MCN for Neonatology
West of Scotland
Neonatal Guideline

Evaluation of the floppy infant

This guideline is intended to guide the investigation of babies with unanticipated floppiness in the neonatal period. Users should refer to appropriate guidance where the cause is known, including guidance on HIE, hypoglycaemia, sepsis and other systemic illnesses. Users should also refer to relevant drug monographs.

The word floppy can be used to mean:

- Decrease in muscle tone (hypotonia)
- Decrease in muscle power (weakness)
- Ligamentous laxity and increased range of joint mobility.

Hypotonia

Definition of tone:

It is the resistance to passive movement around the joint.

- Phasic tone: assessed by the response of the muscle to a rapid stretch (tendon reflexes).
- Postural tone: measured by the response of the muscle to a sustained low-intensity stretch (maintaining posture against gravity= significant head lag on pull-to-sit, rag-doll posture on ventral suspension, slipping through the hands when the infant is held under the arms).

History:

- Antenatal history of reduced fetal movement, or polyhydramnios.
- Family history of muscle disease, stillbirth or consanguinity.
- Delivery , resuscitation, Apgar scores and cord gases
- History since delivery: respiratory effort, ability to feed, level of alertness, level of spontaneous activity and character of cry.

Diagnostic approach

NB - It is important to exclude systemic illness such as sepsis, hypoglycaemia etc.

It is important to determine whether the problem is of an upper motor neurone type (central hypotonia), or of a lower motor neurone type (peripheral hypotonia). In the neonatal period, central causes account for two-thirds of cases with HIE being the most common.

Please note that some of the muscle and nerve disorders (peripheral disorders), can be part of an underlying condition that also affects the brain (Central Disorder), e.g. Arthrogryposis/Metabolic disorders as well as some of the genetic muscle disorders can have a central component.

Indicators of **Central** hypotonia	Indicators of **Peripheral** hypotonia
• Normal strength (Normal antigravity movements). • Dysmorphic features. • Normal or brisk tendon reflexes. • Irritability +/- loud cry. • History suggestive of HIE, Birth Trauma, or symptomatic hypoglycaemia. • Seizures.	• Reduced strength (reduced or absent spontaneous anti-gravity movements). • Reduced or absent reflexes. • Muscle fasciculation (rarely seen but very important if seen). • Myopathic face (open mouth with tented upper lip, poor lip seal when sucking, lack of facial expression, ptosis). • Weak cry. • Look bright.

- Note that during the acute stage of some central causes the infant may appear weak.
- Some of the congenital muscular dystrophies are associated with brain malformations.
- Metabolic causes and those which are multi-system diseases can be difficult to differentiate central from peripheral.
- Babies with profound central hypotonia may have absent deep tendon reflexes.
- contractures are a clue to a muscle cause in a floppy child

Causes of hypotonia

Central hypotonia	Peripheral hypotonia
1. Acute Encephalopathies: • HIE (hypoxic ischaemic encephalopathy). • Hypoglycaemia. • Intracranial haemorrhage. 2. Chronic Encephalopathies: • Cerebral malformations. • Inborn errors of metabolism (mucopolysaccharidoses, aminoaciduria, organic acidurias, lipidoses, glycogen–storage diseases, Menkes syndrome). • Chromosomal disorders (Prader-Willi syndrome, Trisomy 21). • Peroxisomal disorders (neonatal adrenoleukodystrophy, Zellweger's syndrome), • Endocrine (hypothyroidism). • Metabolic (renal tubular acidosis). 3. Connective Tissue disorders: • Ehlers-Danlos syndrome. • Osteogenesis imperfecta. • Congenital Ligamentous laxity.	1. Spinal cord: • Spinal Cord. • Syringomyelia. 2. Anterior horn cell: • SMA (spinal muscular atrophy). 3. Neuro-muscular junction: • Transient Neonatal Myasthenia: caused by transplacental transfer of maternal auto-antibodies against the acetyl choline receptor (AChR) • Congenital myasthenic syndrome , Neuromuscular junction dysfunction secondary to various genetic mutations 4. Muscular disorders: • Congenital muscular dystrophies (CMD) (Walker-Warburg, Fukuyama, Muscle-eye-brain disease, merosin-positive CMD), FSHD (facial scapular humeral Dystrophy) • Congenital myopathies (nemaline rod myopathy, myotubular myopathies, central core disease, mini-core disease). • Congenital myotonic dystrophy. 5. Peripheral nerves: • Congenital hypomyelination neuropathy. 6. Metabolic myopathies: • Acid maltase deficiency (Pompe Disease). • Carnitine deficiency. • Mitochondrial disorders. • Other metabolic myopathies. 7. Arthrogryposis (can be caused by either central or peripheral causes)

Investigations

Central hypotonia

First line Investigations:

