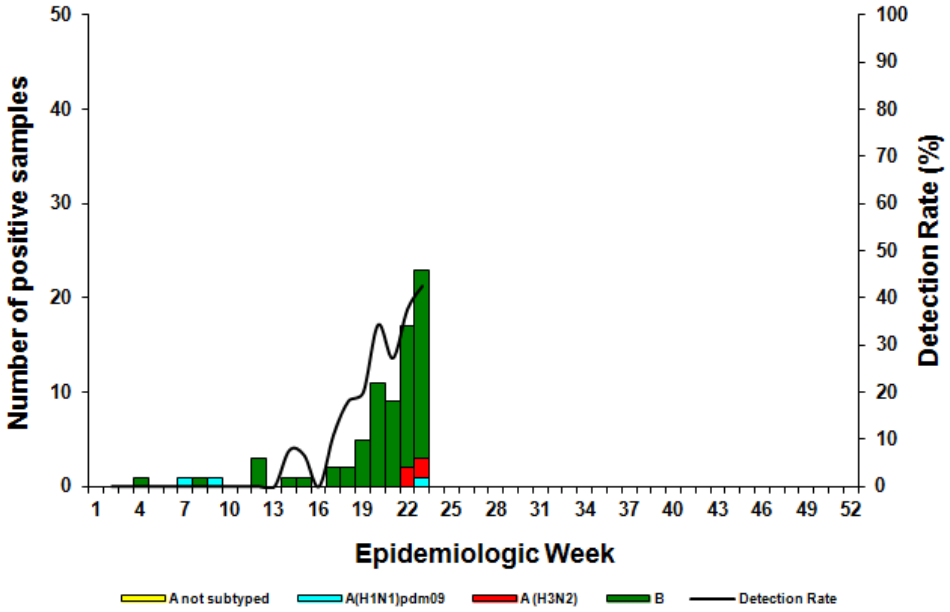


Figure 3. Number of positive samples by influenza types and subtypes and detection rate by epidemiological week of the year, Viral Watch, 2016

c A case of severe influenza B infection where MERS-CoV was suspected

A 41-year-old male South African office worker presented in Cape Town to an emergency unit of a Western Cape Province hospital with a two-day history of fever, cough, sore throat and rigors. The symptoms occurred two days after the patient returned from a camel farm in Hudaibiah, Saudi Arabia, where he was in close contact with camels. There was no history of consumption of camel milk or meat. He revealed that he also had had contact with elderly fellow travellers with upper respiratory tract symptoms. Examination revealed a normal BP, fever (temperature 39˚C), tachycardia (138 bpm). Initial blood tests showed a marginally elevated CRP (11 mg/L), marginally low white cell count (3.66 x 10^9/L), normal liver function tests and a normal neutrophil count. The patient's chest X-ray showed no infiltrates. He did not have any chronic illnesses. He had received meningococcal vaccine prior to departure; however he had not received the influenza vaccine.

Due to the patient's history of travel to Saudi Arabia, close contact with camels and with individuals with upper respiratory symptoms, attending clinicians considered Middle East respiratory syndrome coronavirus (MERS-CoV) infection as part of the differential diagnosis. A sputum sample was submitted to the NICD for testing. The patient was immediately isolated with appropriate infection control and prevention measures for airborne transmission. The specimen tested positive for influenza B virus and negative for MERS-CoV at the NICD Centre for Respiratory Diseases and Meningitis.

MERS-CoV is a betacoronavirus in the Coronaviridae family, discovered in 2012. It is endemic in countries in the Arabian Peninsula. As of 9 June 2016 there has been a total of 1 385 laboratory confirmed cases of MERS-CoV infection in Saudi Arabia including 592 deaths (case fatality rate 42.7%). The most recent case was reported from the region of Tabuk in Saudi Arabia. Travel-associated cases have also been reported in Algeria, Austria, China, Egypt, France, Germany, Greece, Italy, Malaysia, Netherlands, Philippines, South Korea, Thailand, Tunisia, Turkey, United Kingdom and United States of America.

Surveillance and phylogenetic studies suggest a bat origin of MERS-CoV with transmission to dromedary camels, which are responsible for the human infections. Symptoms may range from a mild upper respiratory tract illness to a lower respiratory infection with progression to acute respiratory distress syndrome (ARDS). A high mortality rate has been found in elderly patients with underlying co-morbidities. Spread to close contacts and the capacity for nosocomial transmission is of particular concern within the healthcare setting, highlighting the need for immediate identification and institution of infection prevention measures and contact tracing. Treatment is largely supportive.

In severely ill persons with respiratory disease, a diagnosis of MERS-CoV should be considered in any patient with fever (≥38°C) and cough with pneumonia or acute respiratory distress syndrome (ARDS) (based on clinical/radiological) AND one or more of

the following: 1) A history of travel within 14 days before onset of illness to the Arabian Peninsula or in countries where MERS-CoV is known to be circulating or where human infections have recently occurred; or 2) Close contact with a symptomatic traveller who developed fever and acute respiratory illness within 14 days after travelling from countries in or near the Arabian peninsula; or 3) A history of being in a healthcare facility, within 14 days before onset of illness, in the country where hospital-associated-MERS-CoV infections have been reported; or the patient is associated with a cluster of patients with severe acute respiratory illness of unknown aetiology that occurs within a 14-day period, without regard to place of residence or history of travel.

Patients where MERS-CoV is being considered should undergo routinely available laboratory tests as clinically indicated according to local management guidelines for community-acquired pneumonia to determine the presence of other potential primary aetiologies of pneumonia (e.g *Streptococcus pneumoniae*, *Haemophilus influenzae* serotype b, *Mycoplasma pneumoniae*, *Legionella pneumophila*, *Mycobacterium tuberculosis* and respiratory viruses including influenza, and respiratory syncytial virus (RSV)). These investigations include at least a full blood count, blood cultures, chest radiography, lower respiratory specimens, nasopharyngeal swabs or aspirates and oropharyngeal swabs for detection of viral and atypical pathogens and sputum for *Mycobacterium tuberculosis* microscopy, and/or molecular detection.

