PEDIATRIC NEWBORN MEDICINE CLINICAL PRACTICE GUIDELINES

Management of Neonatal Microcephaly



Implementation Date: September 22, 2022

Clinical Practice Guideline: Management of Neonatal Microcephaly

Points of emphasis/Primary changes in practice include:

1. Expanding knowledge on the diagnosis and workup of microcephaly
2. Head circumference should be measured upon NICU admission by RN and at minimum every week during hospital stay
3. A head circumference <3% defines microcephaly and should utilize this guideline even if baby is IUGR/SGA
4. If HC <3% and confirmed by repeated measurement microcephaly should be added to the hospital problem list (ICD 10 code Q02)
5. Recommendations for which infants diagnosed with microcephaly should receive a neurology consult and/or brain MRI
6. When MRI is indicated in preterm infants, ideally it should be obtained at term equivalent age
7. Recommendations for discharge coordination and outpatient follow-up

July 2022

1. Use Olsen preterm growth charts for all babies born ≤41 weeks gestation
2. For all infants >41 weeks gestation use WHO growth chart
3. Recommend measuring HC at admission and at least once a week in conjunction with the dietician
4. Recommend neurology consult and brain MRI for any baby with a z score >-3
5. Consider a neurology consult and brain MRI for any baby with a z score <-2 to -3

Rationale for change:

This guideline was created to assist providers in recognizing the importance of microcephaly and how to best manage and refer these patients; this guideline was created by the NNCC working group with a goal to maximize use of best practices.

Questions? Please contact: Director of Neonatal Neurocritical Care

Clinical Guideline Name	**Management of Neonatal Microcephaly**
Effective Date	10-26-2021
Revised Date	09-22-2022
Contact Person	Director of Neonatal Neurocritical Care
Approved By	Clinical Practice Council _____ Department of Newborn Respiratory ____ Department of Newborn Medicine _____ Department of Neonatal Nursing ____
Keywords	Microcephaly- IUGR

This is a clinical practice guideline. While the guideline is useful in approaching microcephaly in infants, clinical judgment and/or new evidence may favor an alternative plan of care, the rationale for which should be documented in the medical record.

I. Purpose and Background

To provide clinical guidelines for physicians, practitioners and registered nurses to screen, identify and evaluate for the presence of congenital or acquired microcephaly in the newborn.

Microcephaly is an important clinical finding that can be a sign of various congenital, genetic, or acquired neurologic conditions. Microcephaly indicates reduced brain volume and is associated with a wide spectrum of neurodevelopmental outcomes (1-3). Microcephaly is categorized as either primary microcephaly or acquired microcephaly. Primary microcephaly is detected at birth, and or prior to 36 weeks gestation, and often reflects failure of neurogenesis (4). There is some correlation between the degree of congenital microcephaly and severity of cognitive impairment (1). Secondary (acquired) microcephaly is a condition in which the brain is the expected size at birth and then fails to grow normally. Acquired microcephaly may result from a large number of etiologies, including in utero or perinatal brain injury. When there is no injury, acquired microcephaly may reflect reduction in dendritic processes and synaptic connections (4) and manifests as a normal head circumference at birth with subsequent slowed growth rate (5). Early detection and recognition of microcephaly is crucial for determining underlying etiologies and initiating appropriate treatment and therapies. Because the etiologies and neurodevelopmental implications of microcephaly are highly variable, a multidisciplinary approach to management may be necessary (i.e., Neurology, Genetics, Infectious Disease, PT/OT consults).

