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

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CONTENTS

1 VACCINE-PREVENTABLE DISEASES

a Diphtheria

Update on the outbreak in KwaZulu-Natal Province

The outbreak of diphtheria in KZN is ongoing, with a number of additional cases being reported since the last Communique (May 2015). During the past month, a new category, i.e. 'possible case', was included in the case definition. A possible case is defined as "A person who meets the clinical case definition for respiratory diphtheria and has no epidemiological link to a laboratory-confirmed case." This definition is to accommodate for cases where the clinical presentation is typical of diphtheria, but swabs are negative for *C. diphtheriae.* A negative swab does not conclusively rule out diphtheria s the organism may not be detected if the specimen or specimen transport is inadequate, or the specimen is not processed correctly. Presently there are 15 cases (10 confirmed, 2 probable, 3 possible and none under investigation) and 3 asymptomatic carriers of laboratory-confirmed toxigenic *C. diphtheriae*. Two carriers are epidemiologically linked to two confirmed cases from Margate (all siblings from the same family). One carrier is epidemiologically linked to a possible case from Umlazi. Three persons under investigation were found to have alternative causes of membranous pharyngitis, namely *Arcanobacterium haemolyticum* and Group A streptococcus (2 cases). To date, diphtheria case-patients have been reported from two (Ethekwini and Ugu) of the 11 districts in KwaZulu-Natal Province. Cases range in age from 4 to 41 years (median 10 years). Children aged <15 years accounted for 73% (11/15) of the cases, with 40% (6/15) occurring in those aged 5 to 9 years. Males accounted for 60% (9/15) of cases. Amongst cases ≤22 years old (n=13), vaccination history is known for 38% (5/13) of the cases. Of these (n=5), only a patient aged 11 years with probable diphtheria, had received all age-appropriate diphtheria-containing vaccine doses. He had presented with pharyngitis, a bull-neck and fever, and his throat swab grew *C. diphtheriae* which was negative for toxin production by ELEK test. Further laboratory tests are being conducted on the isolate. Figure 1 illustrates diphtheria cases by date of onset of illness and district as at 19 June 2015.

The KZN Department of Health, University of Kwa-Zulu Natal and NICD together with a consultant from the WHO are reviewing the epidemic to determine the appropriate next steps, both locally in terms of preventive efforts and nationally, in terms of understanding factors contributing to the epidemic.

Source: Division of Public Health Surveillance and Response, NICD-NHLS; Microbiology Laboratory, NHLS KwaZulu-Natal Academic Complex; Diagnostic Media Production Laboratory, NHLS Green Point Complex; Clinicians at hospitals in eThekwini and Ugu Districts, KwaZulu-Natal Province; KwaZulu-Natal Province Department of Health; eThekwini Municipality; Ugu District Department of Health, University of Pretoria, Zoonotic Diseases Division.

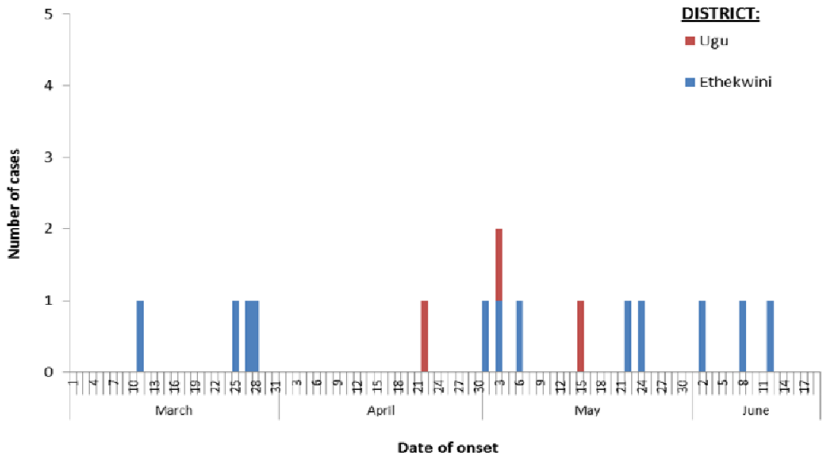


Figure 1. Epidemic curve illustrating the number of diphtheria cases by date of illness onset and district, KwaZulu-Natal Province, March to 19 June 2015

b Measles

The Centre for Vaccines and Immunology at the National Institute for Communicable Diseases (NICD) reported three confirmed measles cases from the Cape Town Metropolitan District in the Western Cape Province, after being alerted by Pathcare private laboratory who had tested the original samples. Two of the cases, a 17-year-old female and a 52-year-old male, presented at an oncology unit of a private hospital and the third case is a 47-year-old male who was a close contact of one of the cases. The diagnosis was made by PCR on clinical specimens, as the index patient was immunocompromised and never mounted an immune response with IgM antibody. Nosocomial transmission most likely accounted for these cases. The source is yet to be determined. A fourth measles case, from the West Coast District of the Western Cape Province, was confirmed and is not linked epidemiologically to the three cases described above. Since the beginning of 2015, there have been a total of nine laboratory-confirmed measles cases in South Africa, with onset of symptoms between the 1st of January and the 11th of June. The cases are from the Eastern Cape, Northern Cape, North West and Western Cape provinces, with ages ranging from 5 months to 52 years.

Molecular testing was conducted by CVI using specimens obtained from the two oncology patients, both of whom demised. This revealed that both were infected with a genotype D8 strain of the measles virus. This genotype is currently circulating in Europe, Australia, Brazil, North America and Asia. It is different from the genotype B3 that caused the recent measles outbreak at the end of 2014 in the Northern Cape and Gauteng provinces.

Measles is one of the most contagious viral infections and causes significant morbidity and mortality worldwide. The occurrence of an outbreak at the end of 2014 in South Africa, coupled with measles outbreaks in other parts of the world, including the USA and Europe, is a reminder for all health care professionals to be vigilant. All suspected cases (any patient with fever, rash, and either cough, coryza or conjunctivitis) should have a blood sample sent for testing at the NICD along with a case investigation form and should be notified prior to blood results being available. Measles is prevented by vaccination with a live attenuated vaccine strain, which is routinely given at 9 months and 18 months according to the South African Expanded Program for Immunization schedule, or to older children and adults during mass vaccination campaigns. Severely immune compromised patients (such as people on prolonged corticosteroids at high doses, organ transplant recipients on immunosuppressive treatment or oncology patients on chemotherapy), should not receive measles vaccine. Protection of such patients against measles is achieved by administration of immunoglobulin and vaccination of contacts and staff of health facilities.

Nosocomial transmission of measles is well described, therefore control measures in response to the cases from the Western Cape described above included vaccination of health care workers and administration of human immunoglobulin (prepared from pooled human serum) to at least two exposed oncology patients. Concern was raised by staff at the oncology facility regarding the risk of transmission of vaccine strain to oncology patients, as vaccine-strain-virus is occasionally shed from immunocompetent recipients post-vaccination. A careful literature search and correspondence with international measles experts revealed no case reports of measles attributable to transmission from a vaccine recipient, and consensus is that this is exceedingly unlikely to occur. Therefore vaccination of immunocompetent staff in an oncology ward represents no risk to patients.

Source: Centre for Vaccines and Immunology, NICD; Pathcare, Western Cape; Western Cape Department of Health; Outbreak Response Unit, NICD.

