EVALUATION OF EUROIMMUN ZIKA VIRUS IGG AND IGM ELISA KITS

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OBJECTIVES

- Examine the sensitivity and specificity of Euroimmun kits
- Determine kit suitability for routine diagnostic use in Asia/Pacific region.
- Provide interpretative guidelines for reporting these results

METHODS

- Two part evaluation
  - Retrospective
  - Prospective

Retrospective Evaluation

- 310 samples were tested for IgG (100 positive for Zika) and 320 samples were tested for IgM (100 positive for Zika).
- All samples tested by Euroimmun IgG & IgM ELISA, in house IgG & IgM IFA & neutralisation using a 90% endpoint.
- All neutralisation positive samples were retested for IgM and IgG by neutralisation following removal of IgG or IgM, respectively.

Prospective Evaluation

- No attempt is made to choose samples
- Patient's are tested because clinicians request them
- On-going but already false positives have been found in both IgG and IgM
- Continuing for another 2 to 3 months

RETROSPECTIVE RESULTS

IgG Test

	Confirmed Positive	Confirmed Negative
Euroimmun positive	91	25
Euroimmun negative	9	185
Total	100	210

Sensitivity 91% Specificity 88.1%
NPV 95.4% PPV 78.5%
Negative LHR 0.10 Positive LHR 7.64

IgM test

	Confirmed Positive	Confirmed Negative
Euroimmun positive	89	17
Euroimmun negative	11	203
Total	100	220

Sensitivity 89.0% Specificity 92.3%
NPV 95.0% PPV 84.0%
Negative LHR 0.12 Positive LHR 11.52

CONCLUSIONS

- Euroimmun assays did not provide the very high levels of specificity that were reported in initial evaluations by others.
- Cross reactions were more common with IgG than IgM
- Cross reactions with dengue were the most common and cross absorption studies indicate that cross reaction between dengue and Zika goes in both directions.
- Zika virus seropositivity in this study was relatively high, at 32%
- In Australia, the expected Zika seroprevalence low, which would have an impact on the expected positive predictive value.

CONCLUSIONS

- Early infections were missed by the Euroimmun assays in some cases.
- Euroimmun kits are potentially useful as a first line test to screen out negatives particularly if two suitably timed samples are used.
- Positive IgM and/or IgG should be submitted for confirmatory testing against a panel of flaviviruses.
- False positive fourfold rises in Zika antibody titres due to cross reactions were also noted in both IgG and IgM.

CONCLUSIONS

- Zika IgM detected for 6 to 8 weeks if primary flavivirus infection but not always detected in secondary infection
- False positive IgMs were noted with non-arboviral conditions (i.e. CMV, EBV and ANA)
- IgG positive only samples it is suggested that comments include the following or similar: "These results may suggest past infection with Zika virus. Cross reaction with another flavivirus or flavivirus vaccination cannot be excluded. If further differentiation is required neutralisation testing may be necessary".

CONCLUSIONS

- IgM pos IgG neg: "These results may suggest early infection with Zika virus. We recommend submitting a second sample 21 days post onset to demonstrate IgG seroconversion to confirm the result and exclude cross reaction with another flavivirus/es. If submitting additional samples please provide full travel and clinical history as this greatly assists interpretation."

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- Questions/Concerns/Comments → linda.hueston@health.nsw.gov.au