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 Update on rabies in South Africa

The National Institute for Communicable Diseases confirmed the diagnosis of rabies in a six-year-old girl from Clocolan in the eastern Free State Province on 20 July 2016. She presented with symptoms in keeping with rabies and passed away on 19 July at a Bloemfontein hospital. Neither the patient prior to her death, nor her family, reported or recalled exposure to a suspected rabid animal. However, rabies is endemic in South Africa amongst dogs, jackals and mongooses, and can be transmitted from infected animals to humans through minor, seemingly harmless exposures to rabid animals. Scratches to the skin, or licks of mucous membranes such as the eyes or nose, may constitute an exposure. Sequencing of the patient sample identified the rabies virus as canid biotype. It is therefore most likely that the infection was contracted from a rabid dog, cat or other domestic animal. This is the second human case reported for South Africa for 2016 to date. The first case was diagnosed in KwaZulu-Natal Province in January 2016.

A countrywide shortage of human rabies immunoglobulin (or HRIG) has been reported since May 2016. As the shortage is expected to last several months, provision has been made for the emergency importation of equine-derived rabies immunoglobulin (or ERIG) under Section 21 licensing. The indication for the use of ERIG is the same as for HRIG, i.e. category 3 rabies virus exposures. The dosage of ERIG is 40 IU/kg (versus 20 IU/kg for HRIG) and it is important to observe recipients of the product for at least 30 minutes due to very small risk (1 in 150,000 administrations) of anaphylactic shock. More information about ERIG and rabies post-exposure prophylaxis can be obtained from the guidelines section of the NICD website (http://www.nicd.ac.za/?page=guidelines&id=73).

Since 16 April to 7 July 2016, rabies has been confirmed in 10 jackals, 4 cattle, 2 dogs and 1 honey badger in Gauteng Province by Gauteng Veterinary Services and Agriculture Research Council - Onderstepoort Veterinary Institute. Although sporadic cases of rabies are reported from Gauteng Province historically, the spike in the jackal cases in the past two months is concerning. Efforts to vaccinate pets in the affected areas have been ongoing and pet owners are reminded that they are responsible to ensure that their cats and dogs are vaccinated for rabies according to the required schedule.

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

b The yellow fever outbreak in Angola and Democratic Republic of Congo

An epidemic of yellow fever (YF) is ongoing in Angola since January 2016. Laboratory investigation of suspected cases of viral haemorrhagic fever from Angola indicated that the outbreak was already in progress in December 2015. Despite intense mass vaccination efforts, human cases of YF are still being reported. In Angola, a cumulative total of 3552 suspected cases has been reported up to 1 July 2016 (Figure 1). The total includes 875 confirmed cases and 355 deaths (case-fatality rate of 10%). Confirmed cases have been reported from 16 of the 18 provinces with the majority from Luanda Province (487; 55.7%).

Since March 2016, a total of 1307 suspected cases of YF has been reported from the Democratic Republic of Congo (DRC). Clear epidemiological information from the outbreak is not yet available. Many cases have a travel history to Angola, but autochthonous transmission is likely as the provinces proximate to Angola seem to be affected. A number of cases may have been acquired in the city of Kinshasa, which is of concern because of the its dense population of about ten million.

Due to the massive uptake of YF vaccine in a short period of time, vaccine shortages are being reported. More than 10 million people residing in Angola (40% of the population) have been vaccinated as of 10 June 2016. Dose-sparing has been recommended by the World Health Organization to balance supply with demand. Dose-sparing entails administration of 1/5th of a dose per immunization. Currently, the dose-sparing regimen is only in effect in outbreak zones and does not effect travel-related vaccination.

Several cases of YF in travellers have been re-

ported in Kenya and the People's Republic of China. No cases of YF have been diagnosed in returning travellers to South Africa to date. Seven countries (Brazil, Chad, Colombia, Ghana, Guinea, Peru and Uganda) are currently reporting YF outbreaks or sporadic cases that are not linked to the Angolan outbreak.

