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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.*

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LMN's are NOT

- *Brain-Related*
  - ✓*ABI, CP*
  - ✓*Pelazius Merzbacher, Canavan's, etc.*
- *Spinal Cord-Related*
  - ✓*SCI*
  - ✓*MMC*
- *Connective Tissue-Related*
  - ✓*Marfan Syndrome*

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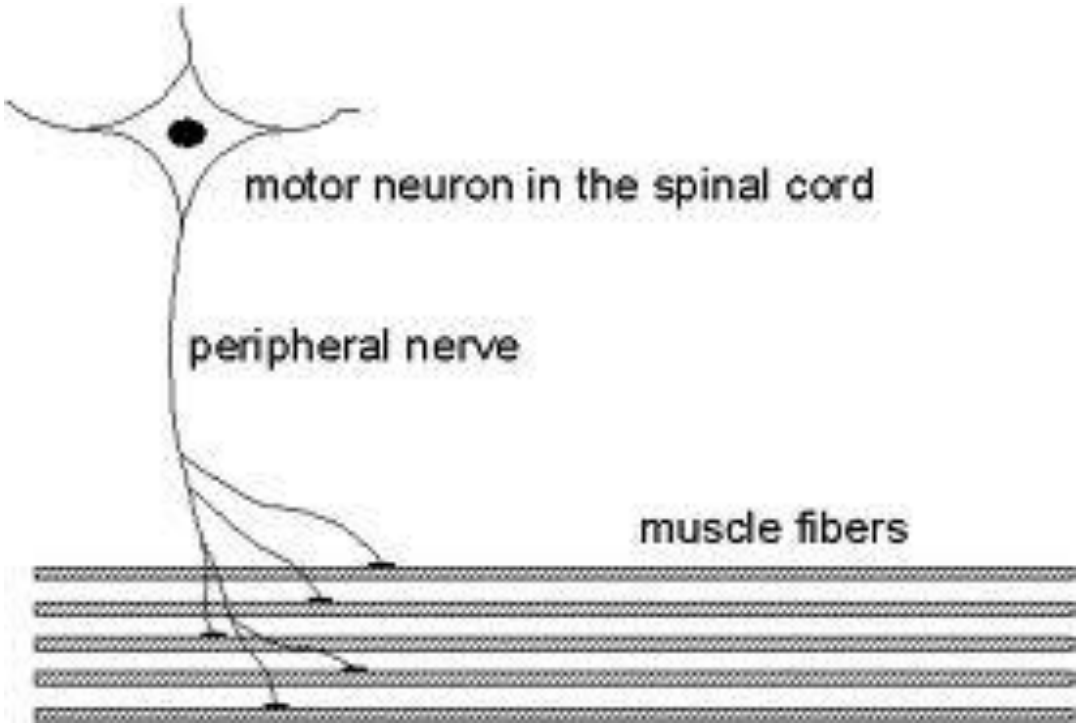
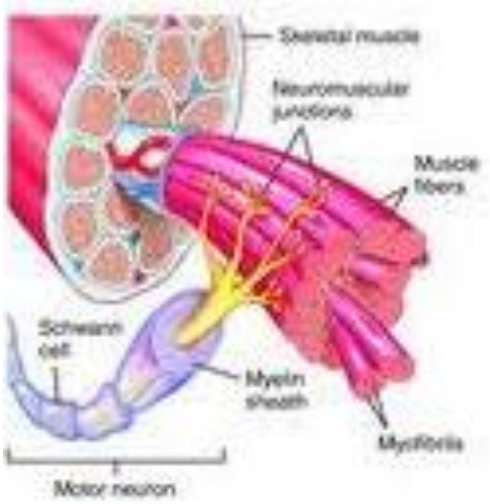
Lower Motor Neurons and Muscles





