

Head Size: is it important?



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The assessment of growth in general and more particularly the measurement of the head circumference is an integral part of the Paediatric Neurological Examination. Very important clues can be revealed from the head size and shape which will guide the differential diagnosis and the need for further investigations. The head grows through to adulthood as is demonstrated in the head circumference charts (Figure 1 overleaf). It is also known from forensic studies that the timing of complete suture closure depends on the site of suture, the sex and the ethnic group, and the process continues till the age of 50.¹

Head size and cranial volume

In early infancy the skull bones are not fused together to allow for brain growth. The head grows rapidly antenatally and in the first three months. The rate of increase in head circumference is 3cm per month. The anterior fontanelle closes between 9-18 months. Between 4-6 years of age the head circumference increases by one cm per year.

The skull is filled with three compartments: brain, cerebrospinal fluid and blood. Expansion of one compartment is at the expense of another. The thickness of the skull bones also plays an important role in head size.

Head circumference (HC) is used as a surrogate measurement of brain size and brain growth

but it is only imperfectly correlated with brain volume. The head circumference is determined by measuring the greatest occipitofrontal circumference (from the occipital prominence to the frontal prominence – taking the biggest measurement of three). The accuracy of the measurement is influenced by the presence of fluid beneath the scalp i.e. oedema, blood, cephalohaematoma, and by the head shape. A round head has larger volume than an oval shaped head and a head with a relatively larger occipitofrontal circumference has a larger volume than a head with a relatively large biparietal diameter. Obviously measurements over time are more informative and should be plotted to the appropriate chart for sex and conceptional age.

Macrocephaly

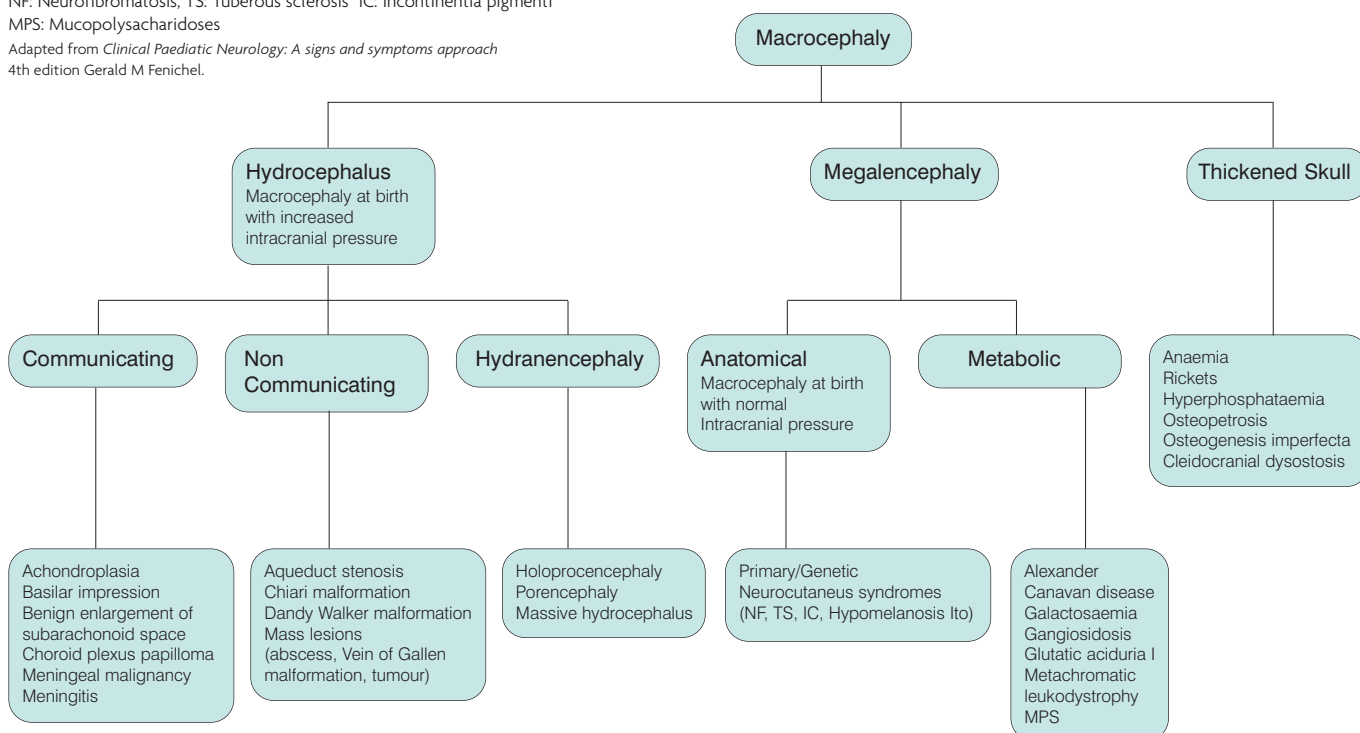
Macrocephaly denotes a large head which is larger than two standard deviations from the normal distribution. That means that 2% of the normal population is macrocephalic, often with a familial tendency. It is therefore essential to measure the HC of the parents before considering further investigations.

