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CONTENTS

1 ZOONOTIC AND VECTOR-BORNE DISEASES

a Dengue in returned travellers

In recent years there has been a dramatic increase in the prevalence of dengue fever in endemic countries. This has resulted in more cases amongst travellers returning home from the dengue-endemic regions: South-East Asia, the Western Pacific, the Americas (Central and the northern parts of South America), Central, West and East Africa and the Eastern Mediterranean. The NICD has documented 17 laboratory-confirmed dengue cases up to and including October during 2015. All cases were amongst travellers returning from known dengue-endemic countries, including Thailand, India, Philippines, Papua New Guinea and Uganda. In October 2015, acute dengue infection was confirmed in four travellers returning to South Africa from Papua New Guinea, India and Thailand. We describe these four cases, all of whom recovered without complication.

1) A 27-year-old man from Gauteng became ill after visiting Papua New Guinea in mid-October 2015. He reported an influenza-like illness and skin rash. Blood tests demonstrated a thrombocytopenia (128 x10^9/L and leucopenia (0.5 x 10^9/L). Negative smear, antigen and PCR tests excluded malaria as a diagnosis. Blood collected three days after symptom onset tested positive by RT-PCR for dengue, confirming an acute dengue infection.

2) A 39-year-old female South African traveller returned from Thailand on 17 October 2015 and developed fever, headache, photophobia, severe lower back and joint pain. The patient presented with a macular rash on the face and body. She was admitted to a Cape Town hospital on 22 October 2015. Abnormal blood findings included leucopenia (3.5 x 10^9/L) and elevated liver transaminases (ALT 280 IU/L) on admission. Blood collected on day five post-onset (24 October) tested positive by RT-PCR, confirming acute dengue fever.

3) A 62-year-old female spent two weeks in India's westernmost state Gujarat, visiting her relatives in the cities of Vadodara and Surat. On her way from Vadodara to Mumbai she experienced a single febrile episode, followed by weakness, nausea, gastric distress, and mild muscle pain. She was given antibiotics (ofloxacin) and stayed in a hotel in Mumbai to recover before returning to South Africa. Upon arrival in East London on 29 October 2015, she consulted her general practitioner who observed a fine petechial rash over her lower legs. Blood tests revealed thrombocytopenia (28 x 10^9/L) and elevated transaminases (ALT 181 IU/L, AST 292 IU/L). A diagnosis of dengue fever was made by RT-PCR and serology.

4) A 10-year-old girl returned from Thailand 10 days prior to onset of symptoms which included high fever, headache and rash. Blood collected three days after onset of illness tested positive for dengue by RT-PCR.

The differential diagnosis of fever in a traveller returning from Asia, South- and Central America, West, Central and East Africa includes malaria, dengue, hepatitis A, typhoid fever, invasive bacterial diarrhoea, rickettsial infections, or causes not related to travel. The typical clinical presentation in uncomplicated dengue includes fever, severe headache, pain behind the eyes, muscle and joint pains, nausea, vomiting, swollen glands and a maculopapular rash. The NICD provides laboratory diagnostics for dengue. The timing of sample collection after disease onset is important for the interpretation of laboratory results. The presence of dengue virus is consistent with acute-phase infection and is typically detectable within 1 to 2 days following infection and up to 9 days after disease onset. Antibodies to the dengue virus may be detected by day 3 – 7 after symptom onset. If initial antibody tests are negative, a convalescent blood sample with the second specimen collected two weeks after the acute phase of infection will demonstrate seroconversion. Serology may be useful if blood was not collected during the viremic (acute) phase of infection.

At a public health level, viraemic travellers returning from endemic areas present a risk of introducing dengue into non-endemic countries where the specific vectors are present. While dengue is not found in South Africa, the mosquito vector of dengue fever, *Aedes aegypti* is present in certain regions of South Africa, namely the KwaZulu-Natal coastline.

Source: Centre for Emerging and Zoonotic Diseases, NICD-NHLS; Pathcare East London

b Rabies

Eight confirmed cases of human rabies have been diagnosed by the NICD in South Africa during 2015 to date. These cases were reported from Limpopo (n=3), KwaZulu-Natal (n=1), Free State (n=1) and the Eastern Cape (n=3) provinces. A probable case of rabies from KwaZulu-Natal could not be verified by laboratory testing but the patient had a clinical and exposure history compatible with a rabies diagnosis.

Two cases of rabies have been confirmed in the past month from the Eastern Cape Province. The first case involved a 36-year-old male from Bizana. He was attacked by a neighbour's dog two months before falling ill. The dog was reportedly aggressive and also attacked two other people, but nothing further was known about the dog. The patient received one dose of rabies vaccine. On 27 October 2015, he became ill. Hydrophobia was noted. The patient died on the same day. A number of saliva and cerebrospinal fluid specimens were submitted for ante-mortem diagnosis of rabies at the NICD but tested negative. Rabies was confirmed on post-mortem brain tissue by fluorescent antibody testing and RT-PCR.

The second case was in an 8-year-old boy also from Bizana. The patient was bitten on the cheek by a stray dog on the 1st October 2015. The child was taken to a local clinic for follow up but no rabies vaccine or immunoglobulin was reportedly available. The child was admitted to hospital with hydrophobia and restlessness and died on the 7th November 2015. A saliva swab collected post mortem tested negative for rabies by reverse transcription PCR. The patient's blood, collected one day before death was positive for anti-rabies IgG and IgM antibodies. In the absence of a history of rabies vaccination, this finding supports a clinical diagnosis of rabies. Rabies antibodies in the blood and CSF typically develop after the first week of illness. Few patients survive into the second week of illness without intensive care. Generally serology is not useful for the diagnosis of rabies in the acute presentation

A case of rabies was also confirmed in a 6-year-old boy from in the Thulamele Local Municipality, Limpopo Province. The child was reportedly scratched by a dog on the lower legs in February 2015 and had sustained only minor wounds. The patient did not present to a facility for care. The child was admitted to hospital in the third week of October 2015 suffering from fever, headache, vomiting, confusion, agitation, delirium, hyperactivity, autonomic instability, insomnia, paraesthesia at the site of the healed wounds and hypersalivation. Saliva specimens were submitted to the NICD for rabies investigation and one of the samples tested positive by real time reverse transcription PCR. The child died and no further specimens were collected for post mortem verification of rabies.

Rabies is invariably fatal after onset of symptoms, but disease is preventable by the administration of rabies post-exposure prophylaxis. An updated poster, published in 2015 summarizing the guidelines for rabies post-exposure prophylaxis is available on the NICD website (www.nicd.ac.za). The root cause of post-exposure management failures in these three tragic cases is inadequate awareness of the risk of rabies and failure to administer post-exposure prophylaxis. Patients with a possible rabies exposure should receive wound management (antibiotics and a tetanus toxoid booster) and rabies post-exposure prophylaxis (rabies immunoglobulin and rabies vaccine as described in the national guidelines).

