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

Communicable Diseases Communiqué

JANUARY 2016, Vol. 15(1)

CONTENTS

1 ZOONOTIC AND VECTOR-BORNE DISEASES

a Rabies update

A total of eight laboratory-confirmed cases of human rabies was reported in South Africa during 2015. The most affected provinces were Limpopo and the Eastern Cape (EC) with three reported cases each. Single cases were also verified from KwaZulu-Natal (KZN) and the Free State provinces. In addition, there were three probable cases, of which two originated from the EC and one from KZN. A single suspected case was reported from the EC. In 2014, there were seven confirmed human rabies cases and five probable cases, and the same number reported in 2014.

The first case of rabies in 2016 was confirmed in a 16-year-old boy from Zululand District, KZN Province who developed a fatal encephalitis. He had been bitten by a domestic cat approximately eight weeks prior to becoming symptomatic. The cat was owned by his grandmother, and had reportedly started attacking people. The boy presented to his local clinic two days after being injured and was given tetanus toxoid, paracetamol and a single dose of rabies vaccine. Rabies is well documented in cats in South Africa. Given the behaviour of this cat, full rabies post-exposure prophylaxis should have been administered. In this case, molecular typing of the patient's rabies virus confirmed a canid biotype.

Rabies is invariably fatal after onset of symptoms, but disease is preventable by the administration of rabies post-exposure prophylaxis (PEP). All instances of exposure to animal bites should be evaluated to determine the risk of rabies virus transmission and the need for PEP. A rabies risk assessment is based on the presence of broken skin, and animal factors including the species of animal, the behaviour and condition of the animal and the animal's rabies vaccination status. The local prevalence of canine rabies is an important consideration when assessing risk.

Most rabies exposures will result in a category III injury (break in skin or lick of mucous membrane). Post-exposure prophylaxis must include rabies immune-globulin and a four dose course of rabies vaccine following thorough wound cleaning. An updated poster, published in 2015 summarizing the South African guidelines for rabies PEP is available on the NICD website (www.nicd.ac.za).

In South Africa, reasons for failure of PEP include: 1) lack of awareness of rabies risk and poor health-seeking behaviour following bite wounds amongst the public; 2) incorrect risk assessments by health care workers (HCW), who may not administer PEP or who prescribe PEP incorrectly (this may happen if the injury is a seemingly minor scratch, or small laceration, and the attending HCW does not consider rabies, or incorrectly judges that rabies transmission is unlikely); 3) incomplete adherence to the PEP regimen—for example if the victim is correctly initiated on PEP but fails to complete the vaccination schedule.

Human rabies case definitions*

Confirmed: Laboratory confirmed through detection of rabies viral antigen in human tissue by

- Fluorescent antibody test
- Animal inoculation
- PCR

Probable: Clinically compatible with rabies and a history of contact with a suspected rabid animal.

Suspected: Clinically compatible with rabies: – a person presenting with an acute neurological syndrome (encephalitis) dominated by forms of hyperactivity, (furious rabies) or paralytic syndrome (dumb rabies) progressing towards coma and death, usually by respiratory failure, within 7-10 days after the first symptom if no intensive care is instituted.

*Case definitions obtained from 'WHO recommended standards and strategies for surveillance, prevention and control of communicable diseases.'
http://www.who.int/rabies/epidemiology/Rabiessurveillance.pdf

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

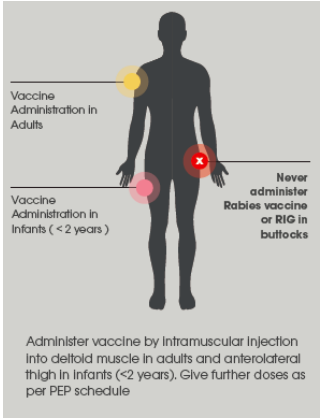

Figure 1. Sites of appropriate or inappropriate administration of rabies vaccine (An excerpt from the new poster describing PEP available on the NICD website).

2 SEASONAL DISEASES

a Malaria update, and insecticide resistance in northern KwaZulu-Natal

Malaria in South Africa during 2015

The number of malaria cases reported to the National Department of Health in 2015 decreased to 11 245, compared to 13 988 cases in 2014. There was a corresponding decrease in deaths, from 174 in 2014 to 135 in 2015. Figure 1 describes the numbers of reported cases and deaths by month over 2015. It is anticipated that the number of cases will increase during the first quarter of 2016 in keeping with seasonal trends.

Travellers to malaria endemic areas in South Africa and surrounding countries 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 (Coartem ®) 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).

Insecticide resistance monitoring

The control of malaria vector mosquitoes in South Africa's endemic provinces is primarily based on indoor spraying of long-lasting residual insecticides. South Africa's National Malaria Control Programme has adopted a malaria elimination agenda and has scaled up vector control activities accordingly. However, despite these plans local transmission continues and is most likely due to outdoor feeding by populations of the major vector species *Anopheles arabiensis.* An outdoor *Anopheles* surveillance system has been set up in three sections of the Mamfene district in northern KwaZulu-Natal Province in order to assess the extent of outdoor resting *An. arabiensis* in Mamfene and to assess the current insecticide susceptibility status of this population. The *An. arabiensis* samples tested showed evidence of resistance to deltamethrin (pyrethroid), DDT (organochlorine) and bendiocarb (carbamate), and full susceptibility to the organophosphates pirimiphos-methyl and fenitrothion. These results affirm the presence of pyrethroid and DDT resistance previously detected in this population and also indicate the comparatively recent emergence of resistance to the carbamate insecticide bendiocarb. The implications of these findings are that special attention and commitment needs to be given to the principles of insecticide resistance management as well as to investigations into alternative control techniques designed to target outdoor-resting *An. arabiensis* in northern KwaZulu-Natal Province. Full details of these findings can be found in the South African Journal of Science at http://dx.doi.org/10.17159/sajs.2015/20150261.

