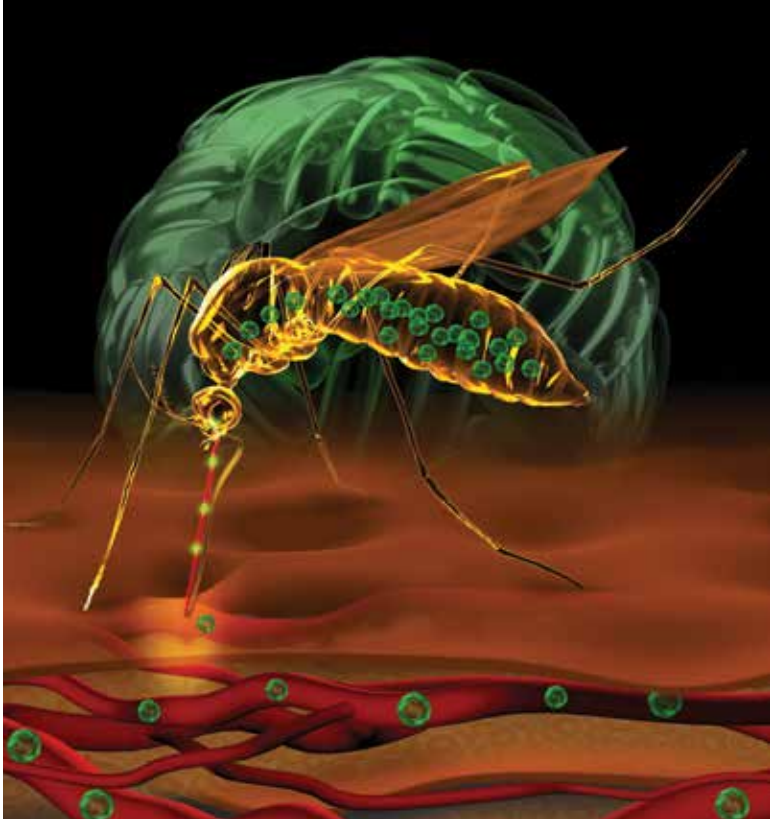

Zika virus infection

Current evidence and implications for practice

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The WHO has declared Zika virus infection a public health emergency of international concern due to the recent outbreak in the Americas and the coinciding increased rates of microcephaly and neurological complications. The 54 cases so far identified in Australia were all acquired overseas but *Aedes aegypti*, the mosquito vector responsible for most cases, is occasionally found in Far North and Central Queensland.

KEY POINTS

- The Zika virus (ZIKV) outbreak is now confirmed in 64 countries.
- ZIKV is transmitted by infected *Aedes* mosquitoes and semen.
- Most ZIKV infections are mild or asymptomatic.
- A causal link with microcephaly and fetal abnormalities has now been established for ZIKV infection.
- Serology and molecular testing methods are available for diagnosis of ZIKV infection.
- There are no specific antiviral therapies currently available for ZIKV infection, nor a vaccine.

Zika virus (ZIKV) is an enveloped, single-stranded RNA virus of the family *Flaviviridae*, genus *Flavivirus*. There are two geographically distinct lineages, African and Asian, with the latter primarily responsible for the current large outbreaks of ZIKV infection in the Pacific Islands and Americas. It is also an arbovirus, with *Aedes* species mosquitoes being the primary vector. The WHO declared ZIKV infection a 'Public Health Emergency of International Concern' on 1 February 2016 due to the recent outbreak in the Americas and the coinciding increased rates in infants of microcephaly and neurological complications including Guillain–Barré syndrome (GBS).[1] As of 13 May 2016, there have been 54 cases of ZIKV infection identified in Australia, all acquired overseas.[2]

This article aims to review the current understanding of the clinical manifestations, epidemiology, diagnostic methods, treatment and preventative measures relevant to ZIKV infection.