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

c Tick bite fever

A middle-aged female patient presented in late October to Helen Joseph hospital complaining of fever, prominent headache, and myalgia. She was initially diagnosed with an influenza-like syndrome, but when a rash developed the following day (Figure 1) this diagnosis was reconsidered. The patient lived on the outskirts of Johannesburg on a large property and was reported to own many dogs, one of which slept on her bed at night. She did not report a history of travel, nor of exposure to ticks or tick bites. On examination she was found to have an

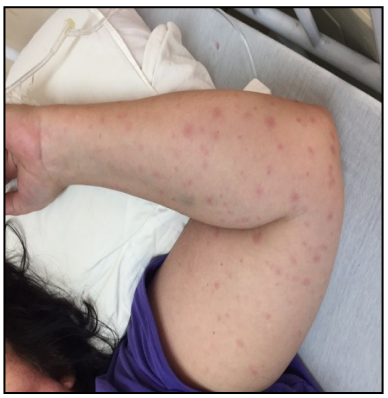

Figure 1. A maculopapular rash in a patient presenting with clinical signs and symptoms of tick bite fever. Photograph courtesy of Dr Jeremy Nel.

eschar in the scalp. (Figure 2). Blood tests were normal. On the basis of this history and clinical findings, notably the eschar, a diagnosis of tick bite fever was made. The patient was treated with doxycycline, and responded well. Initial serology for rickettsial (IFA), done 8 days after symptoms first started, was negative, but a subsequent specimen done 3 days after that was positive.

While the above case is typical of the majority of cases of tick bite fever (TBF), a number of severe cases have been reported by the NICD in the last few months, one of which was fatal despite doxycycline therapy. Severe tick bite fever may present initially with typical signs and symptoms, but cases deteriorate rapidly. Haematological abnormalities including leucopenia, thrombocytopenia and raised transaminases, and a rash which may be haemorrhagic are often reported. The differential diagnosis includes viral haemorrhagic fever, or overwhelming sepsis secondary to bacterial pathogens. The impact of HIV infection on the clinical course of tick bite fever is not well understood.

Two *Rickettsia* species are thought to be responsible for TBF in South Africa. *R. conorii* is associated with a periurban environment and dog ticks, and causes disease that resembles classical Mediterranean spotted fever. Patients are at risk of severe or even fatal complications. *R. africae* is associated with rural and wilderness areas, and is associated with milder illness, less prominent rash, and uncommonly progresses to complicated disease. In terms of the diagnosis of TBF, serology may be negative early on in the course of illness. In this case, a convalescent specimen may be helpful to confirm the diagnosis. The NICD offers a PCR-based assay for *Rickettsia*, which may be done on blood, or on a dry swab taken from the eschar. PCR tests tend to be positive early on in the course of illness. Both *Rickettsia* species respond well to doxycycline therapy.

Treatment of *Rickettsial* infections is with oral doxycycline, 100mg bd. An intravenous quinolone such as ciprofloxacin is effective if oral medication is not possible.

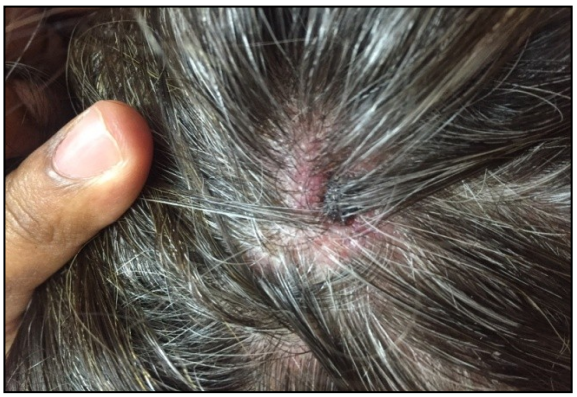

Figure 2. An eschar in a patient presenting with clinical signs and symptoms of tick bite fever. Photographs courtesy of Dr Jeremy Nel.

Reference: Frean J., Blumberg L., Ogunbanjo GA. Tick bite fever in South Africa. SA Fam Pract 2008;50 (2):33-35. accessible at http://www.nicd.ac.za/assets/files/Tick%20bite%20fever%20in%20South%20Africa.pdf

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

d Crimean-Congo haemorrhagic fever

Crimean-Congo haemorrhagic fever (CCHF) was confirmed in a 25-year old male from Wepener, Free State Province. The patient was reportedly bitten by ticks before falling ill. The patient was originally clinically diagnosed with tick bite fever, but in the absence of favourable response to doxycycline treatment and considering the clinical presentation of the patient, an alternative diagnosis of CCHF was considered.

Blood results collected around day four after symptom onset revealed thrombocytopenia (39X 109/L) and raised liver transaminases (AST 94 IU/L; ALT 105 IU/l). Two consecutive blood specimens were collected and submitted for CCHF investigation at the NICD. Both specimens tested positive for CCHF by real time reverse transcription PCR and serology: One specimen tested anti-CCHF IgM positive and the second positive for anti-CCHF IgG and increased level of anti-CCHF IgM antibodies. The patient had no haemorrhagic manifestations, and made an uneventful recovery. No secondary cases have been reported.

This case is the first confirmed case in 2015, and the 200th human case of CCHF from South Africa confirmed by the NICD from 1981 to date. Cases of CCHF have been reported from all nine provinces of South Africa, but predominantly from the Free State, Northern Cape, North West and Western Cape Provinces (Figure 3). Contact with ticks, either by bites or through squashing of ticks (whilst re-

moving them) have been most frequently implied as the route of exposure of patients confirmed with CCHF in South Africa. The virus may also be transmitted, albeit less frequently, by contact with infected blood and tissues from infected animals. Nosocomial transmission in South Africa has been recorded on four occasions since the disease was originally reported in the country.

Amongst South African cases, the mortality rate of CCHF ranges from 5-30%. Presentation may vary greatly from mild disease to fulminant haemorrhagic manifestation. The disease typically includes sudden onset of fever with muscle aches, back ache, headache and photophobia. Sore throat, nausea, vomiting, swollen glands, abdominal pain may also be present. This may progress to include haemorrhagic findings such as petechial rash, ecchymosis, purpura and other forms of bleeding. There is no specific treatment for CCHF, and management is mainly supportive. The efficacy of ribavirin treatment has been the subject of much contention, but it may be useful during the early stages of the disease.

