

Measuring head circumference

Update on infant microcephaly

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Abstract

Objective To provide an evidence-based update emphasizing the importance of measuring head circumference (HC) in infants, with a focus on microcephaly.

Quality of evidence PubMed and EMBASE (OvidSP) were searched. Search terms used were *head circumference* and *infants* and *measurement*; *microcephaly* and *infants* and *measurement*; *idiopathic microcephaly* and *infants*; and *congenital microcephaly* and *infants*. Most of the references for this review were published in 2000 or later. Most evidence is level II.

Main message Serial measurement of HC should be incorporated into routine well-child care. Measure the distance around the back of the child's head with a nonelastic tape measure held above the eyebrows and ears, and plot the measurement on an age- and sex-appropriate growth chart. Microcephaly is HC more than 2 SD below the mean. The most common disability associated with microcephaly is intellectual delay; other common concomitant conditions include epilepsy, cerebral palsy, language delay, strabismus, ophthalmologic disorders, and cardiac, renal, urinary tract, and skeletal anomalies. An interdisciplinary approach to microcephaly is warranted. Although there are no specific interventions to enhance brain growth, dietary or surgical interventions might be helpful in some cases. Infants with microcephaly who show developmental delays might benefit from early intervention programs or developmental physical and occupational therapy.

Conclusion Early identification of HC concerns by family physicians can be a critical first step in identifying disorders such as microcephaly, leading to referral to pediatric specialists and, as needed, provision of family-centred early intervention services.

Mesurer la circonférence crânienne

Mise à jour sur la microcéphalie chez le nourrisson

Résumé

Objectif Présenter une mise à jour fondée sur des données probantes mettant en évidence l'importance de mesurer la circonférence crânienne chez les nourrissons, en particulier pour détecter une microcéphalie.

EDITOR'S KEY POINTS

- Measuring head circumference (HC) in infants is a quick, simple, noninvasive, and reliable procedure for determining underlying brain size. After plotting the measurement on sex- and age-appropriate charts, family physicians can determine if HC is within normal limits, too large (megacephaly), or too small (microcephaly).
- Microcephaly is HC that is more than 2 SD below the mean based on normative growth charts. It is frequently associated with developmental delay. Serial HC measurements during well-child visits are critical to screening young children for possible cognitive or motor delays.
- Family-centred early intervention services might be appropriate for infants or young children with microcephaly.

POINTS DE REPÈRE DU RÉDACTEUR

- La mesure de la circonférence crânienne chez les nourrissons est une procédure rapide, simple, non invasive et fiable pour déterminer la taille du cerveau sous-jacent. Après avoir inscrit la mesure sur un graphique de croissance approprié en fonction du sexe et de l'âge, les médecins de famille peuvent observer si la mesure du crâne se situe dans les limites normales ou si elle est trop grande (mégacéphalie) ou trop petite (microcéphalie).
- La microcéphalie désigne une taille de 2 écarts-types inférieure à la moyenne selon les fiches de croissance normales. Elle est fréquemment associée à un retard développemental. La mesure répétée à chaque visite lors des cliniques du bien-être de l'enfant est essentielle pour dépister chez les enfants des retards cognitifs ou moteurs éventuels.
- Il pourrait être approprié d'offrir des services d'intervention axés sur la famille pour les nourrissons ou les jeunes enfants ayant une microcéphalie.

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Qualité des données Une recherche documentaire a été effectuée dans PubMed et EMBASE (OvidSP) à l'aide des expressions en anglais suivantes : *head circumference* et *infants* et *measurement; microcephaly* et *infants* et *measurement; idiopathic microcephaly* et *infants*; et *congenital microcephaly* et *infants*. La plupart des références tirées de cette recension ont été publiées en 2000 ou après. Les données probantes sont en majorité de niveau II.

Message principal Il y a lieu de réitérer systématiquement la mesure de la circonférence crânienne lors des visites en clinique du bien-être de l'enfant. Il s'agit de mesurer la circonférence de la tête de l'enfant avec un ruban à mesurer non élastique tenu au-dessus des sourcils et des oreilles, et d'inscrire la valeur sur un graphique de croissance approprié, selon l'âge et le sexe. La microcéphalie se définit par une mesure de 2 écarts-types inférieurs à la moyenne. L'incapacité la plus fréquente associée à la microcéphalie est un retard intellectuel; parmi les autres problèmes concomitants courants se trouvent l'épilepsie, la paralysie cérébrale, un retard de l'élocution, le strabisme, des troubles ophtalmologiques, de même que des anomalies cardiaques, rénales, des voies urinaires et squelettiques. La microcéphalie justifie l'adoption d'une approche interdisciplinaire. Même s'il n'y a pas d'interventions particulières pour améliorer la croissance cérébrale, des interventions alimentaires ou chirurgicales pourraient être utiles dans certains cas. Les nourrissons qui ont une microcéphalie et accusent des retards développementaux pourraient bénéficier de programmes d'intervention ou de thérapies du développement physique et d'ergothérapie administrés très tôt.