In addition, infection control and prevention interventions should be implemented as soon as a patient is suspected of having infection due to MERS-CoV. Guidelines for the diagnosis, management and prevention of MERS-CoV are found on the NICD website (www.nicd.ac.za).

Source: NHLS laboratory, Groote Schuur Hospital (nokwazi.nkosi@nhls.ac.za); Centre for Respiratory Diseases and Meningitis, NICD-NHLS (cherylc@nicd.ac.za)

d *Legionella* infection in a hospitalised neonate

A 14-day-old neonate was hospitalised in a Gauteng public hospital following a diagnosis of neonatal sepsis. The neonate was born at the same hospital on 8 March 2016, spent one night in the postnatal ward and was discharged the next day. During this time the infant was not bathed or formula-fed. Following discharge, mother and infant were well until 18 March 2016 when the infant developed symptoms including cough, blocked nose and mild fever. Following assessment at a local clinic, the infant was referred to the same hospital and admitted on 21 March. The neonate tested positive by PCR from a nasopharyngeal swab for *Legionella* spp. on 22 March. The same swab additionally tested negative for other respiratory pathogens including adenovirus, enterovirus, human metapneumovirus, parainfluenza virus 1-3, respiratory syncytial virus, rhinovirus, influenza, *Streptococcus pneumoniae*, *Bordetella pertussis*, *Mycoplasma pneumoniae* and *Chlamydia pneumoniae*. All other investigations were negative. Additional specimens were collected from the infant on 5 April 2016 and were tested for *Legionellas*: nasopharyngeal swabs were culture and PCR-negative for *Legionella* spp. A urine specimen was negative for *L. pneumophila* serogroup 1 on urinary antigen test but positive for *Legionella spp*. by PCR (Cycle threshold value 41). Due to the low bacterial load (high Ct value) in the specimens, the species of *Legionella* could not be determined.

The unusual detection of *Legionella spp*. in an infant, as well as the potential for hospital-acquired infection prompted the NICD and NHLS to conduct an environmental risk assessment at the hospital and patient's home. The hospital assessment revealed a number of challenges including a cold water tank and the coal-powered boiler not being in working order and some wards having hot water temperatures below the recommended hot water temperature of 55°C. Temperatures of hot and cold water to the hospital were not monitored. Tap filters that were examined were clogged. Of 16 water samples collected from various parts of the hospital plumbing system, two (from adult high care, and neonatal intensive care unit (NICU) respectively) were found to be positive for *L. pneumophila* serogroup 1. All four water samples collected from the patient's home were culture-negative for *Legionella* spp. The diagnosis of *Legionnella* species in this patient, and the isolation of *Legionella pneumophila* serogroup 1 from hospital environmental specimens is concerning.

While the hospital water supply cannot be conclusively identified as the source of the infant's infection, this case serves to highlight the importance of preventive maintenance in this hospital's water supply. Legionellosis is a notifiable disease under South African law. Nosocomial and institutional transmission can be prevented through adherence to guidelines for maintenance of water systems. Guidelines for the diagnosis, prevention and management of

Legionnaires disease are found on the NICD website (www.nicd.ac.za).

For further information, please contact Dr Nicole Wolter at Centre for Respiratory Disease and Meningitis 011-555-0352, nicolew@nicd.ac.za; or Rob Stewart at NHLS Charlotte Maxeke Infection Control Laboratory 011-489-8578 rob.stewart@nhls.ac.za;

Source: Centre for Respiratory Diseases and Meningitis, NICD-NHLS; Division of Public Health Surveillance and Response, NICD-NHLS; NHLS Infection Control Laboratory, Charlotte Maxeke Johannesburg Academic Hospital (annev@nicd.ac.za; nicolew@nicd.ac.za; rob.stewart@nhls.ac.za)

3 SEASONAL DISEASES

a An investigation of a cluster of malaria cases in Gert Sibande, Mpumalanga Province

A 23-year-old male resident of an isolated homestead in Gert Sibande District, Mpumalanga Province, which is non-endemic for malaria, was admitted to the local hospital on 21 April 2016 and diagnosed with malaria. His family members, an 8-year-old boy and a 54-year-old man, were subsequently admitted on 3 and 5 May 2016 respectively, and also diagnosed with malaria. These cases were notified to the district through the malaria surveillance system and an investigation was prompted. Staff from the Mpumalanga Provincial and Gert Sibande District Departments of Health, the NICD, and the Mpumalanga Provincial Malaria Control Programme visited the homestead and conducted entomological and epidemiological investigations to determine the source of the outbreak and conduct appropriate investigations.

The homestead, comprising 34 households, was situated in an isolated area, approximately 2 km from the N17 highway (Figure 4). The community is sustained through dependence on social grants, and has limited access to health care. Interview of the patients and community members allowed generation of a timeline (Figure 5). None of the cases reported travelling to malaria endemic regions. However, the community had received visitors from Mozambique in December 2015. Blood specimens from community members were taken, 84 malaria rapid diagnostic tests (RDTs) and 96 blood smears were done. An additional symptomatic person, who was also positive on RDT, was identified and treated for malaria.

Entomological investigations revealed several mosquito breeding sites around the homestead. A number of adult *Anopheles* adult mosquitoes and larvae were caught, none of which were common vectors of malaria. Amongst the identified species were *An. quadriannulatus* and *An. vaneedeni*, the latter species currently under investigation as a possible vector. ELISA testing of a single adult female *An. vaneedeni* mosquito failed to reveal *P. falciparum* sporozoites. In response to these findings, staff of the provincial malaria control programme conducted indoor residual spraying in 171 rooms in the homestead from 12th to 20th May 2016. All breeding sites were treated with larvicide (Starycide 48% SC, Triflumuron) on two occasions. Malaria awareness campaigns were conducted in the community and prompt health seeking advised. Anti-mosquito bed nets were distributed to the two affected families. No additional cases have been reported since.

