# Macrocephaly

## Definition / Supporting Information

Macrocephaly is defined as a head circumference > 2 standard deviations above the mean (about the 97th percentile) based on age and sex.

## Essential History

If there is any suspicion of increased intracranial pressure, evaluate only after the ABCs (airway, breathing, and circulation) of resuscitation have been addressed.

**Ask about:**

- Antenatal history
- Birth history
  - Gestation
  - Birth weight
  - Neonatal intensive care unit (NICU) stay
- Age of onset
  - A large head circumference at birth:
    - Presupposes a cause of prenatal origin
    - Necessitates a detailed prenatal history
- Significant events of ill health
- Family history of any genetic, neurological, and developmental conditions
- History of large head in family members

## ‘Red Flag’ Symptoms and Signs

If there is any suspicion of increased intracranial pressure, evaluate only after the ABCs (airway, breathing, and circulation) of resuscitation have been addressed.

**Ask about:**

- Symptoms suggestive of increased intracranial pressure
  - Developmental delay
  - Seizures
  - Lethargy
  - Vomiting
  - Behavioural changes

**Look for:**

- Signs of increased intracranial pressure
  - Bulging fontanelle
  - Distended scalp veins
  - Visible sclera above iris of eye (sun-setting sign)
- Abnormal neurological signs
  - Abnormalities in muscle tone (eg, hypotonia) and posture
  - Asymmetries
  - Persistence of primitive reflexes
  - Hyperreflexia
  - Sixth cranial nerve palsy
- Dysmorphic features
- Skin Abnormalities (eg, café-au-lait spots, axillary freckling, ash-leaf spots)
- Eye Abnormalities (eg, papilledema, cataract, retinal abnormalities)
- Cognitive impairment
- Autistic features
- Learning disabilities
- Behavioural difficulties
- Abdomen
  - Hepatosplenomegaly
- Serial Head circumference measurements, if available
- Parental head circumference

## Differential Diagnosis / Conditions

- Hydrocephalus
  - Enlargement of the ventricular system
  - May be congenital or acquired
- Hydrocephalus with Chiari type II defect
  - Present in 80% of children with myelomeningocele
- Dandy–Walker malformation
  - Cystic dilatation of the fourth ventricle with:
    - Macrocephaly (commonly the first manifestation)
- Congenital aqueductal stenosis
  - May occur sporadically or be transmitted by X-linked inheritance
- Benign accumulation of extracerebral fluid, probably subarachnoid
  - May be seen in many children with macrocephaly who have an unremarkable neurological examination
  - The exact nature of fluid collection is not clearly established and is also known as:

        - Benign macrocephaly
        - External hydrocephalus
- Megalencephaly
    - Benign or idiopathic megalencephaly
        - Large head
        - No significant collection of extraventricular or intraventricular fluid
        - Normal neurological examination and developmental history
        - No signs of increased intracranial pressure
        - Family history of large head sizes in normal adult
    - Anatomical megalencephaly
        - Usually associated with neurodevelopmental impairment
        - The brain is abnormally large because of an increase in the size and number of its cells
        - Overgrowth syndromes
            - Sotos syndrome (facial dysmorphism and neurodevelopmental deficits, such as poor co-ordination and cognitive and behavioural problems)
    - Neurocutaneous syndromes such as:
        - Neurofibromatosis
        - Tuberous sclerosis
    - Hypomelanosis of ito
    - Achondroplasia
        - Megalencephaly
    - Short stature
        - Shortened proximal arms and legs (rhizomelia)
    - Dysmorphic facial features (see Congenital Malformations)
        - Normal intelligence
        - Cardiofaciocutaneous syndromes
    - Autism
        - Compared with the general population, a disproportionate number of autistic children have enlarged heads
        - The relationship between acceleration in head growth and behavioural and developmental regression remains unclear
    - Fragile X syndrome
        - Macrocephaly
        - Longish face with prominent ears
        - Joint hyperextensibility
        - Enlarged testes
    - Metabolic megalencephaly
        - Mucopolysaccharidoses (MP)

        - Hurler's syndrome—the most severe MP
            - Enlarging head that quickly crosses percentiles during infancy
            - Coarse facial features
            - Frontal bossing
            - Corneal clouding
    - Leucodystrophies
        - Infantile form of Canavan's disease
            - Irritability
            - Poor visual fixation (head lag / motor delay)
    - Alexander's disease
        - Macroencephaly
        - Spasticity
        - Seizures
        - Developmental regression
    - Glutaric aciduria
- Thickening of the skull
    - Haemolytic anaemia (such as β-thalassaemia)
        - May exhibit frontal bossing attributable to expansion of extra-medullary cavity
    - Cleidocranial dysostosis
        - Autosomal dominant disorder of abnormal bone formation characterised by:
            - Delayed closure of fontanelles
            - Widening of the head circumference
            - Other skeletal abnormalities
- Space-occupying lesions
    - Arteriovenous malformation
    - Brain tumours
    - Subdural effusion as a complication of bacterial meningitis in infants may produce:
        - Enlarging head circumference
        - Bulging anterior fontanelle
        - Signs of increased intracranial pressure
    - Subdural haematoma may present with macrocephaly in infants, but is usually associated with other symptoms

## Investigations

If there is any suspicion of increased intracranial pressure, evaluate only after the ABCs (airway, breathing, and circulation) of resuscitation have been addressed and manage according to the increased intracranial pressure decision support tool.

