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IPOPI Position Statement
Zika Virus

Zika virus was first identified in Uganda in 1947 and the first human infections were reported in the early 1950's. In recent months significant outbreaks of Zika virus in different regions and particularly in Central and South America have caught the attention of health authorities worldwide. Zika virus has been declared a public health emergency of international concern (PHEIC) by the World Health Organisation (WHO) after a substantial spike of cases of microcephaly in newborns and Guillain-Barré Syndrome (GBS) in the Americas. WHO defines a PHEIC as "an extraordinary event which is to constitute a public health risk to other states through the international spread of disease and to potentially require a coordinated international response"[i]

Symptoms

It should be noted that only 20% of individuals infected with Zika virus become symptomatic.[ii] The main symptoms of Zika virus disease are usually mild fever, skin rash and conjunctivitis, lasting for 2-7 days. Following the recent outbreak in Brazil (2015), clusters of GBS and pregnant women giving birth to babies with microcephaly (unusually small heads and abnormally developed brains) have been temporally associated with Zika virus transmission in some settings. Whilst a causative link between Zika virus and microcephaly / GBS remains to be firmly established, due to the absence of another explanation for these clusters and in keeping with good public health practice, the WHO highlighted "the importance of aggressive measures to reduce infection with Zika virus, particularly among pregnant women and women of childbearing age"[iii].

Transmission

Zika virus disease is mostly transmitted by Aedes mosquitoes. These are the same mosquitoes that transmit dengue, chikungunya and yellow fever. Other rarer forms of transmission have been described. These include transmission from a pregnant mother to her baby during pregnancy or around the time of birth[iv]. Spread of the virus through blood transfusion and sexual contact have also been reported[v].

The US Food and Drug Administration (FDA) issued on August 26th 2016 a revised guidance[vi] recommending universal testing of donated whole blood and blood components for Zika virus in the US. The revised guidance recommends that "*all States and U.S. territories screen individual units of donated whole blood and blood components with a blood screening test*".

As the FDA explained: "*expanded testing will continue to reduce the risk for transmission of Zika virus through the U.S. blood supply and will be in effect until the risk of transfusion transmission of Zika virus is reduced"*.

Zika virus and Immunoglobulins

Plasma-derived medicinal products (PDMPs) are life-saving treatments used to treat various rare conditions, including a large majority of primary immunodeficiencies (PIDs). They are

developed from donated human plasma. Immunoglobulin replacement therapy (IG Therapy) is the main PDMP used to treat PIDs. It contains immunoglobulins (IGs) from healthy donors, which help to protect against a range of infections and reduce autoimmune symptoms.

Zika virus is a flavivirus of relatively large size (about 40nm) diameter. The Flaviviridae are a family of positive, single-stranded, enveloped RNA viruses. Zika virus is similar to other lipid-enveloped viruses such as Dengue fever or West Nile Virus. It is therefore highly probable that it will be inactivated and removed by viral inactivation and reduction techniques (solvent-detergent, heat treatment and nanofiltration) applied during the manufacturing process of PDMPs such as IGs. In a statement published on 4 February 2016, the Plasma Protein Therapeutic Association (PPTA) stated that Zika virus' "*relatively large size and lipid envelope makes it highly susceptible to steps with virus inactivation and removal capacity used during the manufacturing processes, such as solvent-detergent (S/D), low pH incubation, caprylate, pasteurization or dryheat treatments, nanofiltration or fractionation processes. The effectiveness of these processes has been demonstrated on other lipid-enveloped model viruses which are quite similar to Zika virus, e.g. Bovine viral diarrhea virus (BVDV) or Tick-borne encephalitis virus (TBEV), and most importantly the WNV, another Flavivirus which is even more closely related to the Zika virus (…). Based on these data, PPTA is assured that existing manufacturing methods will also be effective against the Zika virus*".[vii]

The European Medicines Agency (EMA), an agency responsible for the scientific evaluation, supervision and safety monitoring of medicines in the European Union, confirmed on September 21st, 2016 that "*there is no increased ris of contamination with the Zika virus for patients who take plasma-derived […] medicines. […] the manufacturing processes used for plasma-derived products, including for example the solvent/detergent method to inactivate viruses, pasteurisation (liquid heat inactivation) and virus filtration, inactivate or remove the Zika virus from the finished product. […] no additional safety measures such as the testing or exclusion of certain plasma donors was necessary*"[viii].

Zika virus and primary immunodeficiencies

As there is no specific treatment or vaccine currently available for Zika virus disease, prevention for PID patients as for anyone else is very important.

Whilst the effects of Zika virus in PID patients have not been documented or studied, because of their susceptibility to develop infections and potentially a more severe form of the Zika virus disease, PID patients should take all possible precautions to prevent infection with Zika virus. Whilst immunoglobulin replacement therapy provides protection against a range of infections, it does not guarantee immunity against Zika virus.

IPOPI* would recommend PID patients to avoid whenever possible travelling to Zika virus endemic areas. IPOPI would further recommend that PID patients who have to travel to or live in endemic areas should consult with their doctor to receive personalised recommendations about prevention and protection measures. If travelling to countries or regions where Zika virus or other viruses spread by mosquitoes (i.e. West Nile Virus, Dengue

fever) are prevalent, the general prevention measures described by the WHO[ix], CDC[x] and ECDC[xi] should be followed. These include but are not limited to:

- Using mosquito-repellents, always following the product label instructions
- Wearing long-sleeves shirts and long pants
- Staying in places with air conditioning or that use window and door screens to keep mosquitoes outside.
- Using a mosquito bed net if you are outside and are not able to protect yourself from mosquito bites
- Treating clothing and gear with permethrin or purchase permethrin-treated items

When it comes to sexual relations, people with PIDs should ensure that they practise safe sex to avoid any type of infections.

IPOPI is closely monitoring this situation and will provide updated information as it becomes available.

This IPOPI position statement was revised on September 27th, 2016

** IPOPI is the Association of national patient organisations dedicated to improving awareness, access to early diagnosis and optimal treatments for primary immunodeficiency (PID) patients worldwide. As such IPOPI acts as the global advocate of the PID patient community in all relevant policy, legislative and regulatory matters. Primary Immunodeficiencies (PIDs) represent a large group of more than 280 chronic and rare diseases in which the immune system or parts of the immune system do not function correctly.*

References

[i] http://www.who.int/ihr/procedures/en_ihr_ec_faq.pdf?ua=1
[ii] http://www.cdc.gov/zika/disease-qa.html
[iii] http://www.who.int/mediacentre/news/statements/2016/1st-emergency-committee-zika/en/
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