Vaccination of travellers to YF endemic countries is required by international regulations. Travellers are required to be vaccinated at least 10 days before travel in order to develop protective immunity before their trips. Selected groups are exempted from YF vaccination, including infants less than 9 months of age, pregnant or otherwise immunocompromised individuals. For more advise in this regard please consult your travel clinic.

For more information, please visit:
(WHO YF situation report) or http://wwwnc.cdc.gov/travel/notices/watch/yellow-fever-democratic-republic-of-the-congo (Centers for Disease Control and Prevention).

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

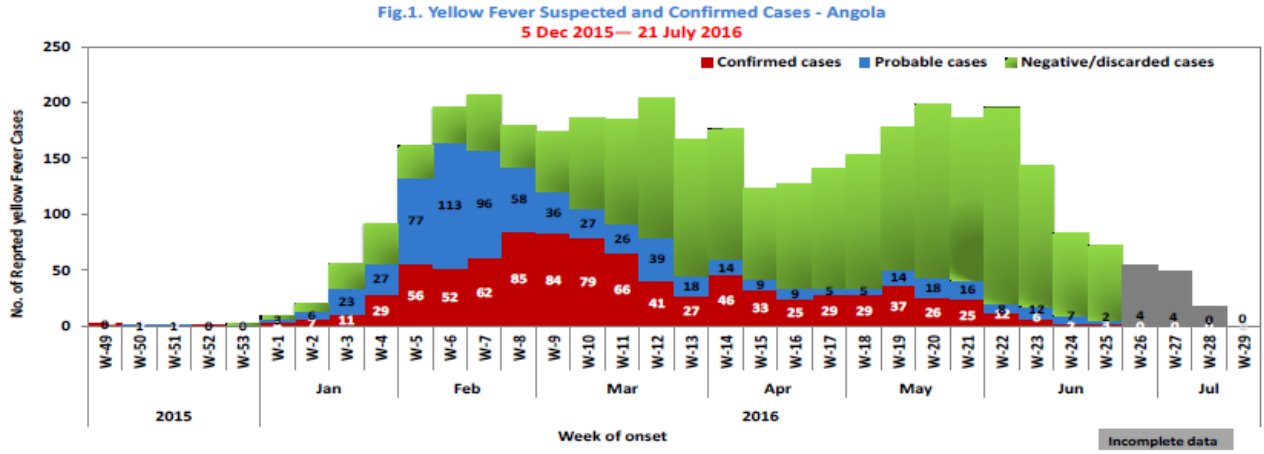


Figure 1. Epidemic curve of confirmed and suspected yellow fever cases in Angola as of 24 July 2016. Source: Yellow fever outbreak situation report 6 June 2016, incident management team, Ministry of Health Angola. http://www.afro.who.int/en/yellow-fever/sitreps/item/8856-situation-report-yellow-fever-outbreak-in-angola-24-july-2016.html

c Zika virus update

Two confirmed cases of Zika virus disease (ZVD) were detected in South African travellers by the National Institute for Communicable Diseases in June 2016:

1. A non-pregnant 43-year-old female from Durban, KwaZulu-Natal Province had travelled to Panama for ten days. Upon returning to South Africa she developed a flu-like illness with documented fever. A blood sample collected on day four after illness onset tested positive for Zika by RT-PCR.
2. A 50-year-old male travelled to the Venezuelan capital, Caracas. Upon returning the patient developed a fever, sore throat and shoulder pain. A blood sample collected on day four after onset tested positive by Zika RT-PCR. Confirmatory serological testing on convalescent blood samples from both patients are pending submission of follow-up specimens.

As of 13 July 2016 62 countries and territories have reported evidence of mosquito-borne Zika virus (ZIKV) transmission to the World Health Organization since 2015. Eleven countries have reported human-to-human transmission likely by the sexual route. A total of 13 countries has reported microcephaly and other central nervous system malformations potentially associated with ZIKV infection. The WHO states that, based on the research to date there is scientific consensus that ZIKV infection is a cause of microcephaly and Guillain-Barré syndrome.