Clinical manifestations

Most ZIKV infections are asymptomatic. The clinical manifestations of infection are nonspecific and difficult to distinguish from those of other arboviral diseases including dengue and chikungunya. The incubation period is not clearly defined but ranges between three and 12 days, and symptoms usually last two to seven days.[1,3-5] Common symptoms include fever, headache, arthralgia, myalgia, maculopapular rash and conjunctivitis (Box 1).[1,3-5] In contrast to dengue virus infection, retro-orbital pain is uncommon in ZIKV infection, maximal body temperatures are lower and the incidence of rash (which occurs earlier in the course of infection) is greater. The rash is generally pruritic and has craniocaudal

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1. CLINICAL FEATURES OF ZIKA VIRUS INFECTION*

Common symptoms

- Fever
- Headache
- Arthralgia
- Myalgia
- Maculopapular rash, caudal to peripheral
- Conjunctivitis

Less common symptoms

- Retro-orbital pain
- Guillain–Barré syndrome
- Myelitis
- Meningoencephalitis
- Postviral fatigue

* Approximately 80% of infections are asymptomatic.

TABLE. REGIONS AND COUNTRIES WITH CURRENT AUTOCHTHONOUS ZIKA VIRUS TRANSMISSION

Region	Countries
Oceania/Pacific Islands	American Samoa, Fiji, Marshall Islands, Micronesia, New Caledonia, Samoa, Tonga
Asia	Philippines, Vietnam
South America	Bolivia, Brazil, Colombia, Ecuador, French Guiana, Guyana, Paraguay, Suriname, Venezuela
Central America	Costa Rica, El Salvador, Guatemala, Honduras, Mexico, Nicaragua, Panama
The Caribbean	Aruba, Barbados, Bonaire, Cuba, Curacao, Dominica, Dominican Republic, Guadeloupe, Haiti, Jamaica, Martinique, Commonwealth of Puerto Rico, Saint Martin, Saint Vincent and the Grenadines, Trinidad and Tobago, US Virgin Islands
Africa	Cape Verde

spread (from the face to the hands and feet) with resolution after one to four days.[6] Rarely gastrointestinal upset (pain, constipation or diarrhoea) and oral aphthous ulcers develop.[7] Neurological complications, including GBS and postviral fatigue, have been reported in the outbreaks in French Polynesia and Brazil.[5,8,9]

Epidemiology

ZIKV was first recovered in 1947 from rhesus monkeys in Ziika Forest, Uganda, and then from *Aedes africanus* mosquitoes collected in 1948 from the same region.[10] Human infections have been documented since 1952.[10] Although sporadic cases were recorded in Pakistan, Malaysia and Indonesia in the 1970s, large outbreaks have been recognised only recently – in the Yap Islands (Micronesia) in 2007 and in French Polynesia in 2013.[3,10] It was estimated that 11% of the population was infected during the outbreak in French Polynesia, although cases were not always confirmed in the laboratory.[5] The first human cases of ZIKV infection in Brazil were notified in May 2015, followed by rapid spread to involve most of the Americas.[8] The current outbreak in the Americas is estimated to have affected between 440,000 and 1,300,000 people.[8] As of 18 May 2016, transmission of ZIKV has been documented in 64 countries and territories.[11]

Successful transmission of ZIKV requires competent vectors and susceptible hosts with little or no pre-existing immunity. *Aedes* mosquitoes are the primary vectors for ZIKV transmission. *A. aegypti* is common in tropical and subtropical regions and responsible for most cases. Other *Aedes* species, including *A. albopictus* and *A. polynesiensis*, which are present in nontemperate climates, may also transmit ZIKV, but this has only been demonstrated within the African continent.[3] In Australia, *A. aegypti* is occasionally found in Far North and Central Queensland.[12] Humans and other primates act as the primary reservoir of ZIKV.[4] Regions with current ongoing circulation of ZIKV are listed in the Table.[11,13,14] ZIKV has been detected in an Australian who was bitten by a monkey in Bali and in another after a brief visit to Jakarta, both in Indonesia.[15,16] *A. aegypti* is found in both these regions but there is no current evidence of autochthonous transmission (i.e. there is no evidence to confirm circulating ZIKV in Indonesia).

