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Division of the National Health Laboratory Service

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CONTENTS

1 RESPIRATORY DISEASES

a Diphtheria: Two confirmed cases in KwaZulu-Natal Province, May 2016

A toxigenic strain of *Corynebacterium diphtheriae* was isolated from a throat swab of an 18-year-old female, hospitalised in eThekwini on 10 May 2015. The patient reported feeling ill since 25 April 2016 with a minor sore throat. She used home remedies initially, but on 10 May, presented to a local clinic, which referred her immediately to a local hospital. On examination, the patient was observed to have a fever, difficulty swallowing, and swelling of the neck. The emergency unit ('Casualty') at that hospital referred her immediately to a tertiary level facility where she was admitted. Nasal and throat swabs were taken, which the next day yielded growth of *C. diphtheriae*. The isolate was submitted to the Centre for Respiratory Disease and Meningitis (CRDM) NICD where the identification of the organism was confirmed, and PCR for the *tox* gene found to be positive. The patient was treated with intravenous penicillin, which was changed to azithromycin 500 mg PO daily. The patient did not receive diphtheria antitoxin (DAT), and currently appears well with no evidence of myocarditis.

A second patient in eThekwini presented to a local clinic on 19 May 2016 and was referred to hospital on 21 May 2016 with typical signs and symptoms of diphtheria. A throat swab yielded growth of *C. diphtheriae*, which was confirmed by CRDM NICD to carry the *tox* gene.

The confirmation of this case following last year's outbreak is concerning. From March until June 2015, 15 cases of diphtheria were identified (11 confirmed, three probable, one possible) in eThekwini and Ugu districts, with four deaths. Cases ranged from three to 41 years with children <15 years accounting for 12/15 of the cases, and six children within the range 5-9 years. Males accounted for nine cases. Where the road-to-health card was available (n=5), one was up to date for age, four had missed one or more doses. Over the course of the outbreak, the KZN Department of Health implemented active contact tracing, taking throat swabs and administering of post-exposure prophylaxis, booster vaccination in schools amongst children aged 6-12 years, dissemination of clinical guidelines and sensitisation of clinicians, and community health promotion activities. The NICD and NHLS issued revised laboratory diagnostic guidelines, implemented routine culturing of throat swabs onto Hoyle's medium (potassium tellurite agar) and enhanced existing laboratory diagnostic and confirmatory capacity for *C. diphtheriae.*

Regarding the present cases, contact tracing and post-exposure prophylaxis administration have been conducted by the Ethekwini Outbreak Response Team. A strategic supply of diphtheria antitoxin for possible additional cases is in the process of being sourced. The NICD, provincial and national departments of health are convening meetings to consider a strategic response.

Source: Ethekwini Municipality; KZN Provincial Department of Health; Centre for Respiratory Diseases and Meningitis, NICD-NHLS; Division of Public Health Surveillance and Response, NICD-NHLS.

2 ZOONOTIC AND VECTOR-BORNE DISEASES

a Yellow fever outbreak in Angola and neighbouring Democratic Republic of Congo

A yellow fever outbreak in Angola was reported in January 2016. Initial cases were diagnosed by the National Institute for Communicable Diseases Centre for Emerging and Zoonotic Diseases on 19 January 2016. Specimens were also submitted to the WHO-AFRO Collaborating Centre for Yellow Fever at the Institut Pasteur, Dakar, Senegal who confirmed the outbreak on 20 January 2016. Subsequently the outbreak escalated dramatically and currently is the largest yellow fever outbreak globally in the past decade and the first in Angola in nearly three decades. In addition, cases have been identified in the Democratic Republic of Congo (DRC) and Uganda amongst residents with no travel history.

The WHO situation report issued on 19 May 2016 indicated a total of 2 420 cases, of which 736 are laboratory confirmed. There have been 298 deaths. The Luanda Province is most affected, accounting for 64% of the cases, followed by the Huambo

(17%), Bengela (7%), and Huila (4%) provinces (Figure 1). Eight percent of cases have been reported from the provinces of Bie, Cuanza Sul, Cunene, Uige, Bengo, Cuanza Norte, Zaire, Malanje, Cabinda and Namibe collectively. Only four of the country's provinces, located in the eastern part of the country, (Lunda Norte, Sul, Moxico, Cuando Cubango) remain unaffected.

As of 19 May, 44 laboratory confirmed cases and five probable cases have been reported by the DRC. While 42 cases are reportedly imported from Angola, the possibility of locally-acquired infection is under investigation in the Kinshasa and Kongo central provinces. The Ministry of Health in Uganda reported 60 cases of yellow fever, of which seven are laboratory confirmed. However, according to sequencing results, these cases are not epidemiologically linked to the outbreak in Angola. These cases represent infection with local strains prevalent in Uganda. In addition, Kenya and China have also reported imported cases amongst unimmunised travellers returning from Angola.

On 19 May 2016, the WHO Director-General under the International Health Regulations (IHR 2005) convened an Emergency Committee (EC) regarding the yellow fever outbreak in Angola. The WHO reports that "Following the advice of the EC, the Director-General decided that the urban yellow fever outbreaks in Angola and DRC are serious public health events which warrant intensified national action and enhanced international support. The events do not at this time constitute a Public Health Emergency of International Concern (PHEIC)".

No cases of yellow fever have been reported in South Africa. The NICD has tested 37 specimens for yellow fever in 2016 (Table 1). Five samples sent from Angola in January were positive by PCR. Reports of yellow fever infection in non-immunised, returning travellers emphasise the need to reinforce the implementation of vaccination requirements in accordance with the International Health Regulations (2005). All South Africans travelling to yellow fever endemic areas require vaccination, or a vaccine waiver letter indicating ineligibility for vaccination.

For case definitions, diagnostic testing and contraindications to the vaccine, please consult the NICD Communique, April 2016 edition available at www.nicd.ac.za.