South African travellers to the Olympic Games in Brazil 2016 should follow the advice given in the June 2016 edition of the NICD Communiqué. The NICD offers the following tests for ZVD: 1) RT-PCR testing (clotted blood/serum) and 2) virus culture (clotted blood/serum), which are both useful dur-

ing the transient viraemic stage of infection (1 – 5 days post-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. Interpretation of serology results 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 as such 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.

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

2 SEASONAL DISEASES

a The influenza season, South Africa, 2016

The 2016 influenza season that started in week 19 (the week starting 09 May 2016), continues. To date (21 July 2016) influenza has been detected in 400/3406 individuals tested for influenza from 3 surveillance programmes carried out by the NICD. Influenza B accounts for the majority of these detections i.e. 316/400 (79.0%), influenza A(H1N1) pdm09 for 21/400(5.3%), and influenza A(H3N2) for 63/400 (15.8%).

Although influenza B still accounts for the majority of influenza detections, the percentage of influenza B detections has declined from 100% in April to 60.7% in July. At the same time the percentage of influenza A(H3N2) detections has risen from 5.5% in May to 30.3% in July (to date).

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

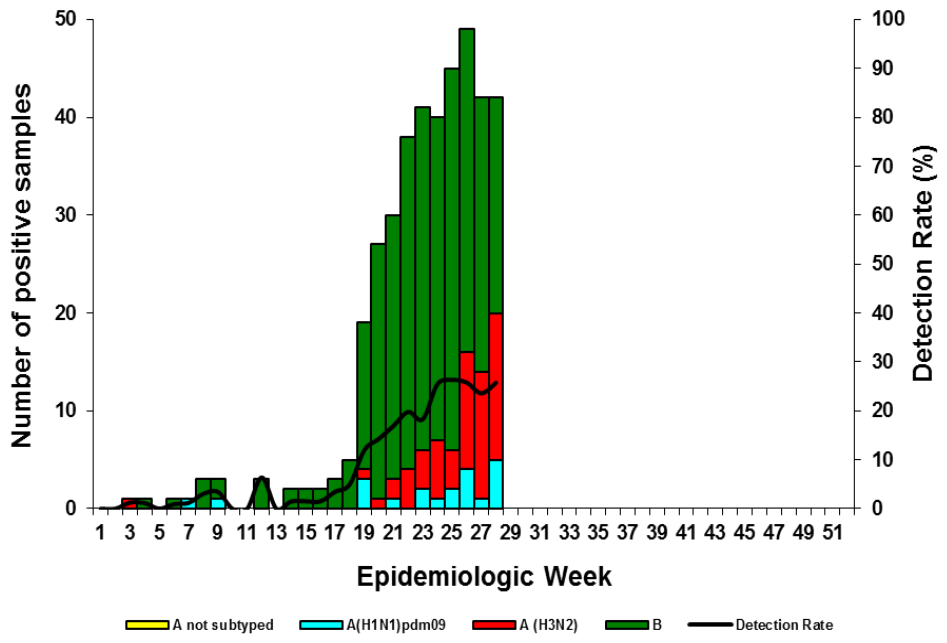


Figure 2. The number of positive influenza results by type and subtype, and the corresponding detection rate by epidemiological week of the year, according to data obtained from influenza-like illness (viral watch and public health clinics) and pneumonia surveillance programmes, 2016.

3 VACCINE-PREVENTABLE DISEASES

a A case of *Haemophilus influenzae* meningitis, and review of surveillance records

In the month of July, a one-year-old infant was admitted to a hospital in the Amajuba district, KwaZulu-Natal Province, with *Haemophilus influenzae* type b (Hib) meningitis. The infant was HIV-unexposed and had missed the 14 week and 9 month routine immunisations. The infant presented with gastroenteritis and signs and symptoms suggestive of bronchopneumonia. The clinician called the NICD hotline to enquire if post-exposure prophylaxis is required for contacts of the child.