Sexual transmission of ZIKV has been documented, transmission occurring via both vaginal and anal intercourse from infected men to both female and male partners.[4,17-19] ZIKV has also been isolated from semen; however, the duration of infectivity of semen has not been established.[19] The virus has been detected in the blood of newborn babies and tissues of terminated fetuses, confirming its vertical transmission.[3,7,17] Transfusion of infected blood products is another potential means of virus transmission, ZIKV having been detected by reverse transcription polymerase chain reaction (RT-PCR) in 2.8% of blood donors in French Polynesia during the 2013 outbreak.[20]

Association between perinatal infection, microcephaly and GBS

There has been a marked increase in the reported rates of microcephaly in conjunction with the recent ZIKV infection outbreak in the Americas.[21-23] Perinatal transmission is not unique to ZIKV, other flaviviruses (including dengue and West Nile viruses) and arboviruses (such as chikungunya virus) also being able to be transmitted vertically.[8] Using Shepard's criteria for 'proof' of human teratogenicity and the Bradford-Hill criteria for evidence of causation, Rasmussen and colleagues have proposed that there is sufficient evidence to infer a causal relationship between ZIKV and microcephaly in the absence of an alternate cause.[24]

Between 22 October 2015 and 30 January 2016 more than 4700 notifications of microcephaly or CNS anomalies had been reported to the Brazilian Ministry of Health.[21] Of these, 404 cases from nine Brazilian states have been confirmed to have microcephaly and/or CNS anomalies suggestive of congenital infection, of which only 17 have been attributed to ZIKV infection using pathogen-specific serology or nucleic acid amplification tests.[21] The US Centers for Disease Control and Prevention (CDC) have been testing cerebrospinal fluid (CSF) from a cluster of 35 microcephalic infants born to mothers living in or visiting ZIKV endemic areas, 74% of whom reported a ZIKV-compatible illness during pregnancy; all 27 infants for whom neuroimaging studies were performed had cerebral anomalies.[21] An increase in fetal neurological abnormalities was also recorded in French Polynesia in 2014; 13 cases of fetal cerebral anomalies were diagnosed compared with four and three in the preceding two years.[23]

Case reports have strongly implicated vertical transmission of ZIKV. Investigators of two cases during the French Polynesian outbreak demonstrated maternal ZIKV viraemia via RT-PCR and positive ZIKV-specific serology within two days of delivery.[7] One infant was ZIKV RT-PCR positive on day four of life, this coinciding with low-grade fever and development of a rash; the other infant was RT-PCR positive on days five and seven of life. A retrospective review of ZIKV cases in French Polynesia recently identified 19 cases of congenital CNS malformations, with and without microcephaly; ZIKV was detected by RT-PCR and viable virus was recovered in four of five microcephalic cases but none of the nonmicrocephalic cases.[25]

ZIKV has also been detected in tissue from a terminated foetus. Vertical transmission has been described in a previously well European woman living in northeastern Brazil who developed a febrile illness consistent with ZIKV infection characterised by myalgia, retro-orbital pain and generalised maculopapular rash at 13 weeks of gestation.[22] Fetal ultrasounds reported normal morphology at 14 and 20 weeks but abnormalities were detected at 29 weeks. The 32-week scan demonstrated intrauterine growth retardation, a calcified placenta of normal size, microcephaly (below second percentile for gestation), moderate ventriculomegaly and numerous intracerebral calcifications. The pregnancy was terminated and ZIKV was detected in fetal brain tissue at autopsy by RT-PCR, immunohistochemistry, electron microscopy and next generation sequencing. Testing for other pathogens, including flaviviruses, chikungunya virus, cytomegalovirus, rubella virus, varicella zoster virus, herpes simplex virus, parvovirus B19, enterovirus and toxoplasma, returned negative results.