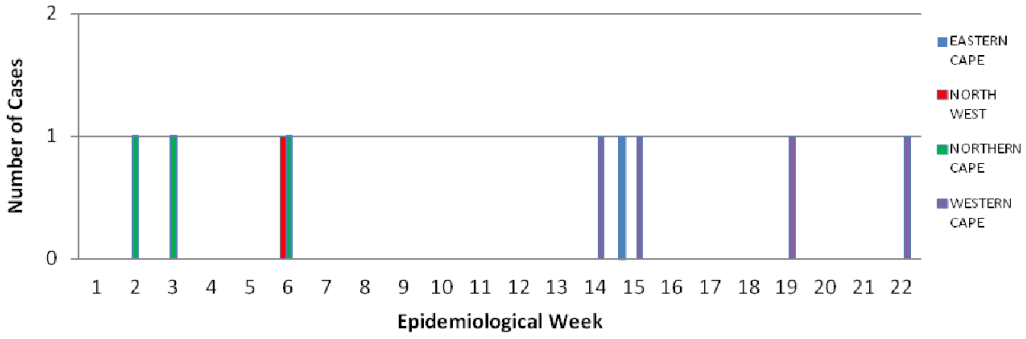


Figure 2. Cases of measles in South Africa with laboratory confirmation reported by Centre for Vaccines and Immunology, NICD, from weeks 1 to 22 (June 11th), 2015

c Pertussis

Increased detection of *Bordetella pertussis* in the pneumonia and influenza-like illness surveillance programmes

Introduction

Worldwide, pertussis is an increasingly recognised disease even in countries with high vaccination coverage rates. This increase in disease may be attributed to waning immunity and to the absence of widespread community-level circulation of the organism which may have boosted immunity in the community. In addition there is increasing recognition of the importance of pertussis not only in infants (among whom severe morbidity and mortality risks are highest), but also in adolescents and adults who usually present with atypical clinical manifestations of pertussis and so contribute to a reservoir of infection for younger children. Although it is a notifiable condition in South Africa, there are few data on the seasonality or periodicity of pertussis in South Africa. Available data suggest that there is an annual peak of pertussis detection in the winter months, although the timing of this peak varies year on year. Data also suggest a periodicity of three years, with a higher number of cases every three years. This is comparable to other countries, for example the United States where peaks in disease are seen every 3-5 years.

Methodology

The National Institute for Communicable Diseases (NICD) has been conducting active, prospective, hospital-based sentinel surveillance for severe acute respiratory illness (SARI) since February 2009. In 2012, the surveillance was further expanded at the two enhanced surveillance sites (Edendale and Klerksdorp-Tshepong Hospital Complex (KTHC)) to include expanded testing of specimens (naso- and oropharyngeal swabs and aspirates) for additional pathogens and collection of additional specimens (induced sputum and oral washes) from patients with severe respiratory illness (SRI). Also in 2012, the NICD initiated a programme of systematic influenza-like illness (ILI) surveillance at public health clinics. Two primary health care clinics serviced by the two enhanced SRI surveillance sites (Edendale Gateway clinic and Jouberton Clinic in Klerksdorp) commenced systematically enrolling patients with ILI. All patients are enrolled based on a clinical case definition of SARI and ILI respectively (1). These programmes have been described previously (7).

Results

A total of 152 cases of pertussis have been identified in the surveillance programme. (April 2012 to May 2015). In 2012 and 2014 the peak months were July and August (detection rates between 3% and 6%) but in 2013 the peak was later in the year (November, peak detection rate 6%). The detection rate in 2015 has been above 2% since January 2015 (Figure 3). Cases were identified in individuals of all age groups, except for the >65 year age group where no cases have been detected to date. The highest detection rate is in the under-3-months of age group. (Figure 4).

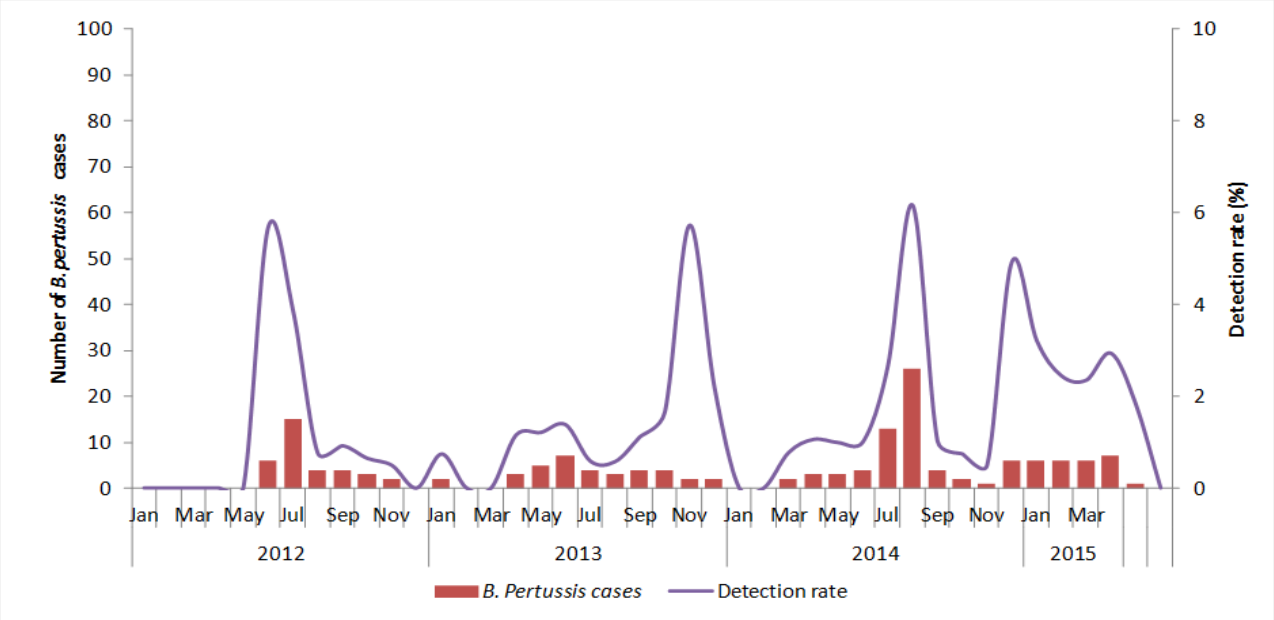


Figure 3. Number of cases of *B. pertussis* by month, year and detection rate, South Africa 2012 to 2015

Cases were detected at both surveillance sites and the majority of cases were SARI/SRI patients (62%, 104/168) while 28% of patients had influenza-like illnesses (ILI) (48/168).

Conclusion

Our surveillance suggests that the number of pertussis cases may be increasing in 2015, as the detection rate has remained above 2% between January and April in 2015. It is too early to comment on whether this increase is part of the expected periodicity of pertussis infections or whether it is independent of periodicity. We encourage healthcare workers throughout South Africa to familiarise themselves with the broad clinical presentation of pertussis and conside the diagnosis in patients meeting the case definition.

Pertussis case definition

In the absence of a more likely diagnosis, a cough illness lasting≥2 weeks, with at least one of the following signs or symptoms:

- Paroxysms of coughing; OR
- Inspiratory whoop; OR
- Post-tussive vomiting; OR
- Apnoea (with or without cyanosis) (for infants only)

In infants the definition may be applied to acute illness of any duration.

The diagnosis of pertussis should be considered in persons of all ages and in all infants with apnoea. It is essential for healthcare workers to familiarise themselves with patient treatment, infection prevention and control, and post-exposure prophylaxis recommendations (available on the NICD website at http://www.nicd.ac.za/?page=guidelines&id=73)

The SARI and ILI programmes will continue to describe the detection of pertussis in South Africa. Ongoing systematic collection of surveillance data will be helpful to monitor future trends.

