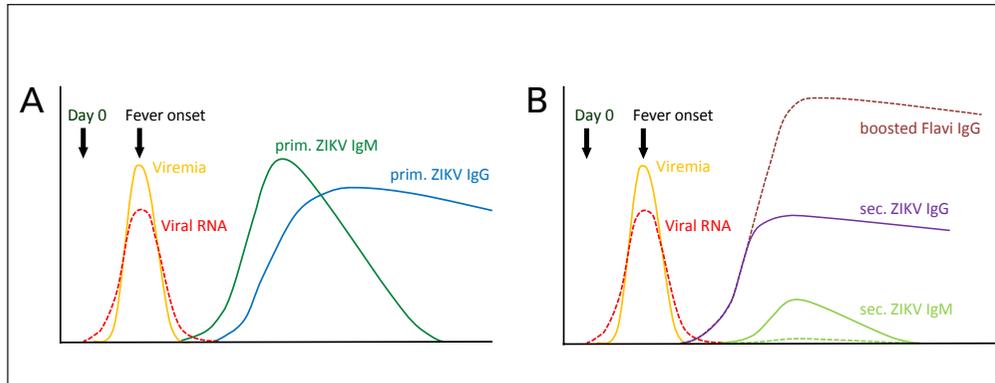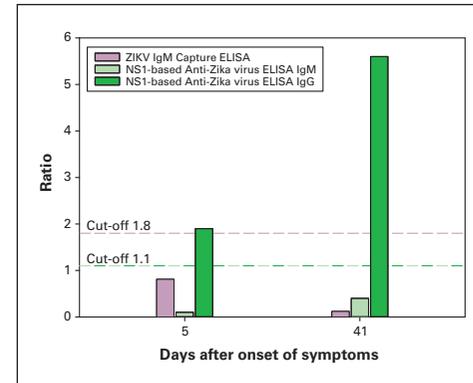# Absence of specific IgM in week six post symptom onset in a patient with confirmed Zika virus infection

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Schematic time courses of specific IgM and IgG titers in primary (A) and secondary (B) ZIKV infections

Patient's anti-ZIKV IgM and IgG titer at day 5 and 41

Days after onset of symptoms	Ratio		
	IgM Capture ELISA Cut-off: 1.8	NS1-based ELISA IgM Cut-off: 1.1	NS1-based ELISA IgG Cut-off.1.1
5	0.81	0.1	1.9
41	0.12	0.4	5.6

Introduction

Subsequently to the severe outbreak of **Zika virus (ZIKV)** infections in the Americas, CDC recommends nucleic acid testing in samples collected within two weeks after symptom onset. Serum samples collected after day 14 and up to day 84 should be tested for anti-ZIKV IgM antibodies assuming that these are present any time from near day four post symptom onset to up to twelve weeks.

However, absence of specific IgM has been frequently reported in patients with secondary **Dengue virus (DENV)** infections. Since DENV and ZIKV are related flaviviruses immunological response may be comparable in ZIKV infections.

Methods

A Colombian woman of 42 years with ZIKV infection as confirmed by RT-PCR five days after appearance of the first symptoms was additionally tested for specific IgM and IgG antibodies. Serum samples taken at day five and day 41 post symptom onset were analysed using ZIKV IgM Capture ELISA, based on the full virus antigen (cut-off ratio 1.8; InBios, USA) and NS1-based Anti-Zika virus ELISA IgM as well as IgG (cut-off ratio 1.1; Euroimmun AG, Germany) according to instructions of the manufacturer.

Results

The two serum samples revealed negative results in both IgM assays. Ratios in the IgM Capture ELISA ranged from 0.81 (day 5) to 0.12 (day 41), and measurements with the Anti-Zika virus ELISA IgM revealed ratios of 0.1 (day 5) and 0.4 (day 41). In contrast, testing for IgG yielded positive results at day 5 (ratio 1.9) as well as day 41 (ratio 5.6).

Conclusion

Both available serum samples of this patient dated from the suggested anti-ZIKV IgM-positive time frame (12 weeks) but were tested IgM-negative independently of the antigenic substrate used – full virus or NS1.

Instead, the two samples revealed an increasing IgG titer suggesting that parallel testing for anti-ZIKV IgM and IgG in two consecutive serum samples should be performed to detect either seroconversion or a significant IgG titer increase in order to avoid missing patients tested anti-ZIKV IgM-negative.