Based on these findings, it is difficult to draw conclusions as to the origin of these malaria cases. The proximity of the area to recognised low-risk malaria areas, and to a major road, suggests that the cases may have originated from an imported, infected mosquito (that is, Odyssean malaria). The cases presented within 18 days of each other, a time period within the average lifespan of a female mosquito (around 30 days under optimal conditions). The *Anopheles* mosquitoes and larvae found in close proximity to the homestead were not common malaria vectors. Thus the cases were unlikely to have arisen as a consequence of a newly-established malaria transmission site. Unfortunately parasite genotyping to establish if the infections were caused by the same strain of *P. falciparum* was not possible, as patient specimens were not available.

Source: Mpumalanga Malaria Control Programme; Mpumalanga Department of Health; Gert Sibande Department of Health; Centre for Opportunistic, Tropical and Hospital Infections, NICD-NHLS; Division of Public Health, Surveillance and Response, NICD-NHLS; Field Epidemiology Training Programme, NICD-NHLS (johnf@nicd.ac.za)

Figure 4 (left). An aerial photograph (courtesy Google Maps) of the affected area showing proximity to the N17 national road, the homestead and the breeding sites.

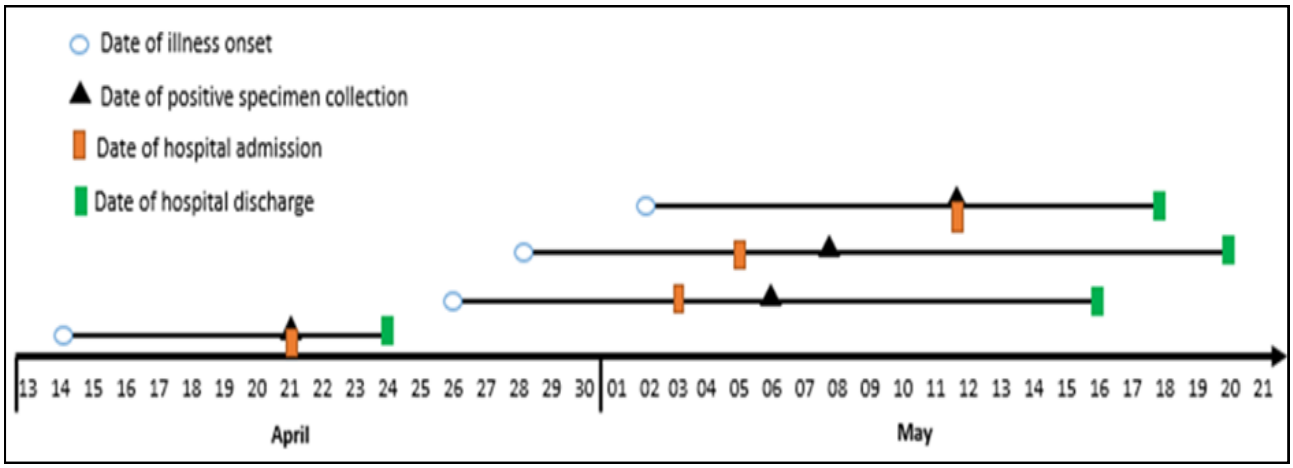


Figure 5. A timeline of the malaria outbreak, Gert Sibande District, Mpumalanga Province, April – May 2016. Each line represents a hospitalised case.

b A case of recrudescent *Plasmodium ovale* malaria presenting following cardiothoracic surgery

A 75-year-old male, resident in White River, Mpumalanga Province, underwent cardiothoracic surgery at a Johannesburg hospital in early May 2016. The patient had cardiac valvular disease secondary to rheumatic fever as a child. He had undergone a nephrectomy for polycystic kidney disease years before this presentation. The patient's surgery was uneventful but his post-operative recovery was complicated by urinary retention and haematuria, leading to a haemoglobin level of 7 g/dl, and fever. Peri- and post-operatively, the patient received numerous transfusions of blood and blood-related products. All investigative tests to identify the source of fever were negative. A full month after surgery, examination of the peripheral smear of a blood specimen taken while the patient had a pyrexia of 39.5°C revealed malaria parasites, with a 1.7% parasitaemia. This finding was confirmed by a malaria antigen test, which showed a negative result for *P. falciparum* antigen, but a positive result for pan-*Plasmodium* species antigen. Blood smear microscopy and PCR done by both the private laboratory and the NICD confirmed a *Plasmodium ovale* infection (Figure 6). The patient was treated with Coartem (artemether-lumefantrine), and will receive primaquine in due course.

Malaria infection in this patient may have originated

from several potential sources, as follows: 1) Through transfusion of malaria-containing blood or blood products; or 2) Through a needle-stick injury or through accidental sharing of needles or intravenous solutions (e.g., such as heparin vials) from other patients with malaria infection concurrently on the ward; or 3) Through the bite of an infected mosquito brought into the hospital inadvertently from a malaria area ('odyssean malaria') – a single case of odyssean malaria due to *P. ovale* has been documented locally; or 4) Following acquisition of *P. ovale* months or years prior to presentation either during travel to an affected area (or locally, as he lives on the border of the malaria transmission area in South Africa), with development of recrudescent infection following surgery. On further investigation, the patient had an extensive occupation-related travel history to malaria-infested areas (always with Malanil prophylaxis), but no travel within 3 months prior to surgery. The patient reported an uncomplicated episode of malaria in 1997 that had been successfully treated with chloroquine. Since 2004, initially every two years, and more recently, annually, the patient experienced an episode of fever, chills, headache and tender abdomen especially in the right upper quadrant. These episodes lasted on average a week. The patient had consulted various medical practitioners, however, no diagnosis had been made. Given the history of antecedent fevers, and multiple potential opportunities for acquisition of *P. ovale* malaria, this is the most likely explanation and source of the patient's infection. Unfortunately no blood specimens pre-dating the patient's surgery were available for testing to confirm this hypothesis.

