

NZPSU Study of Possible Congenital Zika Syndrome – Protocol

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Please make a notification on the monthly NZPSU email or card of an infant or young child under your care that meets the case definition below.

An infant or child <6 months of age with

- Head circumference >2 standard deviations below the mean for gestational age and sex (equivalent to <3rd percentile), whose mother (or her partner) has spent time in a country with active Zika transmission during (or 3 months prior to) pregnancy
OR
- Any neurological abnormality requiring investigation whose mother (or her partner) has spent time in a country with active Zika transmission during (or 3 months prior to) pregnancy
OR
- Head circumference >3 standard deviations below the mean for gestational age and sex (equivalent to <0.1th percentile)

Please notify your staff involved in the primary assessment of infants of this study. We believe that they will be aware of the association between Zika and microcephaly and other neurological abnormalities, but may not be aware of Zika's presence in many parts of the Pacific and parts of South East Asia such as Thailand.

Head Circumference (HC)

- Ideally the HC should be measured at 24 hours after delivery after molding settled.
- For the purpose of this study we are asking for reports to be based on a HC >2 standard deviations below the mean (equivalent to a HC <3rd percentile) for gestational age and sex based on the charts used at each unit.
 - If HCs were normally distributed 2.3% of infants would have a HC below this. However the actual percentage is likely less than this, with one US study finding the birth prevalence of microcephaly defined in this way was 0.6%.
- Severe microcephaly is defined as a HC >3 standard deviations below the mean, which would suggest that approximately 0.1% of infants have a severe microcephaly. The actual percentage is anticipated to be less, probably in the order of 1 per 10,000.
 - Based on the Intergrowth-21st study, for male term infants of average birth weight, the HC >3 standard deviations below the mean was ≤ 30.7 cm and for female ≤ 30.3 for female term infants.
- The distribution of HC by sex, age, weight and length found in the Intergrowth-21st study can be accessed at <http://intergrowth21.ndog.ox.ac.uk/>. A link to this is on the NZPSU website (under Current Studies/Congenital Zika syndrome).

- If you are uncertain whether an infant/child meets the criteria please contact NZPSU@otago.ac.nz.

Area with active Zika transmission

- Information on the current Zika status of countries is regularly updated by the European Centres for Disease Prevention and Control (ECDC) and the US Centres for Disease Control (CDC).
- ECDC updates weekly its report on countries having had confirmed indigenous vector-borne Zika virus in the previous nine months.
(http://ecdc.europa.eu/en/healthtopics/zika_virus_infection/zika-outbreak/Pages/Zika-transmission-past-9-months.aspx)
 - In July 2016, as well as most countries in South and Central America, this was reported by many in the Pacific Region, including Samoa, Tonga, Fiji, Marshall Islands, Papua New Guinea, New Caledonia, American Samoa, the Federated States of Micronesia meet this criterion, and also in SouthEast Asia (including Thailand, Indonesia, the Philippines and Viet Nam).
- The NZPSU website (under Current Studies/Congenital Zika syndrome) include a link the ECDC website.

“Any neurological abnormality”

- The NZPSU has included “Any neurological abnormality” significant enough to require investigation whose mother (or her partner) spent time during pregnancy in a Zika area.
- This generic term has been included in the case definition as the full range of significant manifestations of CZS is still evolving. In general, we are interested in obtaining reports of structural CNS abnormalities.
 - In a prospective study of pregnant women with Zika in pregnancy a range of abnormalities, including choroid plexus cysts, cerebellar atrophy, cerebellar and cerebral periventricular calcifications etc, were found, and a number of ophthalmologic abnormalities. As some of the pregnancies were ongoing when the study was published the proportion that would result in microcephaly was not known.
- If you are uncertain whether an infant/child meets the criteria for any neurological abnormality please contact NZPSU@otago.ac.nz.

Questionnaire

- Follow receipt of a notification to the NZPSU through the monthly mail-out, information will be sent on how to access a web-based questionnaire.
 - A pdf will be made available for those who prefer, but we believe it is much easier to complete online.
 - There is the option of stopping the questionnaire at the end of any section and resuming later, and if you choose this you will be given a code that will be needed to resume.
- The questions are designed to capture basic information on the microcephaly or other neurological abnormalities, travel to a Zika area by the mother or her

partner, symptoms of Zika in the mother, and investigations on the infant/child and the mother that might confirm or refute Zika infection.

- Information on laboratory testing in the infants/children are given in *Interim Guidelines for the Evaluation and Testing of Infants with Possible Congenital Zika Virus Infection — United States, 2016* published by the US CDC and available at http://www.cdc.gov/mmwr/volumes/65/wr/mm6507e1.htm?s_cid=mm6507e1_w.htm .
- There is discussion on investigations available to confirm Zika infection in adults in New Zealand in an editorial *Zika virus threat* by Lance Jennings and John Mackenzie published in the NZMJ in April 2016. The authors recommend consultation with a microbiologist or infectious diseases specialist to advise on choice and interpretation of laboratory tests.
- While the questionnaire is primarily to confirm or refute Zika infection as a cause of microcephaly or other neurological abnormalities, a few questions will be asked that might suggest an alternative aetiology.
- Depending on the findings a decision will be made on the need for a follow up questionnaire.

Dissemination

The findings will be discussed with the Ministry of Health as they are received, and the findings of the first 6 months disseminated to the participating paediatricians.

Further Information

Please contact NZPSU@otago.ac.nz if you have comments, or require clarification or information.