Source: Centre for Respiratory Diseases and Meningitis, NICD-NHLS

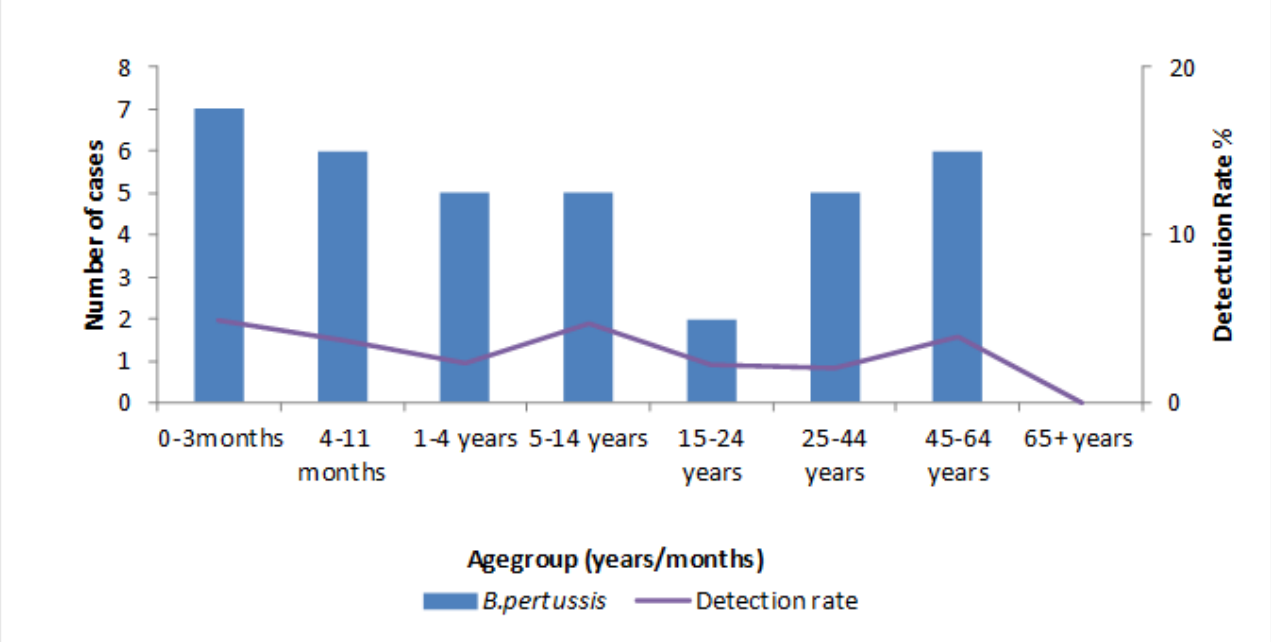


Figure 4. Number of *B. pertussis* cases by age group and detection rate, South Africa 2012 to 2015

2 SEASONAL DISEASES

a Influenza

Influenza data from Viral Watch
The influenza season that started in epidemiologic week 19 (week ending 10 May) continues. The number of specimens submitted by Viral Watch sites have continued to increase and have risen to an average of 75 per week during the last week of May and the first two weeks of June.

To date (10 June), influenza has been detected in 200/440 (45%) of specimens submitted by Viral Watch sites. Influenza A (untyped as yet) has been detected in one patient, influenza A(H1N1)pdm09 in 112, influenza A(H3N2) in 77, and influenza B virus in 10 patients (Figure 5). In addition, 27 specimens have been received from patients at a point of entry into South Africa; influenza was detected in 17 of these patients. So far, the predominant strain circulating in 2015 is the influenza A (H1N1)pdm09, which has been one of the influenza strains circulating every year, since 2010.

Influenza data from national syndromic surveillance for pneumonia programme
From 01 January to 10 June, 1494 specimens from patients admitted with severe respiratory illness were tested from the six sentinel sites in the national syndromic surveillance for pneumonia programme. Influenza A(H1N1)pdm09 was detected in 23, influenza A(H3N2) in 27, influenza A (untyped as yet) in two and influenza B in six of these specimens. In addition, other respiratory viruses were detected in specimens of 561 patients; respiratory syncitial virus (257/561, 46%) accounted for the majority followed by rhinovirus (199/561, 35%).

Recommendations
Although the influenza season is well underway it is not too late to vaccinate for influenza. Healthcare workers are encouraged to vaccinate individuals in the groups that are targeted for influenza vaccination; this includes, among others, pregnant women at any stage of pregnancy, and those vulnerable due to underlying medical conditions or risk factors. Recommendations on target groups, dosages and contraindications for the 2015 influenza vaccine, and influenza antiviral treatment are available in the Healthcare Workers Handbook on influenza 2015, which can be accessed at: http://www.nicd.ac.za/assets/files/Healthcare%20Workers%20Handbook%20on%20influenza%20in%20SA_%205%20May%202015.pdf.

Source: Centre for Respiratory Diseases and Meningitis, NICD-NHLS

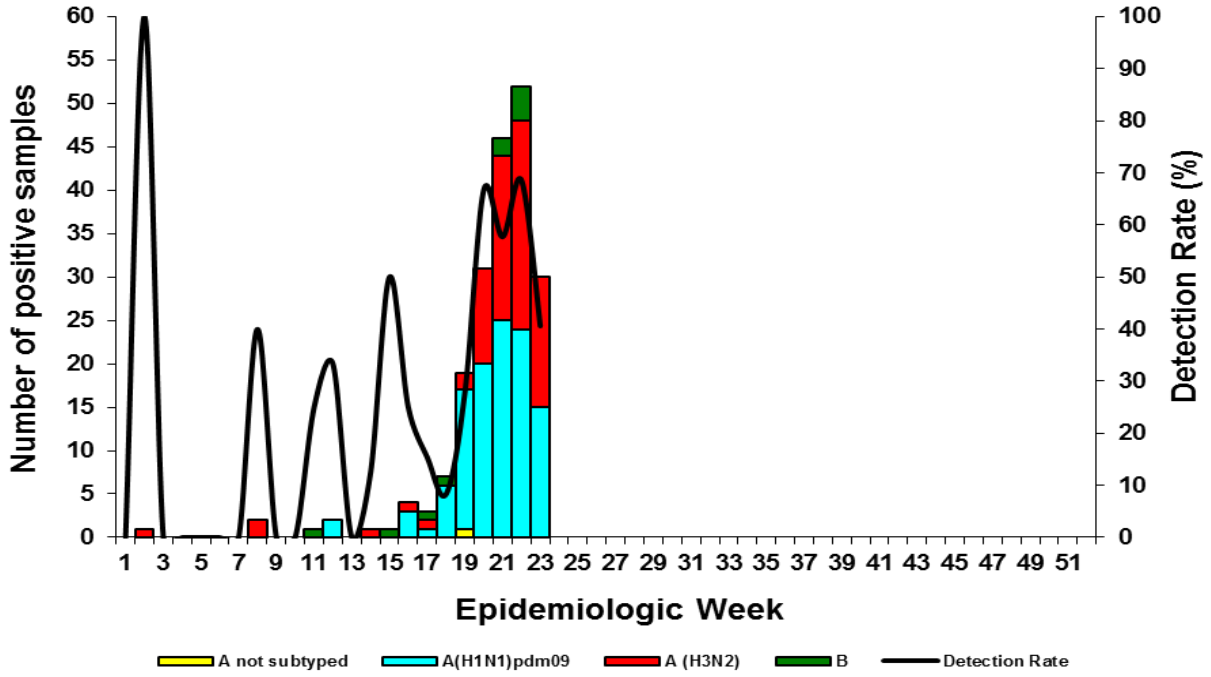


Figure 5. Number of positive samples by influenza types and subtypes and detection rate by week, Viral Watch programme, 2015

b Meningococcal disease

In South Africa, meningococcal disease is endemic with cases occurring year-round, but with seasonal peaks in winter and early spring. In addition, there is a natural cyclical pattern of meningococcal disease with peaks of disease occurring every 5 to 10 years. Current rates of meningococcal disease in South Africa are at a nadir and we are expecting an increase in rates based on known periodicity.

