Joint UKBTS Professional Advisory Committee ([1])

Position Statement

Zika Virus (ZIKV)

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Approved by: Standing Advisory Committee on Transfusion Transmitted Infections.

Background

Zika virus (ZIKV) is a member of the flaviviridae family and is transmitted to humans through the bite of infected mosquitoes. It is related to other pathogenic vector borne flaviviruses including dengue, West Nile and Japanese Encephalitis viruses.

ZIKV was first isolated in 1947 from a monkey in the Zika Forest in Uganda, then in mosquitoes (*Aedes africanus*) in the same forest in 1948 and in a human in Nigeria in 1952. ZIKV was subsequently only found in tropical Africa and parts of South East Asia until 2007 when an outbreak occurred on the Pacific island of Yap, with further outbreaks occurring in the Pacific region and a major outbreak on French Polynesia in 2013-14. The major outbreak in Central and South America, including some movement into mainland US, and in the Pacific region, confirmed ZIKV to be a significant emergent infectious agent in 2016.

There are two ZIKV lineages - the African lineage and the Asian lineage, the Asian lineage having emerged in the Pacific and which is the lineage that has recently spread into the Americas (the American subclade) and parts of the Caribbean.

ZIKV disease is a self-limiting febrile illness. The incubation period for ZIKV ranges from 3 to 14 days. Symptoms are usually mild and last for 2 to 7 days. Infection may go unrecognised or be misdiagnosed as dengue, chikungunya or other viral infections which give rise to fever and rash. However, as seen with other flaviviral infections such as dengue and West Nile fever, asymptomatic infections are common and only 20-25% of infected individuals develop symptoms. The most common symptoms of ZIKV disease include low-grade fever, transient arthritis/arthralgia with possible joint swelling, mainly in the smaller joints of the hands and feet, maculo-papular rash often spreading from the face to the body, conjunctivitis and a number of general non-specific symptoms such as myalgia, asthenia and headaches.

Immunity following infection is seen and appears to be long lasting. Currently, the only treatment available is symptomatic. No vaccine is available although more than 10 candidate vaccines have advanced to phase 1 clinical trials and one has started phase 2 clinical trial. However, a particular challenge is the waning incidence of ZIKV.

Because no large outbreaks of Zika virus were recorded before 2007, little was known about the complications of the disease. Whilst most infected individuals recover fully without severe complications and hospitalisation rates are low, ZIKV infection has been reported to be associated with a small number of deaths, although there is currently insufficient evidence to substantiate any direct linkage. Association with neurological complications such as Guillain-Barré syndrome was first suspected during the French Polynesia outbreak and again during the recent outbreak in the Americas.

In 2016, a WHO statement noted the scientific consensus was that ZIKV infection caused microcephaly and Guillain-Barre Syndrome (GBS). The WHO Zika Causality Working Group

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had convened an expert panel of 18 members with specialist knowledge in the fields of epidemiology and public health, virology, infectious diseases, obstetrics, neonatology, and neurology. The data reviewed and analysed indicated that overall the risk of congenital brain abnormalities was estimated to be around 50 times higher in mothers who had ZIKV infection in pregnancy compared with those who did not. In laboratory studies, ZIKV had been shown to cross the placenta and replicate in human brain cells. In respect of GBS the odds of having had a recent ZIKV infection were more than 30 times higher in patients with GBS than those without.

Whilst the main route of ZIKV infection is through the bite of an infected mosquito, there is evidence that Zika virus can also be transmitted to humans through blood transfusion, sexual contact and perinatally; virus has been found in blood, urine and saliva during the acute phase and in seminal fluid after the acute phase. However, the reservoir for the virus is currently unknown, although previously primates and rodents have been suggested as possible reservoirs in affected areas in Africa.

There have been six cases of transfusion transmission of ZIKV reported in Brazil, although it is possible that this number is an underestimate.

