Zika Virus
Information and recommendations of the Swiss Expert Committee for Travel Medicine (ECTM)*
(Update April 2019)

*members listed below

Background: In 2015 an explosive spread of the Zika Virus occurred in Latine America, and the Caribbean (LAC). Zika virus infection during pregnancy can cause birth defects such as microcephaly and/or other neurological disorders.

Pathogen: The Zika virus (ZIKV) belongs to the virus family Flaviviridae, which include the viruses that cause dengue fever, yellow fever, tick-borne encephalitis (TBE), japanese encephalitis, and West Nile fever.

Reservoir: Monkeys, humans

Vectors: Mosquitoes (*Aedes* genus, subgenus *stegomyia*, mainly *Aedes aegypti*)

Geographical distribution: ZIKV was first isolated in 1947 from a rhesus monkey in the Zika Forest in Entebbe, Uganda. Until 2007, only isolated cases or small clusters had been diagnosed in Africa and in Southeast Asia. In 2007, the Yap islands (Federated States of Micronesia), Western Pacific, reported a first ZIKV outbreak that was followed by a large outbreak in French Polynesia and other territories in the Pacific in 2013-2014. Between 2013 and 2015, ZIKV was probably introduced from the Pacific to Brazil leading to an outbreak from 2015 onwards that further spread to almost all countries of the Americas and the Caribbean. In 2016 – 2017, there were also ZIKV outbreaks reported in the Pacific islands, Cape Verde, Singapore and Florida. The current distribution of ZIKV and areas with outbreaks can be seen at: https://wwwnc.cdc.gov/travel/page/zika-travel-information

Transmission:
a) Vector-borne (main transmission route): ZIKV is transmitted through *Aedes* (subgenous *stegomyia*) *aegypti / albopictus* mosquitoes in tropical and subtropical regions. These mosquitoes are mainly active during the day and early evening hours. *Aedes* mosquitoes are quite aggressive and prefer to bite humans. They are mainly found in cities. Zika cases transmitted by mosquitoes are the predominant way of infection in humans.

b) Sexual: ZIKV can be transmitted by sexual intercourse. This is possible from both asymptomatic and symptomatic persons through genital, and anal intercourse. Sexual transmission is possible from male to female, male to male, and female to male (Baud et al., 2017). Up to date, the maximal documented time of sexual transmission is 44 days after symptom onset, most reports indicate shorter intervals (Baud et al., 2017, CDC, 2018). Infectious ZIKV particles have been detected through semen up to 69 days after symptom onset (Arsuaga et al., 2016), and in the female genital tract up to 2 days after symptom onset. ZIKV RNA detection has been reported in semen for more than 12 months; however, most cohorts report a shorter interval with an estimated mean time to ZIKV RNA clearance of 54 days (Mead et al., 2018). In the female genital tract, ZIKV RNA was detected up to 180 days after onset of symptoms (Reyes et al., 2019). However, the presence of ZIKV RNA in genital fluids is not necessarily associated with infectivity; hence, the exact duration of possible sexual transmission remains unknown.

c) Transfusion: Transmission via a blood transfusion is possible.

d) Materno-fetal: Perinatal transmission was first reported in 2013
during the French Polynesian outbreak and has since been confirmed in the Brazilian outbreak and elsewhere from 2015 onwards, including in pregnant travellers upon return.
As of current knowledge, vertical transmission occurs in around 30% all ZIKV infected pregnant women, and around 50% of all infected foetuses will have symptomatic congenital infections (Pomar, BMJ 2018). The risk of birth defects is similar for symptomatic and asymptomatic infections (Honein, JAMA 2017), and there was a higher risk of birth defects in women who were infected around the preconception period or during the first pregnancy (Hoen, NEJM 2018). Consequently, clinically relevant damages to the child were found in around 5 to 15% of ZIKV positive mothers (Honein, JAMA 2017; Hoen, NEJM 2018, Pomar, BMJ 2018), which is comparable to other congenital diseases such as CMV. Prolonged detection of viral RNA in pregnant women might be the result of viral replication in the foetus or placenta. Infectious ZIKV particles have been detected in breast milk, but no transmission to neonates by breastfeeding has been reported to date.

Risk assessment of ZIKV infection for travellers: ZIKV infection is possible where the ZIKV is endemic. Because of the reported congenital infections during the ZIKV outbreaks in the Pacific and Americas, risk of ZIKV infection with risk of birth defects has to be considered and should be discussed during pre-travel consultation.

