A Comprehensive Approach to Neuromuscular Disorders in Children

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Objectives

- Understand the function of lower motor neurons (LMNs)
- Understand How lower motor neuron diseases cause weakness
- Be Able to Recognize and help care for Children with LMN Diseases
- Be familiar with medical and therapy interventions for children who have low tone.
LMN’s are NOT

- **Brain-Related**
  - ABI, CP
  - Pelazius Merzbacher, Canavan’s, etc.

- **Spinal Cord-Related**
  - SCI
  - MMC

- **Connective Tissue-Related**
  - Marfan Syndrome
Lower Motor Neurons and Muscles

Diagram: A motor neuron in the spinal cord is connected to a peripheral nerve, which in turn connects to muscle fibers.
Lower Motor Neuron Diseases

- Anterior Horn Cell
- Peripheral Nerve
- Neuromuscular junction
- Muscle
1. Anterior Horn Cell
2. Peripheral Nerve
3. Neuromuscular Junction
4. Muscle
Lower Motor Neuron Diseases

- Anterior Horn Cell - SMA
- Peripheral Nerve – Guillian-Barre, Charcot-Marie, HMSN
- Neuromuscular junction- Botulism, Myasthenia Gravis
- Muscle – Duchenne Muscular Dystrophy, BMD, FSHMD, Myotonic Dystrophy
1. **Anterior Horn Cell**
2. **Peripheral Nerve**
3. **Neuromuscular Junction**
4. **Muscle**
Spinal Muscular Atrophy (SMA)

- **Autosomal Recessive / 5q13**
- **Incidence is ~7/100,000**
- **Generalized hypotonia and muscle weakness**
  - (proximal weakness > distal weakness)
  - (lower extremities weaker than UE)
- **Generally Higher IQs**
- **Types 1-3**
SMA Type 1

- **Werdnig-Hoffman**
- **Onset is birth-6 months**
- **Weak suck, poor feeding**
- **Labored and paradoxical breathing**
- **Tongue fasciculations (~60%)**
- **Absent MSR’s (75%)**
- **Never sits without support**
- **Death by age 2 years**
SMA Type 2

- Onset before 18 months
- Tongue fasciculations in 50-70%
- Almost all have finger trembling
- Muscle atrophy is worse than in SMA 1
- Sitting is achieved
- No standing or walking
- Death after 2 years of age (with good support 98% survive to age 10 and 77% survive to age 20) – Lifespan = 30-50 years
SMA Type 3

- Kugelberg-Welander syndrome
- Onset after 18 months old
- Sits, stands and walks
- Hyperlordosis, trendelenburg gait
- Weakness, but normal life expectancy
Which finding is most common in spinal muscular atrophy?
1. Brisk reflexes
2. Weakness and atrophy
3. Sensory loss
4. Urinary retention
A 2 year-old patient with spinal muscular atrophy type 2 (intermediate form) presents with a 25 degree C-shaped scoliosis. What is the best treatment option at this time?

1. Muscle Strengthening
2. Electrical Stimulation
3. Spinal Fusion
4. Spinal Orthosis
1. Anterior Horn Cell

2. Peripheral Nerve

3. Neuromuscular Junction

4. Muscle
The Nerve!

Figure 1a
- Nerve Impulse
- Nerve Fibre
- Myelin Internodes
- Nodes
- Muscle contracts

Figure 1b
- Nerve Impulse fails to conduct
- Destruction of myelin by macrophages and lymphocytes
- Muscle does not contract
Diseases of the Peripheral Nerve

- **Acute Inflammatory Demyelinating Polyradiculopathy (AIDP) = GBS**
- **Chronic Inflammatory Demyelinating Polyradiculopathy (CIDP)**
- **Hereditary Motor Sensory Neuropathy (HMSN types 1-4)**
- **Toxic Neuropathies**
1. Anterior Horn Cell
2. Peripheral Nerve
3. Neuromuscular Junction
4. Muscle
Diseases of the Neuromuscular Junction
Diseases of the NMJ

**Myasthenia Gravis**
- Ideopathic
- Transient neonatal myasthenia
- Congenital myasthenia (GFPT1)
- Autoimmune myasthenia
  - (Acetylcholinesterase inhibitors)
  - Immunomodulators

**Botulism**
- Infantile Botulism (75%)
- Non-infantile (6 weeks-9 months)
- Peak 2-3 months
1. Anterior Horn Cell
2. Peripheral Nerve
3. Neuromuscular Junction
4. Muscle
Muscular Dystrophy

DMD
1:3,500
DMD

- Xp21
- Lack of Dystrophin = sarcolemmal membrane instability
- Muscle Breakdown
The Story
- **Functional History**
- **Physical Exam**
- **Labs** - Elevated CK on blood test
- **Single Condition Amplification/Internal Primer sequencing (SCAIP)** - 2003
- **Gene Therapy** (Exon skipping, forced read through of premature stop codons)
Milestones

- Lose ambulation - mean 9.4 years (range 6-15 years)
- Become power wheelchair dependent, 14.6 years (11-28)
- Need assistance for eating and drinking, 18.2 years (12-23)
- Begin assisted ventilation, 19.8 years (14-31)
- Estimated median survival = 35 years
**DMD- Goals**

- Maximize function (bracing, therapy)
- Glucocorticoids (prednisone)/aquatic therapy to decrease rate of muscle loss
- Manage Contractures and scoliosis
- Maximize Nutrition
- Monitor Bone Density
- Optimize respiratory function (flu shot/pneumovax)
- Scoliosis Management (35 degrees?)
- Monitor Cardiac function (ACE inhibitors, Beta-Blockers)
- Follow Mental Status (sleep, dystrophin isoform)
A (PM&R) Board Question

On physical examination, an 8-year old patient stands on his toes and has increased lumbar lordosis. He has a trendelenburg gait with circumduction. What else would you expect to find on his exam?