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

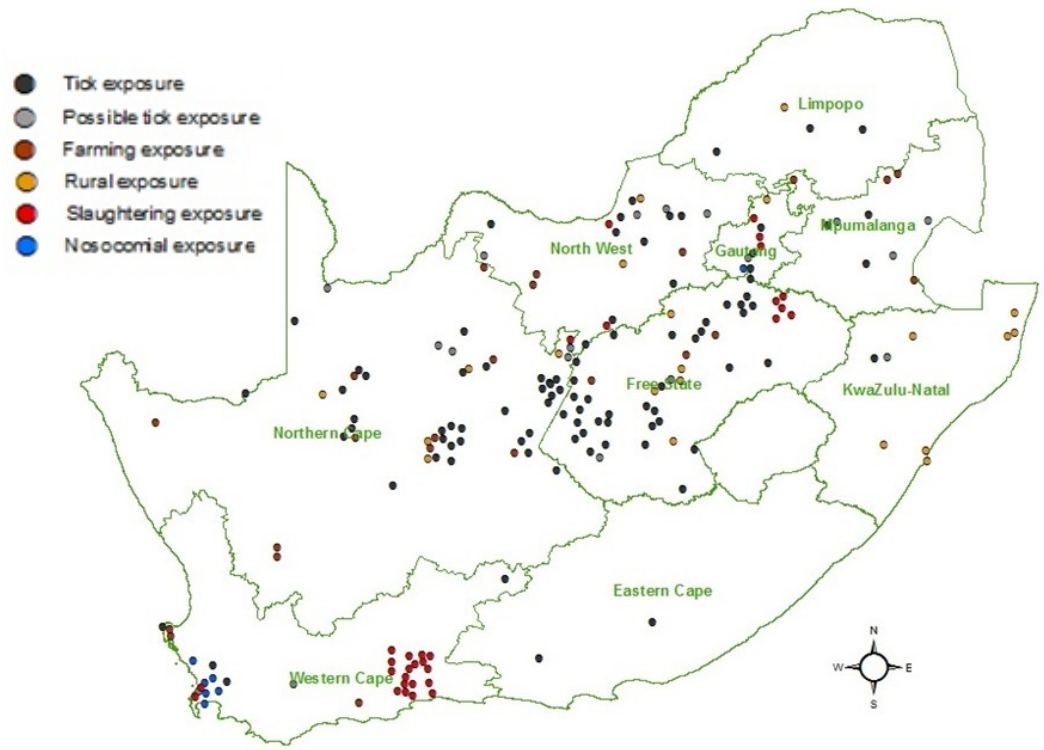

Figure 3: The geographical distribution of laboratory confirmed human CCHF cases in South Africa for the period, 1981-2015. The colour of the indicators depicts the route of exposure recorded for these cases.

2 TB AND HIV

a Surveillance for resistance to anti-retroviral drugs

INTRODUCTION

South Africa (SA) is afflicted with dual epidemics of tuberculosis (TB) and human immunodeficiency virus (HIV). The country has the world's largest antiretroviral (ARV) program, with approximately 3 million people ever started ARV therapy (ART) by 2015. The National Department of Health adopted a public health approach by using standardised combinations of ARVs: first line ART consists of tenofovir (TDF) or zidovudine (AZT) and lamivudine (3TC) or emitricitabine (FTC) with either efavirenz (EFV) or nevirapine (NVP). As of April 2015, all patients with CD4 cell count <500 cells/µl, advanced WHO staging and TB-HIV co-infection were eligible for life-long ART. Clinical and laboratory monitoring recommends that CD4 and HIV viral load testing be performed at 6 and 12 months, and viral loads repeated every 12 months thereafter. Routine testing for HIV drug resistance (HIVDR) is not performed at ART initiation or NNRTI-based regimen failure - patients failing on these regimens are switched to a standardised protease inhibitor-containing 2nd-line regimen after intensified adherence counselling. HIVDR testing is available for PI regimen failure and is a prerequisite for access to 3rd-line regimen selection.

The NICD Centre for HIV and STIs established an

integrated TB-HIV surveillance study in 2014/15 by building on the GERMS-SA hospital-based enhanced surveillance platform. The study introduced surveillance for rifampicin and other drug-resistance in persons initiating TB treatment and/or HIVDR surveillance in persons initiating ART in the same clinic. A single primary health clinic in each province has been selected on the basis of convenience from clinics with high TB and HIV case loads. Enrolment has started in the Eastern Cape (Feb 2015), North West (Jan 2015) and Mpumulanga provinces (Oct 2014). At each clinic, a dedicated surveillance officer (SO) identifies and enrols eligible patients (i.e. patients initiating TB therapy or ART according to routine clinic procedures). Where consent is obtained, SOs interview the participants using a standard questionnaire and available medical records to collect relevant clinical and epidemiological data, and collect sputum or whole blood specimens from the participants. We report on HIVDR data in patients initiating ART.

RESULTS

By September 2015, 219 specimens have been collected for HIVDR testing, 40 (18%) from EC, 24 (11%) from MP and 155 (71%) from NW. Sixty-eight percent of all enrolled participants are female, average age is 33 years (IQR 27-40 years), and median recent CD4 count is 216 cells/µl (IQR 135 – 381 cells/µl). Of 214 case report forms with available data, prior exposure to ART (as PMTCT and/or previous ART) was reported in 57 (27%) participants. Twenty-nine of these reported receiving PMTCT, and 44 had previously received standardized ART for clinical management, between 1 and 5 years prior to current ART re-initiation for an average period of 18 months. Fifteen of these patients had received both PMTCT and ART.

HIVDR testing was successful in 94% of specimens, with amplification failure primarily due to viral loads <1000 copies/ml. NNRTI resistance was detected in 17% of specimens, and dual NRTI/NNRTI drug resistance in 2%. When analysed according to prior ART exposure, HIVDR was present in 30% of participants with any prior ART vs. 15% of those with no reported prior ART (Figure 4).

Whilst study enrolment is at early stages, the data show high proportions of patients are re-initiating ART (27%), and high proportions of NNRTI HIVDR (17%) are present, which may compromise the effectiveness of the NNRTI drug in the standardised first-line regimens.

Sentinel site surveillance, while not population-based and therefore not necessarily generalizable to all clinics, does provide good assessments of prevalence and trend data. The extent to which the facilities surveyed herein are similar to facilities elsewhere and to what extent the patients enrolled are similar to those in the national program needs to be determined in order to ascertain the representivity of this data. However, surveillance through the GERMS platform allows for valuable, consistent and intensified data collection over longer periods of time.

Source: Centre for HIV and STI, NICD-NHLS

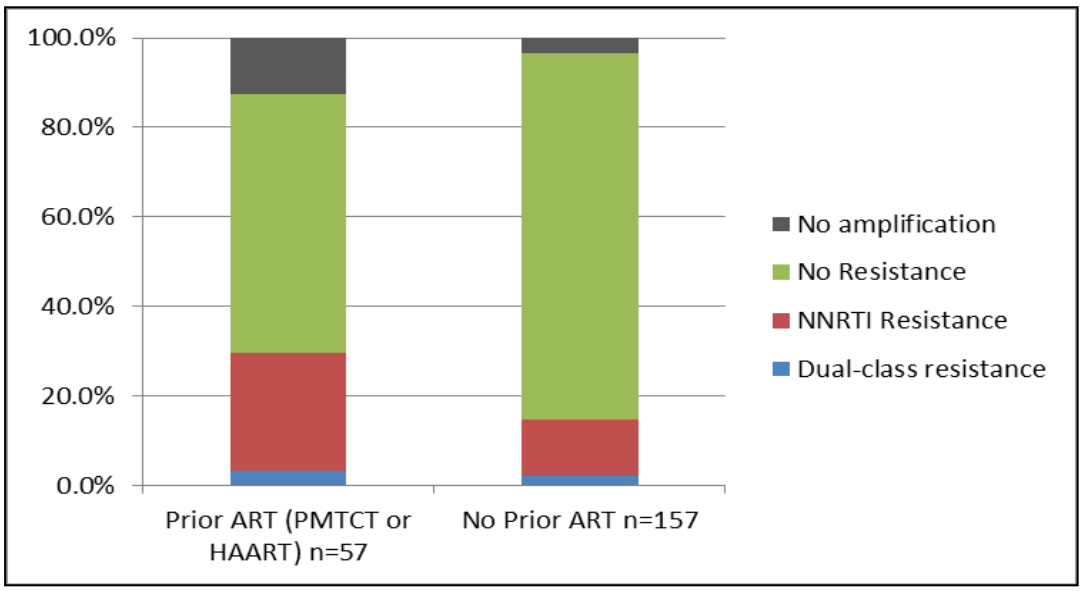

Figure 4. HIV drug-resistance genotyping outcomes amongst 214 participants enrolled in NICD HIVDR surveillance, February – October 2015, according to participants' prior exposure to anti-retroviral therapy.

