Evaluation of the Hypotonic Infant and Child

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Disorders of the peripheral nervous system can generally be divided into three major categories, based on anatomic localization:

- **Neurogenic disorders**, including *nerve and motor neuron diseases*
- Disorders of the *neuromuscular junction*
- **Myopathies**, including *muscular dystrophies*
Clinical approach to neuromuscular disorders of infancy and childhood

NEONATES, INFANTS and CHILDREN

- Hypotonia
- Muscle Weakness
Hypotonia

Outline

- Hypotonia
  - Definition
  - Assessment
- Neuromuscular diseases in the hypotonic infant and child
- Hypotonia
  - Stepwise diagnostic approach
Muscle tone

Definition

Muscle tone is the resistance of muscle to stretch

- Postural tone (i.e. antigravity)
- Phasic tone
Hypotonia

**Definition**
Reduction in postural tone (i.e. antigravity), with or without an alteration in phasic tone (muscle stretch reflexes)
Hypotonia

Differential anatomic diagnosis

- Brain
- Spinal cord
- Anterior horn cell
- Peripheral nerve
- Neuromuscular junction
- Muscle fiber
Hypotonia

Assessment

History

Physical examination
  • General physical examination
  • Motor examination
  • Primary neonatal reflexes
  • Sensation
  • Hypotonia-focused examination
General physical examination

- Normal examination
- Dysmorphic features
- Organomegaly
- Cardiac failure
- Abnormalities of genitalia
- Respiratory irregularities/failure
- Dislocation of the hips
- Arthrogryposis
Hypotonia in utero

- Dislocation of the hips
- Arthrogryposis
Hypotonia

Physical examination

- General physical examination
- Passive manipulation of the limbs
- Muscle power, muscle stretch reflexes
- Appearance (flaccid), motility (e.g. antigravity)
- Neonatal reflexes, sensation
- Traction response ("head lag")
- Vertical suspension ("slips through")
- Horizontal suspension ("drapes over")
- "Scarf" sign, "Heel to ear or chin"
Courtesy NP Rosman, MD, Boston City Hospital
Hypotonia

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THE TRACTION RESPONSE
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HYPOTONIA

PHYSICAL EXAMINATION

<table>
<thead>
<tr>
<th>HEEL TO EAR</th>
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<tbody>
<tr>
<td><img src="heel_to_ear" alt="Diagram" /></td>
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<th>VENTRAL SUSPENSION</th>
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<td><img src="ventral_suspension" alt="Diagram" /></td>
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Approach to diagnosis

- **Cerebral or central hypotonia** (about 2/3)

- **Lower motor unit or peripheral hypotonia** (about 1/3)
Cerebral (central) hypotonia

- History consistent with a CNS insult
- Global developmental delay, seizures
- Microcephaly, dysmorphic features
- Malformation of other organs

- Weakness less than degree of hypotonia (non-paralytic hypotonia)
- Movement through postural reflexes
- SRs: Normal or brisk, clonus, Babinski sign
- Brisk and/or persistent infantile reflexes
Fig. 7
The asymmetrical tonic neck reflex.
ATNR
Lower motor unit (peripheral) hypotonia

- No abnormalities of other organs
- No global delay, delayed gross motor development
- Muscle atrophy, fasciculations
  - Weakness in proportion/excess to hypotonia (*paralytic hypotonia*)
  - Decreased antigravity limb movements
  - Failure of movement on postural reflexes
  - Absent or depressed SRs
Combined cerebral and motor unit hypotonia

- Congenital myotonic dystrophy
- Congenital muscular dystrophies
- Peroxisomal disorders
- Leukodystrophies
- Mitochondrial encephalomyopathy
- Neuroaxonal dystrophy
- Familial dysautonomia
- Asphyxia secondary to motor unit disease
Hypotonia

Systemic diseases

- Sepsis
- Congenital heart disease
- Hypothyroidism
- Rickets
- Malabsorption, malnutrition
- Renal tubular acidosis
Muscle tone

Determinants

- Gamma/alpha motor system
- Visco-elastic properties of muscle and connective tissue
- Joint and tendon resistance
Hypotonia

Connective tissue disorders

- Marfan syndrome
- Ehlers-Danlos syndrome
- Congenital laxity of ligaments
Cerebral (central) hypotonia

- Chromosomal disorders
- Other genetic defects
- Acute hemorrhagic and other brain injury
- Hypoxic/ischemic encephalopathy
- Chronic non-progressive encephalopathies
- Peroxisomal disorders (Zellweger syndrome, neonatal ALD, etc.)
- Metabolic defects
- Drug intoxication
- “Benign” congenital hypotonia
# Neuromuscular diseases in the hypotonic infant and child