Currently, sporadic cases of meningococcal disease continue to be reported across the country, with no noticeable seasonal increase of laboratory-confirmed cases as yet. A possible case (laboratory results pending) in a college student in Potchefstroom was the subject of a number of recent media reports. There are inherent delays in laboratory-based reporting, which lags behind clinical reports. In addition, because our laboratory-based surveillance system excludes disease diagnosed clinically without laboratory confirmation, rates reported through laboratory surveillance represent a minimum estimate of the true burden of disease.

By the end of epidemiological week 22 (week ending 31 May 2015), a total of 31 laboratory-confirmed cases was reported to the Centre for Respiratory Diseases and Meningitis (CRDM), NICD-NHLS (Table 1). The highest burden of disease is seen usually in young children. Amongst the <2-year age group, 7 (22%) cases have been reported so far; a higher number of cases for the equivalent time period and age group in 2014 (n=14, 30%) were reported. Eight cases have also being reported in the 10 to 19-year-old age group.

The reported cases were caused by diverse serogroups, which is in keeping with sporadic endemic disease in the country. Serogroup data were available for 22/31 (71%) of cases. Serogroups B, W* and Y have been identified most commonly this year (7/22, 32% serogroup B; 8/22, 36% serogroup W* and 5/22, 23% serogroup Y). There were also 2 cases of serogroup C disease.
As the meningococcal season is due to start and an increase in cases may be expected this year, clinicians should have a high index of suspicion for meningococcal disease in patients who present with an acute febrile illness and nonspecific early signs and symptoms. Disease typically has a rapid progression and should be managed as a medical emergency in order to reduce morbidity and mortality. All cases of suspected and/or confirmed meningococcal disease (meningitis and sepsis) should be notified telephonically to the Department of Health.

A quadrivalent meningococcal conjugate vaccine is now available in South Africa and is recommended for certain high risk groups (Table 2). Recommendations in Table 2 are not yet officially endorsed, but are advised by local experts. Please discuss with CRDM consultants if clarification is required.

Table 1. Number of laboratory-confirmed meningococcal disease cases reported until

Province	Year 2014	2015
Eastern Cape	11	8
Free State	2	3
Gauteng	15	4
KwaZulu-Natal	2	5
Limpopo	0	0
Mpumalanga	0	1
Northern Cape	0	0
North West	0	1
Western Cape	17	9
	47	31

Source: Centre for Respiratory Diseases and Meningitis, NICD-NHLS

Table 2. Proposed recommendations for meningococcal vaccine use in South Africa*

Population Group	Vaccine choice	Recommendation	Primary dosing	Booster
Healthy children and infants	Quadrivalent conjugate vaccine MenACYW	Should be considered	According to Menactra package insert: Children 9 months to 24 months: 2 doses 12 weeks apart Children >24 months: 1 dose	
Healthy adolescents or young adults entering university or college (particularly if staying in hostels)	Quadrivalent conjugate vaccine	Should be considered	Single dose prior to entry into university or college	
Hajj pilgrims and travellers to Saudi Arabia	Quadrivalent conjugate vaccine	Required	Single primary dose	
Persons with medical conditions at high risk of acquiring infection:	Quadrivalent conjugate vaccine	Recommended	Two-dose primary schedule 8 weeks apart	Booster every 5 years
Complement component deficiencies				
Anatomical or functional asplenia	Quadrivalent conjugate vaccine	Recommended	Two-dose primary schedule 8 weeks apart	Booster every 5 years
HIV infection	Quadrivalent conjugate vaccine	Should be considered	Two-dose primary schedule 8 weeks apart	Booster every 5 years
Other immunocompromising conditions	Quadrivalent conjugate vaccine	Should be considered	Two-dose primary schedule 8 weeks apart	Booster every 5 years

*These recommendations are not yet officially endorsed, but are advised by local experts. Please discuss with CRDM consultants if clarification is required.

3 ZOONOTIC AND VECTOR-BORNE DISEASES

a Rabies

A case of rabies was confirmed in an 8-year-old boy child from Eastern Cape Province. The child was admitted to hospital on the 15th May presenting with restlessness and had weakness in his upper limbs which later extended to lower limbs. He was placed on a ventilator shortly after admission and passed away on the 23rd May 2015. A single saliva specimen was submitted to the NICD and tested positive by rabies RT-PCR. The family was not able to provide a definitive history of a dog bite before the patient fell ill, but as rabies transmission may occur even with small wounds such as scratches or nicks, and even licks on mucosal membranes, it is likely that the child did not report these to his family. Including this case, a total of four cases of human rabies has been laboratory confirmed in South Africa for the current year to date. These cases were reported from KwaZulu-Natal, Eastern Cape (case discussed here) and Limpopo provinces (n=2). All cases, except the Eastern Cape case, reported exposures to dogs and either received no or incomplete rabies post-exposure prophylaxis. In addition, a suspected case of rabies was reported in an 11-year-old boy from the Eastern Cape. The patient presented with restless behaviour, difficulty breathing, vomiting and diarrhoea. The patient died

after a short hospital stay without a confirmed diagnosis. A single saliva specimen was submitted for testing to the NICD but resulted negative with rabies RT-PCR. This finding does not exclude the diagnosis of rabies, as the virus is shed only intermittently in saliva. No definitive history of exposure to dogs or other animals could be provided in this case. Given the clinical presentation and outcome of the patient, but the lack of laboratory confirmation and/or history to support the probable diagnosis of rabies, the case may be classified as a suspected case only.

Cases of human rabies are reported from South Africa annually (Figure 6), with an average of 8 cases per annum in the past 5 years. Since 2010, cases were reported from Limpopo, KwaZulu-Natal, Mpumalanga, Free State and Gauteng provinces.

The first international meeting of the Pan-African Rabies Control Network was held in South Africa from 9th to 11th of June 2015 (https://paracon.rabiesalliance.org). This meeting brought together countries from sub-Saharan Africa in an effort to strategize regional and continental approaches for the control of rabies in dogs and the prevention of human cases. A recent study[1] has estimated 59 000 human rabies cases occur globally per year. More than two-thirds of all human cases occur in African countries, which can be explained by the fact that these countries have the lowest investment in dog rabies control in the world[1]. The most economical and effective approach for preventing human rabies cases remains the vaccination of dogs which are the main vector of the disease to humans. In South Africa, the law states that the responsibility for rabies vaccination remains with the pet owner. Post-exposure guidelines for rabies are available on the NICD website by following http://nicd.ac.za/assets/files/Rabies%20Poster%202011.pdf

1.Hampson K, Coudeville L, Lembo T, Sambo M, Kieffer A, Attlan M, *et al.* (2015) Estimating the global burden of endemic canine rabies. PLoS Negl Trop Dis 9(4): e0003709. doi:10.1371/journal.pntd.0003709

