NHS BLOOD AND TRANSPLANT

ORGAN DONATION AND TRANSPLANTATION

ZIKA VIRUS AND TRANSPLANTATION OF SOLID ORGANS FROM DECEASED DONORS

KEY POINTS

- Zika virus is endemic in parts of Africa and Asia and has recently spread to other parts of the globe, including South and Central America. It is a flavivirus that is spread to humans by a bite from an infected mosquito
- Viral infection is usually asymptomatic or associated with very mild symptoms but an association between maternal Zika virus infection and foetal microcephaly has been observed
- Patients are viraemic for a short period (around 2 weeks) after infection but the virus may be found in other tissues after the viremia has cleared
- There are no commercially available, widely accessible tests for Zika virus in the UK
- There are reports of possible Zika virus transmission by blood transfusion and it is probable that infection may also be transmitted by organ transplantation
- The impact of immunosuppression on the natural history of Zika virus infection is unknown
- Donor characterisation includes a full recent travel history; when the potential donor has travelled to Latin America or other affected areas, the SNOD should enquire whether the donor had been bitten by mosquitos and about any associated illness: this should be documented on the Donor Characterisation Form
- Recipient clinicians should balance the risk and possible consequences of a donor-transmitted infection and the risks of harm by declining the organ.

Note: these notes have been prepared by Dr Ines Ushiro-Lumb and Professor James Neuberger following discussions with microbiology and clinical colleagues. The knowledge base is changing rapidly and users should interpret these notes in the light of any further information.

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ZIKA VIRUS AND SOLID ORGAN TRANSPLANTATION

The spread of the Zika virus epidemic in the Americas is likely to continue as the competent vectors *Aedes aegypti* and *Aedes albopictus* mosquitoes are widely distributed there.

This is an emerging situation that has begun fairly recently and is evolving relatively rapidly. Diagnostic tools are not widely available yet and the utility of available in house developed tests in the context of screening asymptomatic donors need to be considered with care; there are no commercially available tests.

Incidence of microcephaly and Guillain-Barre Syndrome has been reported to be higher in affected areas and investigations are ongoing to clarify the possible causative links.

To date, no cases of transmission through tissues or organs have been reported. Possible transfusion-associated and sexual transmission have been described.

In the UK, cases will be seen amongst travellers returning from affected areas as the vector is not present here. As of 25th January 2016, 6 cases have been diagnosed in UK travellers since 2014.

Understanding of ZIKV pathogenesis and associated clinical presentation and complications is evolving. Viraemia is believed to be short lived and only 1 in 5 infected people develop symptoms. Deaths are rare but have been described, including one adult with co-morbidities, who was on immunosuppressant drugs.

Currently in the UK, there is no routine NAT screening for any of the other flavivirus in an asymptomatic deceased donor who has been to an area where there is ongoing transmission. However, this is a new and rapidly evolving situation where there are significant gaps in knowledge and a strong suggestion that ZIKV may be neurotropic, at least *in utero*. The following precautionary measures may be considered, subject to revision, as more information becomes available:

Potential donor scenario	Consider	Comment
Asymptomatic traveller returning from affected area	The travel history should include, wherever possible, area visited with dates, mosquito bites, and any symptoms. Taking blood samples from the donor for testing should be considered if <28 days date of return. Samples will be stored at NHSBT NTMRL until validated tests become available.	No evidence currently available; seek specialist advice and assess individual cases in context. A negative NAT in plasma may inform assessment and a decision to test should be made on a case by case assessment basis.
Laboratory confirmed ZIKV infection or symptoms compatible with Zika-like syndrome whilst in affected area or within 28 days from returning from affected area	Prolonged viraemia is not thought to occur but ZIKV dynamics not fully clarified. Distribution of virus within body compartments is not known. A cautious approach should be used for donation within the first 6 months from disease onset.	No evidence currently available; seek specialist advice and assess individual cases in context. A negative NAT in plasma may inform assessment
Current symptomatic illness high likely or confirmed to be caused by ZIKV	Decline for deceased donor organ transplantation except in exceptional circumstances	