Causes of macrocephaly – Table 1

Macrocephaly can be due to hydrocephalus (increased CSF fluid), megalencephaly (enlarge-

Table 1: Causes of macrocephaly

NF: Neurofibromatosis, TS: Tuberosus sclerosis IC: Incontinentia pigmenti
MPS: Mucopolysaccharidoses
Adapted from *Clinical Paediatric Neurology: A signs and symptoms approach*
4th edition Gerald M Fenichel.



ment of the brain) or thickening of the skull.

Investigations for macrocephaly – Table 2
Start with a thorough history and examination. Previous measurements of the head circumference, the rate of growth and full developmental history are critical. Initial neuroimaging (preferably MRI) will guide the clinician for further investigations and management. If the cause is hydrocephalus referral to neurosurgery will be necessary. If other causes are suspected then a basic metabolic screening along with baseline biochemistry tests and possible referral to a clinical geneticist will be

Table 2: Investigations of Macrocephaly

- History
- Examination including auscultation of the skull for bruit
- Development
- Rate of head growth – serial measurements
- CT head/MRI head preferably
- FBC
- Urea/electrolytes
- Bone profile
- Thyroid function test
- Plasma amino acids
- Urine amino acids and organic acids, glycosaminoglycans

required.

Specific causes of macrocephaly

The Dandy Walker malformation consists of a triad of partial or complete agenesis of the cerebellar vermis, cystic dilatation of the posterior fossa communicating with the fourth ventricle, and hydrocephalus. The hydrocephalus may not be present at birth but develops later. In two thirds of cases other malformations are found, the commonest of which is agenesis of the corpus callosum. The presentation is with macrocephaly, occipital bulging and symptoms of posterior fossa compression such as apnoea, nystagmus, ataxia and brisk leg reflexes. MRI brain scan is the investigation of choice. The management is neurosurgical with decompression of the cyst and a ventriculoperitoneal (VP) shunt of the lateral ventricle and the posterior fossa cyst.

Benign enlargement of the subarachnoid space (also called external hydrocephalus, extra ventricular hydrocephalus and benign subdural effusions). This is a self limited disorder of unknown aetiology. A genetic cause is likely but not as yet identified. It is more common in males and a large head is the only feature. The anterior fontanelle is large but soft. Neurological examination, development and cognition are normal. Neuroimaging reveals an enlarged subarachnoid space, widening of the sylvian fissure and normal ventricular size. The latter distinguishes the condition from cerebral atrophy. These infants do not require any intervention or repeat scans after the diagnosis is established. They are reviewed clinically with monitoring of the

Table 3: Causes of microcephaly HIE: hypoxic ischaemic encephalopathy

Adapted from *Clinical Paediatric Neurology: A signs and symptoms approach* 4th edition Gerald M Fenichel.

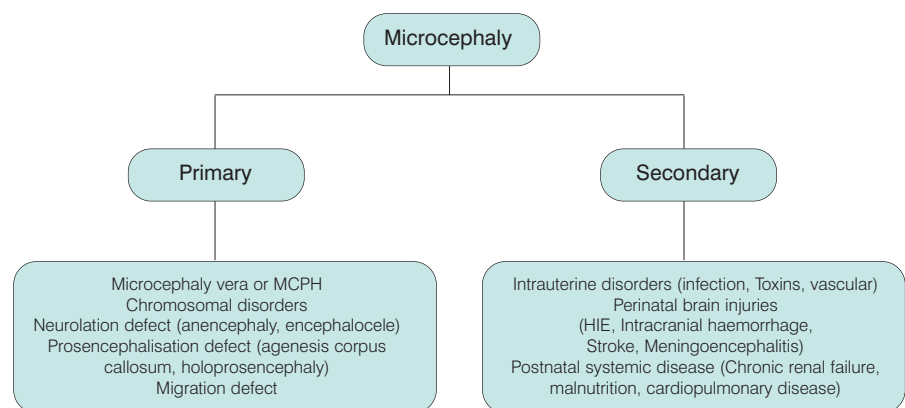
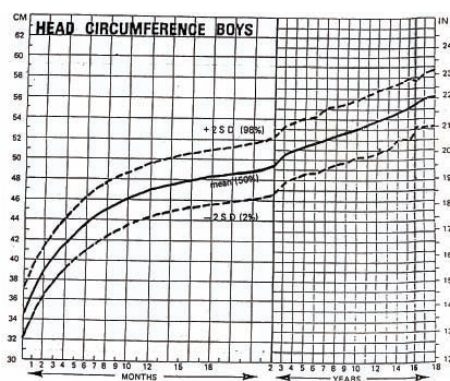


Figure 1



head circumference which should follow the 98th centile.