Conclusion L'observation précoce d'anomalies dans la circonférence crânienne par les médecins de famille peut se révéler une première étape critique dans le dépistage de troubles comme la microcéphalie, qui mènera à une demande de consultation en pédiatrie et, au besoin, à la prestation sans délais de services d'intervention axés sur la famille.

Measuring head circumference (HC) is a quick, noninvasive method of determining if infant head size is too large (megacephaly) or too small (microcephaly).¹ When compared with normative growth curves, serial HC measurements are extremely important in monitoring infant health. The procedure has been described as "the most simple, inexpensive and quick available [tool] to assess the development of the central nervous system and identify neonates at risk of neurodevelopmental disorders."² Although HC is often measured in infants at risk (eg, preterm or low-birth-weight infants, or those with known genetic disorders) few clinicians

include serial HC measurements within routine well-baby checkups¹ or as part of regular care for infants and children admitted to hospital for reasons other than growth concerns (ie, opportunistic growth measurements).³

The objective of this review is to provide an evidence-based update emphasizing the importance of measuring HC in infants, with a focus on microcephaly.

Quality of evidence

To locate evidence, PubMed and EMBASE (OvidSP) were searched. Search terms used were *head circumference* and *infants* and *measurement; microcephaly* and *infants* and *measurement; idiopathic microcephaly* and *infants*; and *congenital microcephaly* and *infants*. Most of the references for this review were published in 2000 or later. Levels of evidence are described in **Table 1** and are indicated throughout the article. Most evidence was level II.

Table 1. Levels of evidence

LEVEL	DEFINITION
I	At least 1 properly conducted randomized controlled trial, systematic review, or meta-analysis
II	Other comparison trials, non-randomized, cohort, case-control, or epidemiologic studies, and preferably more than 1 study
III	Expert opinion or consensus statements

Main message

Definition of microcephaly. The most common definition of microcephaly is "HC that is >2 standard deviations (SD) below the mean compared to age- and gender-matched population-based samples,"⁴ a definition supported by child neurologists,⁵ developmental pediatricians,⁶ pediatric endocrinologists, and geneticists.⁶ The term *severe microcephaly* is used for HC more than 3 SD below the mean.⁶ Although HC measures skull size, it typically also reflects overall brain volume^{7,8} and has been described as a "widely used proxy of neural growth and brain size."⁹ Brain size outside of normal values is an important risk factor for cognitive and motor delay.^{6,10} Microcephaly at birth has been termed *primary microcephaly* and that acquired after birth is *secondary microcephaly*.⁶

Measurement and plotting of HC. Measuring occipital-frontal HC is quick and easy, involving a nonelastic tape measure and 1 to 2 minutes of a clinician's time to measure (at least twice) and plot the measurement on the appropriate growth chart.⁶ According to MedlinePlus of the US National Library of Medicine, HC is a measure of the largest area of a child's head or the distance around the back of the head with the tape measure held above the eyebrows and ears.¹¹ In a recent reliability study of 57 adults from the lay public and 25 mothers of typically

developing children, all were provided with a measuring tape and written instructions, including a diagram, on how to measure either their own HC or that of their children.⁹ High rates of interrater reliability were reported for the lay assessors' measurements relative to HC measurements taken by 2 trained researchers; the 95% CIs for the intraclass correlation coefficients were not statistically different between the lay groups and the researchers,⁹ thus supporting the simplicity and accuracy of HC measurements. Even in infants with positional plagiocephaly or brachycephaly, standardized HC measurements have been shown to be highly reproducible.¹²

The HC measurement should then be plotted on an age- and sex-appropriate growth chart (**Box 1**)^{8,13-15} to determine its percentile. If HC is more than 2 SD below the mean (third centile) and similar to height and weight, it is defined as *proportional microcephaly*; if length and weight are well above the third centile but HC is at or below, then the term *disproportionate microcephaly* is used.⁶