b WHO Global Tuberculosis Report 2015: Highlights

The World Health Organization (WHO) released the Global Tuberculosis Report 2015 on 28 October 2015. The report indicated major advances: TB mortality has fallen 47% since 1990, with nearly all of that improvement taking place since 2000, when the Millennium Development Goals (MDGs) were set. The MDG target to halt and reverse TB incidence has been achieved on a worldwide basis, in each of the six WHO regions and in 16 of the 22 high-burden countries that collectively account for 80% of TB cases. Globally, TB incidence has fallen by an average of 1.5% per year since 2000 and is now 18% lower than the level of 2000.

Notably, the global total for new TB cases was higher than reported previously. The WHO attributes this to improved national data rather than increase in disease burden. As an example, based on findings of a prevalence survey in Indonesia, the burden of TB is double the previous estimate. These revised estimates have further led to TB ranking alongside HIV as a leading cause of death worldwide. The estimated number of people that died of TB globally during 2014 was 1.5 million, while 1.2 million deaths were attributed to HIV during the same period. Surveillance systems have been overlooked as an important element in TB control efforts and the renewed emphasis on finding and treating new TB cases as well as improving surveillance systems will hopefully prevent further unpleasant surprises. Although it is comforting to know that the number of deaths due to TB globally has actually halved since 1990, the number is still staggering. The report emphasizes that a reduction in mortality cannot be achieved at a population level unless the gap between identifying TB cases (including cases of drug-resistant TB) and treating TB cases is closed.

The Global Report 2015 shows South Africa second in the world in terms of incidence rates for TB, closely behind neighbouring Lesotho. The WHO country profile for South Africa reports marginal decreases in TB mortality (from 48 (95% CI 28-73) to 44 cases (95% CI 41-48)/100,000) and incidence (from 860 (95% CI 776-980) to 834 cases (737-936)/100,000) (Figure 5). Case notifications decreased from 328 896 in 2013 to 318 193 in 2014. Amongst the 2014 cohort, 93% of TB cases had known HIV status, and 79% of HIV-positive TB cases were on anti-retroviral therapy (ART) compared with 90% with known HIV status and 66% of HIV-positive TB cases on ART in 2013.

Overall, the results from the Global TB Report are disappointing as South Africa has introduced a number of interventions including Xpert MTB/RIF, and worked hard at strengthening aspects of the TB control programme. While South Africa attained the MDG to halt and reverse TB incidence, we were not able to halve TB mortality compared with 1990 levels, which remains equivalent to that in 1990 (just under 50 cases/100,000). The news that TB mortality leads HIV deaths is not a surprise as the 2011 report from Statistics South Africa revealed TB as the number one killer in the country. Although the anti-retroviral (ARV) program used in controlling HIV/AIDS, has been shown to have a positive impact on the incidence of microbiologically-confirmed pulmonary TB (mPTB), the implementation of the Xpert MTB/Rif assay in this country has not increased the number of TB patients on treatment nor did it have any impact on patient-relevant outcomes, such as mortality. Similarly, the effect of the isoniazid preventive therapy (IPT) has been shown to be short-lived once treatment is stopped and, with high default rates for TB generally, IPT is unlikely to have a significant population level impact. The TB control strategy in this country will need to be more patient centered, aiming to reduce stigma and incentivizing people to enter care and improve adherence to treatment.

All is not bleak however, as TB is on the decline globally. In the longer term, South Africa has shown a decline of 9% between 2008 and 2012 in microbiologically-proven pulmonary TB (mPTB). These positive trends are exemplified by the change in the longstanding slogan "STOP TB", to the new slogan, "END TB" – the game plan aiming to drastically accelerate reductions in the TB burden in South Africa and world-wide. Much more can and should be done. We need to ensure that policies are informed by real population-based data with patient-relevant outcomes as a key end point. The Global TB Report report highlights the fact that most of the successes were observed since 2000 when the Millennium Development Goals were set – thus aspirational targets backed by funding and sustained effort can make the difference.

Reference: WHO Global TB Report 2015 accessed at http://www.who.int/tb/publications/global_report/en/ on 16 November 2015

Source: Centre for Tuberculosis, NICD-NHLS

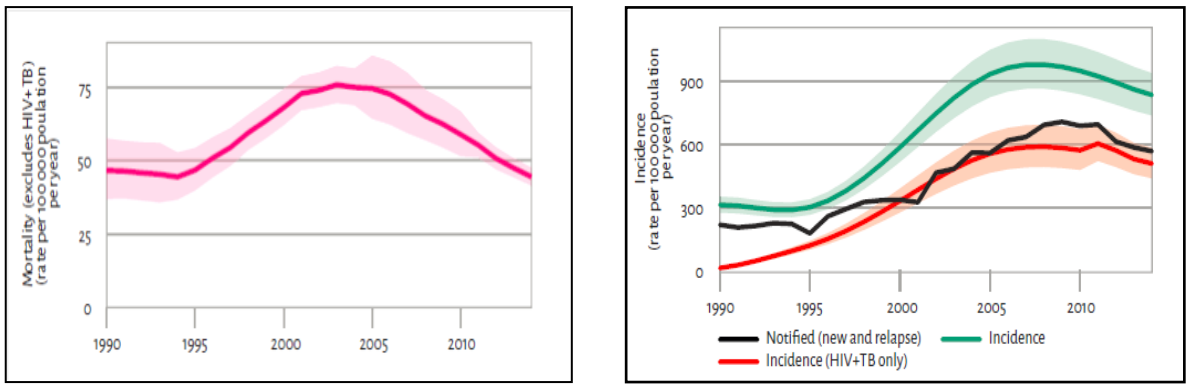

Figure 5. Mortality and incidence of TB per 100,000 population from 1990 to 2015 according to the WHO Global TB report 2015.