Microcephaly

Microcephaly means small head – less than 2SD below the mean for age and sex. It is important to note that there are also differences between different ethnic groups and that needs to be taken into account before a diagnosis is made. For example, in a study in Leicester it was found that Asian newborns had smaller head circumference than their Caucasian counterparts.⁷

It is important to investigate cases of microcephaly appropriately and identify the cause, as small head implies a small brain, reflecting poor brain growth. Most full term microcephalic infants represent the extreme end of the normal range. Those with normal neonatal neurological examination will be expected to have normal intelligence at the age of seven. A HC <3 SD at birth usually indicates later mental retardation and learning difficulties.

The causes of microcephaly (Table 3) can be divided into primary and secondary. Primary microcephaly includes conditions in which the brain is small having never formed properly due to genetic or chromosomal abnormalities. The head circumference is small from birth onwards with the exception of some chromosomal abnormalities in which the HC may be normal at birth.

In secondary microcephaly the growth of a normal forming brain is impaired by an

acquired disease process. In these conditions the HC may be normal at birth but the head fails to grow thereafter. Due to the lack of brain growth the force keeping the cranial bones separated does not exist and there may be early closure of the sutures or even overlapping of the skull bones. In these cases the skull shape is normal and the intracranial pressure is not increased. These features distinguish primary microcephaly from craniosynostosis.

Investigation of microcephaly

- History (perinatal – family history)
- Examination – dysmorphic features – malformations
- Development
- Growth – serial measurements of HC
- MRI brain
- Baseline biochemistry, metabolic screen
- Genetic testing – karyotype, molecular genetics
- TORCH screen
- Ophthalmology

MRI brain scan is very informative in distinguishing primary from secondary microcephaly. In the majority of cases the scan would be either normal or abnormal with developmental cerebral malformations (migration, prosencephalisation or neurolation defects). In secondary microcephaly cases there will be evidence of brain atrophy, porencephaly and ventricular enlargement. If primary causes are suspected a referral to the clinical geneticist is required to identify potential chromosomal or genetic abnormalities. Congenital infection screening and basic biochemical and metabolic investigation may be required.

Autosomal recessive primary microcephaly (MCPH)¹

MCPH is a neurodevelopmental disorder with three defining clinical features:

- Congenital microcephaly at least 4 SD below mean for age and sex
- Mental retardation which is non progressive and no other neurological findings such as spasticity or seizures are seen. Even though seizures are very rare their presence does not exclude the diagnosis, and
- Normal height, weight, appearance and

The head size, the growth rate and the shape of the head are important pointers towards benign or more sinister medical conditions

results on chromosome analysis and brain scan.

MCPH is a disorder of foetal brain growth with the cerebral cortex showing the greatest reduction in volume. All data suggest that MCPH is a primary disorder of neurogenic mitosis and not of neuronal migration. All four known genes are expressed in the neuroepithelium and the phenotypic features and brain scans suggest that the MCPH patient has a small brain that functions normally for its size. Patients with a MCPH1 gene mutation may have reduction in height or may have periventricular heterotopias pointing to a more specific phenotypic – genotypic correlation.

There are at least seven MCPH loci and four genes have been identified: MCPH 1 encoding Microcephalin, MCPH encoding CDK5RAP2 (Cyclin Dependent Kinase 5 Regulatory Associated Protein 2) MCPH 5 encoding ASPM (Abnormal Spindle-like Microcephaly Associated) and MVPH 6 encoding CENPJ (Centromere Associated Protein)

From antenatal scans we know that head size is normal up to week 20 whereas a decreased HC is seen by week 32. At birth the HC is 4-12 SD below mean without variations after that. The cerebral cortical gyral pattern is simplified with slight reduction of white matter volume but the architecture of the CNS is normal without evidence of a neuronal migration defect.

Interestingly, patients with MCPH have mild to moderate mental retardation and the early milestones are achieved at expected times. Later motor and social milestones are mildly delayed with speech development consistently delayed. They have good fine motor skills and balance as young adults and they do well in sports. Their affect is 'happy' and they can follow instructions and learn living skills.

The mode of inheritance is autosomal recessive and the incidence is higher in Asian and Arab populations where consanguineous marriage is practised. Prenatal diagnosis and carrier testing are becoming increasingly available.

Conclusion

Head size, growth rate and the shape of the head are important pointers towards benign or more sinister medical conditions. A detailed history, thorough examination, including developmental assessment and serial HC measurements, will give the clinician important clues for the differential diagnosis. The measurement of HC of the parents and the siblings in combination with appropriate neuroimaging will further assist in the diagnosis and ongoing management. Expert assessment by a clinical geneticist is essential as our understanding of the genetic causes of these conditions improves. ♦

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