Zika Virus – General Information

Zika virus (ZIKV) is a flavivirus related to yellow fever, dengue, West Nile, and Japanese encephalitis viruses. In 2007 ZIKV caused an outbreak of relatively mild disease characterized by rash, arthralgia, and conjunctivitis on Yap Island in the southwestern Pacific Ocean. This was the first time that ZIKV was detected outside of Africa and Asia. This arboviral disease has emerged in tropical areas of Latin America, particularly in Brazil and Colombia, as a public health threat in 2015 and has spread into areas to which dengue virus (DENV) and chikungunya virus (CHIKV) are endemic.

Microcephaly in babies has been associated with ZIKV infection. Some infants with possible Zika virus infection have been found to have intracranial calcifications and abnormal eye findings (Ventura, 2016)[4] . It is not clear if Zika virus infection caused any of these abnormalities and work is ongoing to clarify the suggested link.

Transmission: ZIKV is transmitted primarily by Aedes aegypti mosquitoes. These vectors also transmit dengue and chikungunya virus and are found throughout much of the Americas, including parts of the United States.

There is growing evidence that Intra-uterine and perinatal transmission can occur (Besnard, 2014).[1]

There has been one report of possible transfusion-associated transmission and one report of possible spread of the virus through sexual contact (Foy, 2011).[2]

Pathogenesis: Information regarding pathogenesis of ZIKV is scarce but mosquito-borne flaviviruses are thought to replicate initially in dendritic cells near the site of inoculation then spread to lymph nodes and the bloodstream. The incubation period for Zika virus disease is not known, but is likely to be a few days to a week. As with other Flaviviruses, viraemia is thought to be short-lived and last only a few days. To date, infectious ZIKV has been detected in human blood as early as the day of illness onset; viral nucleic acid has been detected as late as 11 days after onset (Lanciotti 2007). [3]

Clinical presentation: An estimated 80% of persons infected with Zika virus are asymptomatic. Symptomatic disease is generally mild and characterized by acute onset of fever, maculopapular rash, arthralgia, or non-purulent conjunctivitis. Symptoms usually last from several days to 1 week. Severe disease requiring hospitalization is uncommon, and fatalities are rare. Guillain-Barré syndrome has been reported in patients following suspected Zika virus infection (Ohler 2014)[5]

Clinical course in immunosuppressed patients has not been described to date and it is not known whether there are groups of individuals at particular risk of complications. Death in a sickle cell patient infected with ZIKV has been reported. Onset of vaso-occlusion in persons with sickle cell disorders is often triggered by inflammation, as has been reported in DENV infections and which probably occurred in the case reported by Arsuza-Ortega (2016).[6]

Specific prevention and treatment: There is no vaccine or specific antiviral.

Laboratory diagnosis: There is no commercially available test for Zika virus antibodies or nucleic acid. The PHE Rare and Imported Pathogens Laboratory is currently the only laboratory in England that offers some arboviral diagnostic testing (PCR).

During the first week after onset of symptoms, Zika virus RNA can be detected in serum. Virus-specific IgM and neutralizing antibodies typically develop towards the end of the first week of illness; cross-reaction with related flaviviruses (e.g., dengue and yellow fever viruses) is common and can pose a diagnostic challenge.

Up to date information: The situation is evolving rapidly and up to date information should be assessed through websites such as

https://www.gov.uk/guidance/zika-virus

http://www.who.int/mediacentre/factsheets/zika/en/

http://ecdc.europa.eu/en/healthtopics/zika_virus_infection/Pages/index.aspx

http://www.cdc.gov/zika/index.html

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6. Laura A-O, Arnulfo P, Giamina P-T, et al. Fatal Zika Virus Infection in Girl with Sickle Cell Disease, Colombia. Emerging Infectious Disease journal 2016;22.

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