REVIEW
O&G Forum 2016;26:10-12

New guidelines for Zika Virus 2016

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Introduction
Zika virus has caused a self- limiting pyrexial illness across Africa and South East Asia for decades. Recently there has been a rapid spread of the Zika virus in South America. However, to date, the zika virus has not been found further south than Uganda in Africa.[1] The vector species, *Aedes aegypti*, is common in South Africa especially in the eastern coastal plains but it may also be found inland. In urban areas, the mosquito breeds in small collections of water such as discarded tyres and buckets or the leaf axils of *Strelitzia nicolae* (banana tress). *Aedes argypti* is made up of 2 subspecies. The African subspecies tends not to bite humans and is probably less susceptible to Zika virus when compared to the American ones.

The outbreak in Brazil is probably associated with the lack of piped water. The resultant storage of water in indoor vats and pails has provided an ideal habitat for the *Aedes aegypti* mosquito to breed. Although a case of imported Zika has been reported by a traveller returning to South Africa, there is minimal risk to the local population.[1] These viruses are not contagious and require the assistance of a mosquito vector between hosts.

On 1 February 2016, the World Health Organisation (WHO) declared the mosquito-borne Zika virus an international public health emergency, due to its link to thousands of birth defects in Brazil. This is only the fourth time the WHO has declared a global health emergency, with others arising from influenza, Ebola and polio.

Epidemiology
Zika virus was first discovered in a Rhesus monkey in Uganda in 1947 and in humans a few years later.[2] The first outbreaks outside Africa and Asia occurred in Micronesia in 2007 and French Polynesia in 2013 - there has since been major outbreaks in other parts of the pacific. The first case of local transmission was reported in Brazil in May 2015. This was followed by a rapid spread of the virus across 23 countries and territories in South/Central America and the Caribbean.

The rapid spread over the South American region is mainly due to 2 factors[3]:

1. The population in this part of the world has not been previously exposed to the virus so lacks immunity
2. The *Aedes* mosquito is present in all these region/ countries in the Americas except Canada and Chile.

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Transmission
Zika virus is transmitted by the bite of an infected female *Aedes* mosquito. Although various species of the Aedes mosquito have the potential to transmit the virus, the disease is most commonly associated with *Aedes aegypti*.[4] After a human is bitten by an infected mosquito, symptoms develop within 3-12 days. Human Zika virus disease is an emerging condition and the current belief is that mode of transmission is mosquito-human and direct human to human transmission does not occur. Although isolated cases of sexual transmission of the virus in human semen and cases of maternal fetal transmission have been reported, more evidence is required to confirm whether this is possible.[5,6] Zika virus can be transmitted by blood transfusion but standard precautions for ensuring safe blood donations and transfusions should prevent this.

Symptoms
The incubation period is 3-12 days. Clinical illness is consistent with Zika virus if two or more symptoms are present: low grade fever, maculopapular rash, non-purulent conjunctivitis and arthralgia. Symptoms usually last for 3-7 days. Serious complications from Zika virus are uncommon however cases of fetal microcephaly, Guillain-Barre syndrome and other neurological and autoimmune conditions have been reported in areas of Zika virus outbreaks.

Diagnosis
The diagnosis should be considered among individuals returning from South or Central America, the Caribbean or the Pacific region who developed symptoms suggestive of zika virus infection while abroad or within 2 weeks of returning to South Africa. The diagnosis is confirmed by a positive reverse transcriptase-polymerase chain reaction (RT-PCR) on serum. RT-PCR may also be performed on amniotic fluid although the sensitivity and specificity of this test for congenital infection is currently uncertain. Antibody testing is less reliable due to possible cross-reaction with antibodies against other similar viruses such as dengue or yellow fever.

Zika virus infection in pregnant women
In October 2015, the Brazilian Ministry of Health reported a rapid increase in the number of babies born with microcephaly and in November 2015 the zika virus infection was declared a public health emergency. There is no evidence that pregnant women are more susceptible to infection or that the infection causes a more serious illness. Although transmission to the fetus has been documented in

all trimesters, infection in early pregnancy is likely to pose the greatest risk.[7] In a study of 72 women in Rio de Janeiro who tested positive for Zika virus during pregnancy, the following were the most predominant clinical features present: pruritic macular or maculopapular rash, arthralgia, conjunctival injection, headache, lymphadenopathy and fever.[8] Fetal ultrasound was performed in 58% (n=42) of women with active infection during pregnancy. Fetal abnormalities were detected in 29% (n=12) of zika-positive women. Adverse findings included fetal death at 36 and 38 weeks of gestation, intra-uterine growth restriction with or without microcephaly, ventricular calcifications or other central nervous system lesions and abnormal amniotic fluid volume or cerebral or umbilical artery flow. Ultrasonographic findings have been confirmed in the fetuses who have been delivered.

Other brain abnormalities that have been reported in association with Zika virus infection are ventriculomegaly, cell migration abnormalities (eg lissencephaly, pachygyria), arthyrogryposis (congenital contractures) secondary to central or peripheral nervous system involvement.