P. ovale is particularly prevalent in sub-Saharan and West Africa, but is also found in India and South East Asia. In Africa infections with *P. ovale* are far less common than *P. falciparum* – reportedly fewer than 5% of malaria cases are due to *P. ovale*. It is generally a mild disease, but severe and complicated cases are occasionally reported. Artemether-lumefantrine has been shown to be comparable with chloroquine for the treatment of *P. ovale* infection, though controlled trials are few. Primaquine administration, following evaluation for glucose-6-

Source: Centre for Tropical and Hospital infections, NICD-NHLS; Division of Public Health, Surveillance and Response, NICD-NHLS; the reporting physicians; Ampath laboratory; South African National Blood Service (johnf@nicd.ac.za)

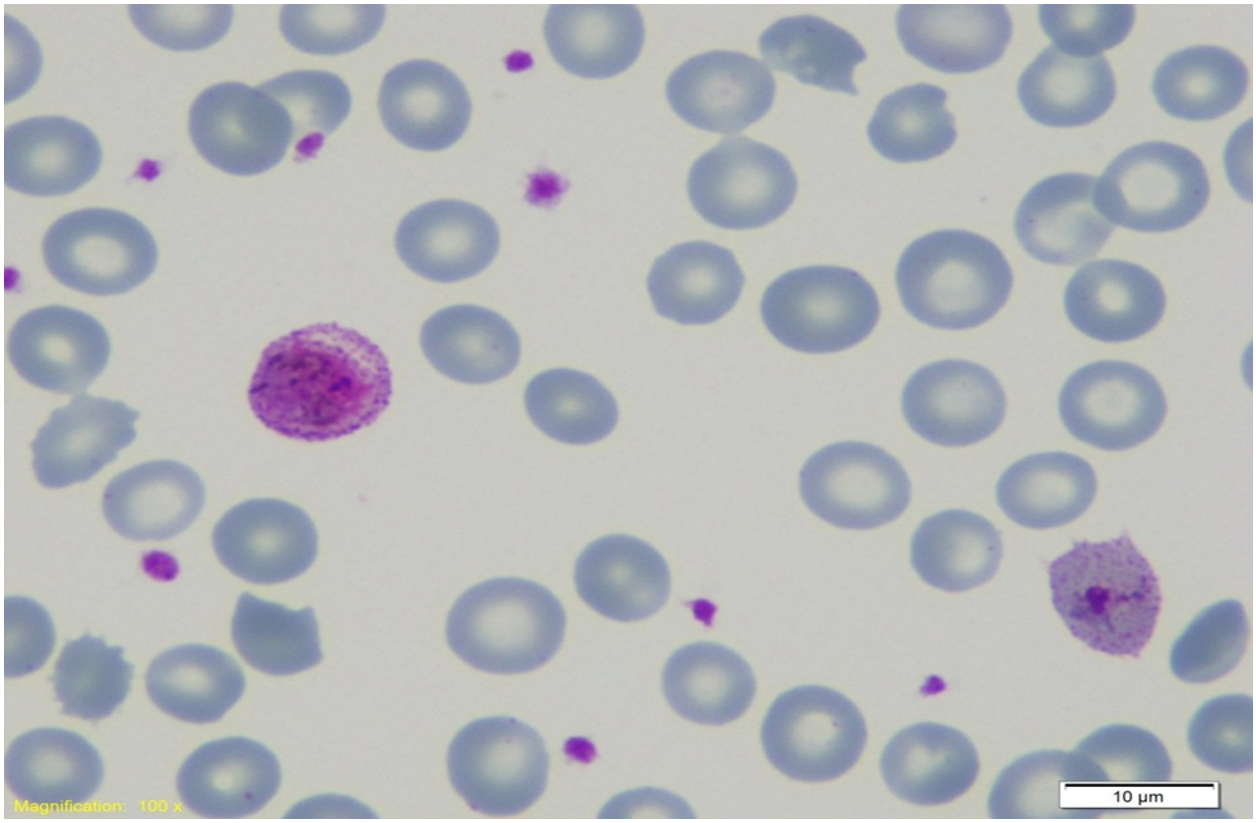


Figure 6. Photomicrograph of the patient's thin blood film showing a gametocyte (left) and trophozoite (right) of *P. ovale*. Note coarse stippling (James' dots) in both infected erythrocytes, and distortion and fimbriation of the red cell on the right. 100 x objective. Photo credit: Lisa Ming Sun, COTHI, NICD-NHLS.

4 DISEASES OF INTERNATIONAL CONCERN

a An update on the Yellow fever outbreak in Angola and Democratic Republic of Congo

New cases continue to be reported in the yellow fever outbreak in Angola. There is a decline in incidence of cases in Angola, but an expansion in the geographical range of cases beyond Angolan borders is noted.

- In Angola, as of 17 June 2016, 3 294 cases have been reported to central level, of which 861 have been laboratory confirmed. In total, 347 deaths have been reported, of which 115 occurred amongst confirmed cases. A quarter of the confirmed cases are in the 9-14 year age group (n=213), followed by the 15-19 year age group (n=170, 20%). The first three cases of the outbreak were confirmed on 19 January 2016 by the NICD. The detection of confirmed cases peaked during epidemiological weeks 8 and 9 (Figure 7). The distribution of cases in Angola with case numbers is shown in Figure 8.
- Since March 2016, international spread through non-immunised travellers to the Democratic Republic of Congo (DRC), Kenya and China has been laboratory confirmed in 59, 2 and 11 yellow fever cases respectively.
- In the DRC, as of 17 June, there have been 1106 reported cases and 75 deaths. Amongst reported cases, 68 are confirmed, of which 59 were imported from Angola, 2 are sylvatic and 7 are autochthonous (local transmission). The reported cases have originated from 22 of 307 health zones in 5 of the 26 provinces. WHO reports that surveillance efforts in DRC have increased, and vaccination campaigns are underway in the capital city-province Kinshasa and Kongo Central provinces, located in the western portion of the country.
- Six additional suspected cases are under investigation in other countries in Africa (Ethiopia, Ghana and Republic of Congo) to determine whether there is a connection with the Angolan outbreak.
- Uganda reported 68 suspected cases but strain typing indicated that these cases are not linked to the outbreak in Angola.