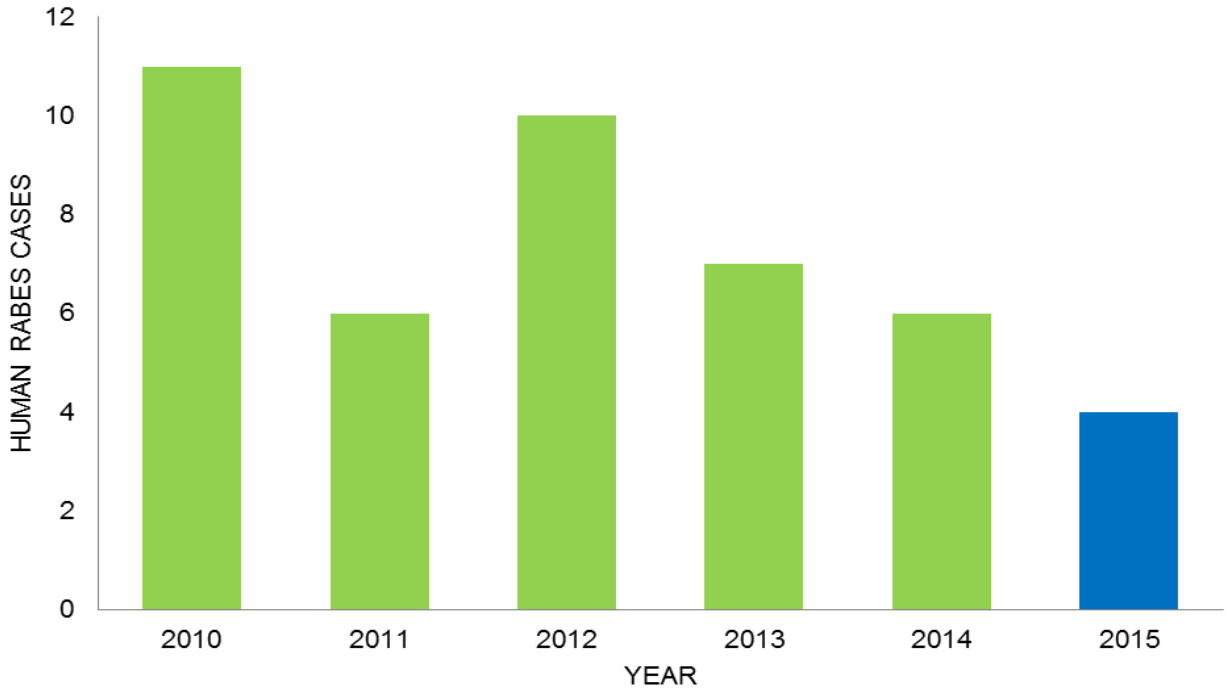


Figure 6. Number of confirmed human rabies cases for South Africa, 2000-2015 (12 June)

Source: Centre for Emerging and Zoonotic Diseases, Division of Public Health, Surveillance and Response, NICD-NHLS

b Leptospirosis

A recent case of leptospirosis presenting as acute multisystem illness

Leptospirosis was the likely diagnosis in a 34-year-old resident of Gauteng, South Africa, who presented with an acute febrile illness with significant splenomegaly and multisystem pathology. He had travelled for business to Nairobi, Kenya and Addis Ababa, Ethiopia in the week prior but had not experienced any likely exposures to zoonotic diseases. On return to South Africa, he visited a number of game parks where he had close contact with a number of animals, and opportunity for exposure to *Leptospira* species While visiting a game farm near Bela Bela he became ill.

The course of illness was rapidly progressive with the development of ARDS, renal failure, DIC, liver dysfunction with jaundice, and depressed level of consciousness. The patient required assisted ventilation, inotropic support and renal dialysis. A broad differential diagnosis was considered, he was isolated and was tested for a large number of infectious diseases including zoonotic infections: – viral haemorrhagic fevers including Crimean Congo haemorrhagic fever and Rift Valley fever, dengue, leptospirosis, Q fever, and arboviral infections, all of which were negative in the first week of illness. Malaria was actively sought despite his not having travelled to a known malaria transmission area, but all tests were negative. Blood cultures were repeatedly negative. An initial anaemia (Hb 8.8 g/dL), a WCC of 2.52 x 10^9/L) and thrombocytopenia (28 x 10^9/L) were noted. A normal reactive bone marrow with eosinophil infiltration, and raised hepatic transaminases and bilirubin levels (AST 452 u/L ALT 178 u/L, total bilirubin 157 umol/L, direct bilirubin 107 umol/L, LDH 1748 u/L) was documented. The PT was 11.9 sec, PTT 32.4 sec, INR 1.2, D-dimers >10 mg/L with fibrinogen of 1.94 g/L, indicating a compensated DIC.

The patient received broad-spectrum antibiotic treatment with ceftriaxone, plus a quinolone and doxycycline for possible rickettsial infection or Q fever. The course of illness was biphasic, with an initial favourable response to treatment. The final, fatal event was likely a nosocomial infection.

Negative leptospiral antibodies in the first week of illness with a seroconversion (by Elisa, repeated on three occasions) in the second week of illness was highly suggestive of the diagnosis of leptospirosis, despite a negative PCR test in the first week. The source of the infection and the exact source remains unknown.

Leptospirosis as a human disease in South Africa

Leptospirosis has a worldwide distribution, but has been relatively rarely diagnosed in South Africa. In 1947 Buchanan reported that despite laboratory investigations on more than 200 jaundiced patients over a 20-year period, mainly on the Witwatersrand, no leptospiral infections were detected. Likewise, his examination of 231 rodents of various types revealed no instances of infection. It was not until 1952 that the first South African case of leptospirosis was diagnosed, in a Cape Town fish hawker who died of typical Weil's disease due to *Leptospira icterohaemorrhagiae*, complicated by myocarditis. In 1958 Gear *et al* described 5 cases amongst persons that recovered from leptospiral meningoencephalitis in Johannesburg, and in the 1960s and 1970s further cases of leptospirosis were published from Cape Town, and one from KwaZulu-Natal Province. Several of these were dockworkers. Evidence of animal reservoirs of infection in South Africa dates from the 1950s, and the first isolation of *L. icterohaemorrhagiae* in Cape Town rats was reported in 1964, followed by isolation of *L. pomona* in pigs and dogs in the Western Cape. In the last study, 54% of Cape Town dogs had serological evidence of infection with *L. icterohaemorrhagiae* or *L. pomona* or both. The South African veterinary literature contains many data about leptospirosis in wild and domestic animals, but is not reviewed here. As part of a study of rodent-associated infections in rural and urban areas of South Africa, 2003-2006, serosurveys of rodents and humans in an urban informal settlement in Durban showed that, respectively, 10% and 20% of rodents and humans had serological evidence of exposure. More recently, three human cases, acquiring the infection in rural settings near Johannesburg (cases 1 and 2), and in an informal settlement in Windhoek, Namibia (case 3), were diagnosed by PCR on blood samples and were published in the Communiqué in 2007 (Vol. 6, No. 1, pp. 3-4), with an additional case in a Cape Town flower seller documented in 2008 (Communiqué Vol. 7, No. 5, p. 1).

Leptospirosis diagnostics

Leptospirosis is pathognomonic with variable clinical manifestations and clinical suspicion must be confirmed with laboratory tests. Findings on general laboratory studies include elevated erythrocyte sedimentation rate, thrombocytopenia, leucocytosis, hyperbilirubinaemia, elevated serum creatinine, elevated creatinine kinase and elevated serum amylase. On urinalysis, proteinuria may be

present. Leukocytes, erythrocytes, hyaline casts, and granular casts may be present in the urinary sediment.

Laboratory diagnosis of leptospirosis is usually carried out by culturing the bacteria from blood, urine or tissues, by detecting antibodies, or by demonstrating the presence of leptospires in tissues using antibodies labelled with fluorescent markers. Other methods include darkfield microscopy (the classic method but no longer recommended), polymerase chain reaction (PCR) and staining using monoclonal antibodies.

The definitive laboratory diagnosis of leptospirosis is made by isolation of leptospires from clinical specimens, but it is technically demanding, requiring rapid inoculation of special fresh medium that is not readily available. Routine microbiological laboratories are generally not equipped for leptospire culture, and it is time consuming and subject to contamination and high failure rates. Therefore, serological approaches are used commonly for diagnosis of leptospirosis. However, detection of antibodies is by itself no proof of a current infection as antibodies may persist for months or even years after an infection. In general, seroconversion or a four-fold rise in titre in consecutive serum samples is considered to be diagnostic proof of current or recent infection. Seroconversion may occur as early as 5–7 days after the onset of illness, but sometimes only after 10 days or longer. In the acute phase, leptospires can be found in blood and CSF for 7-10 days and their presence can be confirmed by detecting and identifying specific segments of leptospiral DNA using PCR amplification. However, due to the small number of leptospires present in blood samples, very sensitive diagnostic tests are required and samples should be taken prior to antibiotic treatment. Leptospires are susceptible to most antibiotics, except chloramphenicol. Recommended treatments include high-dose penicillin G or a 3rd generation cephalosporin, alternatively doxycycline, azithromycin or ampicillin. Severe leptospirosis is associated with a cytokine storm and multiorgan failure, requiring skilled supportive treatment in

Source: Centre for Emerging and Zoonotic Diseases, Division of Public Health, Surveillance and Response, NICD-NHLS

c Crimean-Congo haemorrhagic fever (CCHF)

No cases of Crimean-Congo viral haemorrhagic fever (CCHF) have yet been laboratory confirmed in the 2015. In 2014, a total of six laboratory confirmed cases was reported from Free State (n=2) and the Northern Cape (n=4). Five of the patients who were diagnosed with CCHF were male. The case fatality rate was 50%.