Haemophilus influenzae is an aerobic, Gram-negative bacterium that can cause severe illness. Unimmunised children younger than 5 years of age are at an increased risk of contracting Hib, and patients with underlying chronic conditions such as HIV, asplenia, sickle cell disease, radiation therapy/ haemopoeitic stem cell transplants for malignant neoplasms, are at particular risk for invasive disease. The organism enters the body through the nasopharynx where organisms colonise, and may remain only transiently or for several months in the absence of symptoms, in so-called asymptomatic carriers. Hib-related mortality is mainly attributed to meningitis and pneumonia, the most severe clinical syndromes, but invasive disease may also present as epiglottitis, osteomyelitis, septic arthritis, septicaemia, cellulitis and pericarditis. Most Hib disease occurs in young children.

Following the introduction in 1999 of the Hib vaccine into the South African Expanded Programme on Immunisation (EPI), at 6, 10 and 14 weeks of age, there was a significant decrease in the number of cases of invasive Hib disease in young children, especially infants. Following concerns regarding some increases in Hib disease a few years after vaccine introduction, a booster Hib dose was added to the vaccine schedule at 18 months.

In 2015, a total of 322 laboratory-confirmed invasive *H. influenzae* cases was identified by the NICD surveillance system. In children <5 years of age only 21% (17/82) of disease was due to Hib and 65% (11/17) of these children had not received two or more doses of Hib vaccine at the time of admission. Of the remaining 6 children, 5 had underlying medical conditions.

Following confirmation of invasive illness due to *influenzae* type b, post-exposure prophylaxis (PEP) is required for all household contacts who are less than 10 years of age, or who are pregnant, or immunocompromised or asplenic. Rifampicin 20mg/ kg (max 600mg) once daily for 4 days - for children >3months and adults, or 10mg/kg once daily for 4 days for children <3 months, should be given. In addition, children <10 years should be vaccinated against Hib if not already, and other vaccinations should be updated.

It is vital for clinicians to ensure that children receive all appropriate vaccine doses, and continue to report all cases of Hib. We also encourage all microbiology laboratories to report cases to the NICD and send isolates or specimens for identification and serotyping as part of ongoing national surveillance.

Source: Centre for Respiratory Disease and Meningitis, NICD-NHLS (annev@nicd.ac.za); Division of Public Health Surveillance and Response, NICD-NHLS (outbreak@nicd.ac.za)

b Rotavirus season 2016

The NICD conducts hospital-based surveillance for rotavirus diarrhoea at a number of sentinel sites distributed across all South African provinces. The rotavirus season for 2016 has begun, with a detection rate of 33% (4 positive/12 stool specimens) in epidemiological week 24 (commencing 13 June 2016)and a detection rate of 25% (1 positive/4 stool specimens) in week 25 (Figure 3). The start of the rotavirus season is defined as rotavirus detection rate of >20% for two consecutive weeks and the end as rotavirus detection rate <20% for two consecutive weeks. In 2015, the rotavirus season started in week 20 (commencing 11 May 2015) with a detection rate of 24% (4/13) and a detection rate of 22% (6/23) in week 21. The 2015 rotavirus season ended in week 39 (27 September).

For epidemiological weeks 1-27, the numbers of stools testing positive for rotavirus has been signifi-

cantly lower in 2016 (4.4%; 17/388) compared to 2015 (16.7%; 66/395). This may be partially due to the late start to the rotavirus season (week 20 in 2015 versus week 24 in 2016). Healthcare providers are reminded to encourage vaccination of all children with the rotavirus vaccine at 6 and 14 weeks of age and to ensure adequate supplies of oral rehydration solution during the rotavirus season.