Vaccination campaigns have been conducted in Luanda, Benguela and Huambo provinces, and commencing in May 2016, in Cuanza Sul, Huila and Uige provinces (Figure 8). Following advice of strategic partners, vaccination campaigns are to be commenced in border districts, including Cuango, Lunda Norte and Zaire provinces. In DRC a vaccination campaign reaching 2.1 million people in 11 health zones in Kinshasa and Kwango Provinces was completed on 4 June.

On 19 May 2016, the WHO acknowledged that the urban outbreaks in Angola and DRC are serious public health events which warrant intensified national action and enhanced international support, but do not at this time constitute a Public Health Emergency of International Concern. There is presently concern to safeguard and augment the global supply of vaccines. Currently 5.2 million doses of vaccine are available for emergency response. The WHO Strategic Advisory Group of Experts (SAGE) on Immunization is considering fractional dosing to preserve vaccine supply. There is evidence that using a 5th of a standard vaccine dose would still provide protection against the disease for at least 12 months and possibly much longer.

A number of tests for yellow fever have been conducted by the Centre for Emerging and Zoonotic diseases, and all have been negative to date. South African travellers to yellow fever endemic areas are reminded to undergo vaccination against yellow fever at least 2 weeks prior to departure. As of 11 July 2016, according to WHO agreement, the validity of certificates of vaccination for yellow fever is life long for all countries. For case definitions, diagnostic testing and contra-indications to the vaccine, please consult the NICD Communiqué, April 2016 edition available at www.nicd.ac.za.

Sources: Centre for Emerging and Zoonotic Pathogens , NICD-NHLS; Division of Public Health Surveillance and Response (outbreak@nicd.ac.za; cezd@nicd.ac.za)

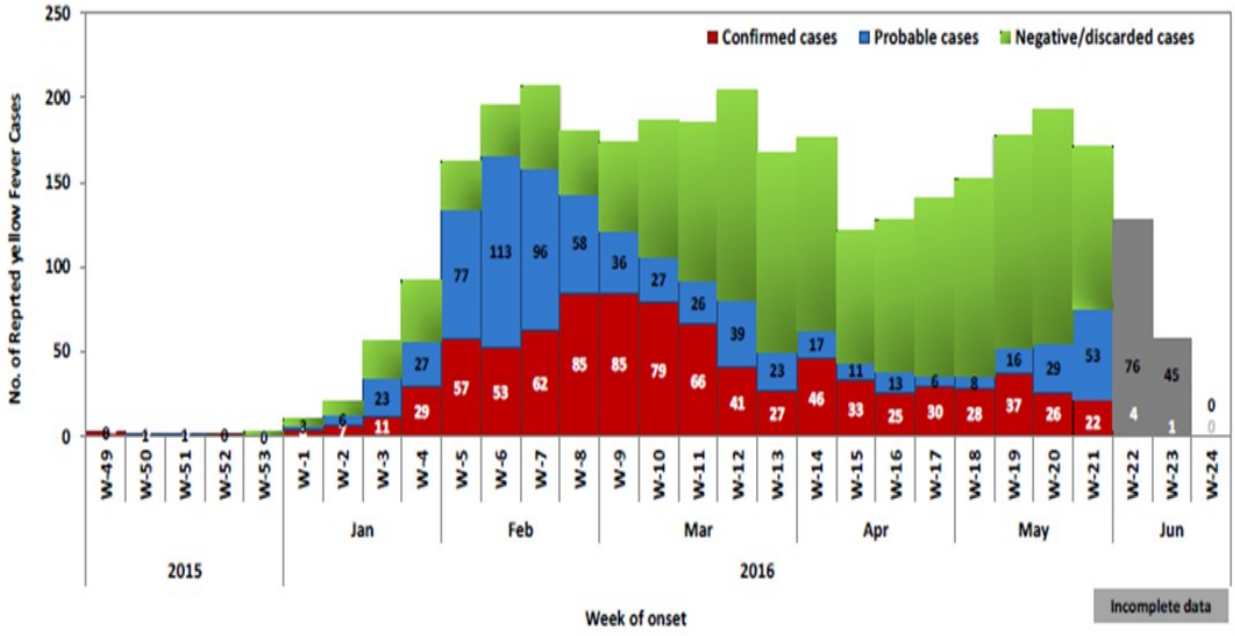


Figure 7. Epidemic curve of confirmed and suspected yellow fever cases in Angola as of 17 June 2016. Source: Yellow fever outbreak situation report 6 June 2016, incident management team, Ministry of Health Angola. http://www.afro.who.int/en/yellow-fever/sitreps/item/8747-situation-report-yellow-fever-outbreak-in-angola-20-june-2016.html

Province	Cumulative (5 Dec 2015— 17 June 2016)					Discarded, Lab with Vacc. History
	Notified Cases	Tested		Confirmed		
		No	%	No	%	
Bengo	21	21	100	6	29	0
Benguela	291	278	96	111	38	11
Bie	33	31	94	16	48	0
Cabinda	37	31	84	1	3	0
Cuando Cubango	6	5	83	1	17	0
Cuanza Norte	61	51	84	5	8	0
Cuanza Sul	103	99	96	16	16	0
Cunene	49	49	100	14	29	0
Huambo	543	487	90	127	23	15
Huila	137	89	65	33	24	0
Luanda	1833	1483	81	489	27	73
Lunda Norte	55	54	98	21	38	0
Lunda Sul	9	8	89	0	0	0
Malange	21	21	100	6	29	0
Moxico	5	5	100	0	0	0
Namibe	13	13	100	2	15	0
Uige	63	61	97	9	14	0
Zaire	14	12	86	4	29	0
TOTAL	3294	2798	85	861	26	99