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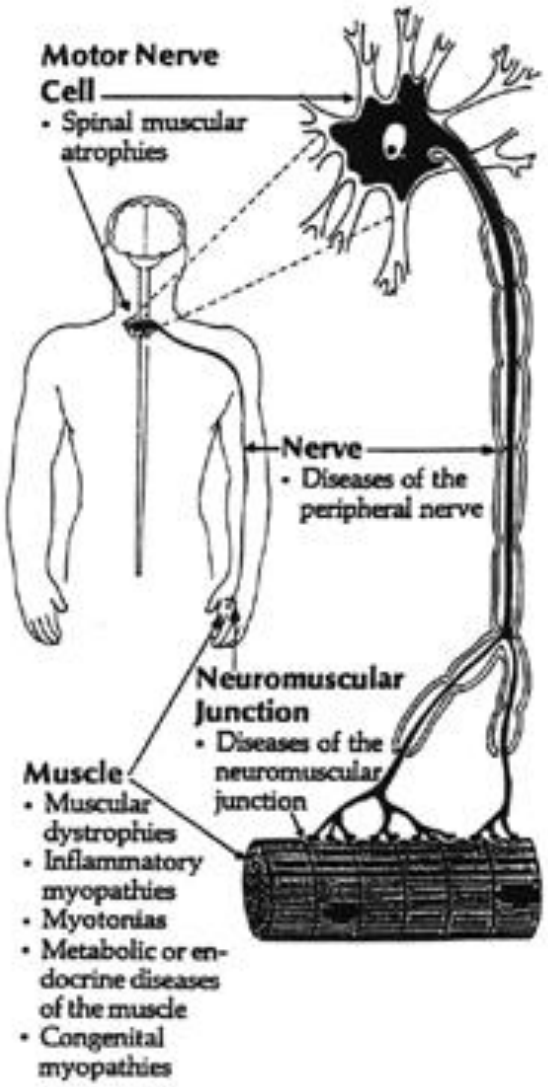
Lower Motor Neuron Diseases

- *Anterior Horn Cell*
- *Peripheral Nerve*
- *Neuromuscular junction*
- *Muscle*



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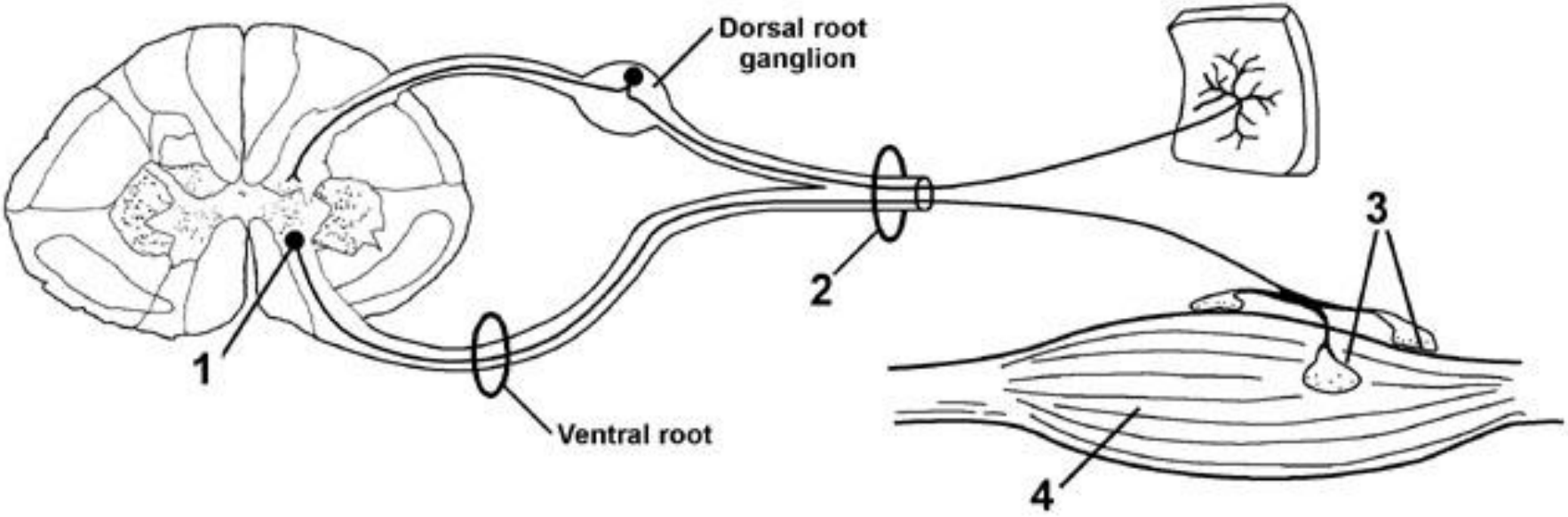
(Horizontal View)