3 SEASONAL DISEASES

a Enteroviral meningo-encephalitis outbreak in Tshwane — a preliminary description

The NICD was alerted regarding a possible outbreak of enteroviral meningitis in the Tshwane District on 3 November 2015. A total of 21 cases of confirmed or suspected enterovirus meningitis were reported from a single private hospital. All the cases were in children, and 5 (24%) had a confirmed diagnosis of enterovirus meningitis. All children had been admitted with symptoms of meningitis/encephalitis or a nonspecific febrile illness with general myalgia and gastrointestinal complaints. Following further enquiries, 18 additional cases of viral meningitis/ encephalitis were reported from other private facilities in the Tshwane area. All cases, except one, were children <10 years of age. To date NICD has obtained residual clinical specimens from 7 of the cases; 3 (43%) of these samples tested positive for enterovirus, of which two had not been previously confirmed.

Enteroviruses belong to the Picornaviridae family and have 2 distinct classes: polioviruses (types 1, 2, and 3) and non-polioviruses (coxsackievirus, enterovirus, echoviruses, and unclassified enteroviruses). The non-polioviruses are responsible for a myriad of clinical syndromes in addition to aseptic meningitis. These include mild respiratory disease, hand-foot-and-mouth (HFM) disease, herpangina, myocarditis and pleurodynia. Reviews of meningitis data from South Africa indicate that there are usually more cases of viral meningitis during dry summer seasons. The most recent viral meningitis outbreak described in Gauteng occurred during the summer of 2010/2011 in Tshwane, and was caused by echovirus 4. Enteroviral infections are under-reported.

Human-to-human transmission of enteroviruses is usually via the faeco-oral route. Poor hand hygiene practices and contamination of food and water sources facilitate transmission. Children younger than 5 years are most frequently affected because of absent immunity. However most cases are self-limiting and the overall mortality rate is extremely low. The most effective way to prevent the spread of enteroviruses is through adequate hand washing and good general hygiene practices. People who are close contacts of viral meningitis patients do not need prophylactic antibiotic treatment.

Although enterovirus or viral meningitis is not a notifiable condition, the recent global increase in the detection of enterovirus D68 and the putative association with acute flaccid myelitis/paralysis in other countries, emphasises the need to closely monitor enteroviruses associated with outbreaks. Please notify outbreak@nicd.ac.za if you are a clinician in the Tshwane area, and identify a case of suspected enteroviral meningitis. Additional samples will allow the NICD together with other healthcare providers to assess the extent of the outbreak.

Source: Centre for Respiratory Diseases and Meningitis, NICD-NHLS; Lancet Laboratories, Vermaak and Partners.

b Malaria advisory and update

The total number of malaria cases reported to the malaria control programme from January to October 2015 is less than the corresponding time period for 2014 (10 561 vs 12 892, Figure 6). The number of malaria deaths are lower in September and October 2015 compared with the corresponding months in 2014 (36 vs 6, Figure 6). This may be a result of fewer cases in these months, and generally dry conditions with late summer rains. However, it is early in the season and the number of cases may rise by the year-end.

Travellers to malaria endemic areas in South Africa and surrounding countries (Figure 7) are advised to take appropriate chemoprophylaxis, as well as observe measures to prevent mosquito bites. Currently recommended chemoprophylactic regimens include one of the following: mefloquine, doxycycline or atovaquone-proguanil.

An acute febrile or flu-like illness in a resident of a malaria endemic area, or traveller recently returned from a malaria area should prompt immediate testing for malaria. Artemeter-lumefantrine (Co-artem ®) is recommended for uncomplicated malaria. Parenteral artesunate is the preferred treatment for complicated malaria, with intravenous quinine as an alternative (with an initial loading dose of 20mg/kg over four hours in 5% dextrose).

In the last month, two cases of *Plasmodium falciparum* malaria have been confirmed in the Madikwe National Park in North West Province. Local transmission has not previously been reported from this area. Entomological investigations are ongoing to determine the likely mode of transmission. Oddysean malaria (acquisition of malaria from a malaria-infected mosquito that was brought into the area through artificial means (e.g. in a motor vehicle, or suitcase)) may be responsible.

Reference: National Department of Health Malaria Prevention Guidelines, accessible at www.santhnet.co.za.

Source: Centre for Emerging and Zoonotic Diseases, Division of Public Health Surveillance and Response, NICD-NHLS; Malaria Control Programme, National Department of Health

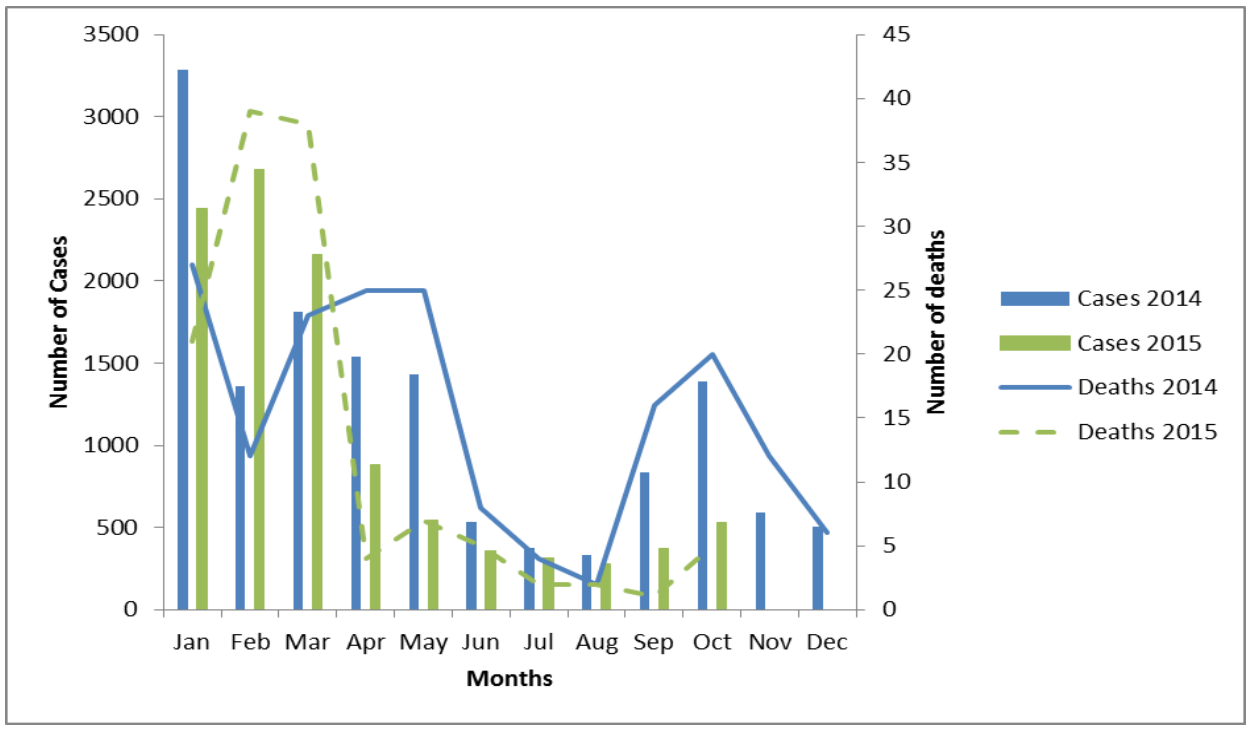

Figure 6. Numbers of malaria cases (left y-axis), and deaths due to malaria (right y-axis) reported to the South African malaria control programme 2014-2015. Data courtesy the South African National Department of Health, Malaria Control Programme.