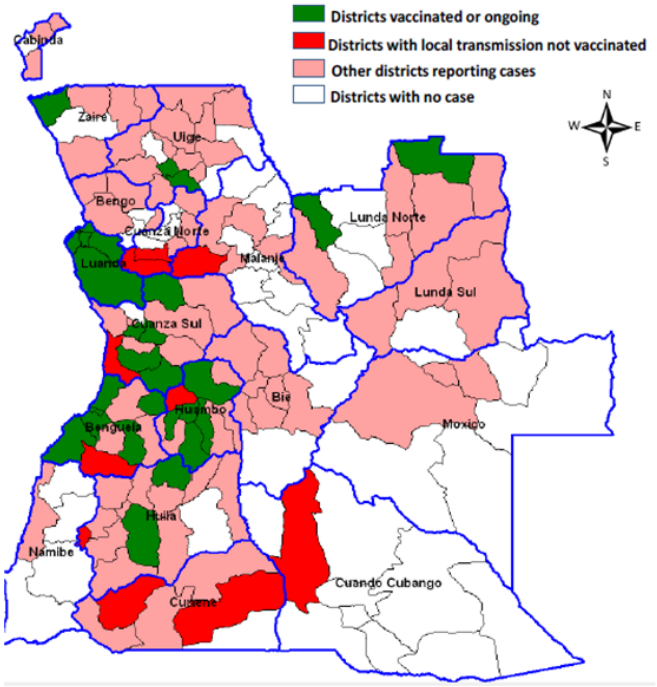


Figure 8. Numbers (table) and distribution of yellow fever cases (map) in Angola of 17 June 2016. Source: Yellow fever outbreak situation report 9 June 2016, incident management team, Ministry of Health Angola. http://www.afro.who.int/en/yellow-fever/sitreps/item/8747-situation-report-yellow-fever-outbreak-in-angola-20-june-2016.html

b Health advice for travellers to the Rio Olympic Games, 2016

Amidst concerns about Zika virus transmission, and risk to participants, the WHO convened a meeting of the Emergency Committee (EC) under the International Health Regulations (2005) on 14 June 2016. After review of available information provided by Brazil and advisors specializing in arboviruses, the international spread of infectious diseases, travel medicine, mass gatherings and bioethics, the Committee concluded that there is a low risk of further international spread of Zika virus as a result of the Olympic and Paralympic Games. The WHO reported that the risk to participants and spectators is minimal, as the intensity of autochthonous transmission of arboviruses, such as dengue and Zika viruses, will be minimal during the Brazilian winter (July). Furthermore, Brazilian authorities are intensifying vector-control measures in and around the venues for the Games which should further reduce the risk of transmission.

Travellers to Brazil should take appropriate advice as follows:

Before travelling to Brazil, travellers should engage with travel medicine providers at least 3-4 weeks prior to departure, in order to ensure adequate time for immunisations and preparation. Travellers to Brazil should be up to date with routine immunisations (including measles) In addition they should receive: 1) influenza vaccine (the currently available 2016 formulation for the southern hemisphere is adequate); 2) hepatitis A vaccine and 3) yellow fever vaccine (all travellers from South Africa require a valid yellow fever vaccination certificate for travel to and from Brazil). Malaria prophylaxis may be required if the itinerary includes areas with known malaria risks (primarily the north-western areas of Brazil; Rio de Janeiro has no malaria risk). Travellers should ensure purchase of effective anti-mosquito preparations.

Whilst in Brazil, to avoid mosquito-borne illnesses, travellers should prevent mosquito bites through: 1) wearing of clothing that covers as much of the body as possible; 2) applying insect repellent containing DEET (diethyltoluamide) or picaridin to skin or clothing especially during the day when *Aedes* mosquitoes are most active. ; 3) use mesh screens or netting materials on windows, or closing doors and windows while indoors and 4) sleep under mosquito nets. Travellers should also practice safe sex or abstain from sex during their stay. While Zika is primarily transmitted through the bite of infected mosquito bites, male-to-female and male-to-male sexual transmission has been documented.

To avoid food- and water-borne diseases, travellers should wash hands before handling and consuming food, ensure that food has been thoroughly cooked, drink safe water and avoid uncooked food except for fruits and vegetables that can be peeled or shelled.

Upon return home, travellers should observe themselves for symptoms of illness especially fever, and seek health care if they are concerned. To prevent onward transmission of Zika virus, and because 80% of persons with Zika infection are asymptomatic, the WHO advises that all returning travellers should practice safer sex, including through the correct and consistent use of condoms, or abstaining from sex, for at least 8 weeks. If men experienced symptoms of Zika (rash, fever, arthralgia, myalgia or conjunctivitis) then they should adopt safer sexual practices or consider abstaining for at least 6 months. Male partners who have travelled to a Zika-area, and who with their partners are planning a pregnancy, should avoid conception within 6 months after return if the male partner has been symptomatic for Zika, or within 8 weeks if asymptomatic. Males have returned from Zika-infected areas and whose partners are pregnant should use barrier prevention (condoms) for the duration of the pregnancy.

The NICD offers the following test for ZVD: 1) RT-

PCR testing (clotted blood/serum) and 2) virus culture (clotted blood/serum), which are useful during the transient viraemic stage of infection (1 – 5 days post-symptom onset); and 3) paired serological testing (clotted blood/serum taken up to 14 days apart). A ZIKV specific IgM and IgG ELISA and a viral neutralisation test are available. Serology is complicated by cross-reactivity with other flaviviruses, including dengue and yellow fever, therefore paired serological testing is essential. Specimens submitted for Zika should also be tested for dengue and chikungunya because of overlapping clinical presentations and should be requested by the referring clinician. Serology for ZIKV may not provide conclusive results.

On request, the NICD will offer testing for Zika to returned travellers from a Zika-endemic area who present with rash, fever, headache or arthralgia within 14 days of return, and to asymptomatic pregnant women with a recent travel history to an active Zika transmission area. Clinicians requesting testing should complete the Zika case investigation form (www.nicd.ac.za) and submit the specimen to the Arbovirus Reference laboratory, Centre for Emerging and Zoonotic Diseases, National Institute for Communicable Diseases, for testing. Clinicians should call or email the laboratory to notify them of incoming specimens at 011 386 6391 / 011 386 6353 / 082 908 8045 or cezd@nicd.ac.za; petrusv@nicd.ac.za Samples should be kept cold (on ice or cold packs) during transport. Testing will not be done after hours.