Recent data from a cohort of 88 pregnant women from the Rio de Janeiro region of Brazil, collected between September 2015 and February 2016, identified that 72 women had ZIKV detected by RT-PCR from blood and/or urine specimens.[26] Fetal ultrasound in 12 cases demonstrated five intrauterine growth retardations and four cerebral calcifications. No abnormalities were observed in the ZIKV-negative women. ZIKV was detected by RT-PCR in amniotic fluid collected from women (two Brazilian and four French Polynesian) with fetal abnormalities.[23,27]

Many questions about the impact of ZIKV disease on human hosts and the pathogenesis of microcephaly remain unanswered. The means by which the virus infects the fetus is also not established. Furthermore, ZIKV may also be transmitted to newborn infants via breast milk, the virus having been isolated from breast milk propagated in cell culture.[28] It remains unknown whether the age of gestation at the time of ZIKV infection alters the clinical course, at what time following infection fetal manifestations should be expected and, most importantly, at what stage it can be safely determined that no complications are expected.

There is also emerging evidence suggesting an association between ZIKV infection and GBS.[29] Of 42 cases of GBS diagnosed during the French Polynesian ZIKV infection outbreak, 41 had anti-ZIKV IgM or IgG detected (all had neutralising antibodies against ZIKV), and 37 presented with a ZIKV-compatible illness within the preceding six days.[30] Diagnoses of GBS in excess of background incidence are also emerging from a number of South American nations including Brazil and El Salvador.[21] Other neurological manifestations include case reports of meningoencephalitis and acute myelitis, with ZIKV detected from CSF by RT-PCR.[31,32]

2. ASSESSING PREGNANT WOMEN RETURNING FROM ZIKA VIRUS-AFFECTED REGIONS (AUSTRALIAN GOVERNMENT DEPARTMENT OF HEALTH RECOMMENDATIONS)[5]

Last potential exposure to Zika virus within the past two weeks

- Symptomatic
  - RT-PCR of blood and urine
  - serology (for acute antibodies)
  - convalescent serology at least two weeks after acute serology and four weeks from last exposure
- Asymptomatic
  - collect and store whole blood and urine for RT-PCR and serum (acute sample) to test retrospectively if convalescent serology is positive
  - convalescent serology at least two weeks after acute serology and four weeks from last exposure

Last potential exposure to Zika virus two to four weeks ago

- Prior symptoms or asymptomatic
  - RT-PCR urine
  - serology, negative results require repeat testing in two weeks