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

Table 1. Number and origin of specimens tested for yellow fever in 2016 by Centre for Emerging and Zoonotic Diseases, NICD

Specimen origin	Number tested
Angola Ministry of Health	11
Namibian Institute of Pathology or other Namibian laboratory	14
Kenyan laboratory	5
South Africans with travel history to yellow fever risk areas	
Angola	4
Other	3

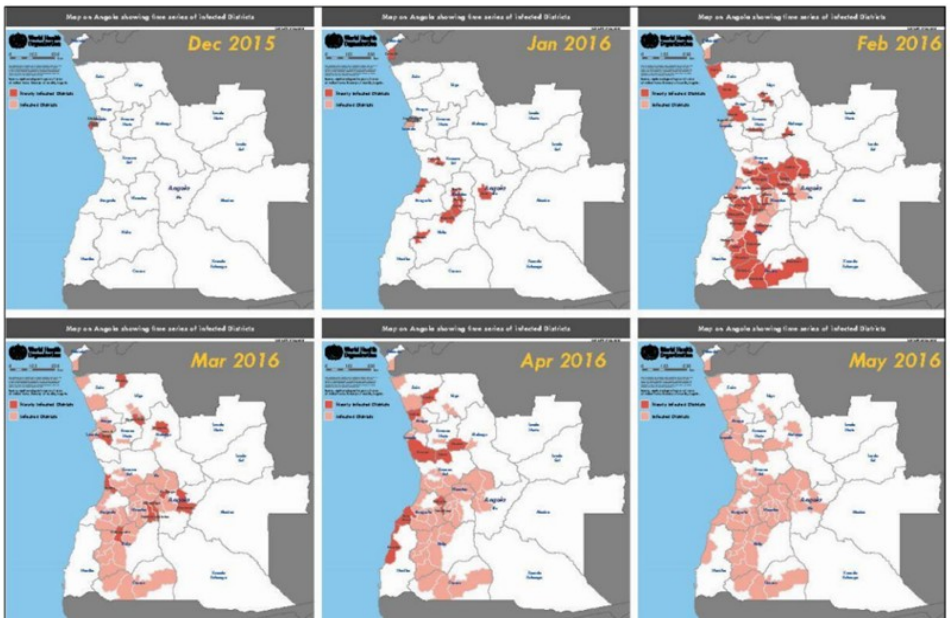


Figure 1. A chloropleth map showing the numbers of cases of yellow fever identified in the provinces of Angola December 2015-May 2016. (courtesy http://www.who.int/emergencies/yellow-fever/situation-reports/20-may-2016/en/)

b Emergence of the Asian strain of Zika virus in Cape Verde

According to the WHO situation report released on 18 May 2016*, 60 countries report continuing mosquito-borne transmission of Zika virus. Argentina is the latest country to report mosquito-borne transmission. Four countries have experienced a Zika virus outbreak between 2007 and 2014, but no longer have ongoing transmission. Complications associated with Zika virus infection, namely microcephaly and Guillain-Barre syndrome (GBS), have been reported in eight and 13 countries respectively. The WHO reports that there is "scientific consensus that Zika virus is the cause of microcephaly and GBS".

In the African region, the Republic of Cape Verde in the Atlantic Ocean off the coast of Africa, is currently experiencing an outbreak, and there is evidence that Zika virus was circulating in Gabon between 2007 and 2014. As of 8 May 2016, there were over 7 500 suspected cases with three cases of microcephaly reported from the Republic of Cape Verde. Available sequencing data indicate that the Zika virus in Cape Verde is an Asian and not African lineage. This has a number of epidemiological implications for countries on the African continent. Although Zika virus was first identified in Africa and appears to be widespread in a number of African countries based on serological surveys, the Asian lineage of the virus appears to have acquired increased and new virulence during the last 20 years. Zika virus may therefore pose an increased risk to public health on the African continent.

The WHO has urged African countries to re-evaluate their level of risk, and increase their level of preparedness and prevention activities. Measures proposed include: 1) increasing or implementing vector surveillance and control; 2) implementing surveillance measures for Zika-associated congenital malformations and GBS; 3) strengthening laboratory capacity; and 4) strengthening community engagement and risk communications. A number of South Africans are preparing to participate or attend the Olympic Games in Rio de Janeiro, Brazil, this year. Team members and visitors have been advised to avoid mosquito bites, seek medical attention should they develop symptoms compatible with Zika virus infection (rash, fever, joint pains or conjunctivitis), and use condoms to prevent potential sexual transmission during or after visiting Brazil.

*http://apps.who.int/irisbitstream/10665/206537/1/zikasitrep_19May2016_eng.pdf

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

c Equine rabies immunoglobulin (ERIG) soon to be available in South Africa

As reported in the Communiqué, April 2016, there is a national shortage of the human rabies immunoglobulin (HRIG) presently being used in the country. The sole supplier of HRIG, the National Bioproducts Institute, has indicated that there will not be any available stock for the period May 2016 to August 2016. The South African National Department of Health is in the process of procuring equine rabies immunoglobulin (ERIG) under Section 21 legislation, as this product is not registered in South Africa. It will take three to six weeks for ERIG to be procured.

ERIG has been widely used for post-exposure prophylaxis (PEP) over many decades in countries with high rates of canine rabies and has been found to be safe and effective. However, compared with HRIG, the use of ERIG does carry a low risk (1 in 150,000 doses administered) of adverse drug reaction, specifically anaphylaxis. **Therefore, ERIG should only be administered in facilities that are equipped to respond appropriately to anaphylactic shock.** ERIG also has a different dosing schedule to HRIG. **The dose of ERIG is twice as high (40 IU/Kg of body weight) as the dose needed for HRIG (20 IU/Kg of body weight).**

All patients who are exposed to a suspected rabid animal should be managed according to current national guidelines for post-exposure prophylaxis. This must include wound management and PEP. PEP includes rabies vaccine with or without rabies immunoglobulin (RIG). The indications for administration of ERIG remain unchanged. As with HRIG, ERIG MUST BE ADMINISTERED in category III wounds. **The vaccine, its schedule and dosing, remains unchanged.** For further information regarding risk assessment, please consult the national rabies guidelines; link provided below.