In a population-based, longitudinal study involving 633 full-term children (level II evidence), Gale and colleagues examined the influence of head growth from birth to ages 1, 4, and 8 years on IQ at 4 and 8 years.¹⁶ Although only HC at birth (prenatal growth) and head growth at 1 year were related to later IQ in the study by Gale and colleagues,¹⁶ authors of a more recent retrospective study (level II evidence) of 680 children with microcephaly recommended that HC should be measured at birth and repeatedly throughout infancy and early childhood.⁶ This recommendation is supported by the American Academy of Pediatrics.¹⁷

In addition to measuring and plotting the child's HC, the initial evaluation should include the child's medical and developmental history, HC measurements for the parents, and a complete physical examination.¹⁸ One conundrum in plotting HC is which growth chart to use (**Box 1**).^{8,13-15} The World Health Organization (WHO) charts¹⁴ were recommended for use in Canada by the Dietitians of Canada, the Canadian Paediatric Society, the College of Family Physicians of Canada, and

Community Health Nurses of Canada.¹⁵ However, the WHO charts have been criticized for under-referring children at 1 year of age because the new second centile is approximately 2 cm smaller than before.¹⁹ As Baxter commented on this discrepancy:

At that age a head circumference that was on the 2nd centile on the old charts would now be between the 25th and 50th centile on the new charts, or a child following the new 2nd centile would be demonstrating a marked acquired, or postnatal, microcephaly on the old charts.¹⁹

The authors of the most recent and largest study of children with microcephaly,⁶ conducted in Germany, recommended the growth charts from the US Centers for Disease Control and Prevention¹³ rather than the WHO charts because the mean occipital-frontal circumference for children in industrialized countries is larger than the standard values provided by WHO. For Canadian infants born preterm (23-37 weeks' gestation), HC reference curves were recently published⁸ by the Canadian Neonatal Network (**Box 1**).^{8,13-15}

Causes of microcephaly. Causes of microcephaly include genetic syndromes, environmental teratogens, or structural brain anomalies. Both primary and secondary microcephaly can result from chromosomal abnormalities (eg, trisomy 13, 18, or 21), specific gene defects, intrauterine infections or teratogens, craniosynostosis, or diseases in the mother⁶; secondary microcephaly can also arise from perinatal or postnatal brain damage.⁶ According to an evidence-based review on evaluation of children with microcephaly, hundreds of different syndromes include microcephaly among their characteristics.¹⁸

In a retrospective review of 51 children with secondary (acquired) microcephaly ages 0.7 to 11.3 years (level II evidence), Baxter and colleagues classified the various causes into 5 categories: idiopathic, familial, syndromic, symptomatic, or mixed (at least 2 of the foregoing causes).²⁰

In their retrospective study of 680 children with microcephaly (level II evidence), von der Hagen et al reported that only 403 of the children (59.3%) received a presumed diagnosis of cause, as shown in the following categories: genetic or presumably genetic (28.5%), perinatal brain injury (26.8%), postnatal brain injury (1.9%), and craniosynostosis (2.1%); cause was unclear for the remaining 277 (40.7%).⁶ Among children for whom primary or secondary microcephaly could be differentiated (n=287), 38% of cases were deemed primary and 62% were deemed secondary.⁶

Disabilities and outcomes. Children with microcephaly often present with concurrent disabilities. Because

Box 1. Sources for growth charts that include head circumference measurement

- Canadian Neonatal Network⁸: <http://pediatrics.aappublications.org/content/131/4/e1158.long>
- US Centers for Disease Control and Prevention¹³: www.cdc.gov/growthcharts
- World Health Organization¹⁴: www.who.int/childgrowth/standards/hc_for_age/en
- World Health Organization growth charts, Canadian Paediatric Society¹⁵: www.cps.ca/tools-outils/who-growth-charts

head size tends to represent brain volume, the most common associated disability is intellectual delay. In their retrospective study (level II evidence), von der Hagen et al reported that 65% of the children had been diagnosed with intellectual disability or neurodevelopmental delay.⁶ In a sample of 1393 children with developmental disabilities identified through chart review at an Israeli child developmental centre (level II evidence), Watemberg and colleagues found that 15.4% of the sample had microcephaly and, of those, 53.7% had intellectual delays ranging from borderline intelligence to severe mental retardation.¹⁰

Of 51 children with secondary (acquired) microcephaly identified in a retrospective chart review (level II evidence), Baxter and colleagues reported developmental quotient (DQ) or IQ scores for 34 children at a mean age of 4.5 years.²⁰ The median DQ or IQ was 63 for this subsample, with the idiopathic group having the highest median score (83) and the syndromic group having the lowest (45).²⁰ Although these results confirm that microcephaly predicts developmental delay overall, the authors found no significant correlation between DQ or IQ and concurrent HC z scores.²⁰

