c An update on Zika virus

Zika virus (ZIKV) is a mosquito-borne pathogen in the flavivirus genus (Flaviviridae), related to other agents of public health importance such as yellow fever, West Nile and dengue viruses. The virus was isolated for the first time from a sentinel monkey in Uganda in 1947 and from *Aedes africanus* mosquitoes the following year, but only recognized as a human pathogen for the first time in 1964. The virus remained confined to the equatorial belt of Africa and Asia, until 2007 when it caused an outbreak on Yap Island in the Pacific Ocean followed by a rapid expansion throughout other islands in the Pacific Ocean. In 2014 ZIKV reached South and Central America and spread explosively. As of 9 March 2016, a total of 52 countries worldwide has reported local transmission of Zika virus since 1 January 2007. The most drastic expansion of transmission occurred from January 2015 onwards, with 41 of the 52 countries reporting transmission in this period, with the Philippines being the most recently affected country. Five of the listed countries are no longer experiencing active transmission while three countries reported locally-acquired infection not related to mosquito transmission, most likely through sexual transmission. In the Americas alone 31 countries have now reported Zika virus active transmission. In Brazil estimation of ZIKV infections ranged from 500 000 to 1.5 million in 2015.

The risk of ZIKV infection to the general South African population is low. Active transmission of the virus has never been detected inSouth Africa. At the time of publication, three imported cases (one confirmed, two probable) have been detected in the country. Zika virus infection was confirmed by RT-PCR in a Colombian visitor to South Africa as reported in the Communiqué, February 2016. Two probable cases of ZIKV infection were diagnosed in twins from Barbados visiting South Africa for several weeks. ZIKV could not be detected by RT-PCR in the two patients, but serological testing (IgM and neutralization assay) revealed the presence of anti-ZIKV reactive antibodies. Serological testing of paired blood samples from these patients is ongoing at NICD. Due to heightened awareness by the public, a total of 28 suspected Zika cases has been investigated by CEZD, of which 6 cases involved pregnant women that travelled recently to affected areas.

Due to increasing case numbers of microcephaly and neurological disorders likely associated with ZIKV infections, the WHO declared this situation as a public health emergency of international concern on 1 February 2016 and this was reiterated at a second meeting of the WHO Emergency Committee on 8 March 2016. Brazil and French Polynesia are the only countries to report an increase in these neonatal malformations following Zika virus introduction and transmission, but similar conditions are under investigation in Colombia. Two cases of neonatal malformations linked to a travel history in Brazil have been reported from the USA and Slovenia. Nine countries have also reported an increase in the incidence of Guillain-Barré syndrome (GBS) in the presence of ZIKV active transmission. There is mounting evidence in the scientific literature of the role of Zika virus in microcephaly and neurological disorders, supported by well-executed case and cohort studies (see references below). The public health emergency of international concern declaration by WHO calls for a more co-ordinated effort to improve surveillance, mosquito control programs and fast-track the development of diagnostic assays, vaccines and antiviral therapeutics for ZIKV, and to investigate the causality of the observed disorders.

Clinical diagnosis of ZIKV disease is complicated due to the non-specific clinical presentation and similarity with other arboviral infections. About 80% of human infections are asymptomatic. Symptoms of ZIKV infection include low-grade fever (37.8-38.5 °C), maculopapular rash, arthralgia (specifically involving the small joints of the hands and feet) and conjunctivitis. Laboratory diagnosis of acute ZIKV infection can be achieved through virus isolation in mice or tissue culture, and molecular testing by ZIKV specific RT-PCR. The required specimen type for ZIKV laboratory diagnosis is clotted blood or serum. Due to the co-circulation of ZIKV, chikungunya and dengue and their common mosquito vector, as well as similar clinical presentation, differential diagnosis is essential when investigating suspected Zika cases. It is highly advisable that all suspected Zika cases also be subjected to testing for chikungunya and dengue. In acute cases, where a patient travelled recently (<14 days) to an affected area and blood was collected within 5 days of onset of compatible symptoms, the patient should be tested by virus-specific RT-PCRs for ZIKV, dengue and chikungunya. Due to transient viremia, acute cases negative by these RT-PCR assays, and convalescent cases (blood collected more than 5 days after disease onset) should be subjected to serological testing. Serological investigation of suspected Zika cases should therefore include IgM ELISA testing for antibodies to ZIKV, dengue and chikungunya. Positive results on either of these IgM assays are followed by virus-specific neutralization assays or

plaque-reduction neutralization assays for confirmation. Cases submitted for laboratory investigation should have an epidemiological link to current ZIKV outbreaks—which implies a recent travel history to an affected country or sexual contact with a male who has travelled to one of the affected countries and presented with possible ZIKV disease. Physicians submitting specimens from suspected Zika cases to NICD should therefore clearly request RT-PCR and/or serological testing for all three viruses to enable proper investigation.

The highest health risk posed by ZIKV is to the unborn of pregnant women travelling to ZIKV affected areas, and possibly the unborn of pregnant woman who have sexual contact with male partners who are infected with ZIKV. On the 8th of February 2016, the South African Department of Health issued a travel advisory recommending that pregnant women avoid travelling to affected areas or if travel is essential, that they should protect themselves against mosquito bites. In addition, the NDoH Environmental and Port Health department are taking steps to reduce the risk of translocation of infected mosquitoes from ZIKV affected countries, including 1) continued mosquito monitoring of arriving aircraft and increased mosquito surveillance to ensure that aircraft are sprayed with insecticide; 2) assessment of ship sanitation to identify possible vector breeding areas and whether steps have been taken to minimize insect breeding, as well as physical inspection of ships for presence of mosquito vectors; 3) continued thermal scanning of all travellers at ports of entry; 4) referral of travellers with compatible symptoms at points of entry to a health care facility for further management; 5) increased monitoring of imported used tyre casings; 6) increased health education and awareness of travellers about ZIKV disease.

Further reading related to Zika virus disease and association with microcephaly

1. Brasil P *et al*. Zika virus infection in pregnant women in Rio de Janeiro - Preliminary Report. N Engl J Med. 2016 Mar 4. [Epub ahead of print]
2. Meaney-Delman D, *et al*. MMWR Morb Mortal Wkly Rep. 2016 Mar 4;65(8):211-4. Zika virus infection Among U.S. pregnant travellers - August 2015-February 2016.
3. Kleber de Oliveira W *et al*. Increase in reported prevalence of microcephaly in infants born to women living in areas with confirmed Zika virus transmission during the first trimester of pregnancy - Brazil, 2015. MMWR Morb Mortal Wkly Rep. 2016 Mar 11;65(9):242-7.
4. Miranda-Filho Dde B *et al*. Initial description of the presumed congenital Zika syndrome. Am J Public Health. 2016 Apr;106 (4):598-600.
5. Tang H *et al*. Zika Virus infects human cortical neural progenitors and attenuates their growth. Cell Stem Cell. 2016 Mar 3. pii: S1934-5909(16)00106-5.
6. Calvet G *et al*. Detection and sequencing of Zika virus from amniotic fluid of fetuses with microcephaly in Brazil: a case study. Lancet Infect Dis. 2016 Feb 17. pii: S1473-3099(16 00095-5.

Related websites:
www.nicd.ac.za
www.cdc.gov/zika/
www.who.int/mediacentre/factsheets/zika/en/

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