- **Incidence**: According to the Center for Disease Control (CDC), approximately 1 in 800-5000 infants are born with microcephaly in the United States (2).
- **Classification:**
  - There have been variations in definitions of microcephaly
  - The (CDC) defines microcephaly as head circumference (HC), also known as occipital-frontal measurement (OFC), more than 2 standard deviations (SD) below the mean for age and gender (Z score less than -2) , which also generally signifies a measurement on or below the 3rd percentile (5). These measurements are indicative of a very small head size, in comparison to other infants, of the same age and sex.
  - Broadly, microcephaly can be qualified as mild or severe
    - **a.** Mild microcephaly can be defined as HC between Z score = -2 to -3) for age, sex, and gender (1).
    - **b.** Severe microcephaly can be defined as greater than Z score less than -3 for age and gender (1).
  - For all infants (including Trisomy 21) ≤41 weeks gestation use Olsen's Growth Curves (**Appendix 1**)
  - For infants (including Trisomy 21) >41 weeks use WHO Growth curve
  - Microcephaly can be symmetric (proportionate) or asymmetric (disproportionate). Microcephaly is considered symmetric (or proportionate) when the HC is less than 3% but proportionate to weight and length. <u>Microcephaly should be investigated whether it is proportionate or not.</u>

- **Method:** Using a paper or cloth tape measure, encircle the entire circumference of head, which should be 1-2 finger breaths above eye brows, over the most prominent part of the brow, and around the most prominent part of the back of the head, usually the occipital protuberance **Appendix 2** (6). Head circumference measurement should be obtained three times. The largest head circumference, measured to the 0.25 of a centimeters, should be documented and plotted along infant growth chart.

- **Clinical significance:** Children with microcephaly are at high risk for developing intellectual or learning disabilities, epilepsy, cerebral palsy, hearing/vision problems (1). Developmental services early in life will often help babies with microcephaly to maximize their physical and cognitive potentials.

- **Etiologies:**
  Microcephaly is associated with variable etiologies. Selected etiologies are summarized in **Appendix-3.** Overall etiologies can be classified into:

  - Isolated/ Syndrome microcephaly is reportedly associated with 15-50% genetic etiology. Moreover, infants with primary microcephaly are more likely to have imaging abnormalities and more severe neurodevelopment impairments (1)
  - Chromosomal Abnormalities
  - Metabolic disorders
  - Neuroanatomy abnormalities
  - Infectious/ Environmental
    - Prenatal/perinatal insult
    - Infections
    - Teratogens
    - Maternal conditions

II. Algorithm for obtaining a neurology consult and neonatal brain MRI for babies with microcephaly (Appendix-4)

- Head circumference should be measured upon NICU admission by RN and at minimum every week during hospital stay (in conjunction with the dietician)
- If HC <3% and confirmed by repeated measurement microcephaly should be added to the hospital problem list (ICD 10 code Q02)
- Send Cytomegalovirus (CMV) PCR Non-blood test using either saliva sample or urine sample (ideally be sent within the first 3 weeks of life) for any infant diagnosed with microcephaly
- Recommended to request a neurology consultation and brain MRI for Z score >-3
- Consider requesting a Neurology consultation and Brain MRI for microcephaly if:
  - Z score -2 to -3 and both biological parents have normal head circumference, i.e., >3rd percentile using Rollins Curves (7) **(Appendix-5)** (3% HC: 52 cm for women, 53.5 cm for men assuming parents >18 years) , or if parents have a neurologic disorder
- If the shape of the head is deformed or if craniosynostosis is suspected, consider neurosurgical consultation. Cranial ultrasound can be also considered to verify suture closure.

- For MRI, please see NICU MRI Guidelines on the Department of Pediatric Newborn Medicine Intranet (under Guidelines and Policies – Neuro) for details. http://www.bwhpikenotes.org/policies/departments/NICU/documents/NICUBWHMRIGuidelines.pdf
- When ordering an MRI, please provide detailed clinical information including the diagnosis of microcephaly as the indication for obtaining the study.
- When MRI is indicated in preterm infants, ideally it should be obtained at term equivalent age
- MRI should be obtained on a 3T scanner at e.g. Lee Bell, Hale, or L1

III. Interpretation of results of MRIs, communication with families, discharge planning, and outpatient follow-up referrals.

Communication of MRI results to families

Microcephaly MRI results should be discussed with families by the primary medical team in conjunction with neurology– i.e. attending neonatologist on service with nurse practitioner, physician assistant, fellow and/or resident. Medical team will describe the process of reviewing the MRI study and reaching a final interpretation. Although a preliminary report may become available shortly after the study is completed, a final interpretation of a study may take up to several weekdays depending on the complexity of the findings. Only final MRI results should be presented to families if abnormal findings consider discussing with neurology prior to discussion with families.