Prevention

There is no vaccine or drug to prevent infection. The *Aedes* mosquito is active mainly during the day; bites are common during mid-morning and late afternoon to dusk. Travellers visiting areas where outbreaks have been reported should minimise the chances of mosquito bites. This includes covering exposed skin, staying in air-conditioned or screened-in areas, treating clothing with permethrin and using N,Ndiethyl meta tolumide based insect repellents. Insect repellents should be re-applied regularly, particularly after swimming.

Both the National Travel Health Network and Centre in the United Kingdom and the Centres for Disease Control and Prevention in the United States advise that pregnant women should consider avoiding travel to countries where zika virus outbreaks are ongoing.[9,10] WHO Director-General, Margaret Chan, has said that delaying travel was something pregnant women should consider, but added that if they need to travel they should take protective measures.

Management of pregnant women who have travelled to an area of zika virus transmission

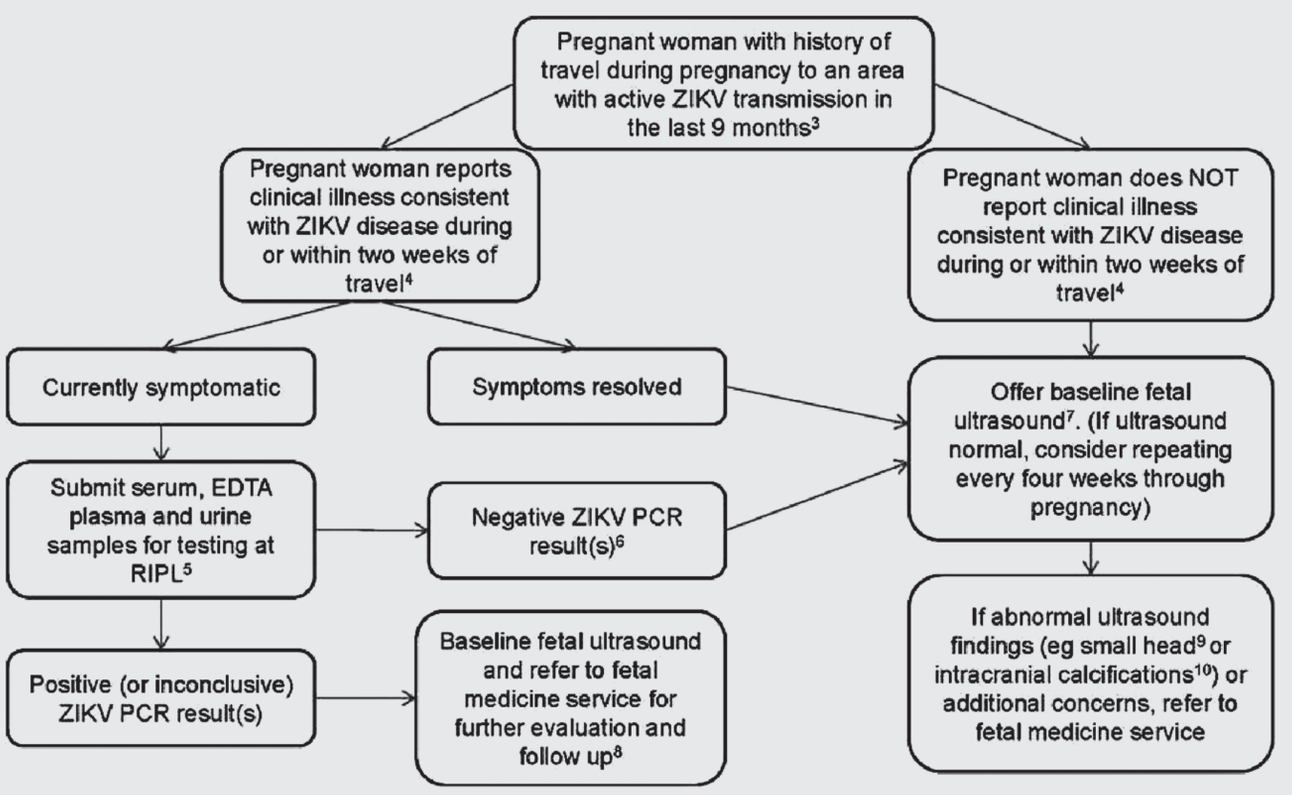
Knowledge and management of zika virus in pregnancy is limited and evolving. Recommendations are based on current information and are likely to be updated to reflect emerging evidence. Healthcare providers should ask all pregnant women about recent travel.

Figure 1 describes the evaluation of pregnant women with a history of travel to an area of zika virus transmission.

Treatment of Zika virus infection

There is no specific antiviral treatment. The infection is usually short-lived and requires no specific treatment. Pregnant women should drink adequate fluids and manage pain and fever with paracetamol and other cooling measures.