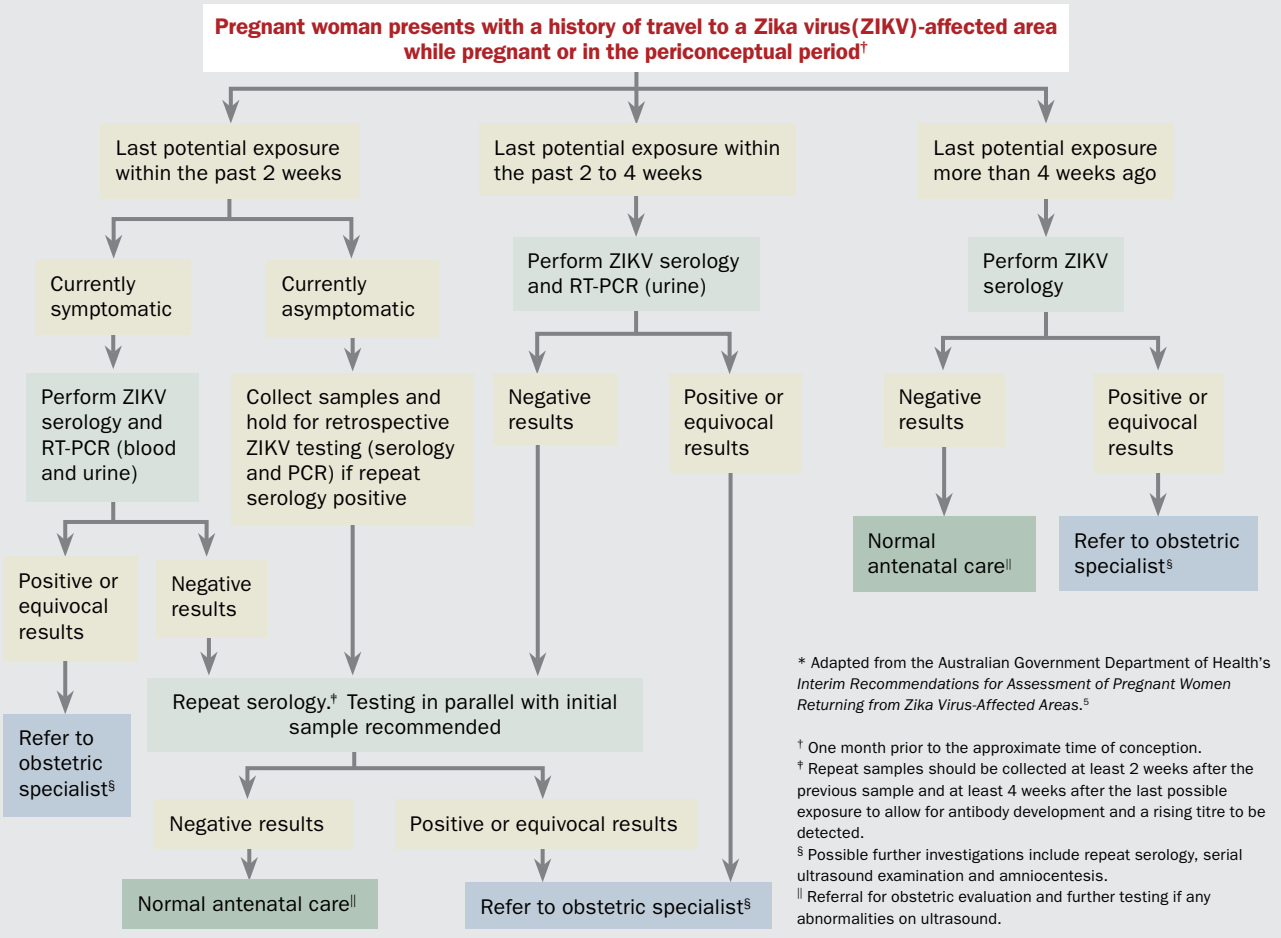
Last potential exposure to Zika virus more than four weeks ago

- Prior symptoms or asymptomatic
  - serology; indeterminate results may warrant a repeat sample two weeks later

Laboratory diagnosis of Zika virus

Laboratory confirmation of all suspected ZIKV infections remains important for

ASSESSING PREGNANT WOMEN RETURNING FROM ZIKA VIRUS ENDEMIC AREAS[5]*



* Adapted from the Australian Government Department of Health's *Interim Recommendations for Assessment of Pregnant Women Returning from Zika Virus-Affected Areas*.[5]

† One month prior to the approximate time of conception.
‡ Repeat samples should be collected at least 2 weeks after the previous sample and at least 4 weeks after the last possible exposure to allow for antibody development and a rising titre to be detected.
§ Possible further investigations include repeat serology, serial ultrasound examination and amniocentesis.
‖ Referral for obstetric evaluation and further testing if any abnormalities on ultrasound.

clinical management and public health. The primary testing methods for ZIKV are ZIKV-specific serology and a nucleic acid amplification test (NAAT), usually RT-PCR. Both methods are useful in confirming the diagnosis in an individual patient, and population-based serological testing allows estimation of ZIKV attack rates (i.e. new cases in susceptible, nonvaccinated populations).

Suitable samples for NAAT include EDTA whole blood and urine collected within one week and four weeks after the onset of symptoms, respectively.[33] Semen, amniotic fluid, cerebrospinal fluid, saliva and breast milk specimens may be considered for NAAT.[5,19] The duration for which ZIKV remains detectable in these samples remains to be established.