Crimean-Congo viral haemorrhagic fever is a tick-transmitted viral disease of humans. It is widespread and highly prevalent throughout the Balkans, southern Federal Districts of Russia, Middle East, and south-west Asia. The disease is infrequently reported in humans in sub-Saharan Africa, where only twelve countries have confirmed CCHF in human cases. Within South Africa, CCHF has been reported throughout the year, although cases are expected during the summer with increased tick activity. Cases originate from across South Africa, but mainly from the central inland plateau including the entire Free State and adjoining parts of the Northern Cape and the North-West provinces. The semi-arid climate conditions in these regions are favourable, and the practice of cattle and sheep farming in that area provides feeding hosts for the ticks involved in CCHF virus transmission. Majority of the infected people are livestock farmers. In half to three-quarters of the cases documented, the infection was acquired through contact with livestock and probable tick exposure. Some 15% of South African cases have been abattoir workers, or butchers or had reported having slaughtered animals recently and acquired the infection directly from the animals. The mortality ratio is high for those that become infected and has been 25% amongst recorded cases in South Africa since 1981. The onset of symptoms is shortly after infection, ranging from 3 to 13 days depending on the route of exposure. There are tests to detect CCHF virus during the acute phase of illness. Antibody tests become positive as early as a week after symptom onset in affected persons. Early recognition and supportive treatment are key contribution factors in the prognosis, survival and recovery from the disease.
More CCHF facts are available from the NICD website: http://www.nicd.ac.za/?page=guidelines&id=73

Source: Centre for Emerging and Zoonotic Diseases, NICD-NHLS

4 INTERNATIONAL OUTBREAKS OF IMPORTANCE TO SOUTH AFRICAN TRAVELLERS AND HEALTHCARE WORKERS

a Middle East respiratory syndrome coronavirus (MERS-CoV) update

Background

Middle East respiratory syndrome coronavirus (MERS-CoV) is a recently identified respiratory virus which causes severe respiratory illness. It was first reported in Saudi Arabia in 2012. Since September 2012 and as of 12 June 2015, WHO has been informed of a total of 1289 laboratory confirmed cases of human infection with MERS-CoV including 455 related deaths.

The number of cases reported has increased sharply since May 2015 as a result of a new outbreak reported in South Korea. To date all the cases reported have been linked to countries in the Arabian peninsula. Middle East countries with laboratory confirmed cases include Jordan, Saudi Arabia, Yemen, United Arab Emirates (UAE), Qatar, Oman, Kuwait and Lebanon. Countries with travel-associated cases include United Kingdom (UK), Tunisia, Egypt, Greece, Germany, Italy, Algeria, Austria, Turkey, Netherlands, Malaysia, Philippines, United States of America (USA), China and South Korea. In South Africa, 37 samples were tested in 2015 and none of these have tested positive. It is important to consider this virus in the differential diagnosis of patients with severe pneumonia and a travel history to a geographically-implicated country in order to identify possible cases early and to allow for implementation of appropriate infection control procedures and public health response.

MERS COV outbreak in South Korea

On 20 May 2015, South Korea notified the WHO of the first laboratory-confirmed case in a 68-year-old man, who had recently travelled between four countries in the Middle East, from 18 April – 3rd May 2015. The index case was asymptomatic at the time of return to South Korea on 4th May 2015. He had no history of exposure to camels or contacts with MERS-CoV patients, or visit to any healthcare facilities while travelling in the Middle East. Investigation of the source of infection is ongoing [WHO website, updated 25 May 2015, Available from: http://www.who.int/csr/don/24-may-2015-merskorea/en/].

The index case had onset of symptoms on 11 May and had sought medical care at several healthcare facilities before a laboratory confirmation was made on the 20th May 2015. Since then, as of June 12, according to the Republic of Korea Ministry of Health, 125 secondary and tertiary cases of MERS-CoV have been confirmed; one case travelled to China where he was hospitalised. In total 126 cases, including 11 deaths have been reported.

Although the cluster in South Korea is the largest identified outside the Arabian peninsular according to available WHO reports, all reported cases are epidemiologically linked to the index case, with transmission limited to other patients, healthcare workers, and visitors in healthcare facilities where case-patients received care. A similar pattern of spread has been reported before in other outbreaks like the nosocomial transmission that followed admission of one case in Jeddah in 2014.

Presentation and clinical course

Patients with MERS-CoV have presented with respiratory infections ranging from mild upper respiratory tract illness to severe lower respiratory disease, with the majority presenting with acute, serious respiratory illness with fever, cough, shortness of breath, and breathing difficulties. Some patients, especially those who are immunosuppressed have presented with fever and diarrhoea. More severe disease has been reported in patients with comorbidities. Primary cases were predominantly symptomatic, leading to high rates of admission to the hospital or intensive care unit ,and death. Secondary infections led to lower rates of symptomatic illness and death, except in those who were already hospitalised. Complications have included severe pneumonia and acute respiratory distress syndrome requiring mechanical ventilation, multi-organ failure, renal failure requiring dialysis and pericarditis. The case fatality ratio is 39%.

Transmission

Although there is evidence that the dromedary camel is a host species for the MERS-CoV and that camels likely play an important role in the transmission to humans, the routes of direct and indirect transmission remain unknown. The virus has spread from person to person through close contact, such as caring for or living with an infected person. The majority of secondary cases are healthcare workers, close contacts of the cases who were visiting the health centres where cases were being cared for, and a number of patients in hospital that have likely become infected in the nosocomial setting. However, there is currently no evidence of sustained spread of MERS-CoV in community settings.

Management
There is no specific treatment for disease caused by MERS-CoV. However, many of the symptoms caused by this virus can be treated and therefore treatment should be based on the symptoms of the patient. There is no available vaccine for the virus yet.

Precautions and infection prevention and control considerations
The increase in numbers of recently-reported cases from healthcare workers and in hospital settings underscores the importance of infection control. Many of the identified cases continue to be caused by nosocomial exposure. When providing care to all patients with symptoms of acute respiratory infection and whenever specimens are collected from cases under investigation, the appropriate infection control guidelines should be followed. (WHO interim guidelines on infection prevention and control of epidemic- and pandemic-prone acute respiratory diseases in health care (2014) http://www.who.int/csr/bioriskreduction/infection_control/publication/en/

WHO does not advise screening at points of entry or travel or trade restrictions.
Travelers returning from the Middle East and South Korea who develop respiratory symptoms either during or within 14 days of their return should seek medical care and inform their health care providers about their recent travel.