<table>
<thead>
<tr>
<th>Anterior horn cell / Peripheral nerve</th>
<th>Neuromuscular junction</th>
<th>Muscle</th>
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<tbody>
<tr>
<td>Spinal muscular atrophies</td>
<td>Transient neonatal MG</td>
<td>Congenital muscular dystrophies</td>
</tr>
<tr>
<td>Hypoxic-ischemic myelopathy</td>
<td>Congenital myasthenic syndromes</td>
<td>Congenital myotonic dystrophy</td>
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<tr>
<td>Traumatic myelopathy</td>
<td>Hypermagnesemia</td>
<td>Infantile FSHD</td>
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<td>Neurogenic arthrogryposis</td>
<td>Aminoglycoside toxicity</td>
<td>Congenital myopathies</td>
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<tr>
<td>Congenital neuromopathies</td>
<td>Infantile botulism</td>
<td>Metabolic myopathies</td>
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<tr>
<td>Axonal</td>
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<td>Mitochondrial myopathies</td>
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<td>Hypomyelinating</td>
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<td>Dejerine-Sotas</td>
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<td>HSAN</td>
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<tr>
<td>Giant axonal neuropathy</td>
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<tr>
<td>Metabolic</td>
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<tr>
<td>Inflammatory</td>
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Spinal muscular atrophy

- SMA, type I (severe)
  - Onset: birth to 6 months
  - Course: never sit unsupported
  - Death: usually < 2 years

- SMA, type II (intermediate)
  - Onset: < 18 months
  - Course: never stand or walk but sit at some time
  - Survival: 98.5% to age 5 years, 68.5% to age 25 years

- SMA, type III (mild)
  - Onset: > 18 months (IIIA <3 years, IIIB >3 years)
  - Course: able to stand and walk at some time
  - Survival: Almost normal life span
Chromosome 5

c840 C>T transition

ESS

ESE

SMN2

90-95%

SMN1

100%

Truncated protein SMNΔ7

Full length SMN protein (294 AA)

SMN full length protein (294 AA)
<table>
<thead>
<tr>
<th>SMA Type &amp; SMN2 Copy Number</th>
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<tbody>
<tr>
<td><strong>SMA I</strong></td>
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<tr>
<td><strong>SMA II</strong></td>
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<tr>
<td><strong>SMA III</strong></td>
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<tr>
<td><strong>Carrier</strong></td>
</tr>
<tr>
<td><strong>Normal</strong></td>
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<tr>
<td><strong>Normal?</strong></td>
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Muscle disorders in the hypotonic infant

- **Classical CMD**
  - Merosin-deficient CMD
    - Primary merosin deficiency
    - Secondary merosin deficiency
  - Merosin-positive CMD
    - Classical CMD without distinguishing features
    - Rigid spine syndrome
    - CMD with distal hyperextensibility (Ullrich type)
    - CMD with mental retardation or sensory abnormalities

- **CMDs with CNS abnormalities**
  - Fukuyama muscular dystrophy
  - Muscle-eye-brain disease
  - Walker-Warburg syndrome
Merosin-deficient CMD (MDC1A)
Myotonic dystrophy syndromes

- Myotonic dystrophy, type 1 (DM1)
- Congenital myotonic dystrophy (DM1)
- Myotonic myopathy, type 2 (DM2, PROMM)
Congenital DM1
Congenital myotonic dystrophy (DM1)

- **Inheritance:** 15%-25% of offspring of affected myotonic dystrophy mothers

- **Features:** hypotonia, poor feeding, facial weakness, club feet, MR

- **Labs:**
  - CK level: usually normal
  - EMG: often no myotonia
  - Large CTG repeat expansion
## Creatine Phosphokinase (CPK)

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<th>Condition</th>
<th>Range</th>
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<tbody>
<tr>
<td>Normal</td>
<td>150–200 U/L</td>
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<tr>
<td>Non-specific</td>
<td>up to 300 U/L</td>
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<tr>
<td>Congenital myopathy</td>
<td>up to 500 U/L</td>
</tr>
<tr>
<td>Spinal muscular atrophy</td>
<td>up to 500 U/L</td>
</tr>
<tr>
<td>Myopathy</td>
<td>500–1000 U/L</td>
</tr>
<tr>
<td>Muscular dystrophy</td>
<td>&gt;1000 U/L</td>
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Approach to Hypotonia and Weakness

- Detailed history and physical examination
  - Exclude systemic illness, congenital laxity of ligaments
  - Test tendon reflexes, antigravity limb movements, etc.

**CENTRAL hypotonia suspected**
- MRI/MRS, metabolic tests, chromosomes/PWS, VLCFAs, LP?

**PERIPHERAL hypotonia suspected**
- Test mother first; if myotonic,
  - DNA test for 19q CTG repeat expansion
  - History of myasthenia gravis in mother?
- Electrolytes, CPK, lactate, pyruvate, carnitine
- Consider EMG/NCS for:
  - Myasthenia (Tensilon test)
  - Botulism
  - Neuropathy, AHC disease
  - Myopathy

**CPK > 10X ULN U/l**
- EMG not crucial
- DNA for FKRP, DMD, or other MD
- Brain imaging (MRI)
- Muscle biopsy (if DNA testing negative)

**CPK < 10X ULN U/l**
- EMG

Neuropathic
- SMN or CMT/DSD testing

Decrement, facilitation
- NM junction defect

Normal, myopathic
- Muscle biopsy
Ευχαριστώ πολύ