Non-specialist practitioners (GP Teams) have an important role in documenting sequential head circumference and growth in the UK 'Red Book'. They can also observe the interaction between the child and the parents.

To be undertaken by specialist practitioners (General Paediatric / Genetic / Paediatric Metabolic / Paediatric Neurosurgery Team(s)):

- (Liaise with) Paediatric Metabolic team for testing for the presence of storage diseases
  - Recommended in a child exhibiting developmental regression
- (Liaise with) Genetic team for testing as appropriate for clinical assessment
- Imaging
  - Head ultrasonography
    - For infants with open fontanelles, useful in identifying hydrocephalus and to a lesser degree intraventricular haemorrhage and intracranial tumours
  - Magnetic resonance imaging (MRI)
  - Computed tomography (CT)
- Skeletal survey
  - May show:
    - Bone age abnormalities in the overgrowth syndromes
    - Abnormalities that may be present in mucopolysaccharidoses
    - Bone dysplasias
    - Trauma
    - Non accidental injury (NAI)

## Treatment Approach

If there is any suspicion of increased intracranial pressure, evaluate only after the ABCs (airway, breathing, and circulation) of resuscitation have been addressed and manage according to the increased intracranial pressure decision support tool.

To be undertaken by specialist practitioners (eg, General Paediatric / Genetic / Paediatric Metabolic / Paediatric Neurosurgery Team(s)):

### Specific Treatment

- Children who have asymptomatic familial megalencephaly do not require treatment

- Hydrocephalus
  - Shunting is the treatment of choice for significant and progressive hydrocephalus.
  - Lumbar puncture
    - Serial lumbar punctures may be used as initial therapy.
  - Medical management
    - Carbonic anhydrase inhibitors (acetazolamide)
    - Other diuretics
- Other
  - Children suspected of having inborn errors of metabolism should be referred for genetic evaluation, treatment, and counselling
    - Treatment for these conditions is mainly supportive and symptomatic
    - Bone marrow transplantation and enzyme replacement therapy are promising interventions for certain disorders
  - Anatomical megalencephaly
    - The association with developmental and cognitive problems warrants early intervention and special education services
  - Subdural haematoma requires further evaluation, including a timely and thorough safeguarding assessment
    - Skeletal survey
    - Retinal examination

## When to Refer

Refer (arrange emergency transfer) to Paediatric Emergency or Intensive Care Team:

- Any child with suspected raised intracranial pressure
- Suspected shunt infection or malfunction

Refer urgently to specialist practitioners (eg, Emergency Department / General Paediatric / Paediatric Metabolic / Paediatric Neurosurgery Team(s)) if:

- Head circumference is crossing percentiles or head growing rapidly
- Suspected child maltreatment [NICE clinical guideline 89]
- Abnormal neurological examination
- Regression in developmental skills or significant developmental delay

Refer non-urgently to specialist practitioners (eg, Emergency Department / General Paediatric / Genetic / Paediatric Metabolic Team(s)) if:

- Head circumference > 2 standard deviations above the mean
- Dysmorphic features (see Congenital Malformations)

## ‘Safety Netting’ Advice

- Inform parent or carer to seek medical advice immediately if there is any change in mental state or seizures

## Resources

### National Clinical Guidance

Child maltreatment: when to suspect maltreatment in under 18s (Web page), NICE clinical guideline CG89, National Institute for Health and Care Excellence.

### Medical Decision Support

UK-WHO Growth Charts (Web page), RCPCH, WHO, Department of Health (also available from Harlow Printing).

### Suggested Resources

***Please note: these resources include links to external websites. These resources may not have national accreditation and therefore PCO UK cannot guarantee the accuracy of the content.***

Seal A. Fifteen-minute consultation on the infant with a large head. Arch Dis Child Educ Pract Ed. 2013;98(4):122-125. [PubMed]

Alvarez LA, Maytal J, Shinnar S. Idiopathic external hydrocephalus: natural history and relationship to benign familial macrocephaly. Pediatrics. 1986;77(6):901-907. [PubMed]

Fenichel GM. Disorders of cranial volume and shape. In: Fenichel GM. Clinical Pediatric Neurology: A Signs and Symptoms Approach. Philadelphia, PA: Elsevier Saunders; 2009.

Glass RBJ, Fernbach SK, Norton KI, et al. The infant skull: a vault of information. Radiographics. 2004;24(2):507-522. [PubMed]

Jones KL. Smith’s Recognizable Patterns of Human Malformation. 6th ed. Philadelphia, PA: Elsevier Saunders; 2006.

Olney AH. Macrocephaly syndromes. Seminars in Pediatric Neurology. 2007;14:128. [PubMed]

## Acknowledgements

**Content Editors:** Dr Srini Bandi and Dr Jan Dudley

**Clinical Expert Reviewers:** Dr Peter Heinz and Dr Colin Powell

**GP Reviewer:** Dr Ian A Dunn

**AAP Reviewer:** Deepak Kamat, MD, PhD, FAAP

**Paediatric Trainee Reviewer:** Dr Sarah Jennifer Gregg

**Update reviewer:** Dr Jyoti Khanna (trainee paediatrician)

**Paediatric Specialty Group:** British Association of General Paediatrics

**Update information**

Created: 2015

Date last updated: 2018

Next review due: 2021