Training will be done before introduction of ERIG at healthcare facilities in South Africa. Training will include indication for ERIG, administration and

dosage, adverse effects and management of these, reporting of adverse effects and referral systems where ERIG is not available. The National Department of Health will issue appropriate communications in the coming weeks. For additional information or rabies-related advice, contact the NICD hotline on 082 883 9920.

Link to the national rabies guideline: http://www.nicd.ac.za/assets/files/B5_rabies_revised_2010%282%29.pdf

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

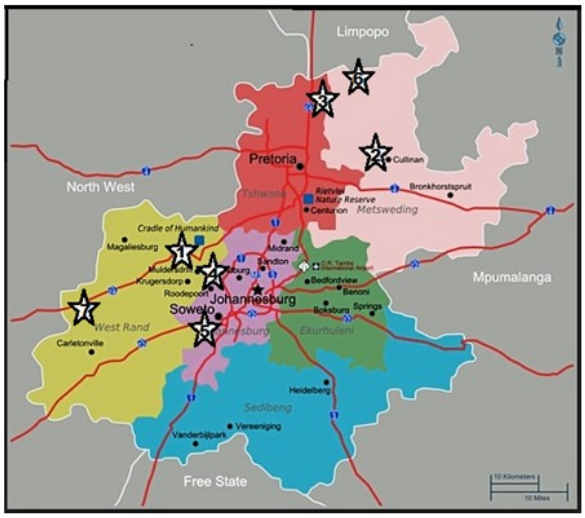
d Animal rabies reported from Gauteng Province

In May 2016, Gauteng provincial veterinary services confirmed the presence of rabies in three jackals. The jackals were found in the Muldersdrift, Broederstroom and Boekenhout (Tshwane) areas in three separate incidents. In one case, the animal appeared unusually tame and entered a building. Three human contacts were given post-exposure prophylaxis (PEP). Two persons required rabies immunoglobulin and rabies vaccine, as they had sustained category three injuries (a scratch or lick to an open wound), while the third required only rabies vaccine as there was no contact with saliva nor injuries sustained. Although cases of rabies in animals in Gauteng are unusual, there have been a number of cases in the past 5 years (Figure 2).

Following exposure to any animal, a risk evaluation should be done to assess the need for rabies post-exposure prophylaxis. Canid biotype rabies circulates in dogs but also in black-backed jackals, bat-eared foxes, genets, African wild cats, aardwolf, polecats, badgers, mongooses, squirrels and suricates. Occasionally cows, domestic cats, cane rats and antelope are infected. Following exposure to any of these animals, an evaluation of the animal behaviour should be elicited. Unusually tame behaviour (in wild animals) or aggressive behaviour in an unwell domestic animal is of concern. The geographical location and known patterns of canine rabies should be considered. A history of vaccination of the offending animal is not necessarily proof that the animal is rabies free. Once it is deemed that PEP is required, the type of exposure should be evaluated: if intact skin is broken the injury is considered a category three injury and PEP consisting of rabies immunoglobulin (RIG) and rabies vaccine should be given. Non-category three exposures require only rabies vaccine. Consult the national rabies guidelines at http://www.nicd.ac.za/assets/files/B5_rabies_revised_2010%282%29.pdf for full details regarding PEP, and see the article in this edition on equine RIG.

Regarding the number of human rabies cases in South Africa, only a single case has been diagnosed to date. A young boy in KwaZulu-Natal Province was exposed to a rabid cat in December 2015, and was diagnosed with rabies in January 2016, prior to his death.

Source: Division of Public Health, Surveillance and Response, NICD-NHLS; Centre for Emerging and Zoonotic Diseases, NICD-NHLS; Gauteng and National Department of Veterinary Services



#	Location	Animal	Month/ year
1	Muldersdrif, Lanseria	2 x jackals	May 2016
2	Doornkraal, Tshwane	Honey badger	April 2016
3	Buffelsdrift, Tshwane	Cat	February 2016
4	Kloofendal, Helledruin, Roodepoort	Domestic dogs	August 2015
5	South-Western Johannesburg	Domestic dogs	2010
6	Boekenhout-kloof, Tshwane	Jackal	May 2016
7	Randfontein	Dog, Jackal, Mongoose	June 2016

Figure 2. Details of the cases of confirmed animal rabies in Gauteng 2010-2016 that are known to the NICD. **NB:** When conducting a risk assessment for animal exposures taking place near the borders of Gauteng, health care workers should consider the prevalence of rabies amongst animals in adjacent provinces.

3 ENTERIC DISEASES

a Typhoid fever cases in South Africa: January-April 2016

The number of typhoid cases in South Africa continues to follow the national monthly trends that have been seen over the last few years (Figure 3), with an annual peak of cases in the early months of the year, and few cases over the winter season.

As of 12 May 2016, a total of 58 laboratory-confirmed typhoid fever case-patients including two deaths has been reported in six provinces across South Africa, with 21 cases reported in January, 19 cases in February, eight cases in March and 10 cases in April (Figure 3). Where age was reported (n=56), age range is 9 months to 68 years with a median of 13 years (IQR 8-30 years). Nine (9/56; 16%) case-patients are children <5-years-old while 18 are adults 20-45 years of age. Females account for 50% (n=29) of cases reported. Diagnosis was based on the isolation of *Salmonella* Typhi in blood culture (88%, n=51), stool specimens (10%, n=6) and urine specimen (2%, n=1). To date, amongst the 45 case-patients in whom travel history is known, 22 (22/45; 49%) reported a history of travel outside their home-town/city within 1 month before the onset of illness. Travel history was to Limpopo Province (n=2), Eastern Cape Province (n=1), KwaZulu-Natal Province (n=2), Zimbabwe (n=10), Malawi (n=2), India (n=2), India/Seychelles (n=1), Bangladesh (n=1) and America (n=1). Of the 23 case-patients without travel history, four had received visitors who had travelled from the Eastern Cape Province (n=1), Gauteng Province (n=2), and Tanzania (n=1) respectively.