Clear risk of ZIKV infection is difficult to assess as several factors (seasonality, other flavivirus cross-immunity, herd immunity, traveller's behaviour…) are most probably involved, and the epidemiological situation of ZIKV has been assessed differently depending on the consulted source (ECDC, CDC, WHO). Moreover, since the peak of the outbreak in 2016, the epidemiological surveillance has decreased and reliable updates are lacking. The Swiss Expert Committee for Travel Medicine (ECTM) assumes the risk to be low to get infected by ZIKV during travel in confirmed or probable endemic areas (with current or past reported ZIKV cases, or area where the vector (mosquitoes) is present). The justification of this assumption is based on the epidemiology observed in Asia and Africa. ZIKV has probably been endemic in Asia and Africa for many decades without revealing an epidemic spread, as it has been the case in 2015-2016 in the LAC or in 2013 in Oceania. Therefore, for pregnant women or women planning to get pregnant, the Swiss ECTM considers the risk to be very low for acquiring a ZIKV infection leading to foetal malformation in confirmed or probable endemic countries.

Based on this background, the Swiss ECTM defines the ZIKV congenital infection risk for travellers as follows:

a) **low risk**= travel (including partner's) in an area with current or past reported ZIKV cases OR in an area where the vector (mosquitoes) is present;
b) **increased risk** = travel (including partner's) in an area with a ZIKV outbreak OR IgM ZIKV+ partner

Incubation Period: Not exactly known, probably 3-14 days.

Disease: Only one out of five infected people fall ill with usually mild symptoms of generally short duration (2-7 days). The main symptoms are a maculopapular rash that is often itchy and spreads from the face to the body, fever (however often missing), conjunctivitis, joint pain in the small joints of the hands and feet, muscle pain, and headache. More rarely, neurological complications are observed (meningitis; or ascending, usually temporary paralysis, the Guillain-Barré-Syndrome). There is evidence that ZIKV infection during pregnancy can cause microcephaly in the unborn child along with other possible neurological damages to the brain, eye (blindness) and ear (hearing loss), known as Congenital Zika Syndrome (CZS). In addition, miscarriage, premature delivery, and impaired intrauterine growth may occur.

Diagnosis and treatment: Since the recent outbreak in the LAC, ZIKV has been recognized as a possible aetiology of fever or neurological symptoms after travel. Like others diseases, diagnostic tools and management are under the responsibility of the medical doctor in charge. The decision to perform one or several ZIKV diagnostic tests (RT-PCR and/or serology) should be discussed in the routine diagnostic evaluation of all fever patients returning from a sub- or tropical country. However, due to the risk of CZS, irrespective of the clinical presentation, and due to its sexual transmission, particular attention should be given to pregnant women. Specific diagnostic guidelines take into account the exposure risk, the period of asymptomatic carriage either in the female genital tract or in the semen and the diagnostic specificity of the respective tests.

In clinical management, medication containing acetylsalicylic acid (e.g. Aspirin®) or non-steroidal anti-inflammatory drugs (such as ibuprofen) should not be used before exclusion of (concomitant) dengue infection. A specific antiviral therapy and/or a vaccination against ZIKV does not exist.

Laboratory Diagnostics of ZIKV (PCR plus serology) can be performed in:
Switzerland:

- Hôpitaux Universitaires de Genève (reference laboratory): http://www.hug-ge.ch/laboratoire-virologie
- Labor Spiez: http://www.laborspiez.ch/de/the/bs/pdf/Diagnostik_von_Zikavirus_Infektionen.pdf
- University Hospitals and some private laboratories will also offer ZIKV testing

Germany:

- Bernhard Nocht Institut: https://www.bnitm.de/aktuelles/mitteilungen/954-empfehlungen-zurdiagnostik-der-zika-virus-infektion/
- Robert Koch Institut in Berlin: https://www.rki.de/EN/Content/Institute/DepartmentsUnits/CenterBioSafety/zbs1/Zika_PCR_standard.pdf?__blob=publicationFile

Mandatory reporting: Since March 5th 2016, reporting of ZIKV infections in Switzerland is mandatory.

*members of the Swiss ECTM, Recommendations Group:
Pietro Antonini, Bernhard Beck, François Chappuis, Gilles Eperon, Hardy Etter, Jan Fehr, Blaise Genton, Christoph Hatz, Pierre Landry, Andreas Neumayr, Anita Niederer-Loher, Daniel Paris, Patricia Schlagenhauf, Cornelia Staehelin, Marcel Stoeckle, Serge de Vallière, Olivia Veit

Recommendations of the Expert Committee of Travel Medicine (ECTM) of Switzerland for evaluating CONGENITAL ZIKV infection:

After ZIKV potential exposure:

Testing for ZIKV after travelling to a ZIVK endemic region **should not be done on a routine basis** after possible ZIKV exposure*. Indeed, ZIKV infection is generally a mild and self-limited infection. Detecting and avoiding congenital ZIKV infection is the aim of these current recommendations.

