

**Question 1:**

True or False: for flaviviruses antibody-dependent enhancement (ADE) is associated with worsening of clinical symptoms only for dengue virus complex.

- True

*Explanation:*

ADE has been confirmed in vitro for several flaviviruses and non-flaviviruses. However up to now there is not clinical or epidemiological evidence that ADE plays a role in the clinical outcome of other viral diseases beyond DENV.

- False

**Question 2:**

True or False: ADE of Zika virus in vitro by pre-existing flavivirus was only confirmed after the 2015 ZIKV epidemic.

- True

- False

*Explanation:*

ADE of ZIKV induced by immune serum of at least other seven flaviviruses, including dengue was described in 1987.

**Question 3:**

True or False: there is strong evidence that Guillain-Barre syndrome and Congenital Zika Virus Syndrome are associated to previous exposure to other flaviviruses.

- True

- False

*Explanation:*

Additional lines of evidence are needed to prove that there is a direct link between a previous flavivirus exposure and specific clinical presentations following ZIKV infection.

**Question 4:**

True or False: From a previous dengue infection antibodies are mainly responsible in modulating the immune response to ZIKV.

- True

- False

*Explanation:*

While it is still unclear the contribution of DENV cross-reacting antibodies, new data indicates that DENV pre-exposure affects not only the quantity but also the quality of the cellular immune responses observed following ZIKV infection.

*Reference:*

Additional information can be found in Grifoni, a et al. DOI 10.1128/jvi.01469-17

**Question 5:**

True or False: The time between a primary DENV and a subsequent ZIKV infection is not a factor that may affect the course of ZIKV infection.

- True

- False

*Explanation:*

Still little is known about the effect of the time elapse between an heterologous flavivirus

exposure on the course of a secondary ZIKV infection. However, from the dengue experience it is plausible to anticipate that the shorter the time between the infections the more likely the DENV cross-reacting neutralising antibodies may contribute to limit ZIKV viremia.