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

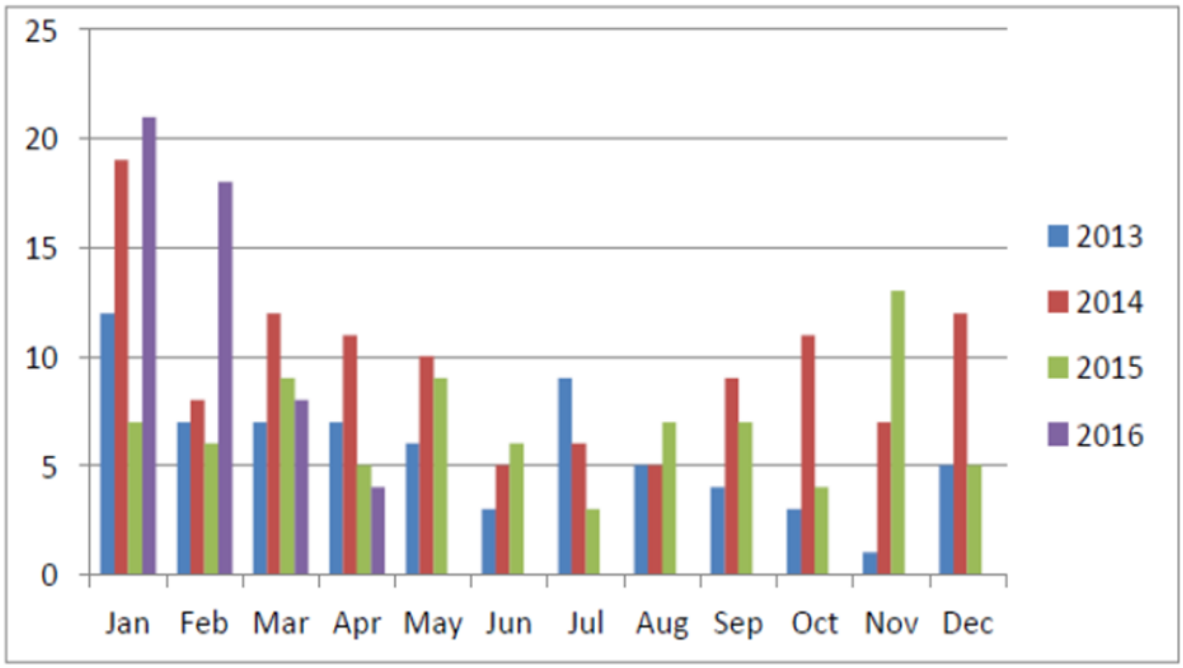


Figure 3. Number of laboratory confirmed typhoid fever cases by month, identified in South Africa 2013-2016. Data courtesy Central Data Warehouse, NHLS

4 SEASONAL DISEASES

a Respiratory syncytial virus infections during 2016

At sentinel sites where surveillance for respiratory viruses is being conducted, the number of cases testing positive for RSV this season continues to increase.

During the first 18 weeks of 2016, 1 Jan 2016 to 8 May, 1 075 patients hospitalised with severe respiratory illness were enrolled at the six pneumonia surveillance sentinel sites. Of these 18% (190/1 075) tested positive for respiratory syncytial virus (RSV). Of the 190 patients that tested positive for RSV, 91% (173/190) were children less than one year. The 2016 RSV season started in week eight (week ending 28 February 2016) when the detection rate rose to and was sustained at ≥10% for ≥2 consecutive weeks. In epidemiological week 18 (week ending 8 May 2016), 51% of all individuals hospitalised with lower respiratory tract infections tested RSV positive.

RSV is the most common cause of bronchiolitis and lower respiratory tract illness (LRTI) among young children. It is highly contagious and interpersonal spread is frequent. RSV-associated bronchiolitis occurs more frequently in infants, a rate 2 to 3 times higher than in children >5 years. Infection with RSV does not result in permanent or long-term immunity and re-infections can occur. In keeping with our observations this season, approximately 40% of patients of all ages and approximately 60% of children aged <5 years who are hospitalised for management of lower respiratory illness, test positive for RSV.

Bronchiolitis is usually self-limiting. Patients present with signs of upper respiratory illness, low grade fever and wheezing. The majority of infants with RSV-associated bronchiolitis do not require hospitalisation, but certain children are at risk of severe disease or require supplemental oxygen. Infants aged <6 months may develop severe disease with inability to feed, hypoxia and severe respiratory distress as evidence by tachypnoea, nasal flaring or lower chest retractions. Some children and infants may develop apnoea. In very young infants, irritability, decreased activity, and breathing difficulties may be the only presenting symptoms. Risk factors for severe RSV-associated disease include prematurity, congenital heart disease, chronic lung disease of prematurity, neurological disease, infants <6 months, immunodeficiency and lack of breast feeding. Environmental factors that are risk factors for severe RSV-associated disease include overcrowding, poverty and day care centre attendance.

Prevention of RSV plays an important role in the management of the disease. Measures include isolation of children with influenza-like symptoms (sick children should not go to crèches for a few days), and teaching children (and adults looking after infants) to practise sneeze and cough hygiene. The use of prophylactic antibiotics for children with upper respiratory tract infections is not recommended. The monoclonal antibody, palivizumab, administered monthly throughout the RSV season to infants and children at high risk of severe RSV disease, has been shown to be effective for prevention. However, high costs and the need for monthly intramuscular injections through the RSV season, limit its use.