In a retrospective chart review of 312 high-risk survivors who had been cared for in a level 3 neonatal intensive care unit in Montreal (level II evidence), 38 (12.2%) were found to have microcephaly at 2 years of age and were also identified as developmentally delayed.⁷ However, the degree of microcephaly did not correlate significantly with the degree of developmental delay.⁷

In a retrospective review of 57 children with secondary microcephaly followed for an average of 4.2 years at 2 Boston medical centres (level II evidence), Rosman et al sought to determine whether growth parameters could predict developmental outcome.²¹ More than 40% of the sample (n=24) had idiopathic microcephaly. Head circumference, body weight, and height were each significant predictors of DQ ($P<.001$). Developmental quotient was also significantly correlated ($P<.05$) with final growth measurements, but the relationship between HC and DQ was the weakest of the 3 ($r=0.13$), possibly owing to the fact that 13 of the children (23% of the sample) had DQs that were within normal limits despite being microcephalic.²¹

Finnish researchers conducted a prospective, longitudinal study of 1056 healthy children born at term (level II evidence).²² Measures of weight, length, and HC were collected at 5, 20, and 56 months of age and compared with scores on cognitive tests at 56 months. For each SD below the mean in HC at birth, the children showed cognitive scores that were 1.31 points lower, thus supporting a relationship between putative congenital brain size and later development even in those without frank microcephaly.²²

In summary, there is a clear predictive relationship between HC at birth and developmental outcomes on

standardized tests, but the absolute correlation between the 2 is relatively weak and sometimes non-significant (a finding which could relate to the small sample sizes in most of the studies).

Another common clinical finding in children with microcephaly is epilepsy. Of the 215 children with microcephaly in the Israeli study, 28.3% also had epilepsy; other associated diagnoses included cerebral palsy (21.4%), language delay (33%), and strabismus (22.3%).¹⁰ In the most recent and largest study of children with microcephaly in Germany, 43% presented with epilepsy. Other comorbidities included ophthalmologic disorders (30%), cardiac anomalies (14%), and renal, urinary tract, and skeletal anomalies (13% to 14% each), leading the study authors to emphasize the need for an interdisciplinary approach to microcephaly.⁶

Interventions for children with microcephaly. Although there are no specific interventions to enhance brain growth, secondary microcephaly can be prevented in some conditions, eg, through dietary interventions in infants with phenylketonuria at birth²³ or through surgical release of sutures for craniosynostosis in infants before 1 year of age.²⁴ For infants born with microcephaly due to inadequate maternal nutrition, enhanced postnatal nutrition has been postulated to account for increased HC.²⁵ Infants with microcephaly who show developmental delays might benefit from early intervention programs or developmental physical and occupational therapy. Such programs, as well as interdisciplinary management by various medical specialists, have been recommended for children with conditions that often include microcephaly (eg, congenital cytomegalovirus infection,²⁶ autism spectrum disorder,²⁷ de Lange syndrome²⁸). Although not specific to infants and young children with microcephaly, a systematic review (level I evidence) of the effects of early intervention showed that specific developmental motor training programs positively influenced infant motor development.²⁹ In a pretest-posttest study of early language intervention for 455 children from birth to 3 years of age with suspected speech or language delay (level II evidence), the 6-month intervention resulted in statistically significant ($P<.001$) improvements in language quotient; about 20% of these children had microcephaly.³⁰

Conclusion

As Holden stated recently in an invited commentary about the largest microcephaly study published to date,⁶ “the time has arrived for the measurement of head circumference to receive the same status and acceptance as obtaining height and weight measurements during routine well-child evaluations.”¹ Family physicians could play a critical role in conducting serial HC measurements for children in their practices. Also, repeated HC

measurements should be incorporated into the Canadian Task Force on Preventive Health Care's upcoming guideline on screening and treatment for developmental delay in early childhood.³¹

Although questions remain about which growth chart to use in measuring and plotting HC, the importance of conducting this measurement cannot be overstated. Both atypically large and atypically small head sizes place infants and young children at risk of a host of different developmental disorders. Early identification of HC concerns by family physicians or community health nurses can provide a critical first step in identifying such disorders, leading to referrals to pediatric specialist physicians and, as needed, provision of family-centred early intervention services.

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Competing interests
None declared

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