For detection of anti-ZIKV IgM and IgG, serum should be collected as early as possible after symptom onset and a convalescent sample collected 14 to 21 days later. In general, ZIKV-specific IgM and IgG are present within five to eight days and seven to 10 days after symptom onset, respectively.[4,5] Positive sera should be tested for other flaviviruses, in particular dengue virus, due to high rates of cross-reactivity. Antibodies against yellow fever, Japanese encephalitis, Murray Valley and West Nile viruses have shown less cross-reactivity in small sample groups.[34] The demonstration of neutralising antibodies against ZIKV can further improve the accuracy of serological diagnosis of the infection.

Several nonspecific laboratory abnormalities are commonly seen in patients with ZIKV infection, including mild derangement of liver function tests, elevated inflammatory markers, leucocytosis and thrombocytopenia.

The Australian Government Department of Health recommendations for assessing pregnant women returning from ZIKV-affected regions are given in Box 2 and the flowchart.

Treatment and prevention

As there are no specific antiviral therapies currently available for ZIKV infection, treatment is supportive. NSAIDs and salicylates should be avoided in the presence of thrombocytopenia because of the

potential risk of bleeding. Perinatal counselling and fetal monitoring should be undertaken in consultation with an obstetric specialist in pregnant women infected with ZIKV.[4,5,13] Monitoring for fetal abnormality via serial ultrasonography and consideration of amniocentesis for ZIKV RT-PCR is recommended by the Royal Australian and New Zealand College of Obstetricians and Gynaecologists.[35]

There is currently no vaccine to prevent ZIKV infection.[4,5,13] Prevention is primarily through avoidance of mosquito bites, and all travellers in areas with transmission should practise mosquito avoidance. *Aedes* mosquitoes usually bite during the day, and measures to minimise the chance of being bitten, and the possible transmission of virus, include wearing long-sleeve and/or permethrin-treated clothing and using insect repellents containing diethyltoluamide (DEET) or picaridin (safe in pregnant women). Insect repellent should be applied after sunscreen. Sleeping inside with either closed or screened windows or under mosquito nets both day and night is advised. Large-scale control of mosquito breeding sites are important public health considerations.

Current recommendations from the WHO, CDC and the Australian Government Department of Health include the following measures to minimise the risk of sexual transmission of ZIKV:[5,13,36]

- for men with confirmed ZIKV infection – condom use or abstinence of any sexual activity for three months after the diagnosis
- for men who have travelled to a ZIKV endemic area and whose partner is pregnant – abstinence of sexual activity for the duration of the pregnancy or use of condoms for all sexual activity.

This advice regarding minimising sexual transmission of ZIKV is cautious and primarily aimed at minimising possible fetal complications. It also has a role in preventing any partner from a secondary acquisition of ZIKV and minimising any risk of further introduction to a mosquito vector.

Current recommendations from the WHO and supported by the Australian Government Department of Health advise women who are pregnant or planning to become pregnant to consider delaying travel to areas with ongoing activity of ZIKV.[13,37]

ZIKV infection is notifiable in Australia. Health professionals in areas of Northern and Central Queensland with *Aedes* mosquito populations should also notify suspected cases prior to laboratory confirmation of infection.[5]

Conclusion

ZIKV infection has rapidly entered public awareness and caused grave concern, particularly in pregnant women and those planning to conceive. Further research to fully understand the pathogenesis, pathophysiology, epidemiology, outcomes and diagnostic methods of ZIKV infection will guide effective disease control and management strategies, including vector control and the development of antiviral therapy and vaccines against the disease. MT

References

A list of references is included in the website version of this article (www.medicinetoday.com.au).

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VITALI SINTCHENKO MB BS, PhD, FRCPA, FACHI