Source: Centre for Opportunistic, Tropical & Hospital Infections, NICD-NHLS; (basilb@nicd.ac.za); Malaria Control Programme, National Department of Health;

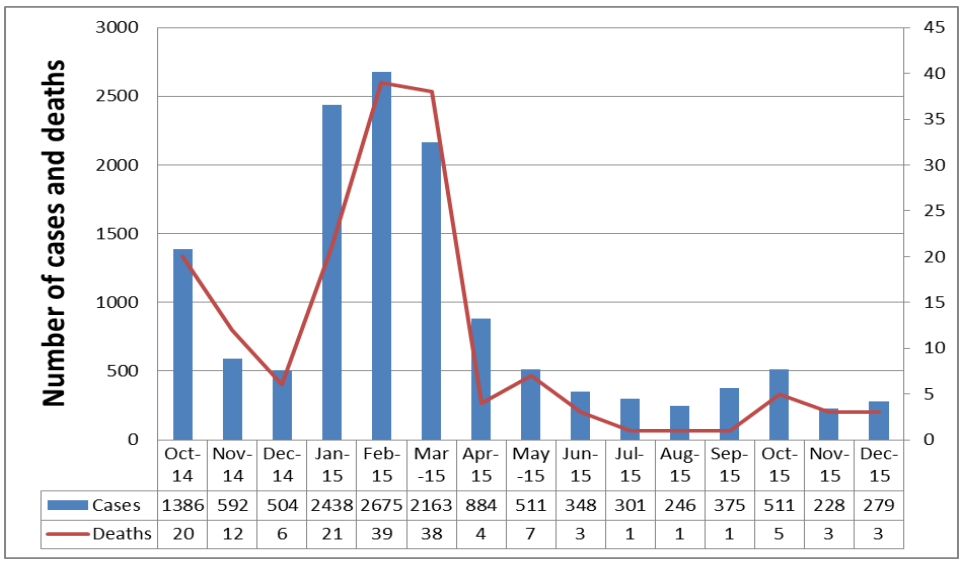

Figure 2. Total malaria cases and deaths reported to the National Department of Health Malaria Control Programme, from October 2014 until December 2015. Data courtesy of the National Department of Health.

b An outbreak of a vesicular rash at the National School Sport Championships, December 2015

The NICD was alerted to an outbreak of peri-oral vesicular lesions affecting learners attending the National School Sport Championships in Tshwane during December 2015. The index case was a 13-year-old male learner from a school in Mpumalanga Province who arrived at the training camp on 7th December with peri-oral lesions. This was followed by a second case on the 8th December. An additional six learners developed symptoms by the 11th December, at which point, medical personnel were notified.

On examination, apart from the peri-oral lesions, no vesicular lesions or ulcers were noted in the oral mucosa or on the hands and feet. Cases had no systemic signs or symptoms, no fever or joint pains and none of the cases were acutely ill. Two cases gave a history of mild diarrhoea. A differential diagnosis of enteroviral infection, herpes simplex and impetigo was made. Three learners were taken to Steve Biko Academic Hospital where specimens were taken for laboratory investigation, and simultaneously, immediate infection control measures were implemented by medical personnel. Infection control measures included advising learners to avoid activities likely to expose them to other persons' saliva, such as sharing eating utensils, water bottles, and toothbrushes, drinking with their mouth directly from water-taps, and kissing. Standard hygiene precautions and adherence to handwashing was reinforced. The medical officer in charge requested to be notified of any further cases. Following implementation of the infection control measures, only five additional cases were reported by the 13th December amongst players from different sports teams, including netball, football, and rugby. Thereafter no further cases were reported. The tournament ended on the 15th December, with all participants returning by bus.

Unfortunately, none of the three cases taken to Steve Biko Academic Hospital had sufficient vesicular fluid, so swabs of the lesions were taken, and transported in viral transport media. Stool specimens were also taken from each of the three patients and submitted for enterovirus PCR testing. The swabs were tested by PCR for enterovirus, herpes simplex virus 1 & 2, Group A streptococcus, *Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarrhalis and Staphylococcus aureus.* All of these molecular tests were negative except for a *Staphylococcus aureus* PCR which was positive in one patient. Two stool specimens were positive for enterovirus. Further molecular typing of the VP1 region suggested infection with a coxsackie A6 virus in one patient. However the other specimen had insufficient titre for molecular characterisation. Although no definite causative agent was identified, timely implementation of appropriate infection control measures successfully contained the outbreak.

Source: Centre for Vaccines and Immunology; Division of Public Health, Surveillance and Response, NICD-NHLS; Medical personnel of the Mpumalanga National School Sport Championship team (outbreak@nicd.ac.za)

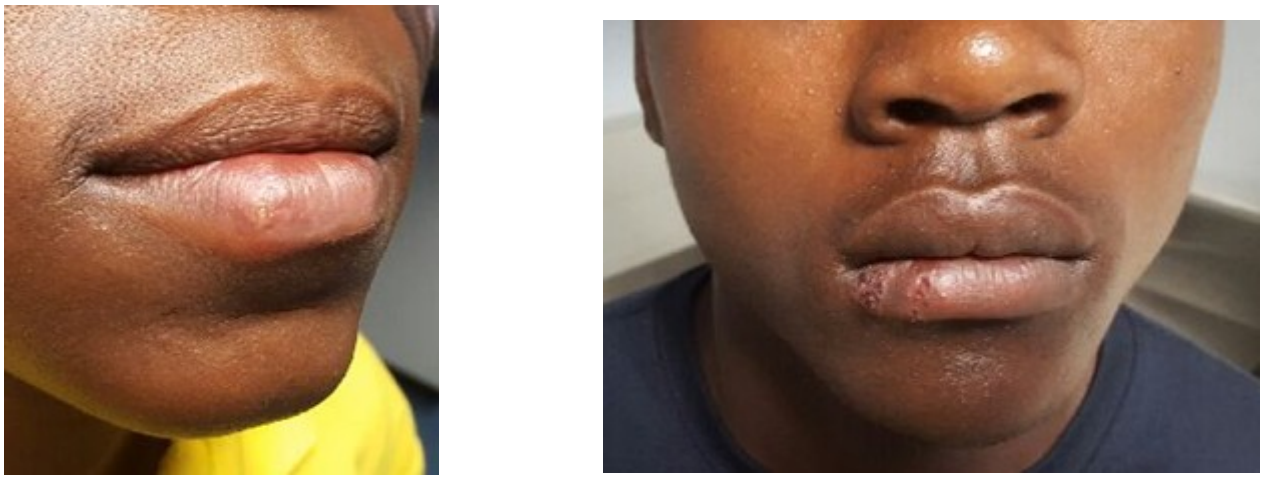

Figure 3. Two learners who attended the National School Sport Championships in Tshwane during December 2015 and who developed vesicular lesions, showing the vesicular lesions with blisters (left) and crusting (right) (Photographs courtesy Mpumalanga team doctor)

3 TUBERCULOSIS AND HIV

a Implementation of a National HIV rapid testing quality assurance and quality improvement programme

Since 2010, the National Department of Health (NDoH) has implemented large-scale HIV rapid testing campaigns to ensure that all South Africans are aware of their HIV status. HIV rapid testing devices (RTD) are the major means for testing for HIV infection in South Africa. The RTDs are robust - laboratory-based evaluations have shown that the performance of these devices in terms of sensitivity and specificity is equivalent to laboratory methods such as ELISAs.