Sources: Centre for Respiratory Disease and Meningitis, NICD-NHLS

b An outbreak of Odyssean malaria in Fochville, Gauteng Province

In the April 2016 Communique, three probable cases of Odyssean malaria were reported from the Fochville area that had occurred in March 2016. The cases involved a 31-year-old female (index case) and two other cases - a 47 year-old grandfather and his six-year-old grandson. All three patients had no travel history over the past 12 months. The two families resided within 180 m of each other, but were otherwise unrelated. All three cases presented to the health system with flu-like symptoms. However the absence of a travel history delayed the diagnoses. The 31-year-old female died, while the other patients recovered with no adverse clinical outcomes.

Fochville is a farming and mining town situated in the Gauteng Province under the West Rand District and within the Merafong City Local Municipality. A

site visit to the residential properties of the patients one week following notification of the cases was conducted. Entomological investigations indoors in the bedrooms where the patients are assumed to have slept around the time of probable infection, revealed no mosquitoes. Similarly, outdoor investigations revealed no breeding sites. There was no evidence of informal settlements near the town and the only major roads of note are the R500 and the N12 highway, which are 600 m and 9 km, respectively, from the two residences.

These three unusual cases once again highlight the importance of clinical vigilance and a high index of suspicion for malaria in anyone with flu-like symptoms. Malaria should be suspected especially when thrombocytopenia (<150 x 10^9/L) occurs in the context of a febrile illness, even in the absence of a travel history. This is especially important in mining and farming areas where migration within and across borders can result in the importation of infectious mosquitoes from malaria-endemic regions within South Africa (Mpumalanga, KwaZulu-Natal and Limpopo provinces) as well as outside South African borders (especially Zimbabwe and Mozambique). Cases of imported malaria commonly increase after holiday seasons and public-holiday periods throughout the year. Malaria is a notifiable disease in South Africa and each diagnosed case must be reported to health authorities. Malaria guidelines are available at http://www.gov.za/documents/guidelines-treatment-malaria-south-africa

Source: Centre for Opportunistic, Tropical and Hospital Infections, NICD-NHLS; Division of Public Health Surveillance and Response, NICD-NHLS; Gauteng Provincial Department of Health, West Rand)

5 HIV AND SEXUALLY TRANSMITTED INFECTIONS

a Universal test and treat implementation: an update on the HIV testing services diagnostic algorithm in adults

The South African National Department of Health announced on the 10 May 2016 that it will implement the two major recommendations of the WHO regarding the timing of anti-retroviral therapy (ART) initiation, and on pre-exposure prophylaxis (PrEP) for HIV. These recommendations are: 1) treatment initiation in all age groups regardless of CD4 count ("Universal Test and Treat", UTT); and 2) prevention of infection using PrEP for high-risk populations in combination with other prevention measures. In South Africa UTT is to be implemented from September 2016 for all HIV-positive persons and PrEP will be provided to sex workers from June 2016, starting in 10 sex-worker programmes. These two policy recommendations are based on clinical trials and observational studies.

The implementation of UTT is likely to be complex as several operational requirements, including HIV diagnostic testing, need to be addressed. In South Africa, HIV Testing Services (HTS) are the key entry points for the continuum of HIV care and treatment. As part of the preparation for UTT, the DoH has updated the HTS policies and guidelines, which are now in line with the WHO HTS 2015 guidelines. The South African HTS diagnostic testing strategy remains a serial testing algorithm but changes aimed at improving the accuracy of results have been made as follows:

- If the screen and confirmatory rapid test are discrepant, guidelines recommend that both screen and confirmatory rapid test should be repeated. If the repeat rapid testing result remains discrepant, only then should a specimen will be sent to the NHLS laboratory for ELISA testing.
- ELISA testing at the NHLS laboratory must follow the standard diagnostic testing for HIV infection namely 4th generation ELISA/EC testing. As before, any initial 4th generation ELISA test that is reactive must be confirmed using a second and different 4th generation ELISA platform. However, if the two 4th generation results are discrepant, a second specimen is to be sent in 14 days.

When discrepant results are observed using rapid tests, a tiebreaker test is no longer recommended. There is evidence to suggest tiebreaker tests may result in an increase in false-positive results. Also, current HIV rapid tests are likely to miss acute/early infections, and combination (antibody + p24 antigen detection) HIV rapid tests have not shown an improvement, most likely because of insufficient sensitivity in detecting p24 antigen. The HTS

guideline does not include confirmation of HIV infection prior to initiation of ARV therapy.

In the South African HTS 2016 guideline, HIV self-testing is acknowledged as a potential way to increase test coverage, particularly amongst males, young persons, and other high-risk groups. The South African Pharmacy Council has approved over-the-counter distribution and use of HIV self-tests. Clearer guidance will likely be developed for self-testing following planned studies to assess acceptability, ease of use and access. The South African HTS 2016 guideline recommends that any reactive (positive) self-test result should be confirmed through standard HTS testing algorithms.

Source: Centre for HIV and Sexually Transmitted Infections, NICD-NHLS.

6 VACCINE-PREVENTABLE DISEASES

a The switch from trivalent to bivalent oral polio vaccine in South Africa

Following the official declaration in September 2015 (see link below) by the World Health Organization (WHO) that wild poliovirus type 2 was globally eradicated, a plan was designed to remove the type 2 strain from the trivalent oral polio vaccine (tOPV). This was a synchronised event in all countries around the world and April 2016 was chosen as the month for the switch from tOPV (containing all 3 types of poliovirus) to bivalent OPV (only containing poliovirus types 1 and 3). Immunity to poliovirus type 2 will be maintained by administration of the inactivated polio vaccine (IPV), which contains inactive virus particles of all 3 poliovirus types, in the national immunisation programs.