WHO should be tested? Screening for ZIKV can be considered in the following situations:

- **Pregnant woman:** All pregnant (symptomatic/asymptomatic) woman with potential exposure* to ZIKV should further be assessed by specialists in gynaecology and medical specialities with experience in ZIKV testing (tropical medicine or infectious disease specialists).

HOW to test: the following investigations for ZIKV may be considered:

A: Laboratory testing:

1. **Symptomatic**** pregnant woman **AND last ZIKV exposure* < 4 weeks :**
   - RT-PCR in serum (up to 4 days) and/or in urine (up to 39 days)
   - Serological testing if > 4 days after onset of symptoms and Serum storage at first consultation
   - Manage "fever after travel return"
   - Consider others investigation including TORSCH (Toxoplasmosis, Rubella, Syphilis, CMV, HSV, VZV)
   - If ZIKV serology and RT-PCR are negative: repeat serology 4 weeks after the first test

2. **Symptomatic AND last ZIKV exposure* ≥ 4 weeks** OR **asymptomatic** pregnant woman
   a) **low risk***** : no intervention
   b) **increased risk***** :
      - Serological testing (IgM and IgG for ZIKV) at minimum 4 weeks of last exposure and serum storage
      - Consider others investigation including TORSCH (Toxoplasmosis, Rubella, Syphilis, CMV, HSV) and VZV

B. Ultrasound diagnostics (US): After **increased*** ZIKV congenital risk infection exposure*** of the pregnant woman OR **symptomatic** (< 4 weeks after exposure*) pregnant woman**, supplementary ultrasound (US) investigations should be considered to assess the risk of developing microcephaly or other neurological disorders in the unborn. In addition to the routine US evaluation performed in Switzerland, a morphological US e.g. 28 weeks of gestation and at least 4 weeks after maternal exposition is recommended. Of note:

- If pregnancy is uncertain, a pregnancy test should be performed
- Safer sex during all pregnancy is recommended in case of **increased*** ZIKV exposure***
- The sensitivity, specificity and positive predictive value of ZIKV laboratory diagnostic tests are not conclusively defined. Therefore, a negative laboratory test (ZIKV PCR and/or serology) does not exclude a ZIKV infection, but one might estimate the risk of infection in a better way by repeated tests
- Detection of ZIKV in blood, urine and amniotic fluid can be negative despite proven foetal infection

ZIKV can be detected in pregnant mothers or amniotic fluids without foetal infection

Definition of a potential ZIKV exposure:** a) history of travel/residence in a possible ZIKV transmission area (low or increased area): https://wwwnc.cdc.gov/travel/page/zika-travel-information; b) unprotected sexual contact with an exposed partner within 2 months after ZIKV symptoms or his/her return from a possible ZIKV transmission area

****Definition of symptomatic:** presence of at least one of these following symptoms: fever, conjunctivitis, arthralgia, myalgia

*****Definition of the ZIKV congenital infection risk:**

a) **low risk**= travel (including partner's) in an area with current or past reported ZIKV cases OR in an area where the vector (mosquitoes) is present;
b) **increased risk** = travel (including partner's) in an area with a ZIKV outbreak OR IgM ZIKV+ partner

Prevention for travellers:

The Expert Committee of Travel Medicine (ECTM) of Switzerland recommends the following:

- **All travellers** with potential ZIKV exposure* should be informed about the risk of the congenital infection and its sexual transmission. Counselling on safer sex practices and on contraceptive methods might be recommended. Protection against mosquito bites (indoors and outdoors) during daytime, evening and early night time hours (especially in the mid-morning and late afternoon to dusk) are recommended by using repellents (DEET), wearing long-sleeved shirts and long pants of light colours that could be impregnated or sprayed with an insecticide.

- Due to congenital complications, **pregnant woman** (regardless of pregnancy trimester) or woman who cannot rule out a pregnancy should be advised to not travel to areas with **increased**** ZIKV congenital infection risk.
  If travel cannot be avoided, special pre-travel advice is necessary including advice of strict protection against mosquito bites and pre-departure serology. A follow-up after travel is recommended (see recommendations "After ZIKV potential exposure").
  If the partner had increased** ZIKV exposure, safer sex practice is recommended during all pregnancy. A serology afterwards may also be proposed.

- **Couples and woman who are planning a pregnancy** should avoid becoming pregnant (safer sex) while travelling and, due to carriage in reproductive track, should wait at least 2 months (Baud, 2018) after symptoms onset (if symptomatic) OR (if asymptomatic) after ZIKV **increased**** risk exposure*.
  A period of at least 3 months (CDC 2018) can be considered in case of medical assisted procreation.
  In certain cases, when delaying conception is not possible (continuous travelling), a serological testing (> 4 weeks after ZIKV increased** exposure*) before conception might be proposed.

