Neonatal Hypotonia

The floppy infant assumes a frog legged position. On ventral suspension, the baby cannot maintain limb posture against gravity and assumes the position of a rag doll.

- Encephalopathy - acute
- No encephalopathy -
Neonatal Hypotonia

- Identification of hypotonia
  - Holding the infant in horizontal suspension
  - The back hangs over the examiner's hand, and the limbs and head hang loosely
  - Passive extension of the legs at the knees no resistance is met
  - Pulling the infant from the supine to sitting position the head lags and continues to lag when the sitting position is reached
Neonatal Hypotonia

Physician must localized to determine etiology:
- Central
- Peripheral
- Clues: History and physical exam
Neonatal Hypotonia

- **History**
  - Apgar scores
  - Trauma
  - Resuscitation requirements
  - Cord gases
Neonatal Hypotonia

• **History**
  • History since delivery
    • Respiratory effort
    • Ability to feed
    • Level of alertness
    • Level of spontaneous activity
    • Character of cry
Neonatal Hypotonia

• **History**
  • Maternal disease
    • Diabetes
    • Epilepsy
    • Myotonic dystrophy
  • Pregnancy and delivery history
    • Drug or teratogen exposure
    • Decreased fetal movements
    • Abnormal presentation
    • Polyhydramnios/ oligohydramnios
Neonatal Hypotonia

• **History**
  • Any significant family history
    • Affected parents
    • Siblings
    • Consanguinity
    • Stillbirths
    • Childhood deaths
Neonatal Hypotonia

• General Physical Examination
  • Clues
    • Hepatosplenomegaly
      • Storage disorders
      • Congenital infections
    • Renal cysts
    • High forehead
    • Wide fontanelles
      • Zellweger’s syndrome
Neonatal Hypotonia

- **Overall Physical Examination Clues**
  - Presence of profound weakness and hypotonia suggest:
    - Disorder of the lower motor neuron
      - A sign of this may be a weak cry
    - Weakness is uncommon in central hypotonia except in the acute stages
Neonatal Hypotonia

- **Neurlogical Examination**
  - **Central Clues**
    - Normal strength
    - Normal or increased DTRs
    - May be seizure
    - May be dysmorphic features
    - Altered mental status - lethargic, encephalopathic
Neonatal Hypotonia

- **Neurological Examination**
  - **Anterior horn cells clues**
    - Generalized weakness
    - Decreased/ absent DTRs
    - Fasciculations
    - Often described as alert
Neonatal Hypotonia

• Examination
  • Nerve clues
    • Weakness, distal>proximal
    • Decreased/ Absent DTRs
    • +/- fasciculations
Neonatal Hypotonia

• *Peripheral nerves*
  • Hereditary sensory motor neuropathies
    • Charcot-Marie-Tooth disease
Neonatal Hypotonia

- **Physical Examination**
  - **Neuromuscular Junction**
    - Weakness, face/ eyes/ bulbar
    - Normal DTRs
    - No fasciculations
Neonatal Hypotonia

• Physical Examination
  • Muscles
    • Weakness, proximal>distal
    • Decreased DTRs
Neonatal Hypotonia

• **Physical Examination**
  • Clues
    • Arthrogryposis (the fixation of joints at birth)
    • Associated with:
      • Neonatal hypotonia – long duration
      • More commonly with lower motor neuron unit
      • Multisystem abnormalities
Neonatal Hypotonia

• **Physical Examination**
  • **Clues**
    • Examination of the mother
      • Congenital myotonic dystrophy
      • Myasthenia gravis
Neonatal Hypotonia

• Physical Examination
  • Clues
    • Abnormal odor
      • Metabolic disorders
    • Hypopigmentation, undescended testes
      • Prader Willi
    • Hepatomegaly
    • Retinitis pigmentosa
      • Neonatal adrenoleukodystrophy
Neonatal Hypotonia

• Physical Examination
  • Clues and Pitfalls
    • Profound central hypotonia may have absent DTR
    • Absent DTR in the first few DOL would not rule out a central cause for the hypotonia
Neonatal Hypotonia

- **Investigation**
  - **Peripheral causes**
    - Creatine kinase: If elevated in an early sample, repeat after a few days.
    - Nerve conduction studies
    - Muscle biopsy
      - Depending on clinical situation, may be delayed until around 6 months of age as neonatal results are difficult to interpret
Neonatal Hypotonia

• **Investigation**
  • Central Causes
    • Neuroimaging
      • Ultrasound scan in the first instance
      • MRI for structural abnormality
      • EEG: if seizures suspected
Neonatal Hypotonia

• **Investigation**
  • Central Causes
    • Genetics review if any dysmorphic features present
    • Karyotype (if dysmorphic features)
    • TORCH screen
    • DNA methylation studies or FISH for Prader-Willi syndrome (if clinically indicated after a genetics review)
    • Metabolic work up
Neonatal Hypotonia

- **Investigation**
  - **Peripheral causes**
    - EMG, NCV, Muscle biopsy
    - Molecular genetics – CTG repeats, deletions in SMN gene
## Differentiating Features of a Floppy Infant according to Site of Involvement