References

1. WHO. WHO statement on the first meeting of the International Health Regulations (2005) (IHR 2005) Emergency Committee on Zika virus and observed increase in neurological disorders and neonatal malformations. WHO statement; 2016. Geneva: WHO; 2016.Available online at: http://www.who.int/mediacentre/news/statements/2016/1st-emergency-committee-zika/en (accessed June 2016).
2. Australian Government Department of Health. Zika virus – notifications of Zika virus infection (Zika). Canberra: Commonwealth of Australia; 2016. Available online at: http://www.health.gov.au/internet/main/publishing.nsf/Content/ohp-zika-notifications.htm (accessed June 2016).
3. Musso D, Nilles E J, Cao-Lormeau V-M. Rapid spread of emerging Zika virus in the Pacific area. Clin Microbiol Infect 2014; 20: O595-O596.
4. Centers for Disease Control and Prevention (CDC). Zika virus. Clinical evaluation and disease. Atlanta, USA: CDC, US Department of Health and Human Services; 2016. Available online at: http://www.cdc.gov/zika/hc-providers/clinicalevaluation.html (accessed June 2016).
5. Australian Government Department of Health. Interim recommendations for assessment of pregnant women returning from Zika virus-affected areas. Canberra: Commonwealth of Australia; 2016. Available online at: http://www.health.gov.au/internet/main/publishing.nsf/Content/ohp-zika-pregnant.htm (accessed June 2016).
6. Simpson DI. Zika virus infection in man. Trans R Soc Trop Med Hyg 1964; 58: 335-338.
7. Besnard M, Lastère S, Teissier A, Cao-Lormeau VM, Musso D. Evidence of perinatal transmission of Zika virus, French Polynesia, December 2013 and February 2014. Euro Surveill 2014; 19: pii=20751.
8. European Centre for Disease Prevention and Control (ECDC). Rapid risk assessment: Zika virus epidemic in the Americas: potential association with microcephaly and Guillain-Barré syndrome – 10 December 2015. Stockholm: ECDC; 2015. Available online at: http://ecdc.europa.eu/en/publications/Publications/zika-virus-americas-association-with-microcephaly-rapid-risk-assessment.pdf (accessed June 2016).
9. Ioos S, Mallet HP, Leparc Goffart I, Gauthier V, Cardoso T, Herida M. Current Zika virus epidemiology and recent epidemics. Méd Malad Infect 2014; 44: 302-307.
10. Lanciotti RS, Kosoy OL, Laven JJ, et al. Genetic and serologic properties of Zika virus associated with an epidemic, Yap State, Micronesia, 2007. Emerg Infect Dis 2008; 14: 1232-1239.
11. WHO. Zika situation report, 19 May 2016. Geneva: WHO; 2016. Available online at: http://www.who.int/emergencies/zika-virus/situation-report/19-may-2016/en (accessed June 2016).
12. Russell R, Currie B, Lindsay M, Mackenzie JS, Ritchie SA, Whelan PI. Dengue and climate change in Australia: predictions for the future should incorporate knowledge from the past. Med J Aust 2009; 190: 265-268.
13. WHO. Zika virus factsheet. Geneva: WHO; 2016. Available online at: http://www.who.int/mediacentre/factsheets/zika/en (accessed June 2016).
14. Centers for Disease Control and Prevention (CDC). Zika virus. All countries and territories with active Zika virus transmission. Atlanta, USA: CDC, US Department of Health and Human Services; 2016. Available online at: http://www.cdc.gov/zika/geo/active-countries.html (accessed June 2016).
15. Leung GH, Baird RW, Druce J, Anstey NM. Zika virus infection in Australia following a monkey bite in Indonesia. Southeast Asian J Trop Med Public Health 2015; 46: 460-464.
16. Kwong JC, Druce JD, Leder K. Zika virus infection acquired during a brief travel to Indonesia. Am J Trop Med Hyg 2013; 89: 516-517.
17. Patino-Barbosa A, Medina I, Gil-Restrepo AF, Rodriguez-Morales AJ. Zika: another sexually transmitted infection? Sex Transm Infect 2015; 91: 359.
18. Deckard DT, Chung WM, Brooks JT, et al. Male-to-male sexual transmission of Zika virus – Texas, January 2016. MMWR Morb Mortal Wkly Rep 2016; 65: 372-374.
19. Musso D, Roche C, Robin E, Nhan T, Teissier A, Cao-Lormeau VM. Potential sexual transmission of Zika virus. Emerg Infect Dis 2015; 21: 359-361.
20. Musso D, Nhan T, Robin E, et al. Potential for Zika virus transmission through blood transfusion demonstrated during an outbreak in French Polynesia, November 2013 to February 2014. Euro Surveill 2014; 19: pii: 20761.
21. European Centre for Disease Prevention and Control (ECDC). Rapid risk assessment: Zika virus epidemic in the Americas: potential association with microcephaly and Guillain-Barré syndrome. Second update, 8 February 2016. Stockholm: ECDC; 2016. Available online at: http://ecdc.europa.eu/en/publications/Publications/zika-virus-rapid-risk-assessment-8-february-2016.pdf (accessed June 2016).
22. Mlkakar J, Korva M, Tul N, et al. Zika virus associated with microcephaly. N Engl J Med 2016; 374: 951-958.
23. Jouannic JM, Friszer S, Leparc-Goffart I, Garel C, Eyrolle-Guignot D. Zika virus infection in French Polynesia. Lancet 2016; 387: 1051-1052.
24. Rasmussen SA, Jamieson DJ, Honein MA, Petersen LR. Zika virus and birth defects – reviewing the evidence for causality. N Engl J Med 2016; 374: 1981-1987.
25. Besnard M, Eyrolle-Guignot D, Guillemette-Artur P, et al. Congenital cerebral malformations and dysfunction in foetuses and newborns following the 2013 to 2014 Zika virus epidemic in French Polynesia. Euro Surveill 2016; 21: pii=30181.

