

Microcephaly in children aged < 12 months

BACKGROUND

Microcephaly is defined as an Occipito-Frontal head Circumference (OFC) more than 2 standard deviations (SD) below the mean for age and gender⁽¹⁾. All newborns should have their OFC measured and plotted, and it should be adjusted for gestational age and gender⁽²⁾. Microcephaly is often associated with signs and symptoms of neurological impairment including seizures and abnormal tone and reflexes. It may also be associated with developmental delay, intellectual impairment, problems with hearing, vision and feeding⁽³⁾.

There are many causes of microcephaly, including: (i) congenital infections: most commonly cytomegalovirus, toxoplasmosis, or rubella, but also Zika virus and rarely herpes simplex virus, syphilis, varicella zoster virus and very rarely HIV (ii) exposure to teratogens in pregnancy (e.g. alcohol, drugs and other toxins) (iii) maternal phenylketonuria (iv) poorly controlled maternal diabetes; (v) severe CNS trauma, ischaemic or haemorrhagic stroke (vi) severe deprivation including malnutrition, and placental insufficiency (vii) chromosomal syndromes (viii) single gene defects (ix) neural tube defects⁽⁴⁾. Microcephaly may occur in isolation or in association with other major or minor birth defects or syndromes⁽³⁾.

Microcephaly is of current interest due to the proven relationship between maternal Zika virus infection during pregnancy⁽⁵⁾ and microcephaly and other abnormalities in newborn infants, with a twenty-fold increase in birth prevalence of microcephaly reported over 5 years from 2010 to 2015 in Northern Brazil⁽⁶⁾. Zika virus is a mosquito borne flavivirus, and can also be transmitted sexually or through blood products from an infected donor, but this is rare. Symptoms are usually mild (fever, fine rash, myalgia, conjunctivitis, arthralgia), and present in only 25% of those infected. The Aedes mosquito which transmits Zika virus is currently only found in Northern Queensland, where local transmission has not been reported but is possible. To consider a diagnosis of Zika associated microcephaly outside Northern Queensland a confirmed history of travel during or 3 months prior to pregnancy to areas with ongoing Zika transmission, for the mother or her sexual partner is required.

Microcephaly is rare in the developed world. The birth prevalence in the USA is reported as 1.1 to 1.6 per 10,000 live births⁽⁶⁾. In Australia, prevalence estimates range from 1.7/10,000 live births to 5.0/10,000 total births (including stillbirths) according to reports from birth defects registers in different state jurisdictions⁽⁷⁻⁹⁾. The wide variation in reported rates may be due to different methods of ascertainment and case definitions for microcephaly with some studies using a cut-off of more than 3 SD below the mean⁽¹⁰⁾.

The APSU study will be the first Australian study to prospectively document cases of microcephaly in infants less than 12 months of age who are seen by paediatricians. This will provide important data on baseline birth and infancy prevalence of microcephaly to enable detection of outbreaks of infectious causes and to inform the timely introduction of public health interventions.

STUDY OBJECTIVES

1. To describe the epidemiology of microcephaly in children aged <12 months presenting to paediatricians.
2. To describe all causes of microcephaly in Australia.
3. To document the infective causes of microcephaly (e.g. congenital Cytomegalovirus infection, congenital rubella, toxoplasmosis, maternal Zika virus infection, etc.) and to describe how infection was acquired.
4. To educate Australian paediatricians about the possible causes of microcephaly including maternal Zika virus infection in women with appropriate travel history of exposure and to disseminate best practice guidelines as these become available or are updated.

CASE DEFINITION

Please report any child < 12 months of age with microcephaly when the OFC is more than **two standard deviations (<3rd percentile) below the mean** for age and gender according to standard growth *charts, presenting to you in the last month and whom you have not previously reported.

*The WHO recommends the Intergrowth Charts (<https://intergrowth21.tghn.org/>)⁽²⁾ which allow for adjustment for gestational age and are based on a wide range of ethnicities. The Intergrowth calculator can be found at <http://intergrowth21.ndog.ox.ac.uk/en/ManualEntry>

NB: It is advised that all children have OFC measured at birth and as part of routine health checks.

Useful resources

If Zika virus is suspected as a potential cause of microcephaly, we recommend that specialist advice from an infectious diseases or public health expert should be obtained before ordering tests on newborn infants for Zika virus.

Australian Government Department of Health: Information for health Professionals - Zika
(<http://www.health.gov.au/internet/main/publishing.nsf/Content/ohp-zika-health-professionals>)

Royal Australian and New Zealand College of Obstetrics and Gynaecology (RANZCOG)
(http://www.ranzcog.edu.au/images/Care_of_women_with_confirmed_zika_virus_infection_during_pregnancy_in_Australia.pdf)

We will circulate via direct email and via the APSU website (www.apsu.org.au) any updates to the above guidelines or release of new guidelines that are relevant to paediatricians.

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10. WHO. Microcephaly Fact Sheet Geneva: WHO; 2016 [cited 2016 March]. Available from: <http://www.who.int/mediacentre/factsheets/microcephaly/en/>.

OTHER USEFUL RESOURCES

- **Centers for Disease Control and Prevention. Interim Guidelines for the Evaluation and Testing of Infants with Possible Congenital Zika Virus Infection – United States.**
(http://www.cdc.gov/mmwr/volumes/65/wr/mm6503e3.htm#F1_down)
- **Zika Virus Disease: A CDC Update for Pediatric Health Care Providers.**
(Karwowski MP, Nelson JM, Staples JE, Fischer M, Fleming-Dutra KE, Villanueva J, et al. Zika Virus Disease: A CDC Update for Pediatric Health Care Providers. Pediatrics. 2016;137(5))
- **Assessment of infants with microcephaly in the context of zika virus.**
(http://apps.who.int/iris/bitstream/10665/204475/1/WHO_ZIKV_MOC_16.3_eng.pdf?ua=1)
- **Practice Pointer: Zika virus – management of infection and risk.**
(<http://www.bmj.com/content/352/bmj.i1062>)
- **Zika: A clinical guide.**
(<http://sandpit.bmj.com/graphics/2016/zika/index.html>)
- **Early Years Learning Framework Practice Based Resources - Developmental Milestones.**
(https://www.dss.gov.au/sites/default/files/documents/05_2015/developmental-milestones.pdf)