The major challenge in the use of HIV RTD is quality assurance of testing. The rapid expansion of HIV testing in South Africa has outstripped the implementation of quality assurance activities. A recent PEPFAR-supported initiative launched in South Africa is the Rapid Testing Quality Assurance and Quality Improvement Initiative (RTQII, Figure 4). The RTQII implementation is led by the NICD in partnership with the National and Provincial Departments of Health (HCT coordinators), CDC-Pretoria, CDC and USAID Development Partners and the NHLS. The initial rollout of the RTQII programme to date has occurred in PEPFAR-selected priority facilities. The focus of the RTQII is training on HIV rapid testing quality assurance (QA) and monitoring the implementation of QA. The monitoring of QA is through the use of a specific tool, the Stepwise Process for improving the quality of HIV Rapid Testing (SPI-RT) checklist. The tool assesses seven elements to determine whether the sites (1) provide accurate and reliable results; (2) are managed appropriately and adhering to quality practices and (3) require support to improve quality of testing. The elements include: training and certification; the physical facility; safety; (EQA). A standardised scoring system is applied and facilities are placed in four possible levels from 0 to 4 of competence with level 0 requiring immediate remediation and level 4 eligible for certification.

From its inception in September 2014 until December 2015, 850 facilities have received training on quality assurance and baseline SPI-RT checklists have been applied in 170 facilities in the Eastern Cape and Free State provinces. One hundred and sixty-eight (168, 98.8%) facilities have started implementing the QA-QI programme. The outcome of the baseline assessments show that sixty-two facilities (37%) attained Level 1 compliance (partially eligible for certification) and 106 (63%) attained level 2 compliance status (close to national site certification). Key problem areas identified included: no training records, no inventory management for storage of test kits, no standard operating procedure documents or job aids; test procedures not adhered to, QC logs not reviewed and no participation in proficiency testing.

The RT-QII programme parallels other NDoH-led initiatives such as the "Ideal Clinic" programme that focus at facility level to improve health services. The triangulation of the different initiatives will be essential to obtain a global perspective on meeting specific requirements for the UNAIDS 90-90-90 targets, which includes accurate HIV testing.

Source: Centre for HIV and Sexually Transmitted Infections, NICD-NHLS (adrianp@nicd.ac.za)

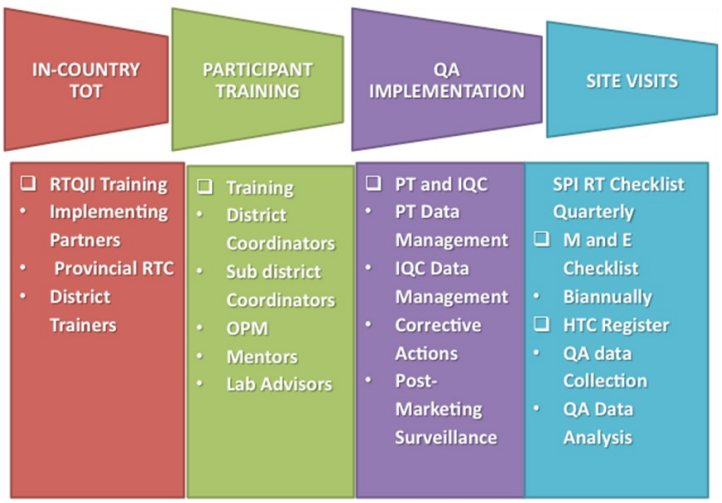

Figure 4. A schematic diagram illustrating the pillars of the Rapid Testing Quality Improvement Implementation (RTQII) strategy for HIV rapid testing. TOT: Train-the-Trainer; RTC: Regional Training Centre; OPM: Operational Manager; PT: Proficiency Testing; IQC: Internal Quality Control; M&E: Monitoring and Evaluation; HTC: HIV Testing and Counselling

4 ENTERIC DISEASES

a Sporadic cases of typhoid in South Africa over January 2016

During the week of 17th to 24th January 2016, four confirmed and one suspected case of typhoid were identified through laboratory alerts in the City of Johannesburg. This prompted an investigation of all typhoid cases reported in South Africa since January 1, 2016, and a review of typhoid case management and public health interventions following identification of a case.

Since January 1, 2016, a total of 19 cases with at least one positive culture for *Salmonella* Typhi has been identified across South Africa. Of these, 10 were reported from Gauteng Province (three from Charlotte Maxeke Johannesburg Academic Hospital, one from Dr Bheki Mlangeni Hospital, two from Edenvale, two from Dr George Mukhari Hospital and a single case each from Chris Hani Baragwanath Hospital and a private Tshwane hospital). The mean age of cases is 19 years (range 0-52 years), with 7 cases presenting in children under the age of 12 years. Four cases had two positive cultures and a single case had three positive cultures. One patient died in an intensive care unit after a delayed diagnosis. By comparison, in the all South African provinces, 72 cases of typhoid were reported in 2015, and 102 cases in 2014. Five cases were reported in January 2015, and 17 in January 2014. Investigation of all 2015 cases including molecular typing techniques on patient isolates, is currently underway to determine sources of infection, and potential interventions to reduce transmission.

Typhoid is endemic within South Africa with an expected seasonal increase in January. Sporadic cases are reported in all provinces every year. Typhoid is spread through the faeco-oral route, and there is ongoing risk of typhoid fever in any area where water quality and sanitation is not optimal. Contamination of water supplies has resulted in numerous large-scale outbreaks. Delmas (Mpumalanga Province) has experienced repeated outbreaks of typhoid fever, with over 1000 cases during 1993, and over 400 suspected cases and three deaths in 2005. In Harare, Zimbabwe, a typhoid outbreak that began in 2012, associated with contaminated water sources, is ongoing, with over 4 000 cases reported.