ZIKV has been shown to persist in semen for up to 370 days after symptom onset and after cessation of viraemia, with the potential for transmission to sexual partners through this route. ZIKV shedding has also been detected in vaginal secretions at a median of 14 days and a maximum of 37 days after symptom onset. A number of cases of sexual transmission have been reported. Results from following-up 5 immunocompetent men with ZIKV infection showed that the median duration of ZIKV viraemia was 22 (range 14–100) days in whole blood and 10 (range 7–37) days in plasma. Whole blood samples from 2 patients remained positive at 14 and 63 days after their plasma samples had become negative. Furthermore, a three-fold prolonged median detection of ZIKV RNA in serum collected from symptomatic women who were pregnant than those who were not, 40 days versus 14 days, respectively has been reported. Another group isolated infectious virus in semen from 8 of 97 men for up to 38 days after initial detection when ZIKV loads were $>1.4x10^6$ genome copy equivalents/ml (Medina F *et al,* JID 2019 219 31-40). These are considerations when looking at sample type, diagnosis as well as donor deferral periods. The recommended duration for taking measures to prevent sexual transmission of ZIKV from an infected partner to a sexual contact has been reduced by WHO from six to three months for men, and two months for women (WHO 2019).

Despite ZIKV having circulated in Africa and Asia in humans, animals and mosquitoes for many years, very few outbreaks have been documented. The first Zika outbreak reported outside Africa and Asia occurred in Micronesia in 2007; it was caused by the Asian strain of the virus. The same strain caused a subsequent outbreak in French Polynesia in 2013 and has since caused large outbreaks in other parts of the Pacific region including the first cases in the Americas on Easter Island in 2014. The outbreak across Central and Southern America, the Caribbean and into mainland US, began in May 2015. The first locally-acquired confirmed case of Zika infection was reported in north east Brazil; in April 2017 the WHO updated its country classification and listed 48 countries in the Americas with confirmed locally-acquired cases and on-going transmission. In 2016, it was felt that the spread of Zika virus in the Americas was likely to continue as the competent vectors *Aedes aegypti* and *Aedes albopictus* mosquitoes were widely distributed and the outbreak in Central and South America and in the Pacific region evolved rapidly. However, by 2017, it was noted that in Brazil where around 206,000 probable Zika infected individuals were recorded in 2016, only around 13,000 had been reported by July

2017, most of whom had been detected by mid-April. Similar falls had been seen throughout the Americas. CDC reported falls in travel related cases and only one transmission incident in the US. By July 2019, by WHO region, there were 13 reports of mosquito-borne ZIKV transmission in Africa, 49 in the Americas, 19 in the Western Pacific, 6 in Southeast Asia and a total of 87 worldwide.

Zika virus in the UK

ZIKV does not occur naturally in the UK, cases are imported in travellers returning from affected countries.

Case numbers of travel-associated Zika infections in the UK peaked in 2016, with 283 reports; there was also one report of likely sexual transmission. Numbers fell to 23 in 2017 and in 2018, 4 travel-associated infections were diagnosed in the UK. Of these, 2 were PCR positive and 2 were Zika-specific IgM positive and reported as highly indicative of recent infection. Nothing has been reported in the UK as of February 2019. In February 2019, the risk for Zika virus transmission in countries was reclassified as either 'risk' or 'very low risk'. In April 2019, ECDC reported that the epidemic in the Americas peaked in 2016 and a fall in infections was seen in most countries in the Americas and the Caribbean. Apparent interruption of transmission was reported in several islands. In Asia, Zika surveillance suggested a wide geographical distribution of infections.

Surveillance is carried out in the UK for ‘transmission competent’ mosquito vectors that included *Aedes aegypti* and also, possibly, *Aedes albopictus*. Both have been detected in Kent and Merseyside in 2016 and 2017.

Information about international outbreaks of ZIKV is available on the National Travel Health Network and Centre (NaTHNaC) website: http://travelhealthpro.org.uk

Visitors to affected areas are excluded from donation for 4 weeks under the current tropical virus deferral guidelines or for six months under current malaria deferral guidelines if the affected area also has a malaria risk. Visitors to these areas who have been, or who have had symptoms which suggest that they may have been infected with ZIKV should not donate blood or tissues for six months from their return to the UK. In addition, donors are excluded from donation if they have had sex in the last 28 days with someone who has had a confirmed Zika virus infection in the 3 months preceding the sexual contact.

Countries affected by ZIKV are shown in the Geographical Disease Risk Index (GDRI) and any associated Change Notifications.

(1) **Joint U**nited **K**ingdom **B**lood **T**ransfusion **S**ervices **Professional Advisory Committee**