Microcephaly MRIs, discharge planning, and outpatient follow-up

In the situation where the infant has had a brain MRI for microcephaly, outpatient follow up should include:

- Direct communication with the primary pediatrician at the time the infant is discharged. If MRI has abnormalities, the attending neonatologist or pediatrician should make efforts to communicate directly with the primary pediatrician what the MRI result is, how it has been presented to the family, and what are the recommendations for follow-up.
- Communication with the outpatient infant follow up program and Neurology clinic the infant is being referred to
- Inclusion of MRI results in the discharge summary with concrete recommendations for developmental follow-up.

- Considering utilizing care coordination to help facilitate a referral to early intervention
- In addition, referrals for additional Physical therapy (PT), Occupational therapy (OT) and/or Feeding therapy services as appropriate (above and beyond what will be provided by early intervention) can be explored. Medical teams can work with the Care Coordination and/or the Developmental Therapy team in making these referrals.

Early Intervention Services

EI Eligibility for services in Massachusetts:

Children with an established diagnosis of microcephaly automatically qualify for early intervention until age 3 years old.

- Can be referred for an EI evaluation by either a medical professional (pediatrician, nurse, developmental therapist, *etc.*) or a parent/caregiver.
- Typically, the regional EI catchment area to which a family belongs geographically conducts a multidisciplinary assessment for each referred child

Appendices:
Appendix 1- Olsen Growth Charts
Appendix 2- How to measure HC
Appendix 3- Selected causes of microcephaly
Appendix 4- Microcephaly management algorithm
Appendix 5- Rollins head circumference growth chart (for parents HC)
Appendix 6- Parents Information Sheet on Microcephaly

References:

1. Ashwal, S., Michelson, D., Plawner, L. et al. (2009). Practice Parameter: Evaluation of the child with microcephaly (an evidence-based review): report of the Quality Standard of the American Academy of Neurology and Practice Committee of the Child Neurology Society. *Neurology*, (73), 887-897
2. Bloom, J. (2020). Microcephaly in infants and children: Etiology and Evaluation. *UptoDate*. Retrieved December 14, 2020 from https://www.uptodate.com/contents/microcephaly-in-infants-and-children-etiology-andevaluation?search=evaluation%20of%20microcephaly&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1

3. Center for Disease Control and Prevention. (2020). Facts about Microcephaly. Retrieved from https://www.cdc.gov/ncbddd/birthdefects/microcephaly.html
4. Cragan, J. (2016, Feburary18). *Surveillance for Microcephaly.* National Center on Birth Defects and Development. (Powerpoint slides) https:// www.cdc.gov/ncbddd/birthdefects/documents/surveillance-microcephaly-webinar.pdf
5. Drutz, J. (2020). The pediatric physical examination: General principles and standard measurements. *UptoDate.* Retrieved December 21, 2020 from https://www.uptodate.com/contents/the-pediatric-physical-examination-general-principles-and-standard-measurements?sectionName=Head%20circumference&search=evaluation%20of%20microcephaly&topicRef=2839&anchor=H798296674&source=see_link#H798296674
6. Passemard, S., Kaindl, A. & Verolesm A. (2013). *Pediatric Neurology Part I, Microcephaly.* (13). 129-141.
7. Rollins JD, Collins JS, Holden KR. United States head circumference growth reference charts: birth to 21 years. J Pediatr. 2010 Jun;156(6):907-913.e2. doi: 10.1016/j.jpeds.2010.01.009. Epub 2010 Mar 20. PMID: 20304425.
8. Villar J, Giuliani F, Fenton TR, Ohuma EO, Cheikh Ismail L, Kennedy SH, for the INTERGROWTH-21st Consortium. INTERGROWTH-21st very preterm size at birth reference charts. Lancet 2016 doi.org/10.1016/S0140-6736(16) 00384-6.
9. (2015, October 1). Retrieved January 10, 2021, from http://eiplp.org/wp-content/uploads/2015/09/EI_DX_List-with-ICD-10-codes-10.2015.pdf

Appendix 1:

Olsen Growth Curves for Intrauterine Growth

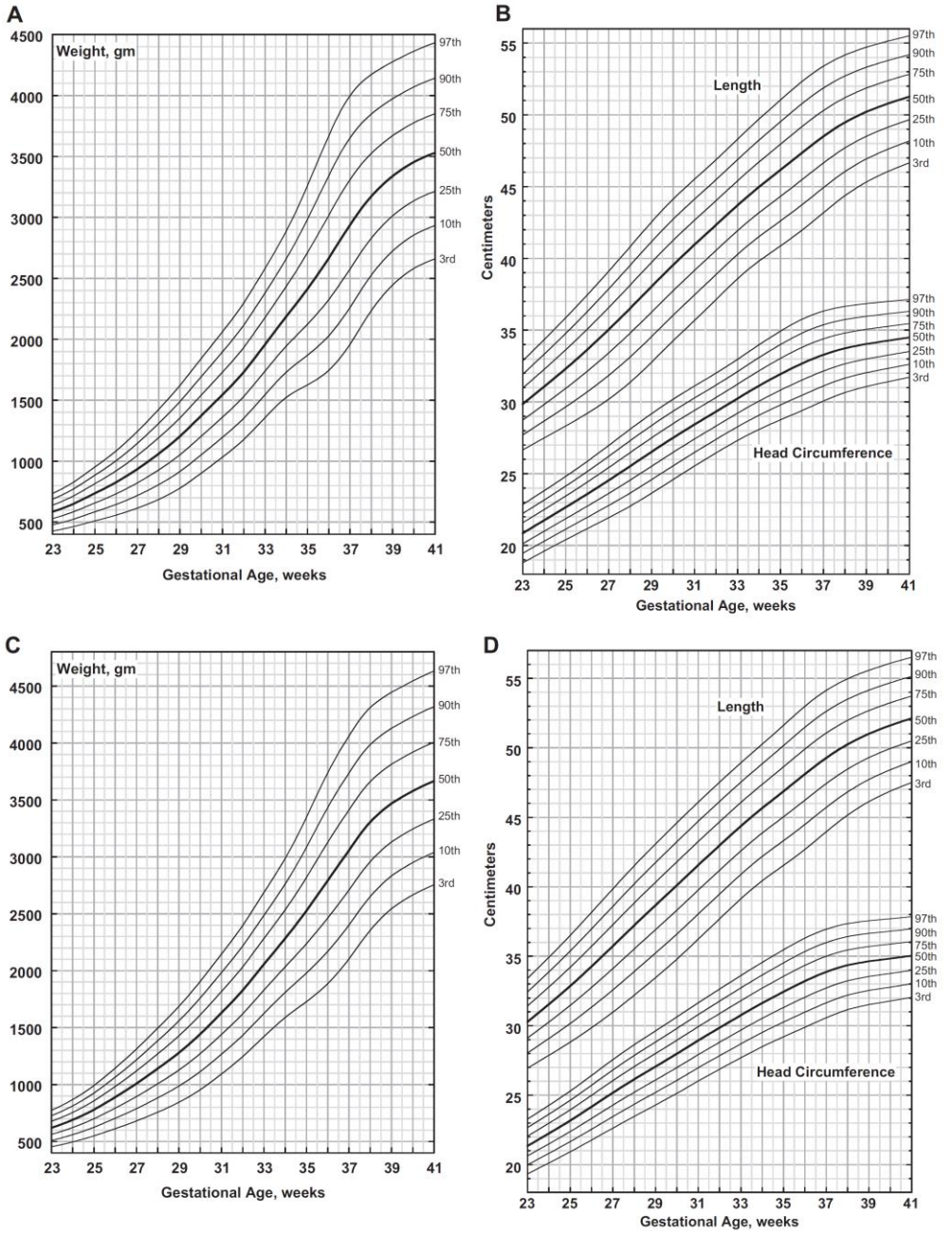
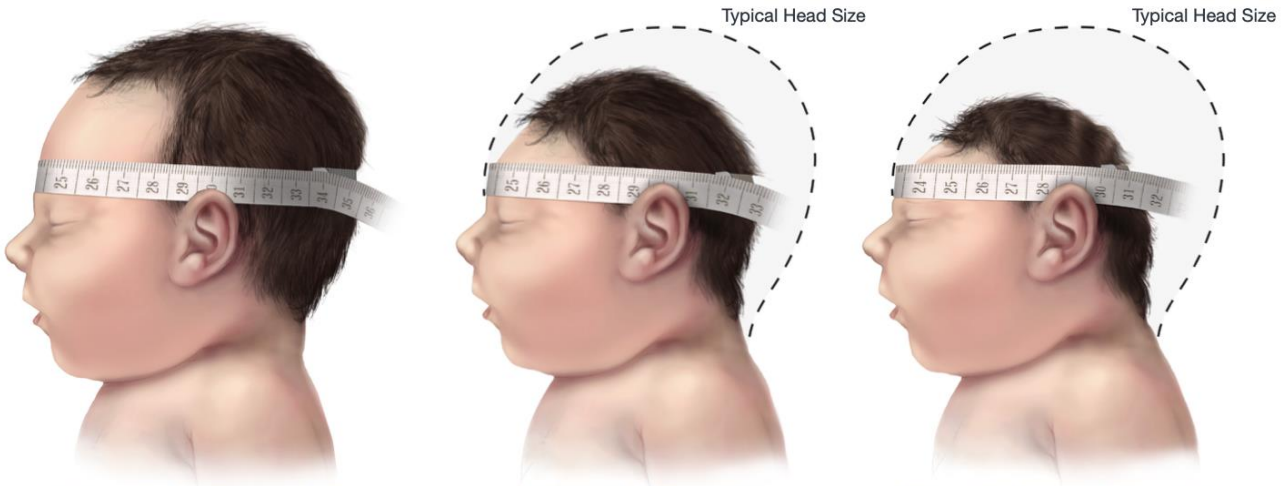