<table>
<thead>
<tr>
<th>Site of involvement</th>
<th>Extent of weakness</th>
<th>Proximal vs. distal weakness</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Face</td>
<td>Arms</td>
</tr>
<tr>
<td>Central</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Anterior horn cell</td>
<td>±</td>
<td>+++</td>
</tr>
<tr>
<td>Peripheral nerve</td>
<td>-</td>
<td>+++</td>
</tr>
<tr>
<td>Neuromuscular junction</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Muscle</td>
<td>Variable</td>
<td>++</td>
</tr>
</tbody>
</table>
Differentiating Features of a Floppy Infant according to Site of Involvement *(Contd.)*

<table>
<thead>
<tr>
<th>Site of involvement</th>
<th>Deep tendon reflexes</th>
<th>EMG</th>
<th>Muscle biopsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central</td>
<td>Normal or increased</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Anterior horn cell</td>
<td>Absent</td>
<td>Fasciculation / fibrillation</td>
<td>Denervation pattern</td>
</tr>
<tr>
<td>Peripheral nerve</td>
<td>Decreased</td>
<td>Fibrillation</td>
<td>Denervation pattern</td>
</tr>
<tr>
<td>Neuromuscular junction</td>
<td>Normal</td>
<td>Decremental / incremental</td>
<td>Normal</td>
</tr>
<tr>
<td>Muscle</td>
<td>Decreased</td>
<td>Short duration small amplitude potential</td>
<td>Characteristic</td>
</tr>
</tbody>
</table>
Neonatal Hypotonia

- **Central Hypotonia**
  - Hypoxic ischemic encephalopathy
  - Intracranial hemorrhage
  - Cerebral malformations
  - Chromosomal abnormalities (e.g. Trisomy 21, Prader-Willi syndrome)
  - Congenital infection TORCH
  - Acquired infections
  - Peroxisomal disorders
  - Drug effects (e.g. benzodiazepines)
Prader Willi Syndrome
Cardinal features

- Profound hypotonia
- Swallowing difficulty
- No respiratory distress
- Low birthweight
- Characteristic facies; fair hair
- Antigravity movement of limbs
Prader Willi Syndrome

- Deletion chromosome 15q
- Imprinting
- Paternal chromosome
- Submicroscopic molecular deletions
- Snpm protein
Neonatal Hypotonia

- **Spinal cord**
  - Birth trauma (especially Breech delivery)
  - Syringomyelia
Neonatal Hypotonia

- **Anterior Horn Cell**
  - Spinal Muscular Atrophy
Spinal Muscular Atrophy

It is characterized by marked hypotonia, sluggish fetal movement, and fasciculation of tongue. The child is alert. Feeding behaviour and cry are poor. Deep tendon reflexes are absent. Muscle biopsy shows neurogenic type of atrophy or that the muscle spindles are atrophied in groups. Disease is inherited as an autosomal may be available. Death occurs by 2-4 years of age.
The Survival of Motor Neurones (SMN) Locus on 5q13

* Total deletion of SMN2 not pathogenic
* Total deletion of SMN1 causes SMA
* Total deletion of SMN1 and SMN2 is lethal before implantation
SMN Gene Testing

- Reliable and unequivocal diagnostic confirmation in 98.5% of cases
- Subtle gene abnormalities in the remaining cases with typical clinical features
- No simple correlation between disease severity and result of the gene test
- Clinical involvement of bulbar and chest muscles determines survival, not age at onset
Neonatal Hypotonia

- **Neuromuscular junction**
  - Congenital myasthenia gravis
  - Transient acquired neonatal myasthenia
  - Infantile botulism
Myasthenia gravis

Myasthenia gravis may occur in about 12 percent of the babies born to mothers with the disease. It is characterized by marked hypotonia, pooling of oral secretions, poor feeding, feeble cry and generalized muscle weakness appearing within 2-3 days after the birth. Baby is alert. Facial weakness manifests by mark-like facies, open mouth and staring look. External opthalmoplegia and ptosis are rare. Deep tendon reflexes are normal. The prognosis is substantiated by improvement in the muscle functions following intramuscular injection of edrophonium chloride 1 mg or neostigmine methyl sulfate 0.1 mg. The condition lasts for 3 to 4 weeks. The child is treated with neostigmine methyl sulphate 0.1 to 0.5 mg IM 10 minutes before each feel for 1 or 2 days followed by neostigmine bromide, 1 to 4 mg orally half an hour before each feed.
Neonatal Hypotonia

- **Muscle**
  - Muscular dystrophies (congenital myotonic dystrophy)
  - Congenital myopathies (e.g. central core disease)
Congenital myopathies

These are rare inherited disorders resulting in a benign congenital hypotonia, with generally good outlook for normal life span. Nemaline myopathy is the most common variant. Other disorders of this group include the central core disease, myotubular myopathy and congenital fiber type disproportion.
Neonatal Hypotonia

- **Metabolic myopathies**
  - Acid maltase deficiency
  - Carnitine deficiency
  - Cytochrome-c-oxidase deficiency