Source: Centre for Enteric Diseases, NICD-NHLS; (nicolap@nicd.ac.za)

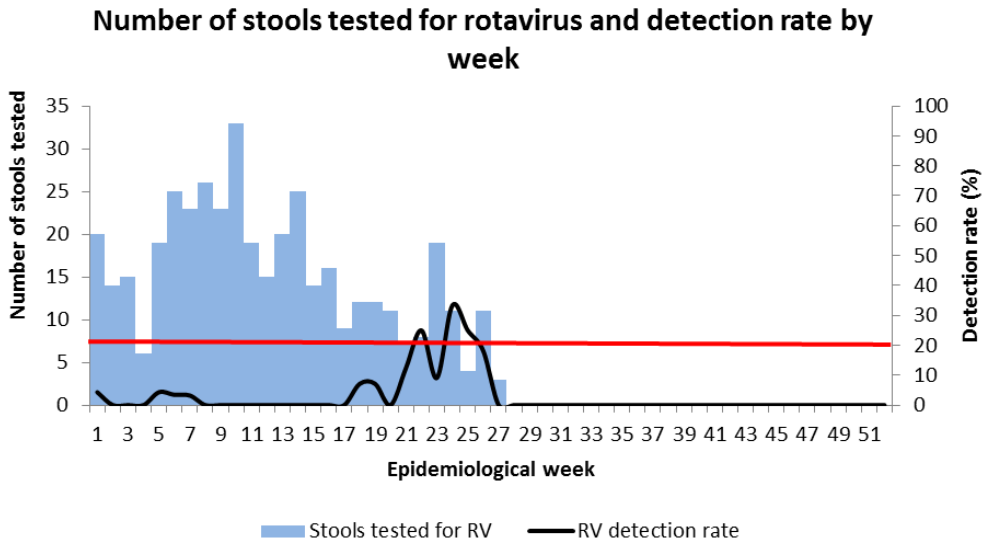


Figure 3. The rotavirus detection rate and the numbers of specimens tested by week for 10 sentinel surveillance sites in South Africa.

4 TUBERCULOSIS

a Results of the 2012-2014 tuberculosis drug resistance survey

The second South African Tuberculosis Drug Resistance Survey (2012-2014) was undertaken by the NICD to determine the prevalence of MDR-TB and other types of drug-resistant TB in all nine South African provinces, and to assess changes relative to the previous survey conducted in 2001-2. The survey enrolled participants in 442 randomly selected health facilities across the country with just over 200 000 people screened. Findings were recently reported by NICD and are available at www.nicd.ac.za.

The current survey confirmed that the prevalence of multidrug-resistant TB (MDR-TB) is stable (2.8% of all TB cases) compared to the previous survey conducted in 2001-2 (2.9%) and is lower relative to that reported globally (7.7% of all TB cases. Although MDR-TB has remained stable nationally, there has been an almost doubling of resistance to rifampicin (1.8% to 3.4%), the main drug for TB treatment, in patients without any previous history of TB treatment. Provincial variation of MDR-TB prevalence was observed, with the highest prevalence observed in Mpumalanga (5.1%), which was also the case in the previous survey. Among those with MDR-TB, 1 in 20 had extensively drug-resistant TB (XDR-TB), which is an even more resistant type of TB.

The NICD is currently undertaking further analyses and additional investigations to inform the TB control programme of risk factors for MDR-TB, including a mapping of hotspot areas for drug-resistant TB, and appropriate control interventions. Early diagnosis and treatment is still the mainstay of TB control and preventing MDR-TB. South Africa has introduced the latest technology (Gene Xpert) that can rapidly detect drug resistance; utilization needs to be closely monitored and diagnosed patients need to be started on treatment as quickly as possible. The findings of this survey and additional analyses currently underway will help inform the allocation of resources and expertise to respond to the TB epidemic.

Source: Centre for Tuberculosis, NICD-NHLS; (naziri@nicd.ac.za)

5 SURVEILLANCE FOR ANTIMICROBIAL RESISTANCE

a *Candida auris* — a global alert

Government agencies in the United States of America and United Kingdom have recently issued alerts for an emerging fungal 'superbug', *Candida auris*.