Any person who presents with a documented fever ≥38.5°C and clinical symptoms compatible with typhoid should be investigated further. Clinical symptoms of typhoid include fever, headache, rigors and gastrointestinal symptoms (abdominal pain, nausea and vomiting, occasionally constipation). Splenomegaly and/or hepatomegaly may be noted. The classic full blood count shows a leucopenia (but a neutrophilia) and a moderate thrombocytopaenia. A travel history within the last month to an area with a confirmed outbreak of typhoid should increase the clinician's index of suspicion for the diagnosis. **Malaria must always be considered and tested for urgently in any pyrexial, returning traveller or resident in a malaria area.**

The gold standard for the diagnosis of acute typhoid is a positive blood culture. Stool cultures may only become positive after the first week of illness. Culture of bone marrow is useful as it may remain positive even after 5 days of antibiotic treatment. Positive cultures are confirmed by agglutination with specific typhoid antisera, including the Vi antigen. The Widal test which looks for antibodies to *S.* Typhi may be suggestive of the diagnosis but is not confirmatory. Acute and covalescent sera are required.

Ciprofloxacin is the drug of choice for treatment of typhoid. Advantages of treatment with ciprofloxacin include oral twice-daily dosing with rapid resolution of symptoms, and frequent eradication of carriage post-treatment. Alternative treatment includes 3rd generation cephalosporins (ceftriaxone), or azithromycin. No high level resistance to ciprofloxacin in *Salmonella* Typhi in SA has been detected at present.

Typhoid can be prevented through adherence to strict hand washing after using the toilet and before handling food; the provision of safe water, and adequate sanitation. Patients with typhoid fever should pay strict attention to hand hygiene and should not be involved in food preparation until they have been shown to be free of infection.

When a case of typhoid is identified, the following steps are necessary:

- Notify the Local Authority and Department of Health using form GW/17 and telephonically
- Confirm the diagnosis by verifying laboratory results, and patient details.
- Review the case management and treatment
- Interview the patient and complete a case investigation form to ascertain risk factors for exposure and likely source of infection
- Follow up the patient after treatment with three stool specimens to confirm that s/he is not a carrier
- Identify contacts at risk of infection, and submit two stool specimens for culture to determine carriage status.

Guidelines for the diagnosis, management and prevention of typhoid are found on the NICD web site www.nicd.ac.za

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

b Investigation of food- and water-borne illness outbreaks.

On account of summer high temperatures and ongoing water supply problems, an increase in the number of food-borne and water-borne illness outbreaks can be anticipated. According to the South African Health Act, 1977 (Act No. 63 of 1977), 'food poisoning, defined as an occurrence of gastro-intestinal symptoms (vomiting, diarrhoea or abdominal pain) amongst two or more persons who have an epidemiological link', is a notifiable medical condition. The following actions are required to facilitate appropriate and timeous investigation of these events:

1. If a food- or water-borne outbreak is suspected, attending health care workers should notify the person in charge of infection control at the facility, or notify the district Communicable Diseases Co-ordinator and the district Environmental Health services as soon as possible.

2. Attending clinicians should ensure that appropriate clinical specimens from the patients are taken, and submitted to the correct NHLS laboratory. Contact details of NHLS public health laboratories are listed below. Ensure that specimens are clearly labelled so that NHLS couriers deliver specimens to the correct laboratory. Clinicians and Communicable Disease Co-ordinators should retain the NHLS bar-code label in order to trace specimens.

- If patients are vomiting, retain specimens of vomitus for laboratory testing
- If patients are complaining of diarrhoea, obtain stool specimens for laboratory testing.
- Blood is not a helpful specimen for investigation of food- or water-borne outbreaks.

4. Environmental Health Officers or Communicable Diseases Co-ordinators should complete a case investigation form for each affected person (see www.nicd.ac.za) and collect specimens of food served at the implicated event, or water if the source is suspected to be water-borne. These should be submitted to the correct NHLS laboratory (Table 1).

5. Finally, an analysis of the data obtained from patient interviews and results of clinical specimens and environmental samples should be conducted. A possible cause for the outbreak should be identified, and appropriate steps taken to prevent future food- or water-borne disease.

The NICD has employed an epidemiologist in each province to assist provincial and district teams with epidemiological data analysis and outbreak investigation. Contact details of provincial epidemiologists are listed in Table 2. Outbreak investigation is a critically important activity that monitors and safeguards public health. Prompt notification will ensure that investigations are done properly and timeously. Alternatively, health care workers can call the NICD hotline for advice on 0828839920, or email outbreak@nicd.ac.za

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

Table 1. Contact details of NHLS public health laboratories for processing of clinical and environmental samples obtained during investigation of food- and water-borne outbreaks

Name of laboratory	Address	Contact person
NHLS Infection Control Service Laboratory, Johannesburg	Wits Medical School, room 3T09, 7 York Road, Parktown, Johannesburg, 2193	Mr Rob Stewart. 011-489-8578/9
NHLS Public Health Laboratory, KwaZulu-Natal	3rd floor, 149 Prince Street, Durban, 4001	Ms Inderani Chetty, Mr Leon Taylor 031-327-6743
NHLS Public Health Laboratory, Port Elizabeth	Corner of Buckingham and Eastborne Road, Mount Croix, Port Elizabeth, 6000.	Ms Vanessa Pearce 041-395-6174

Table 1. Contact details of NICD provincial epidemiologists

Province	Name	Cell	Email
National	Portia Mutevedzi	0826580140	portiamu@nicd.ac.za
Eastern Cape	Riyadh Manesen	0826049701	riyadhm@nicd.ac.za
Free State	Motshabi Modise	0826163642	motshabim@nicd.ac.za
Gauteng	Joy Ebonwu	0824005588	joye@nicd.ac.za
KwaZulu-Natal	*not yet filled*		
Limpopo	Ntsieni Ramalwa	0729779183	NtsieniR@nicd.ac.za
Mpumalanga	Hlupi Mpangane	0765228511	doreenm@nicd.ac.za
North West	Thejane Motladiile	0828945030	thejanem@nicd.ac.za
Northern Cape	*not yet filled*		
Western Cape	Hlengani Mathema	0731774735	hlenganim@nicd.ac.za

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

a Ebola virus disease (EVD) outbreak: situation update

On 14 January 2016 the World Health Organization declared the Ebola outbreak in Liberia over for the third time. Liberia was first declared Ebola free in May 2015; however the Ebola virus was re-introduced twice in the country since then. As Sierra Leone and Guinea had been declared free of Ebola transmission on 7 November and 29 December 2015 respectively, the declaration that Liberia is Ebola-free would have marked the end of the longest and worst Ebola outbreak ever reported in history. However, the announcement signalling the end of the Ebola outbreak in West Africa was short lived. Hours after the pronouncement was made, Sierra Leone reported a case, also identified on 14th January 2016. A patient who fell ill in the northern parts of the country near the Guinean border and later died in Tonkolili district, was tested as part of the 90-day post-declaration enhanced surveillance programme, and found to be Ebola virus positive. Few days later a second Ebola case was confirmed. A second case-patient was identified as a 38-year-old woman who cared for the deceased EVD case reported on 14 January 2016. She developed symptoms on Wednesday 20 January 2016 and was later confirmed as having EVD. The two case-patients were identified after Sierra Leone was declared Ebola free on 7 November 2015. Health officials have identified about 150 contacts of the deceased case, of whom 50 are considered high risk. The investigations into the origin of the infection of the index case and vaccination of associated contacts are underway.