South Africa chose the 20th of April to conduct the switch from tOPV to bOPV. Clearly marked boxes were used for distribution of bOPV throughout the national territory during the weeks prior to the switch date. All provinces and districts were requested to plan their order of tOPV accordingly such that on the 19th of April 2016 there was just enough tOPV for routine vaccination activities. Administration of bOPV commenced on the 20th of April 2016 while all remaining tOPV was removed from the health facilities and vaccine supply chain for destruction. After the switch, the Department of Health, supported by the National Certification Committee, the National Polio Expert Committee, and the National Task Force for Polio Containment, monitored all national, provincial and district storage and distribution points, as well as a select number of health facilities to ensure that tOPV was out of the cold chain and no longer in use, and that only bOPV was in use.

The South African vaccine switch occurred smoothly, with only a small number of districts in which tOPV was found requiring a more intense audit. National, provincial and district distribution points were all compliant, meaning tOPV stocks are no longer available and bOPV is in full use country-wide. As of the 9th of May 2016, 154 of the 155 countries using OPV around the world have switched from tOPV to bOPV.

Congratulations are in order for South African health care workers!
http://www.polioeradication.org/mediaroom/newsstories/Global-eradication-of-wild-poliovirus-type-2-declared/tabid/526/news/1289/Default.aspx

Source: Centre for Vaccines and Immunology, NICD-NHLS.

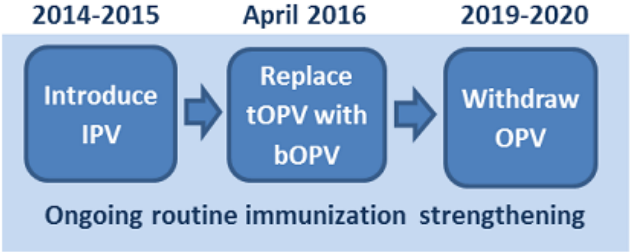


Figure 4. Key dates in the polio end-game. Taken from http://www.who.int/immunization/diseases/poliomyelitis/endgame_objective2/oral_polio_vaccine/planning/en/

7 UNUSUAL PRESENTATIONS OF COMMON PATHOGENS

a A fatal case of hepatitis due to HSV, presenting as a viral haemorrhagic fever

In April 2016, NICD was alerted about a 45-year-old previously-healthy male admitted to hospital with a history of fever (temperature of 39^0C), myalgia and malaise for 3 days with a request for yellow fever testing. On further enquiry, the NICD established that the patient had travelled to Mozambique (Tete Province) 2 months prior to presenting with illness. He had a low blood pressure, was tachycardic with a pulse rate of 122 beats per minute and tachypnoeic, though his CXR was normal. His admission blood test results showed a profound thrombocytopenia (platelets – 6 x 10^9/L) and markedly elevated liver enzymes (ALT – 6 287IU/L; AST – 1 537 IU/L) His clinical condition deteriorated within 36 hours of admission, requiring ICU and ventilation. He progressed to ARDS, arrhythmias, renal and liver failure and significant bleeding and died 4 days after admission. Blood cultures, hepatitis A, B and C, and three malaria smears, were all negative. Clinical specimens were sent to NICD for further testing to exclude Crimean-Congo haemorrhagic fever (CCHF) which is endemic in the area. CCHF testing returned with a negative result; however PCR for herpes simplex virus (HSV) tested positive on blood and was thought to be the cause of the illness.

Herpes simplex virus hepatitis is an unusual but well-described clinical entity following primary HSV infection, and is known to cause fulminant hepatitis in immune-compromised patients, pregnant females and rarely, in immune-competent adults. Two previous cases in immunocompetent adults were described in the NICD Communiqué in 2008 and 2013. The illness typically presents with a short onset of non-specific flu-like symptoms. Patients frequently present with elevated liver enzymes levels, a minimal increase in bilirubin levels, leucopenia and thrombocytopenia. While positive serology and PCR results can be confirmatory for HSV hepatitis, definitive diagnosis is made by liver biopsy. In the absence of muco-cutaneous herpetic lesions, diagnosis of herpes hepatitis is often difficult and delayed. Mortality outcomes are as high as 90% in the event of acute liver failure. The efficacy of intravenous administration of acyclovir is unknown, thought occasional good outcomes have been reported, especially when the diagnosis is made early in disease presentation. However, acyclovir treatment is generally unsuccessful by the time the diagnosis of HSV hepatitis is made.

References:

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- Poley, R. A., Snowdon, J. F., & Howes, D. W. (2011). Herpes Simplex Virus Hepatitis in Immunocompetent Adult. *Case Reports in Critical Care*, 4.
- NICD Communique: January 2008 and April 2013

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

8 SURVEILLANCE FOR ANTIMICROBIAL RESISTANCE

a Detection of carbapenem-resistant *Klebsiella pneumoniae* at a regional hospital in KwaZulu-Natal Province

Over a three-week period in April 2016, carbapenem-resistant *Klebsiella pneumoniae* (CRKP) was isolated from nine infants at in the neonatal intensive care unit (NICU) of a regional hospital in KwaZulu-Natal. All babies were in the NICU for medical conditions that required urgent intervention and intensive monitoring. One of the babies was seriously ill on admission to the unit, and required transfer to a tertiary centre, where the baby subsequently died 10 days later. Isolates from seven of the nine patients were available for further analysis. During the outbreak investigation, CRKP was isolated from six specimens collected from equipment and surfaces in the NICU. Additionally, the on-site laboratory retrieved five stored CRKP isolates from the freezers. The latter

were collected from patients admitted to another section of the hospital between January and April 2016.