Further references:

South African Travel Health Network (www.SaNTHNet.co.za) for yellow fever regulations pertaining to RSA travellers

WHO - http://www.who.int/csr/disease/zika/information-for-travelers/en/

CDC travel advisory for yellow fever and malaria endemic areas in Brazil at http://wwwnc.cdc.gov/

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

5 SURVEILLANCE FOR ANTIMICROBIAL RESISTANCE

a First report of echinocandin-resistant *Candida glabrata FKS* mutants in South Africa

Echinocandins are recommended as first-line agents to treat invasive infections caused by *Candida glabrata* since this organism is less susceptible to azoles. However, owing to the relatively high cost, echinocandin use is largely restricted to the South African private sector. Anidulafungin, caspofungin and micafungin disrupt the synthesis of β-1,3-D-glucan, a fungal cell wall component, by inhibiting β -1,3-D-glucan synthase. Echinocandins bind to Fksp, the catalytic subunit of β-1,3-D-glucan synthase, which is encoded by three related genes: *FKS1*, *FKS2* and *FKS3*. Resistance to echinocandins has been described in *C. glabrata* due to amino acid changes in the hotspot regions of the *FKS1* and *FKS2* genes.

The first two South African *C. glabrata* isolates with echinocandin resistance, mediated by mutations in the *FKS2* gene, have been isolated from urine specimens from private-sector patients in Gauteng Province. For the first isolate, the broth microdilution MIC ranges were 0.5 - 1 µg/ml for anidulafungin (CLSI M27-S4 resistant breakpoint ≥0.5 µg/ml) and 0.25 µg/ml for micafungin (resistant breakpoint ≥0.25 µg/ml). This isolate had a mutation in the hot spot 1 region of the FKS2 gene where serine was replaced by phenylalanine at position 663 (S663F). The anidulafungin and micafungin MICs for a second isolate were both 2 µg/ml by broth microdilution method and a change from arginine to lysine at amino acid position 1377 (R1377K) was detected in the FKS2 hotspot 2 region. Diagnostic laboratories should refer isolates with elevated anidulafungin or micafungin MICs to NICD for confirmation of resistance. Systematic active laboratory surveys, including isolates from cases of non-invasive *Candida* infection, are needed to determine if echinocandin resistance has become more widespread in South Africa.

Further reading:

Naicker S, Magobo R, Zulu G, Maphanga T, Luthuli N, Lowman W, Govender N. Two echinocandin-resistant *Candida glabrata* FKS mutants from South Africa. Medical Mycology Case Reports. 11 (2016) 24-26

Source: Centre for Opportunistic, Tropical and Hospital Surveillance, NICD-NHLS (neleshg@nicd.ac.za)

b Update on carbapenemase-producing *Enterobacteriaceae*

The Johannesburg Antimicrobial Resistance Laboratory and Culture Collection (AMRL-CC) of the Centre for Opportunistic, Tropical and Hospital Infections (COTHI) at the NICD have been testing referred isolates of suspected carbapenemase-producing Enterobacteriaceae (CPE) for the presence of selected carbapenemase genes. 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. CPE surveillance is required to determine the extent of the problem as a first step in order to restrain the emergence and spread of CPE. For May 2016, a total of 118 Enterobacteriaceae isolates were received. One hundred and one isolates were screened, 74 of which expressed carbapenemases (Table 1). Majority of these CPE isolates were *Klebsiella pneumoniae* (61) followed by *Enterobacter* spp. (21).

It is important to note that these figures do not represent the current burden of CPEs in South Africa. Given that CPE infections are currently not reportable or notifiable in South Africa, there is no platform for appropriate surveillance reports and consequently no locally representative data is available. This is of major concern, since meaningful data can inform public health policy and highlight priorities for action. Controlling the spread and limiting the impact of CPEs in South Africa will require 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.co.za)

Table 1. Enterobacteriaceae by CPE enzyme type, AMRL-CC, COTHI, NICD, May 2016 and January-April 2016

Organism	NDM		OXA-48 & Variants		GES		VIM		KPC	
	Jan-Apr 2016	May 2016	Jan-Apr 2016	May 2016	Jan-Apr 2016	May 2016	Jan-Apr 2016	May 2016	Jan-Apr 2016	May 2016
Klebsiella pneumoniae	42	16	66	25	1	-	-	4	-	1
Morganella morganii	-	2	-	-	-	-	-	-	-	-
Providencia rettgeri	4	2	-	-	-	-	-	-	-	-
Escherichia coli	-	1	6	6	-	-	-	-	-	-
Proteus mir-abilis	-	-	1	-	-	-	-	-	-	-
Serratia marcescens	7	2	2	1	-	1	-	1	-	-
Citrobacter freundii	2	-	-	2	-	-	-	-	-	-
Enterobacter spp.	6	3	6	7	-	-	-	-	-	-
Total	**61**	**26**	**81**	**41**	**1**	**1**	**-**	**5**	**-**	**1**

NDM: New Delhi metallo-beta-lactamase; **OXA**: oxacillinase; **GES**: Guiana-Extended-Spectrum; **VIM**: Verona integron-encoded metallo-beta-lactamase;
KPC: *Klebsiella pneumoniae* carbapenemase.

6 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 9 on page 16.

1. Avian influenza A (H7N9 and H5N6) - China

China has reported 11 laboratory-confirmed cases of human infection with avian influenza A (H7N9) virus, including one cluster, on 25 June 2016. Poultry and environmental samples collected from live birds from different settings have tested positive for H7N9 since January 2015 to April 2016. The H7N9 infection has become enzootic in the mainland China but potential for human-to-human spread remains low. One laboratory-confirmed case of human infection with avian influenza A (H5N6) was reported to WHO on 30 May 2016. No human-to-human transmission is documented. WHO advise that travellers to countries where outbreaks have been reported should avoid contact with live poultry markets, poultry farms, contact with surfaces that may be contaminated with animal faeces, or entering poultry slaughter areas.