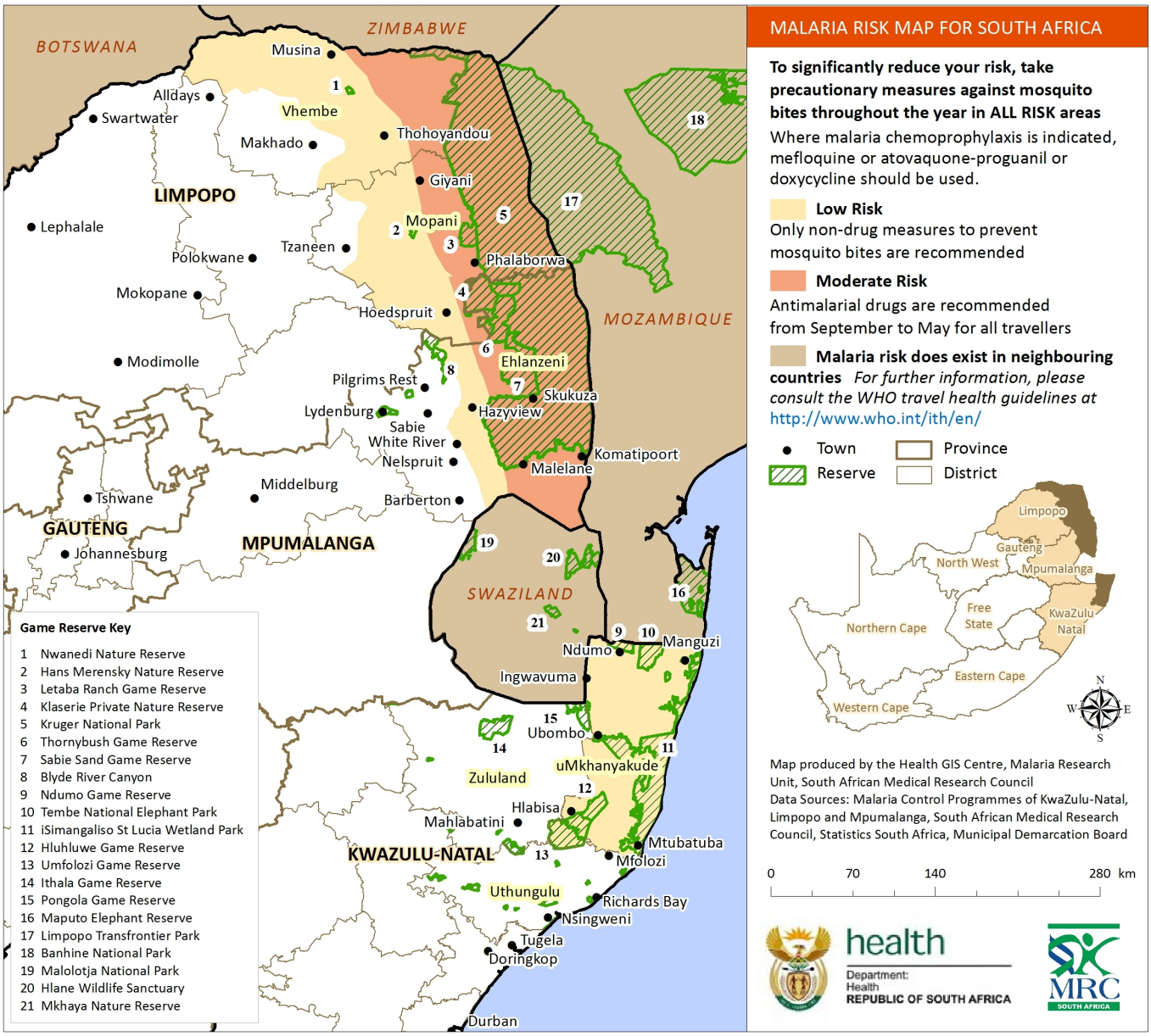

Figure 7. A malaria risk map for South Africa, obtained produced by the National Department of Health and the South African Medical Research Council, current as of March 2015. Obtained from www.santhnet.co.za

4 ENTERIC DISEASES

a Listeriosis-an apparent cluster of cases in Western Cape Province

During September 2015, an increased number of cases of *Listeria monocytogenes* were isolated at NHLS Groote Schuur laboratory: seven cases had been identified since the beginning of 2015, with six occurring between June 2015 and September 2015. Clinical information was available for these six cases, of which four were related to pregnancy, or were infants who had been diagnosed post-partum. Two cases, both adults, had underlying conditions, namely leukaemia and multiple myeloma. One of these patients died. In order to determine whether the cases were epidemiologically linked, attempts were made to contact patients for an interview using a standard case investigation questionnaire. Three interviews were conducted with pregnancy-related cases. In addition to pregnancy, all three

cases had additional epidemiological risk factors for *Listeria* acquisition. The mother of case one worked at a farm three months prior giving birth, planting and harvesting spinach, cucumber and beans in tunnels, while sometimes consuming these foods. She also frequently ate unrefrigerated left-overs. The mother of case two occasionally ate raw fruit while pregnant and case three exclusively consumed ready-to-eat foods such as deli meat and Greek salad three months prior giving birth. No epidemiologic link between these cases has been identified as yet. Six of the isolates have been sent to the Centre for Enteric Diseases at the NICD for molecular genotyping which is ongoing.

Preliminary analysis of listeriosis cases (meningitis and bacteremia) in the Western Cape Province (extracted from the Cooperate Data Warehouse of the National Health Laboratory Services) from January 2012 to September 2015 was done to assess trends in isolation rates. During this period, 72 cases were identified in the Western Cape Province, with fewer cases identified during 2014 compared to other years. Figure 8 shows the distribution of cases by age, gender and year.

Listeria monocytogenes are Gram-positive bacilli, capable of growing at temperatures of 4°C. They may resemble diphtheroids or short chains of streptococci on Gram's stain and therefore be missed on blood culture or cerebrospinal fluid specimens. When over-decolourised, they may be misidentified as *Haemophilus* species. Low concentrations of organisms in the CSF may also lead to false negative CSF culture, and 10 ml of CSF should be collected to optimise diagnostics. The organisms may grow slowly and cold enrichment (incubation of cultures at 4°C) may be required to recover isolates in mixed infections.

Although listeriosis is a relatively rare disease (global incidence of 0.337 per 100 000 people in 2010), it has an estimated global mortality of 24% and a 93% hospitalisation rate. The incidence of listeriosis is at least 10 times higher among pregnant women compared to the general population. In pregnant women, listeriosis precipitates premature labour, or leads to intra-uterine death. Neonates who acquire listeriosis transplacentally may develop septicaemia with or without meningitis. Long-term post-infectious sequelae in neonatal disease include intellectual disability, which may be severe, epilepsy, motor impairment, hearing and vision loss. Infection in older patients is frequently associated with severe immune-suppressive conditions including HIV, malignancy and transplants. *Listeria monocytogenes* was first recognised by WHO as a foodborne pathogen in the 1980s, with soft cheeses recognised as the main sources of listeriosis during outbreaks. Outbreaks associated with raw meat, pâté, fresh produce, seafood and other milk products have since been documented.