- Serum electrolytes, glucose, calcium, Magnesium and phosphate, liver function test, thyroid function test, blood gases, Lactate and ammonia.
- Septic screen including lumbar puncture with CSF goes to both bacteriology and virology.
- Plasma amino acids.
- Urine for organic acids.
- Neuroimaging: USS head.
- Microarray CGH

Second Line Investigations:

- MRI, EEG has prognostic information for brain function.
- Urine for mucopolysaccharide screen= GAG (glycosaminoglycan)
- Very long chain fatty acids.
- Screen for congenital viral infections.
- Consider medical genetics and ophthalmology opinion.
- Consider plasma copper and caeruloplasmin assay(for Menkes)
- Acylcarnitine profile (plasma or blood spot test).
- consider a blood spot to biochemistry for acid maltase

Peripheral hypotonia

First Line Investigations

- Creatine kinase (levels need to be interpreted with caution as tend to be higher at birth, rises in the first 24 hours, and increase with acidosis) so if initial test is high, repeat.
- DNA for myotonic dystrophy (EDTA sample).
- Genetic testing for SMA gene deletion which is present in 95%of cases of SMA type 1.
- EDTA sample for Prader-Willi testing
- CXR/ECHO (cardiomegaly/cardiomyopathy).
- Microarray CGH (for completion)

Second Line Investigations

- Neurology service: EMG/NCS (nerve conduction studies), may distinguish between neurogenic**,** myopathic, myotonic and myasthenic aetiologies, although difficult in the first 6 months of life.
- Muscle biopsy: to be sent for histology, immunohistochemistry, electron microscopy, respiratory chain enzyme analysis).
  Pleases note that genetic testing now supersede muscle biopsy (e.g. congenital myopathy panel, arthrogryposis etc)

*NB – If a diagnosis of congenital myaesthenia gravis is considered it is considered best practice to perform an EMG before considering a challenge with pyridostigmine. If such a challenge is undertaken the appropriate dosage would be:-

Pyridostigmine -
1 milligram/kg/day orally in 6 divided doses, increasing by weekly increments of 1mg/kg/day - up to a maximum 4 mg/kg/day.
Once at the maximum dose of 4 mg/kg/day, continue the dose for 6 weeks to assess response.
Caution: *Pyridostigmine is contra-indicated in some congenital myasthenic syndromes, so need to be discussed with Neurology before initiating any treatment.*

Additional clues which may direct to a specific diagnosis:

- Hepatosplenomegaly; storage disorders, congenital infections.
- Renal cysts, high forehead and wide fontanelles; Zellweger's syndrome.
- Hepatomegaly, retinitis pigmentosa; neonatal adrenoleukodystrophy.
- Congenital cataracts, glaucoma; oculocerebrorenal (Lowe) syndrome.
- Abnormal odour; metabolic disorders.
- Hypopigmentaion, undescended testes; Prader Willi

Principles of Management

- Physiotherapy: stretches aimed at prevention of contractures, positioning.
- Respiratory support.
- Feeding.
- Management of gastro-oesophageal reflux.
- Evaluation and treatment of cardiac dysfunction.
- Later:
  Prevention and correction of scoliosis.
  Prevention and prompt treatment of respiratory infections.
  Follow up of general development and stimulation of learning.

- Please note that with advances in treatment of SMA and potential gene therapy in DMD, early diagnosis as initiation of early treatment as early as possible is recommended for Individuals with infantile-onset (Type 1) and pre-symptomatic SMA
  Please note that with rapid advances in treatment of SMA, Early recognition and Diagnosis is essential in allowing early initiation of gene therapy of SMA. Early treatment is Associated with an improvement outcome, especially for babies with Type I and Pre-Symptomatic SMA. See Appendix which identifies red flags for suspicion of SMA in the neonate

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Appendix – Red flags for SMA in the neonate

RED FLAGS FOR 0-6 MONTHS[1]

1 Does not move his/her head from side to side when lying on back.

Has trouble lifting his/her head when lying on stomach during tummy time (floppy baby).

Has lost the ability to do things he/she was able to do before.

2 Breathing is very fast; only the belly moves, especially when he/she is lying on his/her back.

Cry is weak (hard to hear his/her cry).

It takes a long time to complete his/her feeds.

3 Has a bell-shaped chest.

After feeding, breathing sounds rattly or wheezy.

I have concerns regarding my child's movement and development.

4 Does not move his/her hands to mouth. Does not reach for toys placed in front of him/her.

5 When I pick up my child, it feels like he/ she will slip out of my hands.

Does not squirm.

Seems smaller than other children his/her age and is not gaining weight appropriately.

6 Does not lift his/her legs when lying on movement).

Unable to independently extend legs, and/or his/her legs often remain in a frog-like position.

7 Does not kick his/her legs.