2. MERS-CoV – Saudi Arabia

Between 15 May to 20 June 2016, 12 laboratory-confirmed cases of MERS-CoV including one death were reported to WHO from. Four cases had a history of contact with an index case. Three cases had a history of frequent contact with camels and consumption of raw camel milk. One case had reported no exposure to known risk factors in the 14 days prior to symptom onset. Risk factors in the remaining cases are being investigated. Since September 2012, 1 768 laboratory confirmed cases of MERS-CoV with 630 deaths were reported globally (case fatality rate: 36.2%). People should avoid contact with camels and camel products, such as drinking raw milk or urine of camels or eating meat that was not cooked properly.

3. Diphtheria – India

A fatal case of diphtheria was reported from Kerala on 19 June 2016 – a 15-year-old boy, unvaccinated, was admitted on 06 June 2016. His condition worsened despite treatment with anti-diphtheria serum and he died on 18 June 2016. Two additional symptomatic children are being treated. Prevention of diphtheria is achieved through vaccination.

4. Japanese encephalitis – India and Taiwan

On 17 June 2016, 6 fatal cases of Japanese encephalitis (JE) were reported from Assam state, India. More than 200 people in different villages have been affected. Control measures such as awareness and vaccination campaigns are being implemented to contain the disease during the transmission season in Assam. In Taiwan, the first indigenous case of JE was confirmed on 17 June 2016 as an unvaccinated farmer without any travel history prior to illness onset. JE is endemic in Taiwan and sporadic infections are common during May to October season with a peak in June and July. The *Culex* spp mosquitos are the main vectors for JE infections. JE is a vaccine-preventable disease; vector control, vaccination and avoiding mosquito bites are the only measures for disease control and prevention.

5. Lassa fever – Nigeria

Since January 2016 to the week ending 4 June 2016, 717 cases including 71 laboratory-confirmed cases and 87 deaths were reported (case fatality rate: 12%). During the same period in 2015, 126 cases including 8 laboratory-confirmed cases and 4 deaths were reported (case fatality rate: 3%). Although the WHO has reported a declining trend in the current outbreak, disease awareness, laboratory support, active case finding, contact tracing and monitoring and training of health care workers should continue. Lassa fever-endemic countries in West Africa are encouraged to strengthen surveillance activities.

6. **Measles – New Zealand**

Since April 2016, 60 confirmed measles cases were reported in New Zealand, mostly linked to the town of Hamilton. Residents and visitors to the area are urged to ensure that they are fully immunised against measles.

7. Ebola – Liberia

On 9 June 2016, Liberia passed the 42-day mark after the most recent confirmed Ebola patient tested negative for the second time. The country is now within the 90-day increased surveillance period. This is the 4th time Liberia has been declared Ebola-free. Guinea and Sierra Leone are within their 90-day increased surveillance period: Guinea since 1 June 2016, and Sierra Leone since March.

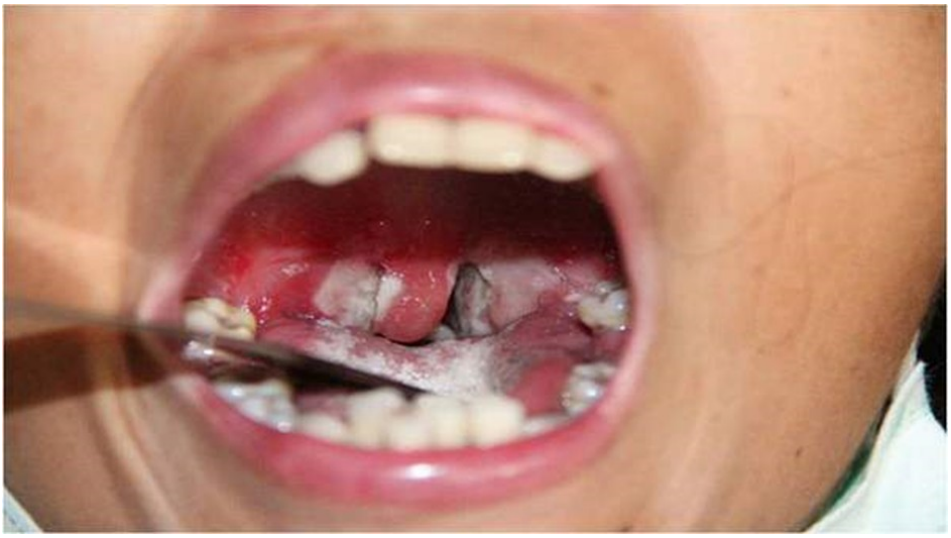
8. Yellow fever – see zoonotic and vector-borne diseases section

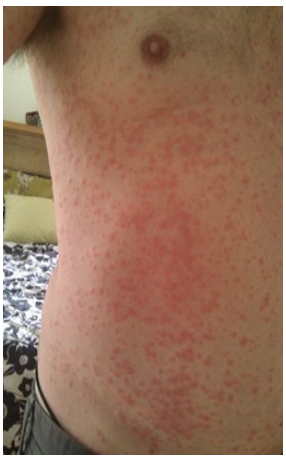
9. Zika virus – see zoonotic and vector-borne diseases section

Source: Division of Public Health Surveillance and Response, NICD-NHLS; (outbreak@nicd.ac.za)

Figure 9. Current outbreaks that may have implications for travellers. Number correspond to text above. The red dot is the approximate location of the outbreak or event

7 PHOTOQUIZ





June Photoquiz (above left)
This 9-year-old boy complained of a sore throat, fever and swelling of the neck for 4 days. What is your differential diagnosis? Please supply your answers in an email to kerriganm@nicd.ac.za with 'June Photoquiz' the subject line.

May photoquiz (above right)
The macular-papular rash illustrated below is typical of a Zika infection; one would also look for conjunctivitis, and ask for a history of althralgia. However the differential diagnosis is broad. In this case, the travel history is helpful: until April 15 2016, Belize was the only central American country that had not reported local transmission of Zika virus. The virus was first reported in an American traveller, diagnosed with Zika on returning to USA. The first case in a local resident was identified on May 16 2016. (Photo courtesy www.google.co.za)