26. Brasil P, Pereira Jr JP, Raja Gabaglia C, et al. Zika virus infection in pregnant women in Rio de Janeiro – preliminary report. N Engl J Med 2016 March 4; epub (doi: 10.1056/NEJMoa1602412).
27. Calvert G, Aguiar R, Melo S, et al. Detection and sequencing of Zika virus from amniotic fluid of foetuses with microcephaly in Brazil: a case study. Lancet Infec Dis 2016 Feb 17; epub (doi: 10.1016/S1473-3099(16)00095-5).
28. Dupont-Rouzeyrol M, Biron A, O'Connor O. Infectious Zika viral particles in breastmilk. Lancet 2016; 387: 1051.
29. WHO. Zika virus microcephaly and Guillain-Barré syndrome – situation report 31 March 2016. Geneva: WHO; 2016. Available online at: http://apps.who.int/iris/bitstream/10665/204718/1/zikasitrep_31Mar2016_eng.pdf (accessed June 2016).
30. Cao-Lormeau V, Blake A, Mons S, et al. Guillain-Barré syndrome outbreak associated with Zika virus infection in French Polynesia: a case-control study. Lancet 2016; 387: 1531-1539.
31. Carteaux G. Zika virus associated with meningoencephalitis. N Engl J Med 2016; 374: 1595-1596.
32. Mécharles S, Herrmann C, Poullain P, et al. Acute myelitis due to Zika virus infection. Lancet 2016; 387: 1481.
33. Gourinat AC, O'Connor O, Calvez E, Goarant C, Dupont-Rouzeyrol M. Detection of Zika virus in urine. Emerg Infect Dis 2015; 21: 84-86.
34. Hueston L. Zika virus fact sheet: serology, 19 Feb 2016. Sydney: Institute of Clinical Pathology and Medical Research, Pathology West; 2016. Available on request from Pathology West.
35. Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG). Care of women with confirmed Zika virus infection during pregnancy in Australia. College Communiques. Melbourne: RANZCOG; 2016. Available online at: https://www.ranzcog.edu.au/images/Care_of_women_with_confirmed_zika_virus_infection_during_pregnancy_in_Australia.pdf (accessed June 2016).
36. Oster AM, Russell K, Stryker JE, et al. Update: interim guidance for prevention of sexual transmission of Zika virus – United States, 2016. MMWR Morb Mortal Wkly Rep 2016; 65: 323-325.
37. Australian Department of Health. Zika virus – information for clinicians and public health practitioners. Canberra: Commonwealth of Australia; 2016. Available online at: http://www.health.gov.au/internet/main/publishing.nsf/Content/ohp-zika-health-practitioners.htm#toc03 (accessed June 2016).