All 18 CRKP isolates tested were susceptible to colistin and tigecycline. Further analysis of the patient and environmental isolates revealed that all possessed the *bla*$_{NDM}$ gene for carbapenamase production. To determine relatedness, pulsed-field gel electrophoresis (PFGE) was performed on all 18 isolates (Figure 5). All strains were related according to Tenover criteria (a cluster was defined as PFGE patterns differing by three or less bands) but two sub-clusters were identified. Sub-cluster A comprised 14 isolates which were indistinguishable. Sub-cluster B comprised four isolates and differed from sub-cluster A by one band. Within sub-cluster B, three isolates were indistinguishable, while one differed by one band. Three of the five retrieved isolates belonged to sub-cluster A and two to sub-cluster B. Of the seven isolates from patients within the NICU, six belonged to sub-cluster A and to sub-cluster B. One of the isolates from the environmental sampling belonged to sub-cluster B , whilst the rest belonged to sub-cluster A.

Isolates belonging to both sub-clusters appear to be circulating in different parts of this hospital. A possible reservoir facilitating transmission within different sections of this hospital needs to be investigated. It is also plausible that the outbreak might have been going on undetected for some time creating the two sub-clusters that differed by one band. Infection prevention measures were reinforced, and ongoing surveillance has not revealed further cases of CRKP over the past four weeks.

Surveillance results over the past years have revealed that CRKP is present in many South African facilities, both private and public, and may also be found circulating in the community. This is especially the case amongst persons who are in frequent contact with healthcare establishments. This outbreak illustrates the importance of adherence to appropriate infection control procedures.

Source: NHLS-Business Unit, KwaZulu-Natal**;** University of KwaZulu-Natal Province; Antimicrobial Reference Laboratory, Centre for Opportunistic, Tropical and Hospital Infections, NICD-NHLS;

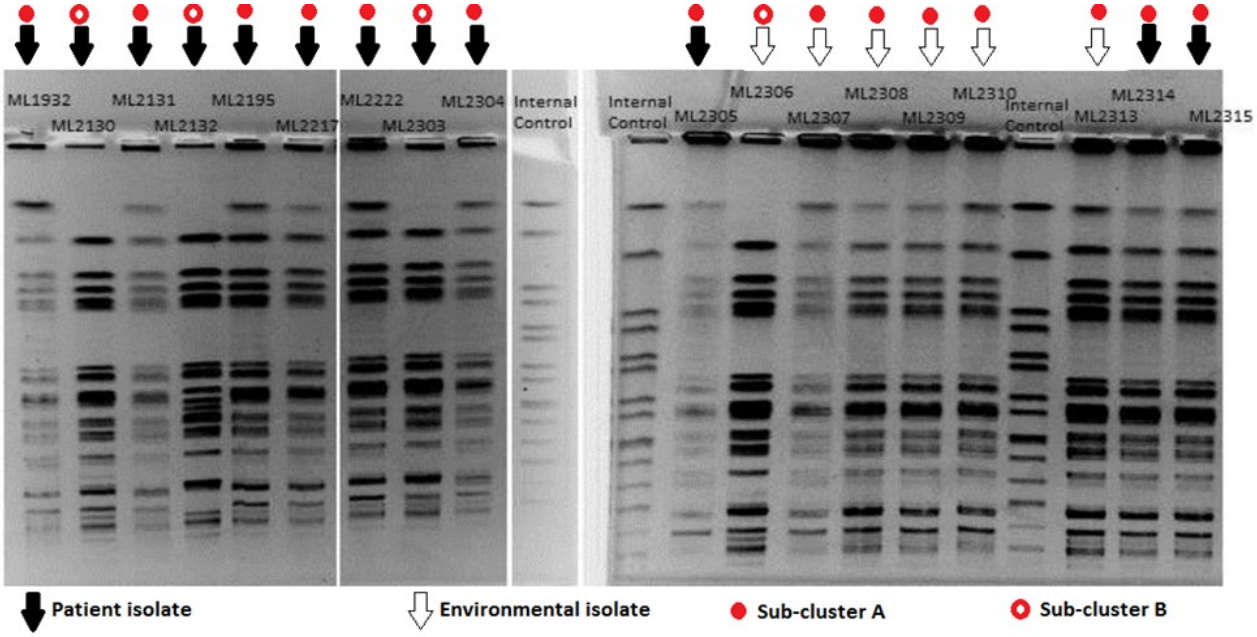


Figure 5. Pulsed-field gel electrophoresis of 18 strains (12 patient and 6 environmental isolates) of carbapenem-resistant *Klebsiella pneumoniae*, isolated from patients in the neonatal intensive care unit of a regional hospital in Kwa-Zulu-Natal Province

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. In April 2016, a total of 135 Enterobacteriaceae isolates were received. One hundred and nine isolates were screened, 97 of which expressed carbapenemases (Table 1). Majority of these CPE isolates were *Klebsiella pneumoniae* (71) followed by *Enterobacter cloacae* (17).

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.za.za)

Table 2. Enterobacteriaceae by CPE enzyme type, AMRL-CC, COTHI, NICD, April 2016 and January-March 2016

Organism	NDM		OXA-48 & Variants		VIM	
	Jan-Mar 2016	Apr 2016	Jan-Mar 2016	Apr 2016	Jan-Mar 2016	Apr 2016
Enterobacter aerogenes	-	-	2	1	-	-
Enterobacter cloacae	7	6	11	3	-	-
Enterobacter kobei	-	-	-	1	-	-
Escherichia coli	1	2	20	11	-	-
Klebsiella oxytoca	-	-	2	1	-	-
Klebsiella pneumoniae	72	46	125	25		1
Klebsiella spp	-	-	-	1	-	-
Proteus vulgaris	-	1	-	-	-	-
Providencia rettgeri	6	1	-	-	-	-
Serratia marcescens	14	1	3	1	-	-
Total	**100**	**57**	**163**	**44**	**-**	**1**

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

9 BEYOND OUR BORDERS

The 'Beyond our Borders' column focuses on selected and current international diseases that may affect South Africans travelling abroad. Numbers correspond to Figure 5 on page 14.