- Public Health England (UK): https://www.gov.uk/government/collections/candida-auris
- Centers for Disease Control and Prevention (US): http://www.cdc.gov/fungal/diseases/candidiasis/candida-auris-alert.html

Reasons for the global alert and recommendation to the South African laboratories and clinicians are listed below:

***C. auris* is difficult to identify in the routine laboratory** using biochemical methods (including automated systems). Vitek 2 YST and VITEK Mass Spectrometry (MS) (BioMérieux) misidentify this as *Candida haemulonii*, API systems (BioMérieux) as *Rhodotorula glutinis* and Auxacolor (Bio-Rad) as *Saccharomyces cerevisiae*. The identification of this pathogen can be confirmed currently using the Bruker MS or molecular methods. Suspect *C. auris* in the laboratory if a cream-coloured yeast-like colony is identified as *C. haemulonii, S. cerevisiae, R. glutinis, Candida sake* or *Candida famata*.

***C. auris* is multidrug resistant**. Almost all isolates are resistant to fluconazole (almost uniformly high minimum inhibitory concentrations (MICs)) and a large proportion are resistant to voriconazole. In other regions, amphotericin B and echinocandin resistance has been seen. As there are no agreed-upon interpretive breakpoints for *C. auris* and any antifungal agent, it may be helpful to refer any isolates with high echinocandin or amphotericin B MICs to the NICD for confirmation. The first-line agent for the treatment of invasive *Candida* infections should ideally be an echinocandin (i.e. caspofungin, micafungin or anidulafungin) but amphotericin B is more easily accessible in the public sector. No amphotericin B resistance has been confirmed in SA to date.

***C. auris* is already endemic in Gauteng Province**. *C. auris* has emerged as a common pathogen in the private sector (hundreds of cases since 2013) and in a few public-sector facilities in Gauteng. A few cases have been identified in neighbouring provinces. Urine, central venous catheter tips and blood cultures are among the most common specimens from which *C. auris* has been isolated in South Africa.

Nosocomial transmission of *C. auris* is likely. Person-to-person transmission is very likely based on findings from molecular epidemiology studies. Contact precautions and terminal environmental decontamination is recommended where feasible. Screening of patients for colonisation has been recommended in high-income countries where cases have not yet been detected, but this may not be feasible or appropriate in SA. Local epidemiologic studies to determine risk factors for *C. auris* invasive infection and patient outcomes are currently underway.

Diagnostic laboratories are requested to continue to send all bloodstream isolates to the NICD as part of routine GERMS-SA candidaemia surveillance. Please contact the Centre for Opportunistic, Tropical and Hospital Infections directly for assistance with identification of any suspicious non-sterile site isolates.

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

b 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 have 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. 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 June 2016, a total of 108 Enterobacteriaceae isolates was received. Seventy-nine isolates were screened, 73 of which expressed carbapenemases (Table 1). Majority of the isolates were *Klebsiella pneumoniae* (44) followed by *Enterobacter cloacae* (12).

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.

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

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

Organism	NDM		OXA-48 & Variants		VIM	
	Jan-May 2016	June 2016	Jan-May 2016	June 2016	Jan-May 2016	June 2016
Citrobacter spp.	5	1	2	1	-	-
Enterobacter aerogenes	-	1	5	1	-	-
Enterobacter cloacae	16	4	19	4	-	-
Enterobacter kobei		1	1		-	-
Escherichia coli	5	2	35	4	-	-
Klebsiella pneumoniae	149	15	170	21	6	1
Providencia rettgeri	9	2	-	-	-	-
Serratia marcescens	17	8	1	9	-	-
Total	**201**	**26**	**233**	**40**	**6**	**1**

NDM: New Delhi metallo-beta-lactamase; **OXA**: oxacillinase; **VIM**: Verona integron-encoded metallo-beta-lactamase.

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 4 on page 9.

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

On 5 July 2016, one fatal case caused by H7N9 influenza was reported in northeast China. A 67-year-old man had become feverish after he butchered a chicken at his home; he was admitted to hospital shortly afterwards and deteriorated.