The finding of these latest cases highlights the importance of the 90-day heightened surveillance period, during which all persons meeting specific case definitions, or unexplained deaths in the affected country, are subject to Ebola testing. Persistence of the virus in sanctuary sites such as semen may account for re-emergence of the disease, although the epidemiology of this is not fully understood. As at 15 January 2016, a cumulative total of 28 602 cases (laboratory-confirmed, probable and suspected) including 11 301 deaths with a case-fatality rate of 40% has been reported in Guinea, Liberia and Sierra Leone. A summary of case numbers and deaths reported is shown in Table 3.

The World Health Organization has been working behind the scenes not only to strengthen affected countries' response to Ebola, but also at a global level to enhance development of diagnostic, preventive and therapeutic products against a list of top emerging diseases likely to cause major epidemics. The list of diseases includes Crimean Congo haemorrhagic fever, Ebola virus disease and Marburg, Lassa fever, MERS and SARS coronavirus diseases, Nipah and Rift Valley fever, but will be updated annually or in response to newly detected threats. The WHO has released a Research and Development Blueprint– a 'global strategy and preparedness plan, aimed at reducing the time between the declaration of an international public health emergency and the availability of effective tests, vaccines and medicines that can be used to save lives and avert crisis'. The plan includes financial support for investment in targeted research and development. More details are available at http://www.who.int/csr/research-and-development/blueprint/en/

As at 15 January 2016 there have been no EVD cases in South Africa associated with the current outbreaks in West Africa. In addition, there are no

suspected cases of EVD in South Africa at present. The risk of Ebola being introduced into South Africa still remains low. However a high index of suspicion is necessary given on-going EVD transmission in West Africa, and occasional risks on the African continent.

Testing for viral haemorrhagic fever viruses (including Ebola virus) in South Africa is only available at the NICD. EVD testing is neither warranted nor useful for persons that are not suffering from a clinical illness compatible with EVD, even in the event of compatible travel histories. The tests cannot be used to determine if the patient has been exposed to the virus and may develop the disease later. Requests for testing (with a detailed clinical, travel and exposure history) should be directed to the NICD Hotline at 082 883 9920 (a 24-hour service, for healthcare professionals only)

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

Table 3. Number of Ebola virus disease cases and deaths in Guinea, Liberia and Sierra Leone (as at 20 January 2016)

Country	Total cases (laboratory-confirmed, probable and suspected)	Total deaths
Guinea	3 804	2 536
Liberia	10 675	4 809
Sierra Leone (as at 7 November 2015)	14 122	3 955
Sierra Leone (since 14 January 2016)	2	1
Total	**28 603**	**11 301**

b Zika virus

Zika virus is an arbovirus belonging to the Flavivirus genus, family Flaviviridae. It was first isolated from a rhesus monkey in Uganda in 1947 and from humans in Nigeria in 1968. Zika virus is transmitted to humans by certain daytime-active Aedes aegypti mosquitoes that also transmit dengue and chikungunya viruses in the urban setting. Symptoms of Zika fever are usually mild and include an acute onset of fever, maculopapular rash, arthralgia, conjunctivitis, myalgia and headache. About 1 in 4 infected persons are symptomatic. Symptoms are self-limited and may persist for 2-7 days. Severe disease requiring hospitalization is rare and to date, no deaths due to Zika have been reported. Treatment is nonspecific and supportive. Zika, dengue and chikungunya present with similar clinical signs and symptoms, and have a similar geographical distribution. Dengue and Zika virus infections may cross-react in serology tests but PCR tests reliably detect and differentiate between viruses. Persons with Zika virus are only viraemic for 2-4 days during the first week of illness, so PCR may not reliably identify older infections.

Prior to 2015, Zika virus outbreaks were intermittently reported in a narrow equatorial band extending from Central Africa through Southeast Asia to the Pacific Islands. In May 2015, the Pan American Health Organization issued an alert regarding the first confirmed Zika virus infections in Brazil. Since then, 18 countries in the Americas have confirmed autochthonous circulation of Zika virus. The Pan American Health Organization (PAHO) and the World Health Organization acknowledged an increase of congenital anomalies (microcephaly, unilateral ophthalmological abnormalities and cerebral calcifications), Guillain-Barre syndrome and other neurological and autoimmune syndromes in areas where Zika virus is currently circulating. Presently, no definite causality can be attributed to Zika virus infection, but investigations are ongoing. On 17 January 2016 the WHO made specific recommendations to member states to establish and maintain the capacity to detect and confirm Zika virus cases, prepare healthcare facilities to respond to a possible increased demand of specialized care for neurological syndromes and to strengthen antenatal care.

In the light of the possible association with congenital anomalies, prevention of Zika virus infection is critical. Efforts to eliminate mosquito vectors through effective vector control strategies should be strengthened and communicated to the

public in areas where Zika is currently prevalent. Mosquito exposure during the first few days of illness should be avoided to prevent other mosquitoes from becoming infected. Personal protection to avoid mosquito bites is essential for travellers visiting areas where the Zika virus is circulating. As a further precaution, pregnant women should delay travel to areas with current outbreaks of Zika virus.

It is important to emphasize that Zika virus has not been found on the African continent further south than Uganda. The vector species, *Aedes aegypti* is common in South Africa, particularly in the eastern coastal plain but also in the cities of the inland plateau. In the urban centres, the mosquito breeds in small collections of water such as discarded tyres and buckets, or the leaf axils of *Strelitzia nicolae* ("banana trees"). The question is, why has Zika virus spread to Indonesia and Brazil but not to southern Africa? We don't have a definitive answer but believe that the reason is probably the same as for yellow fever and the dengue viruses, which also don't occur this far south. One could speculate that numerous introductions of either infected mosquitoes or infected travellers are necessary before a foreign arbovirus can become established in a new area, because the virus needs to be introduced into a capable vector population as well as host population. These arboviruses are not contagious and usually require the assistance of an intermediate vector between hosts. Then there is also the question about vector susceptibility and ability to transmit the virus by bite. *Aedes aegypti* is made up of two subspecies, only one of which occurs predominantly outside of Africa. This subspecies has enjoyed several centuries of adaptation to the urban environment and has developed a preference for human blood. The typical African subspecies, *Aedes aegypti* subspecies f*ormosus*, tends not to bite humans and may well be less susceptible to Zika virus when compared to the South American *Aedes aegypti* subspecies *aegypti*. However, this needs to be established in the laboratory before one can categorically state that it is a competent or poor vector.