Indications for testing
The outbreak in South Korea and previous similar outbreaks highlight the continued risk of healthcare-associated transmission and the need for timely diagnosis and implementation of prevention and control measures. MERS-CoV should be suspected in anyone who develops fever and symptoms of respiratory illness, such as cough or shortness of breath, within 14 days after traveling from countries in or near the Arabian Peninsula and South Korea or to countries where MERS-CoV infection in human cases has been recently identified. This is particularly important for patients who have been in contact with health facilities in these countries. Details of case definitions, indications for testing and appropriate specimens for MERS-CoV can be accessed at the NICD webpage: http://www.nicd.ac.za/?page=guidelines&id=73

Additional information on MERS-CoV can be accessed at the following websites:
WHO website: http://www.who.int/csr/disease/coronavirus_infections/en/
WHO website: http://www.who.int/csr/don/12-june-2015-mers-korea/en/
NICD website: http://www.nicd.ac.za
WHO website: http://www.who.int/csr/bioriskreduction/infection_control/publication/en/
CDC website: http://www.cdc.gov/coronavirus/mers/

Source: Centre for Respiratory Diseases and Meningitis, NICD-NHLS

b Ebola virus disease (EVD) outbreak: update

Ebola virus disease (EVD) outbreak: situation update

As at 21 June 2015, a total of 27 443 (laboratory-confirmed, probable, and suspected) cases of EVD has been reported in Guinea, Liberia and Sierra Leone, with 11 207 reported deaths. The outbreak in Liberia was declared over on 9 May. As at 09 May 2015, a cumulative total cases of 10 666 EVD cases (3 151 laboratory-confirmed, 1 879 probable and 5 636 suspected) including 4 806 deaths had been reported in Liberia. At present the outbreak continues in Guinea and Sierra Leone. However the number of new cases reported has declined to relatively low levels.

A confirmed imported EVD case was reported in Italy on 12 May 2015. The case-patient is a volunteer healthcare worker who travelled from Sierra Leone to Italy on 7 May 2015 and three days later developed symptoms. Following confirmation of Ebola on 12 May 2015, the case-patient was transferred to the National Institute for Infectious Diseases in Rome. Nineteen associated contacts were monitored and all have completed the 21 days follow-up period. The patient was confirmed EVD negative, and clinically well on 9th June 2015.

Countries with widespread and intense transmission (Guinea and Sierra Leone)

As at 21 June 2015, a cumulative total of 16 777 cases (laboratory-confirmed, probable and suspected) including 6 352 deaths with a case fatality rate of 38% has been reported in Guinea and Sierra Leone. In addition, cases have been reported from a widening geographical area. The continued occurrence of cases arising from unknown sources of infection and cases detected after post-mortem testing of community deaths, highlights challenges faced in the finding and elimination of transmission chains. A summary of case numbers and deaths reported is shown in Table 3.

Table 3. Number of Ebola virus disease cases and deaths in Guinea and Sierra Leone as at 21 June 2015

Country	Total cases (laboratory-confirmed, probable and suspected)	Total deaths	Case fatality rate	Number of cases among healthcare workers (number of deaths)
Guinea	3 718	2 473	67%	189 (94)
Sierra Leone	13059	3 928	30%	305 (221*)
Total	**16 777**	**6 401**	**38%**	**494 (315)**

Source: World Health Organization Global Alert and Response: Ebola situation report of 7 June 2015 (www.who.int) . *Data as at 17 February

Situation in South Africa

As at 25 June 2015 there have been no EVD cases in South Africa associated with the current outbreaks in West Africa. In addition, there are no suspected cases of EVD in South Africa at present. The risk of Ebola being introduced into South Africa still remains low. However a high index of suspicion is necessary given on-going EVD transmission in West Africa.

Testing for viral haemorrhagic fever viruses (including Ebola virus) in South Africa is only available at the NICD. EVD testing is neither warranted nor useful for persons that are not suffering from a clinical illness compatible with EVD, even in the event of compatible travel histories. The tests cannot be used to determine if the patient has been exposed to the virus and may develop the disease later.

Requests for testing (with a detailed clinical, travel and exposure history) should be directed to the NICD Hotline at 082 883 9920 (a 24-hour service, for healthcare professionals only).

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

5 ANTIMICROBIAL RESISTANCE

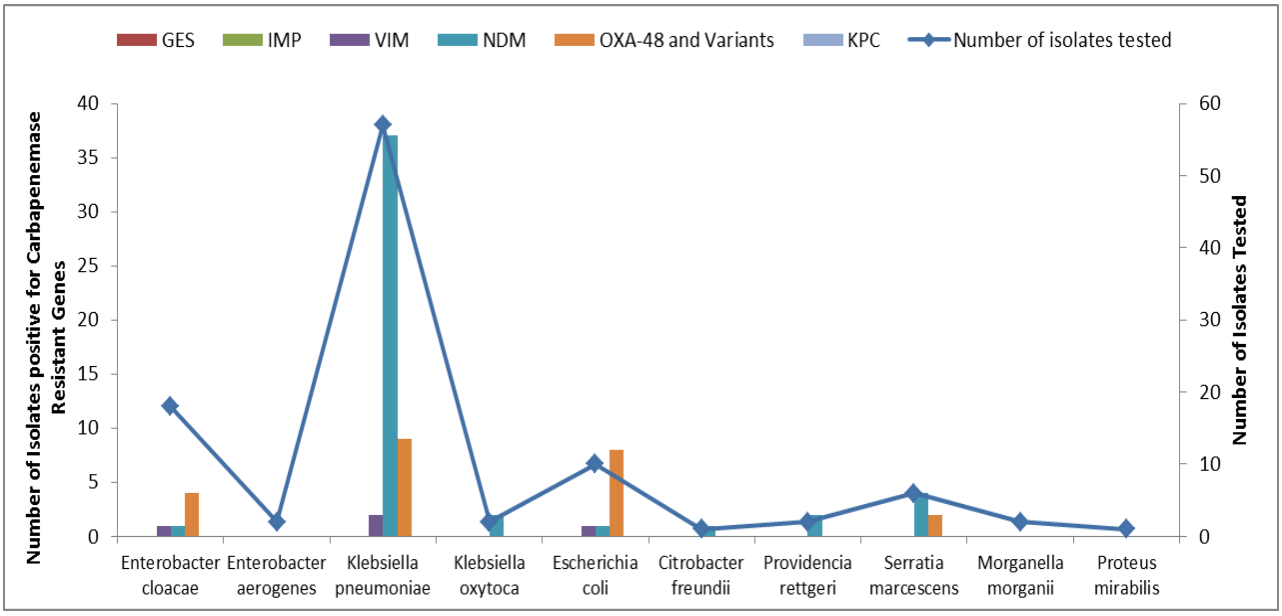
Update on carbapenemase-producing Enterobacteriaceae

Carbapenemase-producing Enterobacteriaceae (CPEs) 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 CPEs. The Johannesburg Antimicrobial Resistance Laboratory-Culture Collection (AMRL-CC) of the Centre for Opportunistic, Tropical and Hospital Infections (COTHI) at the NICD/NHLS has been testing referred isolates of suspected CPE for the presence of selected carbapenemase genes. For May 2015, a total of 102 Enterobacteriaceae isolates were received. One hundred and one carbapenem resistant isolates were screened, 71 of which were CPE isolates. Majority of the isolates were *Klebsiella pneumoniae* (57) followed by *Enterobacter cloacae (18), E. coli (10) and Serratia marcescens* (6) (Figure 7).

Forty-eight bla_{NDM}-positive isolates were identified; four from private hospitals (all from KwaZulu Natal) and 44 from public hospitals – 27 from Gauteng, 16 from KwaZulu-Natal (KZN) and 1 from Eastern Cape. Twenty-three bla_{OXA-48}-positive isolates were identified; five from private hospitals in Gauteng and KZN, and 18 isolates from public hospitals: nine from Gauteng province, seven from the Eastern Cape and two from KZN. Four bla_{VIM}-positive isolates were identified from public hospitals in Gauteng. No other CPE enzyme types were identified in May (Figure 8).