China has reported 11 laboratory-confirmed cases of human infection with avian influenza A (H7N9) virus this year, 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 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

As of 22 Jul 2016, Saudi Arabia has reported a total of 1440 laboratory-confirmed cases of MERS-CoV infection, including 606 deaths (reported case fatality rate 42.1%). To date, 829 persons have recovered. There are currently 5 active cases. 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 and Malaysia

India: Between 15 June to 12 July, 2 fatal cases and 32 confirmed cases were identified. In Malaysia and as of 6 July 2016, there have been 14

confirmed cases of diphtheria. Prevention of diphtheria is achieved through vaccination.

4. Japanese encephalitis – Vietnam
Between 23 June to 1 July 2016, 9 cases were confirmed in the Vietnamese city of Hanoi.

5. Measles – New Zealand, USA and UK
Both the UK and the USA have issued warnings about potential measles outbreaks. In both countries isolated cases have escalated into clusters, apparently amongst people refusing vaccination. In the UK, in the south Devon town of Totnes, 15 children at a high school were diagnosed with confirmed measles. In the USA, a cluster of cases in a detention centre has been linked to officials who refused to show proof of vaccination. In New Zealand, since April 2016, 60 confirmed measles cases were reported, mostly linked to the town of Hamilton. Residents and visitors to the area are urged to ensure that they are fully immunised against measles.

6. Ebola – Liberia, Guinea and Sierra Leone
There continue to be no further reported cases of Ebola in these three countries. Sierra Leone issued a request that persons continue to notify the authorities of all deaths, and that deaths meeting certain criteria will continue to be tested.

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

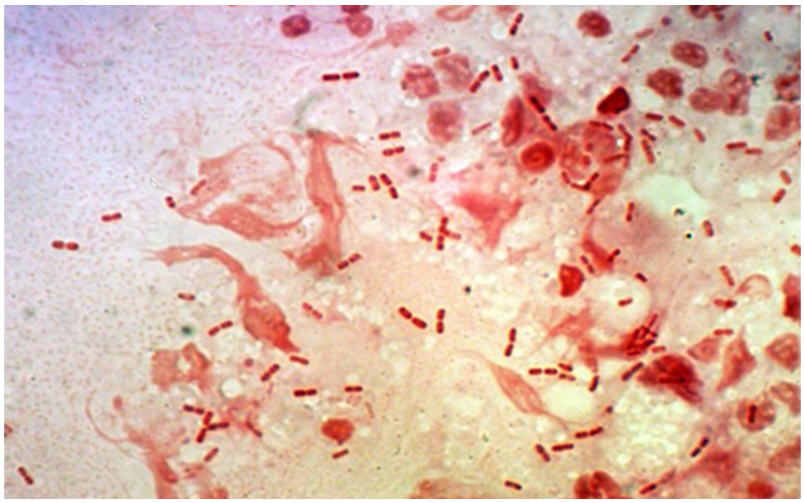
8. Zika virus – see zoonotic and vector-borne

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

Figure 4. 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

July Photoquiz (right)
This eight-month-old infant presented with floppiness, hypothermia and failure to feed. A lumbar puncture was done, and a photograph of the Gram's stain of CSF is shown. What is the likely cause of this infant's condition? Please supply your answers in an email to kerriganm@nicd.ac.za with 'July Photoquiz' the subject line.



June photoquiz (left)
This 9-year-old boy was complaining of a sore throat, fever and swelling of the neck for 4 days. The differential diagnosis was diphtheria (*Corynebacterium diphtheriae*), streptococcal pharyngitis (*Group* A streptococci), oral thrush (*Candida* spp.), or pharyngitis due to *Arcanobacterium haemolyticum*, or Epstein-Barr virus. Diphtheria is distinctive as the white patches are actually necrotic tissue, and are adherent to the pharynx, while with other causes, the white patches are pus or fungal growth. (Photo courtesy https://www.bestonlinemd.com/how-to-avoid-getting-diphtheria/)