Figure 1 Algorithm for assessing pregnant women with a history of travel.
(source–RCOG/RCM/PHE/HPS clinical guidelines. Zika virus infection and pregnancy)[11]



Ultrasound screening following zika virus exposure
The Society for Maternal-Fetal Medicine in the United States has recommended the following screening program for women exposed to zika virus in pregnancy[12]:

- If the head circumference (HC) by prenatal ultrasound is > 2 SD below the mean, a careful evaluation of the fetal intracranial anatomy is indicated. If the intracranial anatomy is normal, fetal ultrasound should be repeated in 3-4 weeks.
- Isolated fetal microcephaly should be defined as fetal HC > 3SD or more below the mean for gestational age. The diagnosis of pathologic microcephaly is considered certain when the fetal HC is > 5 SD. A detailed neurosonographic examination should be performed and follow-up ultrasound done in 3-4 weeks.

The Centre for Disease Control – United States of America recommends that amniocentesis for zika virus testing be offered to all mothers with demonstrated zika virus infection or if ultrasound raises suspicion of fetal infection.[7] It is uncertain if the assay performance on serum and amniotic fluid is similar nor is it known for what duration PCR on amniotic fluid is positive after maternal infection.

Women planning pregnancy
Women should avoid becoming pregnant while travelling to an area with active zika virus infection. On returning, pregnancy should be postponed for a further 28 days. This allows for a maximum two week incubation period and possible two week viraemia.

Women whose partners have been to an area with zika virus transmission
Although zika virus has been identified in semen of infected men, the risk of sexual transmission is thought to be very low. It is uncertain how long the virus persists in semen. Condoms should be used to prevent against infection acquisition:

- For 28 days after his return if he had no symptoms
- For 6 months following recovery if he experienced symptoms suggestive of infection.

Following birth
After birth of a live infant, the following tests are recommended:

- Histopathological examination of the placenta and umbilical cord
- Testing of placental tissue and cord for zika virus-RNA
- Testing of umbilical cord for zika and dengue virus

Babies should be followed up into childhood to monitor signs of congenital infection.

In the case of a fetal loss, samples of fetal tissue, umbilical cord and placenta should be tested for zika virus RT-PCR. These tests are recommended to advance the understanding of the pathophysiology of zika virus in pregnancy.

Other management considerations
The American College of Obstetricians and Gynaecologists recommend breastfeeding after maternal zika virus infection in pregnancy.[7] Very small quantities of the virus has been reported in breast-milk following maternal infection. Any effects of neonatal infection, as with adults, are likely to be mild and of short term consequence.

Table 1: Zika virus: what you need to know

- Zika virus produces a mild illness with non-specific symptoms and may be symptomatic in just one in four cases
- The link between infection in pregnancy and microcephaly is not fully characterised
- Offer pregnant women at risk of infection a monthly fetal scan, and discuss those with symptoms with an infectious disease specialist
- Women who are pregnant or planning pregnancy should consider avoiding travel to affected areas
- Advise men returning from affected areas to avoid unprotected sex with female partners of childbearing potential for 28 days, and for six months if they have probable or confirmed infection

References

1. *National Institute for Communicable Diseases. The Zika virus: What is the risk to South Africa. 2016. http://www.nicd.ac.za/?page=alerts&id=5&rid=636.*
2. *CDC. Zika Virus. http://www.cdc.goc/zika/geo/index.html.*
3. *PAHO Statement on Zika Virus Transmission and Prevention. http://paho.org.hg/index.php?option=com_content&view=article&id=11605&It.*
4. *Hayes EB. Zika virus outside Africa. Emerg Infect Dis 2009;15:1347-50.*
5. *Musso D, Roche C, Robin E et al. Potential sexual transmission of Zika virus. Emerg Infect Dis 2015;2:359-61.*
6. *Foy BD, Kobylinski KC, Chilson Foy JL et al. Probable non-vector-borne transmission of Zika virus, Colorado, USA. Emerg Infect Dis 2011;17: 880-882.*
7. *ACOG. Practice Advisory: Interim Guidance for Care of Obstetric patients during a Zika Virus Outbreak. 2016. http://clacaidigital.info:8080/xmui/handle/123456789/719.*
8. *Brasil P, Pereira JP, Gabaglia CR et al. Zika Virus Infection in Pregnant Women in Rio de Janeiro – Preliminary Report. NEJM 2016:1-11.*
9. *National Travel Health Network and Centre. Zika virus: update and advice for pregnant women. http://travelhealthpro.org.uk/zika-virus-update-and-advice-for-pregnant-women/.*
10. *CDC. Travelers' health. CDC issues interim travel guidance related to Zika virus for 14 countries and territories in Central and South America and the Caribbean. Atlanta, GA: US Department of Health and Human Services, CDC; 2016.*
11. *RCOG. Interim RCOG/RCM/PHE/HPS clinical guidelines. Zika virus Infetion and Pregnancy. Information for Healthcare Professionals. 2016. https://www.rcog.org.uk/en/news/interim-clinical-guidelines-on-zika-virus-infection-and-pregnancy.*
12. *Society for Maternal-Fetal Medicine Publications Committee. Ultrasound screening for fetal microcephaly following zika virus exposure. AJOG 2016: B1-3.*