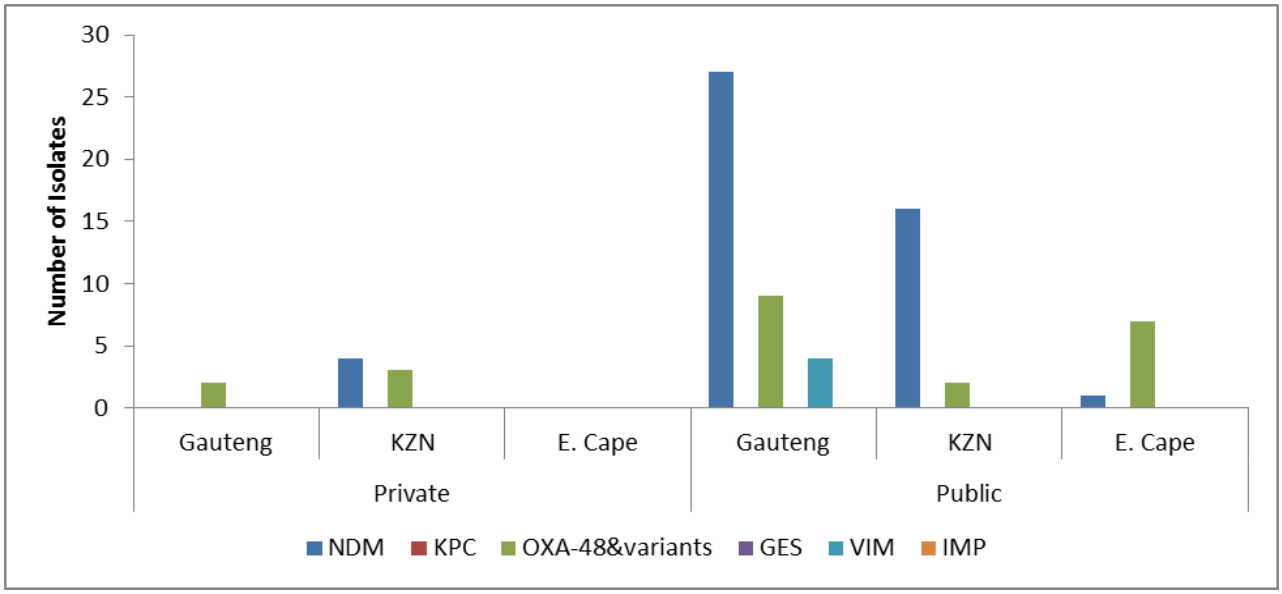
It is important to note that these figures do not represent the current burden of CPEs in South Africa. Given that CPE infections are currently not reportable or notifiable in South Africa, there is no platform for appropriate surveillance reports and consequently no locally representative data are available. 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 the AMRL-CC, NICD/NHLS. Please telephone (011) 555 0342/44 or email: olgap@nicd.ac.za; for queries or further information.



GES: Guiana extended-spectrum; IMP: imipenemase; VIM: verona integron-encoded metallo-beta-lactamase; NDM: New Delhi metallo-beta-lactamase; OXA: oxacillinase; KPC: Klebsiella pneumonia carbapenemase

Figure 7. Enterobacteriaceae isolates screened (n=101) and confirmed CPEs (n=71) at the Antimicrobial Resistance Laboratory-Culture Collection, COTHI (NICD-NHLS), May 2015



GES: Guiana extended-spectrum; IMP: imipenemase; VIM: verona integron-encoded metallo-beta-lactamase; NDM: New Delhi metallo-beta-lactamase; OXA: oxacillinase; KPC: Klebsiella pneumonia carbapenemase

Figure 8. The total number of CPEs (n=71) in the public and private sectors from three provinces, May 2015

Source: Centre for Opportunistic, Tropical, and Hospital Infections, NICD-NHLS

6 BEYOND OUR BORDERS

The 'Beyond our Borders' column focuses on selected and current international diseases that may affect South Africans travelling abroad.

Disease & countries	Comments	Advice to travellers
1. Respiratory diseases continued		
MERS-CoV Saudi Arabia South Korea	Saudi Arabia has reported a total of 1031 laboratory-confirmed cases and 453 deaths as of 14 June 2015. MERS-Cov has spread to South Korea and as of 14 June 2015, 149 cases and 15 deaths have been reported.	Good hygiene and basic infection prevention measures should be practiced. Travellers with diabetes, chronic lung disease and immune-compromised states are at risk of infection and should avoid contact with animals if possible. Strict hand washing must be followed after touching animals. Avoid raw camel milk or undercooked camel meat at all times. Travellers should avoid contact with animals and eat food that is fully cooked. Infection control practices such as regular hand washing must be followed to prevent infection.
2. Water-borne disease		
Cholera Kenya Tanzania Haiti	Kenya has reported a total of 3223 acute cases of cholera and 72 deaths as of the 9 June 2015. Tanzania has reported a total of 4487 suspected cases of cholera as of 28 May 2015. Haiti has reported a total of 15000 cases of cholera and 126 deaths since the beginning of 2015.	Cholera is an acute diarrhoeal illness that causes severe dehydration. Drink lots of safe water (bottled water with an unbroken seal, boiled water or water treated with chlorine tablets). Strict washing of hands with soap and safe water must be practiced. Food must be well cooked before eating. Peel fruit and vegetables before eating.
3. Vector-borne diseases		
Dengue fever Taiwan Ecuador	Taiwan has reported a total of 208 cases of dengue fever since the beginning of 2015. Ecuador has reported a total of 20 800 cases of dengue fever since the beginning of 2015	Dengue fever (like chikungunya) is a mosquito-borne viral infection transmitted by *Aedes* spp. mosquitoes, which bite mostly during the day. Travellers can protect themselves from getting dengue fever by preventing mosquito bites. To protect against mosquito bites they can use insect repellent and sleep in an air-conditioned room. For those sleeping in an area that is exposed to the outdoors, they can use mosquito nets.

Disease & countries	Comments	Advice to travellers
3. Vector-borne diseases cont.		
Chikungunya		
Honduras, French Guiana, Puerto Rico	Honduras has reported a total of 31,460 cases of chikungunya (November 2014); Guiana 5,380 (June 2015) and Puerto Rico 428 (June 2015)	In late 2013 chikungunya virus was found for the first time in the Americas on islands in the Caribbean and in Mexico in 2014. Ongoing outbreaks are occurring in this region as described in the column to the left. Chikungunya is a mosquito-borne viral infection transmitted by *Aedes* spp. mosquitoes, which bite mostly during the day. The most common symptoms of chikungunya virus infection are fever and joint pain. Other symptoms may include headache, muscle pain, joint swelling, or rash. Travellers should wear long-sleeved shirts and long pants during the day and stay in well-ventilated (fan/air-conditioned) rooms.
Colombia, Ecuador, and Peru	Colombia has reported 263,247 cases, Ecuador 14,459 cases and Peru, 11 cases (June 2015)	
Argentina	Argentina has reported no cases	
Trichinellosis		
Argentina	Argentina has reported 9 cases of trichinellosis as of 9 June 2015. The source of the infection is still being investigated.	Trichenellosis is caused by ingesting raw meat of animals infested with the larvae of *Trichinella* species. Infection occurs in wild animals such as bears and cougars and in domestic animals such as pigs. Travellers must avoid eating raw or undercooked meat.
Yellow fever Brazil	Brazil (Goiras) has reported a total of 4 cases of yellow fever to date. The last outbreak in Brazil was in 2008 where 17 people were infected and 10 died.	Yellow fever is an acute viral haemorrhagic disease transmitted by infected mosquitoes. The 'yellow' in the name refers to the jaundice that affects some patients. Vaccination is the most important preventive measure against yellow fever. The vaccine is safe, affordable and highly effective, and a single dose of yellow fever vaccine is sufficient to confer sustained immunity and life-long protection against yellow fever disease. A booster dose is not needed. The vaccine provides effective immunity within 30 days for 99% of persons vaccinated.

References and additional reading:

ProMED-Mail (www.promedmail.org)
World Health Organization (www.who.int)
Centers for Disease Control and Prevention (www.cdc.gov)
Last accessed: 24 June 2015

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