Even though the possibility of an infected traveller introducing Zika virus to South Africa obviously does exist, the short viraemic period in humans would lessen the chance of being transferred to a susceptible mosquito, particularly because local *Aedes aegypti* mosquitoes have very limited flight ranges (measured in a few metres) and tend not to enter buildings (unlike subspecies *aegypti*, which utilize homes in crowded urban settlements). The Brazilian outbreak appears to be associated with lack of piped water and the resultant storage of water in indoor vats and pails, all ideal habitats for *Aedes aegypti* mosquitoes to breed in. For this reason, the best way to eliminate or at least minimize Zika virus is to control the *Aedes aegypti* populations by eliminating their breeding habitats. Aerial spraying of insecticides for *Aedes aegypti*, though appearing to be useful, has failed in the past for various reasons and is not recommended. Brazilian vector control teams are attempting to reduce vector populations by a combination of removing containers that could be used for oviposition by mosquitoes, and deployment of traps for attracting gravid mosquitoes, laced with a larvicide to kill larvae as they hatch out.

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

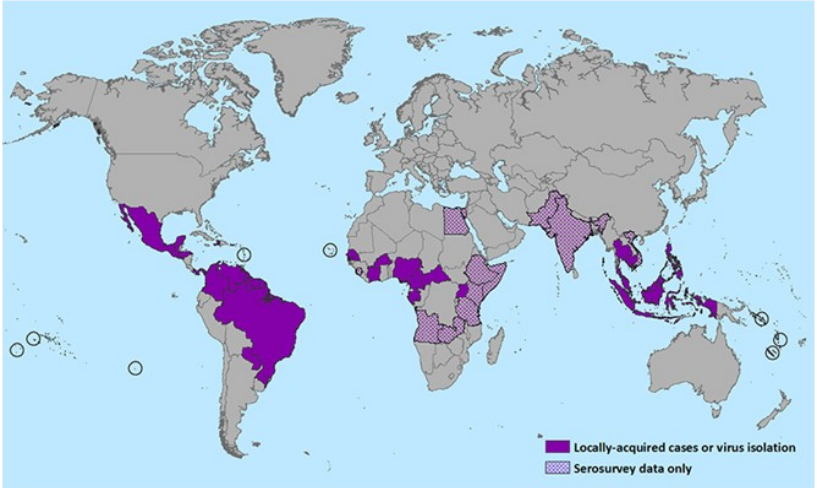

Figure 5. A map showing the distribution of Zika virus as of January 2016 (Source: Centers for Disease Contol, Atlanta, USA)

c Yellow fever in Angola

The Angolan Minister of Health in a press statement on Wednesday 20th January 2016 reported that 23 confirmed cases and seven deaths from yellow fever had occurred among Eritrean and Congolese citizens living in the municipality of Viana, in Luanda. Cases were diagnosed through initial tests conducted by the National Institute for Communicable Diseases. The statement indicated that of a total of the twenty-three (23) reported cases and seven deaths, three severe cases are under special surveillance while the remaining thirteen had been cleared. Among the cases, 22 are male and one is female, aged 20 to 46 years old. The first case was recorded on the 5th December 2015. Up to now, no cases among national citizens have been reported. The World Health Organization is working with the Ministry of Health in the investigation and management of these cases. A vaccination campaign in Viana, Luanda is been planned, in order to protect children, pregnant women, health professionals and the local community. Angola is considered endemic for yellow fever, although there have been no recent outbreaks. Vaccination is mandatory for travellers to the country, and for all those travelling from Angola to South Africa.

Yellow fever is an arbovirus of the *Flavivirus* genus. It infects monkeys, and is transmitted by *Aedes* mosquitoes from animals to humans in sylvatic (rural) and urban cycles. Three to six days after infection, persons enter an acute phase characterised by fever, muscle pain and generalised non-specific symptoms. Resolution of this phase occurs after 3-4 days. Subsequently, a minority of patients enter a second, more toxic phase characterised by fever, jaundice, bleeding, kidney impairment, and death within 15 days. Yellow fever is preventable by vaccination. The introduction of yellow fever into a suburban location may herald the onset of an urban cycle, with outbreak potential. Timeous vaccination campaigns are essential, as protective immunity takes at least 10 days to develop.

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

6 VACCINE-PREVENTABLE DISEASES

a A change in the measles vaccination schedule

The measles vaccination product and schedule in South Africa has been updated since 01 December 2015. A product called MeasBio® (Biovac) replaces the previous product Rouvax® (Sanofi Pasteur) due to the manufacturer discontinuing the previous product. MeasBio® has been in use in other countries for over 30 years. Both Measbio and Rouvax are live attenuated vaccines.

MeasBio® will be administered at the age of 6 months and 12 months, requiring two additional visits in the Expanded Programme on Immunisation schedule. MeasBio®is administered subcutaneously while Rouvax®, licensed for both intramuscular and subcutaneous administration, was usually given intramuscularly.

The reasons for the change in schedule are twofold. Firstly, MeasBio® should be given alone in all vaccination visits. Measles vaccination was previously administered at 9 months and 18 months. Previously, the dose at 9 months was given concurrently with pneumococcal vaccine (PCV) and at 18 months it was given concurrently with the 6-in-1 vaccine, Hexaxim® (Sanofi Pasteur). The schedule change allows measles vaccine to be given as the only vaccine at the scheduled visit.

Secondly, it has been recommended to vaccinate against measles as early as 6 months of age to prevent the high morbidity and mortality associated with the disease in young infants. South Africa had previously used an additional 6-month dose of vaccine during outbreak situations or for those living with HIV. A 6-month dose as part of the routine schedule should prevent serious measles complications in young infants. As vaccine efficacy only becomes optimal after 1 year of age, a second dose is essential to ensure high population immunity rates.

In the interim period during the change in schedule for those children who present at 9 or 18 months, measles vaccination will be given as first preference and the other required vaccine postponed for 4 weeks – namely PCV would be postponed to age 10 months and Hexaxim® to 19 months.