FIGURE 1

New gender-specific intrauterine growth curves for girls' weight-for-age (A), girls' length- and HC-for-age (B), boys' weight-for-age (C), and boys' length- and HC-for-age (D). Of note, 3rd and 97th percentiles on all curves for 23 weeks should be interpreted cautiously given the small sample size; for boys' HC curve at 24 weeks, all percentiles should be interpreted cautiously because the distribution of data is skewed left. Adapted from Groveman.[20]

From: Olsen IE, Groveman SA, Lawson ML, et al. New intrauterine growth curves based on United States data. Pediatrics 2010;125(2):e214-e24.

Appendix 2: Measuring Head Circumference



- Use a measuring tape that cannot be stretched
- Securely wrap the tape around the widest possible circumference of the head
  - » Broadest part of the forehead above eyebrow
  - » Above the ears
  - » Most prominent part of the back of the head
- Take the measurement three times and select the largest measurement to the nearest 0.1 cm
- Head circumference measurements should be taken on the first day of life because commonly-used birth head circumference reference charts by age and sex are based on measurements taken before 24 hours of age

Adopted from CDC (www.cdc.gov/zika)

Appendix 3:

Selected causes of microcephaly

Isolated microcephaly
Autosomal recessive (multiple types)
Autosomal dominant
X-linked microcephaly
Chromosomal abnormalities and syndromes
Trisomies (eg, 21, 18, 13)
Monosomy 1p36 deletion
Seckel syndrome
Smith-Lemli-Opitz syndrome
Williams-Beuren syndrome (7q11.23 deletion)
Cornelia de Lange syndrome
Miller-Dieker lissencephaly syndrome (17p13.3 deletion)
Wolf-Hirschhorn syndrome (4p deletion)
Cri-du-chat syndrome (5p15.2 deletion)
Mowat-Wilson syndrome
Rubinstein-Taybi syndrome
Aicardi-Goutières syndrome
Cockayne syndrome
Bloom syndrome
Angelman syndrome