Optimal treatment of invasive listeriosis includes ampicillin at high doses. An aminoglycoside may be added for synergy. Treatment should be continued for up to two weeks. Second-line treatments include trimethoprim/sulfamethoxazole, erythromycin, vancomycin and fluoroquinolones. *L. monocytogenes* is resistant to cephalosporin antibiotics.

Although there was no common exposure identified among these patients from the Western Cape, persons who are at risk for listeriosis—those with underlying immunocompromising conditions, and pregnant women should avoid known risks, namely unpasteurised milk and milk products, uncooked or undercooked meat, poultry and fish products.

Source: Centre for Enteric Diseases, Field Epidemiology Training Programme, NICD-NHLS; NHLS laboratory Groote Schuur Hospital; Western Cape Province, Department of Health.

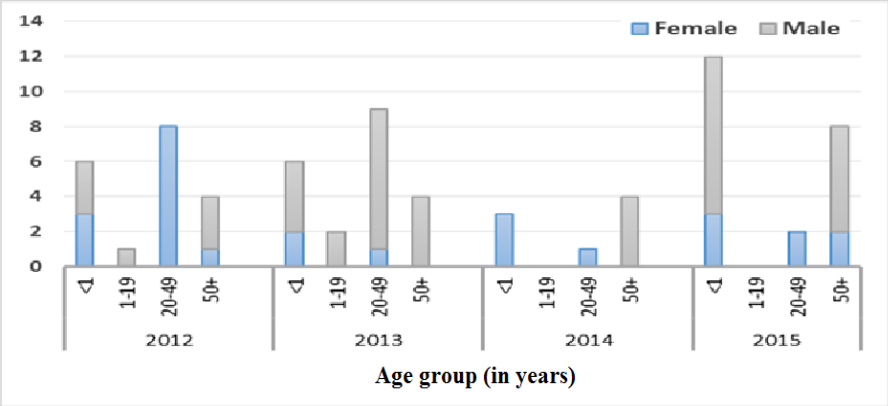

Figure 8. Cases of listeriosis identified by NHLS laboratories in Western Cape Province, 2012 – 2015 by age group and gender. Data courtesy Central Data Warehouse, NHLS.

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

a Ebola virus disease (EVD) outbreak

The EVD outbreak in Sierra Leone was declared over on 7 November 2015, 42 days after the last laboratory-confirmed EVD case twice tested negative on 25 September 2015 (Reference 1). Sierra Leone has managed to interrupt and halt Ebola virus transmission, and there are currently no EVD cases in this country. The World Health Organization (WHO) reports that this outbreak has had a devastating impact on Sierra Leone and much needs to be done to assist the country to recover. Since the first laboratory-confirmed EVD case in Sierra Leone in May 2014, a total of 8 704 laboratory-confirmed EVD cases including 3 589 (41%) deaths have been reported. However, EVD survivors continue to experience health related problems (Reference). Sierra Leone has now entered a 90-day period of heightened surveillance to ensure that any new possible case/s can be rapidly identified. Health officials are maintaining a high level of suspicion as the possibility of re-emergence of the disease still remains.

The outbreak continues in Guinea; however in the week ending 8 November 2015, no new laboratory-confirmed EVD cases were reported. To date, in Guinea 69 contacts are under follow-up, of whom 60 are high risk. As at 8 November 2015, a cumulative total of 28 599 cases (laboratory-confirmed, probable and suspected) including 11 299 deaths with a case fatality rate of 40% has been reported in Guinea, Liberia and Sierra Leone (Table 1).

The Ministry of Health in Liberia reported a new case of EVD in a statement released on 20th November 2015 (Reference 2). There are unconfirmed reports of two subsequent cases. These new cases have arisen some time after Liberia was officially declared ebola-free. A 10 year-old boy, his father and sibling from a suburb in Monrovia are being treated, and a further 153 cases are under observation. It is not yet known how the family contracted EVD. Cross-border transmission is unlikely.

Situation in South Africa

As at 10 November 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 Guinea.

Enhanced surveillance

Following the announcement by the WHO on 7 November 2015 to declare the EVD outbreak in Sierra Leone over, South Africa took a decision to remove Sierra Leone from the list of high-risk countries for EVD transmission. As a result travellers to and from Sierra Leone will no longer be required to apply for permission to travel to South Africa. However several measures for epidemic preparedness and response remain in place to prevent the introduction of EVD into South Africa. Travellers from Sierra Leone will still go through the thermal screening process at the ports of entry. For more information please contact NATHOC on Tel: +27 12 395 9636

Laboratory testing

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 person 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

Reference: (1) World Health Organisation. WHO commends Sierra Leone for stopping Ebola virus transmission. Available at http://www.afro.who.int/en/sierra-leone/press-materials/item/8139 ; (2) Liberian Ministry of Health http://www.mohsw.gov.lr/documents/press%20release%2020151120.pdf

Table 1. Number of Ebola virus disease cases and deaths in Guinea, Liberia and Sierra Leone (as at 8 November 2015)

Country	Total cases (laboratory-confirmed, probable and suspected)	Total deaths	Case fatality rate	Number of cases among healthcare workers (Number of deaths)
Guinea	3 805	2 536	67%	196 (100)
Sierra Leone	14 122	3 955	28%	307 (221)
Liberia (as at 9 May)	10 666	4 806	45%	378 (192)
Liberia (from 29 June)	6	2	33%	
Totals	**28 599**	**11 299**	**40%**	**881 (513)**

Source: World Health Organization: Ebola outbreak - Ebola situation report of 8 November 2015 (www.who.int)

6 SURVEILLANCE FOR ANTIMICROBIAL RESISTANCE

a Update on carbapenemase-producing Enterobacteriaceae

The Johannesburg Antimicrobial Resistance Laboratory and Culture Collection (AMRL-CC) of the Centre for Opportunistic, Tropical and Hospital Infections (COTHI) at the NICD have been testing referred isolates of suspected carbapenemase-producing Enterobacteriaceae (CPE) for the presence of selected carbapenemase genes. CPE have become a threat to healthcare and patient safety worldwide by compromising empiric antibiotic therapeutic choices and increasing morbidity, hospital costs and the risk of death. CPE surveillance is required to determine the extent of the problem as a first step in order to restrain the emergence and spread of CPE. For October 2015, a total of 80 Enterobacteriaceae isolates were received. Seventy-seven carbapenem -resistant isolates were screened, 60 of which were CPE isolates (Table 1 and Table 2). The majority of the isolates were *Klebsiella pneumoniae* (56) followed by *Enterobacter cloacae* (14).