1. Decreased sensation in his feet
2. Anterior tibialis weakness
3. Quadriceps weakness
4. Hyperreflexia at the ankles
A 15 year old patient with Duchenne Muscular Dystrophy complains of new onset morning headaches. What is the most likely cause?

1. Neck extensor tightness
2. Hypercarbia
3. Migraines
4. Vision changes
BMD

- Xp21
- Less or smaller dystrophin
- Same elevated CK
- Progresses more slowly (walking in adulthood)
- Fewer contractures
- Still with cardiac risks/dilated cardiomyopathy
- Goals the same as DMD
FSH MD

- Slowly progressive dystrophy
- Autosomal Dominant
- 4q35 locus
- SCAPULAR INSTABILITY
- FACIAL WEAKNESS
  - Expressionless appearance
  - Trouble whistling, drinking through a straw, smiling
  - Difficulty with eye closure
  - (USUALLY PRESENTS IN ADOLESCENCE)
MYOTONIC DYSTROPHY

- Autosomal Dominant (1 per 8,000)
- 19q13.3 (DM protein kinase)
- Skeletal, smooth muscle wasting (+pain)
- Heart, brain, hair and eyes
- Weakness is DISTAL > PROXIMAL
MYOTONIC DYSTROPHY

- Baldness, Cataracts
- Adults = Long thin face (temporal and masseter wasting)
- Gonadal atrophy
- Constipation
- Cardiac dysrhythmias
- Daytime Sleepiness
- MYOTONIA
Myotonia

- Delayed relaxation or Sustained Contraction of Skeletal Muscles
- Worsens with cold, stress
- Grip myotonia
- **Percussion myotonia**
- Difficulty releasing objects
Other Forms

Myotonia Congenita (autosomal dominant)
- Herculean apperance
- Worsened with rest
- Worsened with cold
- Diagnosis via EMG ("dive bombers")

Paramyotonia Congenita (AD)
- Milder form
- Worsened with rest
- Worsened with cold
- Worse in hands and face
- Myotonic episodes
Care of the Child with Neuromuscular Disease

- Help Identify the Condition
- Optimize Function
- Prevent Secondary Complications
- Provide Appropriate Resources
Help Doctors Make the Diagnosis

- Clinical History
- Family History
- Clinical Exam
- (Electrodiagnosis)-an extension of the PE
- Serum Labs (Creatine Kinase-MM fraction)
- Muscle/Nerve biopsy
- Molecular Genetic Testing
History

- Prenatal
- After delivery
- Developmental milestones
Clinical History

- Floppy baby
- Delayed motor milestones
- Feeding difficulties
- Breathing difficulties
- Abnormal gait, frequent falls
- Muscle pain, muscle wasting
- Weakness
Weakness

- Is it new?
- Is it progressive?
- How fast is it changing?
- Is it proximal or distal or generalized?
- Are there other symptoms or illnesses?
Detailed

- Autosomal dominant
- Autosomal Recessive
- X-linked Dominant
- X-linked Recessive
MALIGNANT HYPERTHERMIA

- Central core myopathy
- DMD
- BMD
- Also
  - LGMD
  - FSHMD
Physical Exam

- LOOK
- Any atrophy?
- Any (pseudo)hypertrophy?
- Any inverted wine bottles?
- Any fasciculations (tongue, fingers)?
- Any rashes?
- Any ptosis?
Functional Exam

- Head control (head lag)
- Bed Mobility
- Transfers
- Sitting
- Standing
- Gait
- Stairs
Functional Exam

- **Difficulty whistling**
- **Scapular Winging**
- **Gower’s sign**
- **Gait exam**
  - Lordosis, Trendelenburg, Toe walking
  - Foot slap, circumduction, hip hike
Optimize Function and Prevent Secondary Conditions
Challenges to Address

- Progressive Weakness
- Decreased Endurance
- Contractures
- Scoliosis / Kyphosis
- Decreased Mobility
- Decreased Pulmonary Function
- Cardiac Abnormalities
- (MR)
Treatment Plan

- Exercise?
- Manage Contractures
- Braces
- Wheelchairs
- Adaptive Equipment
- Spinal Arthrodesis
- Positive and Negative Pressure Ventilation
Treatment Plan (cont.)

- Identify and Manage Dysphagia
- Provide Protein (and Branched-chain Ketoacid?) Supplementation
- Avoid obesity
- Identify Cardiac abnormalities (conduction, MVP, MR)
- Steroids for MD
- Gene Therapy
- Stem Cell Research
Resources

- Muscular Dystrophy Association
  [http://www.mdausa.org](http://www.mdausa.org)

- Muscular Dystrophy Family Association
  [http://www.mdff.org](http://www.mdff.org)

- Families of Spinal Muscular Atrophy
  [http://www.fsma.org](http://www.fsma.org)
### Clinics

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<tr>
<th>Location</th>
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Questions / Discussion