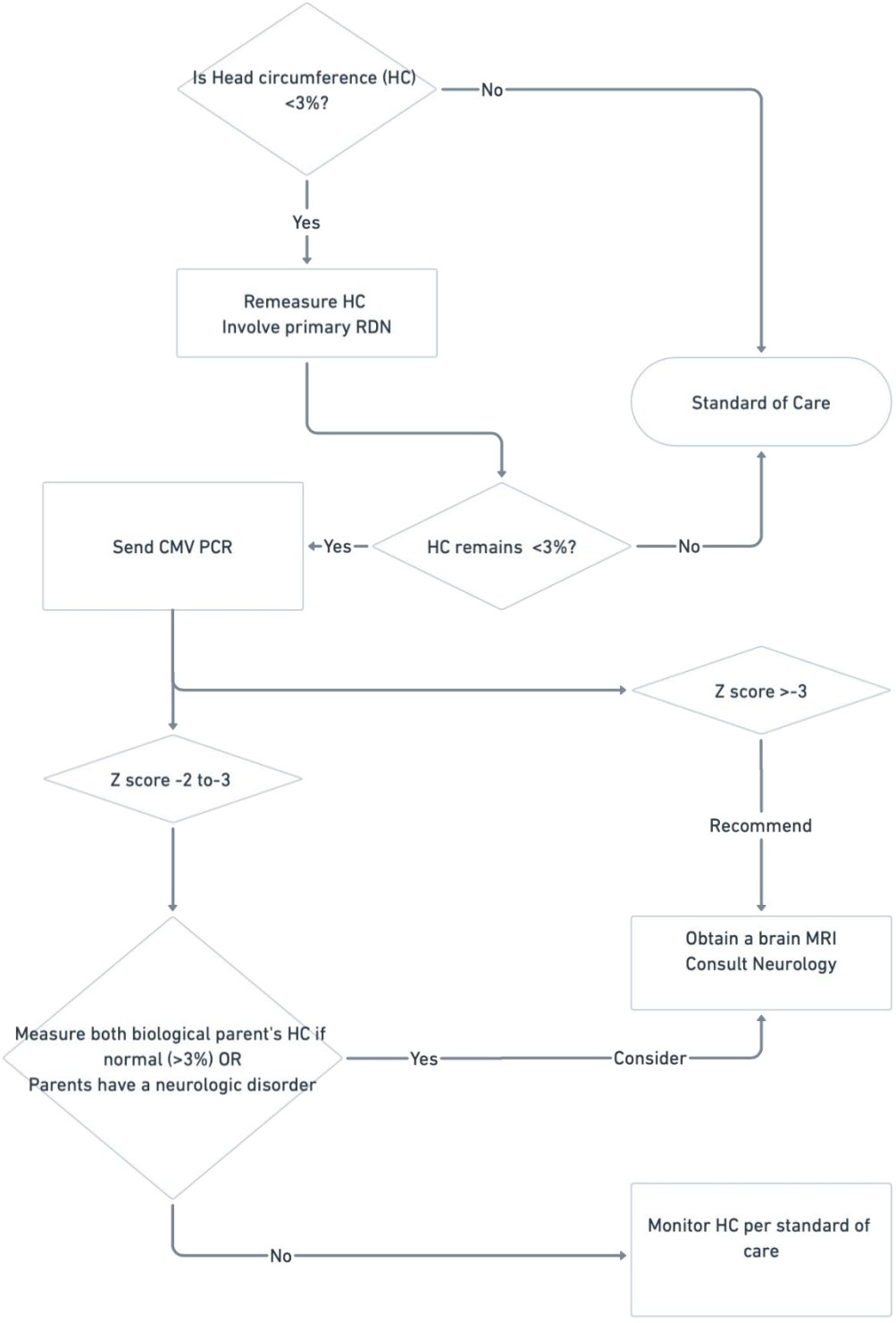
Neuroanatomic abnormalities associated with microcephaly
Neural tube defects (eg, anencephaly, hydranencephaly, encephalocele)
Holoprosencephaly
Atelencephaly (aprosencephaly)
Lissencephaly
Schizencephaly
Polymicrogyria
Pachygyria (macrogyria)
Fetal brain disruption sequence
Metabolic disorders
Maternal diabetes mellitus
Untreated maternal phenylketonuria
Phenylketonuria
Methylmalonic aciduria
Citrullinemia
Neuronal ceroid lipofuscinosis
Environmental causes
Congenital infection (eg, cytomegalovirus, herpes simplex virus, rubella, varicella, toxoplasmosis, HIV, syphilis, enterovirus, Zika virus)
Meningitis
In utero drug or toxin exposure (eg, alcohol, tobacco, marijuana, cocaine, opioid, antineoplastic agents, antiepileptic agents, radiation, toluene)
Perinatal insult (eg, hypoglycemia, hypothyroidism, hypopituitarism, hypoadrenalism)
Anoxia/ischemia