Measles is a highly contagious epidemic-prone disease. Signs and symptoms of measles include high fever and rash with cough, coryza or conjunctivitis. The disease may cause complications such as pneumonia, diarrhoea, blindness,

encephalitis or death. Measles vaccination is a safe, effective and cost effective way of preventing measles morbidity and mortality. Measles is targeted for elimination in the African region by 2020. Health care workers are encouraged to take each opportunity to check child vaccination status and catch up missed vaccinations according to recommended guidelines. It is never too late to catch up measles vaccination.

Source: Centre for Vaccines and Immunology, NICD -NHLS (melindam@nicd.ac.za)

EXPANDED PROGRAMME ON IMMUNISATION – EPI (SA) REVISED CHILDHOOD IMMUNISATION SCHEDULE FROM DECEMBER 2015

Age of child	Vaccines needed	How and where it is given
At birth	**BCG** Bacilles Calmette Guerin	Right arm
	OPV (0) Oral Polio Vaccine	Drops by mouth
6 weeks	**OPV (1)** Oral Polio Vaccine	Drops by mouth
	RV (1) Rotavirus Vaccine	Liquid by mouth
	DTaP-IPV-Hib-HBV (1) Diphtheria. Tetanus, Acellular Pertussis, Inactivated Polio Vaccine and Haemophilus Influenzae Type B and Hepatitis B Combined	Intramuscular/left thigh
	PCV (1) Pneumococcal Conjugated Vaccine	Intramuscular/ right thigh
10 weeks	**DTaP-IPV-Hib-HBV (2)** Diphtheria, Tetanus, Acellular Pertussis, Inactivated Polio Vaccine and Haemophilus Influenzae Type B and Hepatitis B Combined	Intramuscular/left thigh
14 weeks	**RV (2)** Rotavirus Vaccine*	Liquid by mouth
	DTaP-IPV-Hib-HBV (3) Diphtheria. Tetanus, Acellular Pertussis Inactivated Polio Vaccine and Haemophilus Influenzae Type B and Hepatitis B Combined	Intramuscular/left thigh
	PCV (2) Pneumococcal Conjugated Vaccine	Intramuscular/right thigh
6 months	**Measles Vaccine (1)****	Subcutaneous/left thigh
9 months	**PCV(3)** Pneumococcal Conjugated Vaccine	Intramuscular/right thigh
12 months	**Measles Vaccine (2)****	Subcutaneous/right arm
18 months	**DTaP-IPV-Hib-HBV (4)** Diphtheria, Tetanus, Acellular Pertussis, Inactivated Polio Vaccine and Haemophilus Influenzae Type B and Hepatitis B Combined	Intramuscular/left arm
6 years (both boys and girls)	**Td Vaccine** Tetanus and reduced strength of Diphtheria Vaccine	Intramuscular/left arm
12 years (both boys and girls)	**Td Vaccine** Tetanus and reduced strength of Diphtheria Vaccine	Intramuscular/left arm

*Rotavirus Vaccine should NOT be administered after 24 weeks
**Do not administer with any other vaccine

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

A long and healthy life for all South Africans

Figure 6. National Department of Health Expanded Programme of Immunisation (EPI) revised schedule, as from December 2015

b A cluster of rubella cases in Limpopo Province

On 18 December 2015, a general practitioner (GP) from a district in Limpopo Province alerted the NICD of an increase in the number of patients presenting with a fever and a maculopapular rash. At the time there were 9 cases of which 2 were adults. All had presented within a week. According to the alert, none of the patients had cough, coryza or conjunctivitis. Initial serology tests done by the GP on two of the patients were IgM negative for measles and rubella. NICD clinicians suspected rubella, enterovirus or parvovirus infection. A case investigation form (CIF) was drawn up, and epidemiological data and blood samples collected for analysis.

Of the 11 cases, 5 CIFs were completed. Four cases were under the age of 3 years (range 6 months – 27 months), and the fifth case was an adult of 25 years old. In all the cases, the rash was itchy. Three had occipital nodes. None of them had joint pain or arthralgia. Except for the adult case whose two children also had similar symptoms without the rash, there was no epidemiological linkage of note. In all, the disease process was mild with no hospital admissions. A blood specimen from one of the cases was sent to the NICD for serology testing. Rubella IgM tested positive and measles IgM was negative. A final diagnosis of rubella was likely as a cause of this cluster of cases.

Rubella is common in South Africa and may be confused with measles. It is an acute viral infection which occurs most often in children but can also be seen in adults. It is caused by rubella virus, a member of the Rubivirus genus of the Togaviridae family. It is spread in droplets when infected persons cough or sneeze. The incubation period is 12 to 23 days. It is generally a benign infectious disease with age being the most important determinant of disease severity. In most cases, no treatment is required. In pregnant women however, incident rubella infection may lead to birth defects (congenital rubella syndrome) or foetal death.

References: WHO | Rubella.

http://www.who.int/mediacentre/factsheets/fs367/en/. Accessed January 19, 2015.

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

7 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 has 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 December 2015, a total of 132 Enterobacteriaceae isolates were received. One-hundred and thirty isolates were screened, 106 of which expressed carbapenemases (Table 1 and Table 2). The majority of these CPE isolates were *Klebsiella pneumoniae* (84) followed by *Enterobacter cloacae* (9).

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 4. Enterobacteriaceae by CPE enzyme type, AMRL-CC, COTHI, NICD, 2015

Organism	NDM		KPC		OXA-48 & Variants		VIM		GES	
	Dec-15	Jan-Nov-15	Dec-15	Jan-Nov-15	Dec-15	Jan-Nov-15	Dec-15	Jan-Nov-15	Dec-15	Jan-Nov-15
Citrobacter freundii	2	16	-	2		2		2	-	2
Enterobacter cloacae	5	18	-	1	3	12	1	4	-	-
Enterobacter kobei	1	-	-	-	-	-	-	-	-	-
Escherichia coli	1	13	-	2		41		4		2
Klebsiella pneumoniae	35	260	1	6	44	117	3	37	1	8
Morganella morganii	1	2	-	-	-	-	-	-	-	-
Providencia rettgeri	3	20	-	-	-	-	-	-	-	-
Serratia marcescens	5	42	-	-	-	6	-	2	-	1
Total	**53**	**371**	**1**	**11**	**47**	**178**	**4**	**49**	**1**	**13**

Table 5. Enterobacteriaceae isolates by specimen type and province, AMRL-CC, COTHI, NICD, 2015