Of note:

- In case of travel to/ or stay in a ZIKV endemic area during pregnancy, woman (asymptomatic or symptomatic) should inform their gynaecologist for further potential follow up.
- Pregnant woman should discuss their sex partner's possible history of having been in areas with ZIKV transmission and history of illness consistent with ZIKV disease.

***Definition of a potential ZIKV exposure:** a) history of travel/residence in a possible ZIKV transmission area (low or increased area**): https://wwwnc.cdc.gov/travel/page/zika-travel-information; b) unprotected sexual contact with an exposed partner within 2 months after ZIKV symptoms OR his/her return from a possible ZIKV transmission area

****Definition of the ZIKV congenital infection risk:**

a) **low risk**= travel (including partner's) in an area with current or past reported ZIKV cases OR in an area where the vector (mosquitoes) is present;
b) **increased risk** = travel (including partner's) in an area with a ZIKV outbreak OR IgM ZIKV+ partner

References

Literature and Websites:

- World Health Organization (WHO/PAHO): Zika Virus Infection. http://www.who.int/csr/disease/zika/en/
- European Centre for Disease Prevention and Control (ECDC): Zika Virus infection. http://www.ecdc.europa.eu/en/healthtopics/zika_virus_infection/pages/index.aspx
- Centers for Disease Control and Prevention (CDC): Zika Virus. http://www.cdc.gov/zika/index.html
- Centers for Disease Control and Prevention (CDC): Update: Interim Guidance for Preconception Counseling and Prevention of Sexual Transmission of Zika Virus for Men with Possible Zika Virus Exposure — United States, August 2018, MMWR
- Bundesamt für Gesundheit (BAG): https://www.bag.admin.ch/bag/de/home/themen/menschgesundheit/uebertragbare-krankheiten/ausbrueche-epidemien-pandemien/aktuelle-ausbrueche-epidemien/zikavirus.html
- Robert Koch Institut (RKI): Zika Virus Infektionen: http://www.rki.de/DE/Content/InfAZ/Z/Zikaviren/Zikaviren.html
- Bernhard-Nocht-Insitut (BNT): Empfehlung zur Diagnostik bei Zika Viorus Infektion: https://www.bnitm.de/aktuelles/mitteilungen/954-empfehlungen-zur-diagnostik-der-zika-virus-infektion/
- Arsuaga M, Bujalance SG, Díaz-Menéndez M, Vázquez A, Arribas JR. Probable sexual transmission of Zika virus from a vasectomised man. Lancet Infect Dis. 2016
- Baud D, Gubler DJ, Schaub B, Lanteri MC, Musso D. An update on Zika virus infection. Lancet. 2017. https://www.ncbi.nlm.nih.gov/pubmed/28647173
- Driggers RW, Ho C, Korhonen E et al. Zika Virus Infection with Prolonged Maternal Viremia and Fetal Brain Abnormalities NEJM, 2016: http://www.nejm.org/doi/full/10.1056/NEJMoa1601824
- Honein MA, Dawson AL, Petersen EE, Jones AM, Lee EH, Yazdy MM, et al. Birth Defects Among Fetuses and Infants of US Women With Evidence of Possible Zika Virus Infection During Pregnancy. JAMA. 2017 Jan 3;317(1):59.
- Hoen B, Schaub B, Funk AL, Ardillon V, Boullard M, Cabié A, et al. Pregnancy Outcomes after ZIKV Infection in French Territories in the Americas. N Engl J Med. 2018 Mar 15;378(11):985–94.
- Pomar L, Vouga M, Lambert V, Pomar C, Hcini N, Jolivet A, et al. Maternal-fetal transmission and adverse perinatal outcomes in pregnant women infected with Zika virus: prospective cohort study in French Guiana. BMJ. 2018 Oct 31;k4431.
- Mead PS, Duggal NK, Hook SA, Delorey M, Fischer M, Olzenak McGuire D, Becksted H, Max RJ, Anishchenko M, Schwartz AM, Tzeng WP, Nelson CA, McDonald EM, Brooks JT, Brault AC, Hinckley AF. Zika Virus Shedding in Semen of Symptomatic Infected Men. N Engl J Med. 2018. https://www.ncbi.nlm.nih.gov/pubmed/29641964
- Reyes Y, Bowman N.M, Becker-Dreps S, Centeno E, Collins M.H, Liou G-J. A, Bucardo F. Prolonged shedding of Zikva Virus RNA in vaginal secretions, Nicaragua. Emerg Infect Dis. 2019; Apr 25(4):808-810

Last update: 23.04.2019