1. Avian influenza (H7N9 and H5N6) - China
China reported 11 laboratory-confirmed cases of human infection with avian influenza A (H7N9) virus, including four deaths, to WHO on 17 May 2016. From 5-9th May, China reported three new human A (H5N6) virus infections. No human-to-human transmission has been documented. All cases have had exposure to live poultry or slaughtered poultry market and live poultry, while one reported a history of selling pork at a market. 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, and avoid entering poultry slaughter areas. No special screening at entry points, travel or trade restrictions are currently recommended by WHO. However, for travelling or returning individuals who develops symptoms of severe acute respiratory infections (SARI) while travelling, or soon after returning, a diagnosis of avian influenza virus should be considered. Countries are encouraged to continue with influenza surveillance strengthening, including SARI surveillance to detect unusual pattern under the IHR (2005) human infections reporting.

2. MERS-CoV – Qatar and Saudi Arabia
A single case of MERS-CoV has been reported from Qatar in a patient who reported frequent exposure to dromedaries as part of his work. Four cases in Saudi Arabia were identified from 30 April to 5 May 2016. Two cases were reported from Riyadh city, of which one was an asymptomatic contact identified during contact tracing. One case each was reported from Hofuf and Hail cities respectively. Of the four cases, a single case who had reported frequent contact and consumption of dromedaries' raw milk, resulted in a fatality. Since September 2012, 1 733 laboratory-confirmed cases of MERS-CoV with 628 deaths were reported globally (case fatality rate: 36.2%). People should avoid contact with camels and camel products such as unpasteurised camel milk, camel urine or improperly cooked camel meat.

3. Anthrax – Bangladesh
On 17 May 2016, 40 cases of human anthrax infections were reported from one village at Ullapara upazila, Sirajganj. This is the second such incident with 87 people infected to date, from three upazilas (Shahjadpur, Kamarkhand and Sirajganj). It appears that the infections occurred when sick animals were slaughtered, the meat sold, and consumed. A vaccination program for animals in the affected villages was initiated. Persons should avoid slaughtering sick animals and consuming meat from sick animals.

4. Cholera – Asia
India: A total of 25 cholera cases was reported in Jaipur, Rajasthan State, India, and more than 100 cases in Uttar Pradesh State in May 2016.

5. Measles – Pakistan
Following the diagnosis of measles in over 500 children over April and May 2016 in Karachi, Pakistan, the health department has planned to vaccinate over 1.1 million children between the age of 6 months and 5 years.

6. Cholera – Malawi and Kenya
An estimated 266 cases of cholera with 13 deaths were reported within a two-month period from the northern districts of Malawi (Karonga and Rumphi). Two cholera outbreaks were reported in Kenya from the Narok and Mandera areas. At Norak Boys High School, 11 students were admitted to hospital for treatment following severe diarrhoea and vomiting. In the Mandera County outbreak, 320 cases and five deaths were reported. Food inspection and good hygiene practices were emphasised to prevent further spread.

7. Lassa fever – Nigeria
Since January 2016, the Nigerian Federal Ministry of Health has reported 657 suspected Lassa fever cases (63 lab-confirmed) and 75 deaths. In the same period in 2015, 101 suspected cases (8 laboratory confirmed) with three deaths were reported. The reason for the increased number of cases and increased fatality rate this season is unknown.

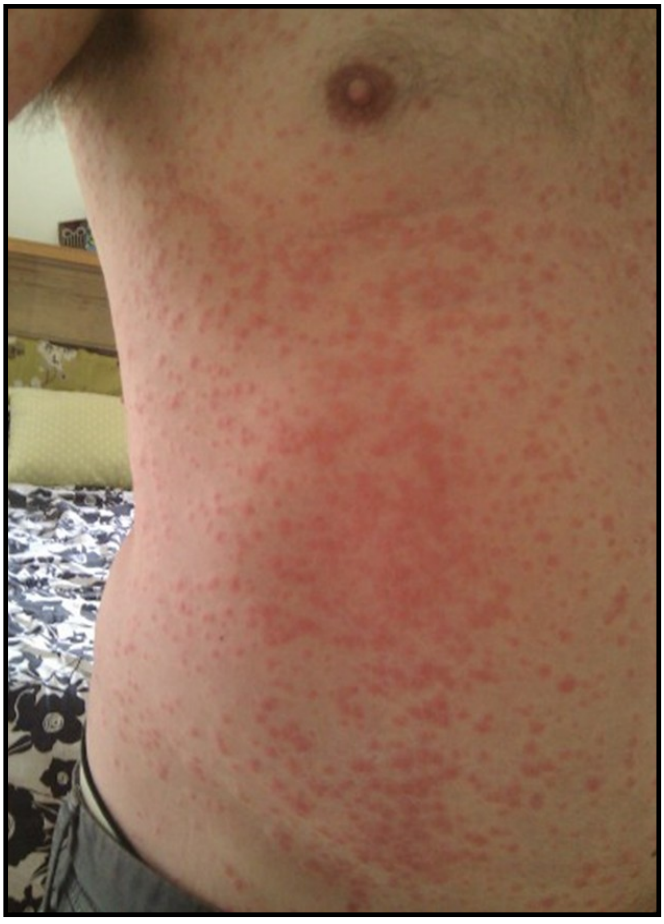
8. Yellow fever - Angola – see page 2

9. Zika virus – Cape Verde – see page 4

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

Figure 6. 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

10 PHOTOQUIZ



May Photoquiz (left)
This rash, along with low-grade pyrexia, developed in a traveller who returned five days ago from Belize. What is your differential diagnosis? Please supply your answers in an email to kerriganm@nicd.ac.za with 'April Photoquiz' the subject line.

April photoquiz (below)
The correct response was 'bubonic plague', caused by *Yersinia pestis*. The photograph was taken by Margaretha Isaacson probably during the Lesotho outbreak in 1968 and was provided by Prof John Frean. The differential diagnosis of a suppurating bubo includes plague, tuberculosis, granuloma inguinale caused by *Klebsiella granulomatis*, or just simply a polymicrobial abscess.