Organism	EC	FS	GA	KZ	WC	Total Dec-15	Total Jan- Nov-15
Citrobacter freundii	-	-	-	1	2	3	16
Sterile	-	-	-		2	2	10
Non-sterile	-	-	-	-	-	-	1
Unknown	-	-	-	1		1	5
Enterobacter cloacae	3	5	8	-	1	17	94
Sterile	2	3	8	-	1	14	61
Non-sterile	1	2	-	-	-	3	16
Unknown	-	-	-	-	-	-	15
Not stated	-	-	-	-	-	-	2
Enterobacter kobei	1	-	-	-	-	1	-
Unknown	1	-	-	-	-	1	-
Escherichia coli	-	-	-	1	-	1	65
Sterile	-	-	-	-	-	-	50
Non-sterile	-	-	-	-	-	-	9
Unknown	-	-	-	1	-	1	6
Klebsiella pneumoniae	12	-	56	25	3	96	447
Sterile	3	-	36	11	3	53	280
Non-sterile	9	-	17	2	-	28	53
Unknown	-	-	3	12	-	15	108
Not stated	-	-	-	-	-	-	6
Morganella morganii	-	-	3	-	-	3	7
Sterile	-	-	3	-	-	3	2
Non-sterile	-	-	-	-	-	-	2
Unknown	-	-	-	-	-	-	3
Providencia rettgeri	-	-	3	-	1	4	20
Sterile	-	-	2	-	-	2	12
Non-sterile	-	-	1	-	-	1	-
Unknown	-	-	-	-	1	1	8
Serratia marcescens	-	-	1	4	-	5	50
Sterile	-	-	1	-	-	1	11
Unknown	-	-	-	4	-	4	38
Not stated	-	-	-	-	-	-	1
Total	16	5	71	31	7	130	1398

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

b Global spread of antimicrobial resistance to colistin

Antibiotic resistance has increased in the last two decades and very few new antimicrobial agents have been discovered. With the limited range of antimicrobials available to treat pan-resistant organisms, clinicians have become increasingly dependent on colistin, a polymyxin antibiotic discovered in 1949. Colistin acts on the bacterial cell membranes to increase permeability, resulting in bacterial cell lysis. Colistin also neutralizes endotoxin by binding to the lipid A component of lipopolysaccharide molecules of Gram-negative bacteria. Colistin is a 'last resort' drug and clinicians avoid using it because of potential renal toxicity.

Chromosomally-mediated mutations that confer resistance to colistin had been reported previously. However, researchers led by Yi-Yun Liu from the South China Agricultural University, recently discovered plasmid-mediated resistance to colistin on a named MCR-1, on plasmids. Because plasmids are mobile, DNA conferring resistance can be easily copied and transferred between different bacteria of animals and humans. The increasing use of colistin to treat multidrug-resistant Gram-negative bacterial infections has led to the emergence of colistin resistance in *Klebsiella pneumoniae* in several countries worldwide. Several factors are reportedly associated with colistin resistance, including inappropriate use of colistin and patient-to-patient transmission. International co-operation and global surveillance for MCR-1 resistance is now essential to try to prevent the spread of polymyxin-resistant bacteria. In South Africa, regulation of antibiotic use in agriculture and human health should be implemented based on South African AMR strategic framework.

Reference: Bogdanovich, T., Adams-Haduch, J. M.,Tian, G. B., Nguyen, M. H., Kwak, E. J., Muto, C. A., Doi, Y. Colistin-resistant, *Klebsiella pneumoniae* carbapenemase (KPC)-producing *Klebsiella pneumoniae* belonging to the international epidemic clone ST258. Clin Infect Dis: 53: 4: 373-6

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

8 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 15.

1. Cutaneous anthrax cases in Matabeleland South Province: Zimbabwe

Cutaneous anthrax has been diagnosed in 36 persons from the Umzingwane District, Matabeleland South Province since early December 2015. Anthrax is highly endemic in Zimbabwe, and the cases have been directly linked to livestock contact. Human-to-human transmission is rare; none have occurred during this outbreak. Risk to travellers is minimal; contact with cattle should be avoided.

2. Lassa fever: Nigeria

According to WHO and other global outbreak alerts, there are 239 suspected cases of Lassa fever of which 44 are confirmed, and deaths (case fatality 34%) from Dec 2015 until 24th January 2016. Lassa fever is an acute viral haemorrhagic illness of 1-4 weeks duration that occurs in West Africa. The Lassa virus is transmitted to humans via contact with food or household items contaminated with rodent urine or faeces. Person-to-person transmission can also occur. Clinical syndromes can result in significant illness. Therefore early supportive care and ribavirin is recommended to improve outcomes. Travellers are advised to report to health facilities immediately if any symptoms and signs are identified during or after a trip to this area.

3. Legionellosis: Spain

As of 30 Dec 2015 there were 228 confirmed cases of *Legionella* sp. infection, 23 of whom were hospitalized; 4 requiring intensive care unit support and 2 deaths following an acute outbreak in the city

of Manzanares. An ornamental fountain at the Manzanares bus station is a suspected source. Initial testing has shown at least 2 strains of *Legionella* are responsible, though further tests are still on-going. The outbreak has since been contained and is unlikely to pose any significant risk to travellers.

4. Pertussis: Canada
According to global outbreak reports, there has been an increase in pertussis cases reported in the city and Ontario district from Oct 2015 – Jan 2016. Ten confirmed cases have been reported, and the outbreak has been seemingly contained within the district. Travellers should ensure that vaccinations are up to date if they are travelling to this area.

5. Dengue fever: Americas, Asia, Africa
Global outbreak reports have identified cases of Dengue fever throughout the Americas, in Asia and Africa in Dec 2015. Travellers are advised to continue exercising precautionary measures in preventing mosquito bites.

6. Middle East respiratory syndrome coronavirus (MERS-CoV): Saudi Arabia/UAE
According to global outbreak and official WHO reports MERS-CoV cases continue to be reported in significant numbers in Saudia Arabia, though other cases were also reported in South Korea during December 2015. There were 167 cases in total throughout December 2015 and 6 cases reported in Saudi Arabia and UAE within the first 2 weeks of January 2016. Travellers should continue to exercise good hygiene practices and avoid contact with camels and camel milk.

7. Yellow fever
See article on page 11

References:
www.promedmail.org
www.who.int

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

Figure 7. Current outbreaks that may have implications for travellers. Numbers correspond to text above. The red dot is the approximate location of the outbreak or event.