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From Bloom J. : Microcephaly in infants and children: Etiology and evaluation. UpToDate. Last accessed 4-12-2021

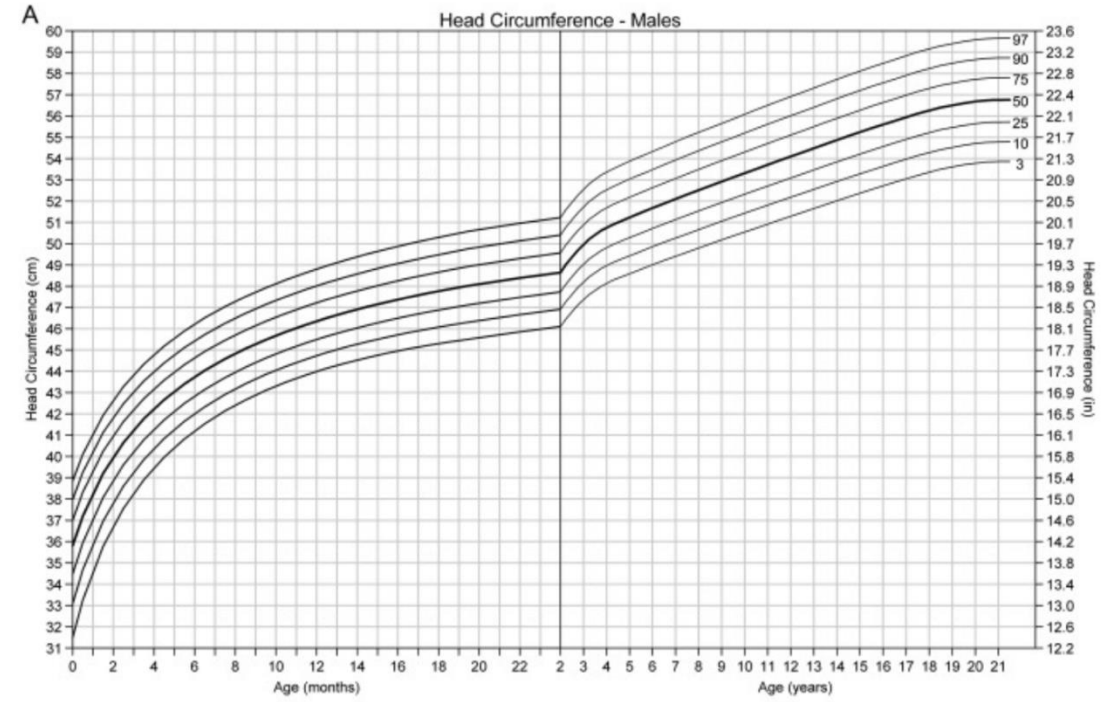
Appendix 4:

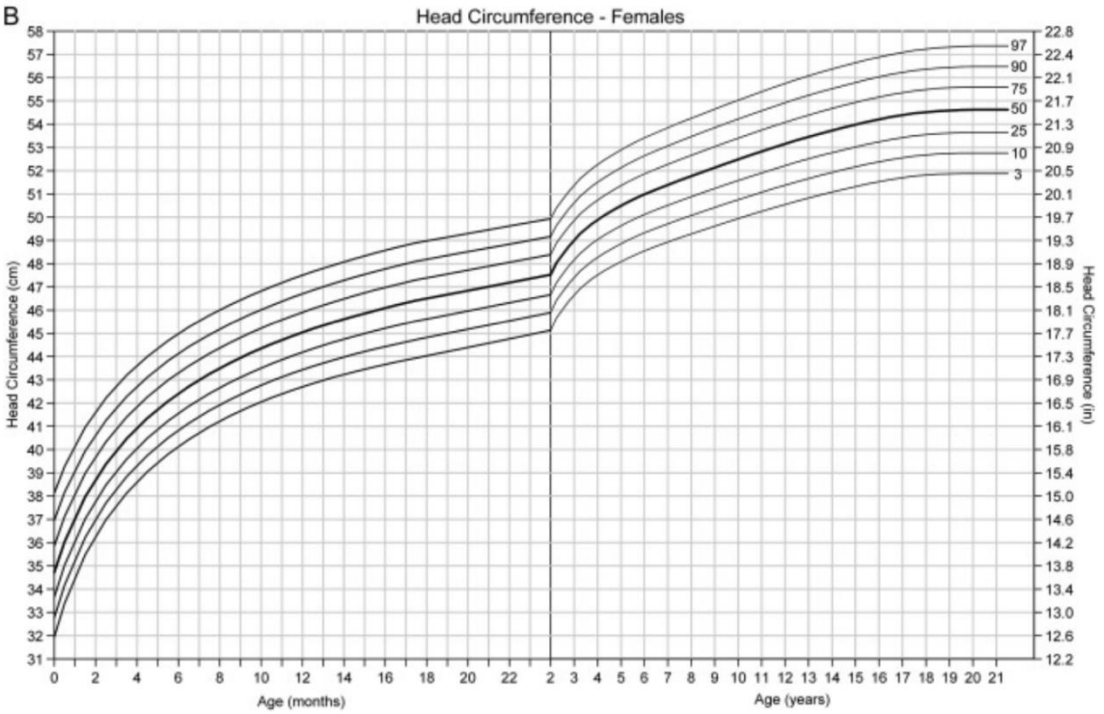
Microcephaly Management Algorithm



Appendix 5:

Rollins Head Circumference Growth Chart (to be used for parents)





From: Rollins JD, Collins JS, Holden KR. United States head circumference growth reference charts: birth to 21 years. J Pediatr. 2010 Jun;156(6):907-913.e2.

BRIGHAM AND WOMEN'S HOSPITAL

Neonatal Intensive Care Unit

Parent Information Sheet: **Microcephaly**

What is Microcephaly?

Microcephaly is a condition where a baby's head is much smaller than expected. During pregnancy, a baby's head grows because the baby's brain grows. Microcephaly can occur because a baby's brain has not developed properly during pregnancy or has stopped growing after birth, which results in a smaller head size. Microcephaly can be an isolated condition, meaning that it can occur with no other major birth defects, or it can occur in combination with other major birth defects.

Causes and Risk Factors:

The causes of microcephaly in most babies are unknown. Some babies have microcephaly because of changes in their genes. Other causes of microcephaly, including severe microcephaly, can include the following exposures during pregnancy:

- Certain infections during pregnancy, such as rubella, toxoplasmosis, or cytomegalovirus
- Severe malnutrition, meaning a lack of nutrients or not getting enough food
- Exposure to harmful substances, such as alcohol, certain drugs, or toxic chemicals
- Interruption of the blood supply to the baby's brain during development

Diagnosis:

A healthcare provider will measure the distance around a newborn baby's head, also called the head circumference, during a physical exam. Diagnosis of microcephaly is given if head circumference is less than the 3rd percentile.

- Consultation with specialists like a pediatric neurologist and geneticist may be needed
- Further testing and brain MRI might be indicated to try to understand the cause of microcephaly

Treatment:

- Microcephaly is a lifelong condition.
- There is no known cure or standard treatment for microcephaly but further management might be guided by the specific cause if identified
- Referral to early intervention and NICU follow up clinic might be indicated



Baby with Typical Head Size



Baby with Microcephaly



Baby with
Severe Microcephaly

CDC

Neonatal Intensive Care Unit
CWN Building, 6th Floor
75 Francis Street
Boston, MA
02115

617-732-5420

Centers for Disease Control and Prevention. (2020, October 23). Facts about Microcephaly. Centers for Disease Control and Prevention. https://www.cdc.gov/ncbddd/birthdefects/microcephaly.html.