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

Table 2. Enterobacteriaceae by CPE enzyme type. Data courtesy AMRL-CC, COTHI, NICD, 2015

Organism	NDM		OXA-48		VIM	
	Oct-15	Jan-Sep 2015	Oct-15	Jan-Sep 2015	Oct-15	Jan-Sep 2015
Klebsiella pneumoniae	26	205	20	65	3	26
Enterobacter cloacae	1	13	1	8	-	4
Serratia marcescens	2	32	-	5	-	2
Providentia rettgeri	-	18	-	-	-	-
E. coli	1	8	-	26	-	2
Citrobacter freundii	1	11	-	-	-	-
Klebsiella oxytoca	3	6	-	2	-	3
Other Enterobacteri-aceae	-	8	-	-	-	-
Total	**34**	**301**	**21**	**109**	**3**	**37**

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

Table 3. Enterobacteriaceae isolates by specimen type and province, January-October 2015 AMRL-CC, COTHI, NICD, 2015

Organism	GP	KZN	WC	FS	EC	Unk	Total Oct 2015	Total Jan-Oct 2015
Klebsiella pneumoniae	**29**	**25**	**-**	**1**	**1**	**-**	**56**	**345**
Sterile	16	10	-	1	-	-	27	184
Non-sterile	8	4	-	-	1	-	13	75
Unknown	5	11	-	-	-	-	16	86
Enterobacter cloacae	**7**	**1**	**-**	**-**	**6**		**13**	**66**
Sterile	3	-	-	-	5	-	8	37
Non-sterile	4	-	-	-	1	-	5	15
Unknown	-	1	-	-	-	-	1	14
E. coli	**1**	**1**	**-**	**-**	**-**	**-**	**2**	**47**
Sterile		1	-	-	-	-	1	23
Non-sterile	1	-	-	-	-	-	1	19
Unknown	-	-	-	-	-	-	-	5
Serratia marcescens	-	**2**	-	-	-	-	**2**	**39**
Sterile	-	-	-	-	-	-	-	8
Non-sterile	-	-	-	-	-	-	-	1
Unknown	-	2	-	-	-	-	2	30
Klebsiella oxytocoa	**1**	**2**	**-**	**1**	**-**	**-**	**4**	**14**
Sterile	1	1	-	1	-	-	3	10
Non-sterile	-	-	-	-	-	-	-	1
Unknown	-	1	-	-	-	-	1	3
Citrobacter freundii	**1**	**-**	**-**	**-**	**-**	**-**	**1**	**13**
Sterile	1	-	-	-	-	-	1	7
Non-sterile	-	-	-	-	-	-	-	1
Unknown	-	-	-	-		-	-	5
Other Enterobacteri-aceae	-	-	-	-	-	-	**-**	**66**
Sterile	-	-	-	-	-	-	-	29
Non-sterile	-	-	-	-	-	-	-	14
Unknown	-	-	-	-	-	-	-	23
Total Jan-Oct 2015	**278**	**194**	**7**	**18**	**77**	**7**	**-**	**590**

7 BEYOND OUR BORDERS

The 'Beyond our Borders' column focuses on selected and current international diseases that may affect South Africans travelling abroad. Numbers correspond to Figure 9 on page 16.

1. Saudi Arabia and the Middle East: MERS-COV and cholera

MERS-CoV: There have been 2 reported deaths of non-healthcare workers in Riyadh province. Since 2012 to 04/11/2015 there has been a total of 1 275 lab-confirmed cases of MERS-CoV. This includes 546 deaths, 722 recoveries, 1 asymptomatic and 8 current cases. Presently, the vast majority of cases are likely to have contracted infection in health care facilities. A small minority have exposure to camels.

Cholera: Approximately 2 500 cases of cholera have been reported from Iraq. Cases have also been reported from Bahrain and Kuwait. It is unclear if cases have been reported from war-torn Syria. Travellers are advised to follow rigorous hygienic measures.

2. USA: Plague

Oregon Health officials have confirmed bubonic plague in a girl who fell ill 3 days after a hunting trip in Heppner, in Morrow County. She probably contracted the disease from a flea bite. No other human cases have been reported. Plague is unlikely in travellers to USA, but avoidance of contact with wild animals especially rodents by humans and pets is advocated.

3. Colombia, Brazil: Zika virus

Zika virus has been reported in high numbers from Colombia and Brazil. Other central and southern American countries fear the emergence of Zika, which is an emerging arbovirus spread through *Aedes* mosquitoes. Disease presents as fever, rash, joint pain and non-purulent conjunctivitis, similarly to chikungunya and dengue, though it is usually less severe. Travellers are advised to avoid mosquito bites.

4. South Sudan: Yellow fever

It emerged that fake yellow fever cards were being sold at Juba International Airport to unvaccinated individuals. The State Ministry of health has subsequently banned the sale. There are reports that some of their own employees are implicated. A yellow fever outbreak occurred in West and South Kordofan in 2013 and Darfur between 2012 and 2013. The importation and exporting of the disease poses a serious public health concern when proper vaccination is not taking place.

5. China: Avian influenza

According to Zhejiang Centre for Disease Control since autumn 2015 there have been 4 cases of human H7N9 avian influenza infections. The WHO had a total of 679 lab confirmed cases reported with 275 fatalities from 2013 - 2015. The Ministry of Agriculture has a number of prevention strategies: improvement of early warning and monitoring programs; strengthening of live bird market regulation and epidemic prevention strategies; improved health and veterinary sector collaboration and emergency preparedness.

6. Mozambique: Contaminated beer

In January 2015 75 persons died and over 150 were hospitalised after drinking contaminated beer at a funeral. This November it was reported that a bacterium, *Burkholderia gladioli* has been found in flour used to make the beer after it was sent for testing in the USA. The organism produces a toxin that has a high case-fatality rate in food poisoning cases. Similar cases have been reported in China (fermented corn flour snacks) and Indonesia (fermented soybean cake). This outbreak has been the largest such occurrence to date.

7. Australia: Pertussis

The Australian Department of Health reports that there have been 8 200 cases since January 2015, centered mainly on the Australian East Coast, and New South Wales. This is the highest number of cases reported in the last four years. Most cases have been in persons under the age of 14 years.

8. Mozambique and Tanzania: Cholera

A cholera outbreak was reported on 5 November 2015 in three districts of Zambezia Province, Mozambique, namely Namula, Malema and Mocuba. There have been 1 237 suspected cases, 49 hospitalizations, 10 lab confirmed cases and 5 deaths. Health authorities are stockpiling medication and conducting social mobilisation campaigns to halt the spread of the disease.

An outbreak of cholera in Tanzania has been reported to WHO this month. A number of districts are affected and over 8 000 cases have been

5 BEYOND OUR BORDERS

reported. Further details are awaited.

10. Zambia: Measles
Following a protracted outbreak of measles in DR Congo, measles has now been reported in Zambia. So far 30 cases are suspected with 1 confirmed. WHO is awaiting further information.

References and additional reading:
ProMED-Mail (www.promedmail.org)
World Health Organization (www.who.int)
Centers for Disease Control and Prevention (www.cdc.gov)

Source: Division of Public Health Surveillance and Response

Figure 9. Current outbreaks (as of 18 November 2015) that may have implications for travellers. Numbers correspond to text above. The red dot is the approximate location of the outbreak or event.