1. *Anterior Horn Cell*
2. *Peripheral Nerve*
3. *Neuromuscular Junction*
4. *Muscle*



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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*

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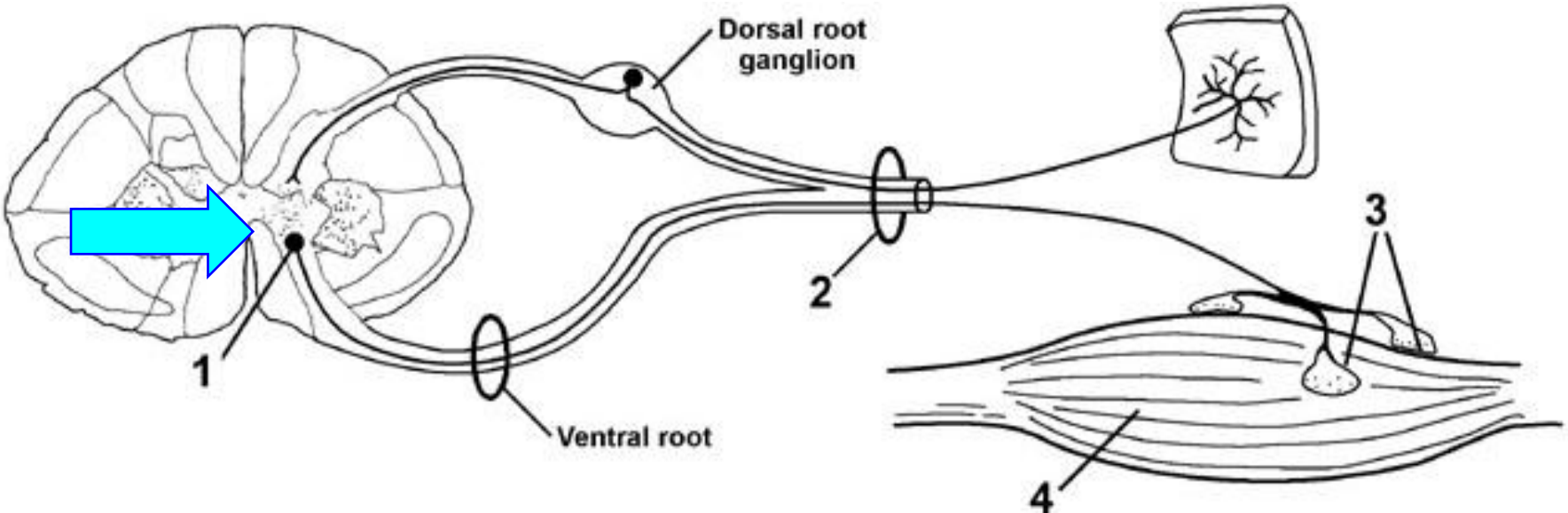

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Motor Neuron Disorders

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*

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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*

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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*

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SMA Type 3

- *Kugelberg-Welander syndrome*
- *Onset after 18 months old*
- *Sits, stands and walks*
- *Hyperlordosis, trendelenburg gait*
- *Weakness, but normal life expectancy*

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A (PM&R) Board Question

- *Which finding is most common in spinal muscular atrophy?*

1. *Brisk reflexes*
2. *Weakness and atrophy*
3. *Sensory loss*
4. *Urinary retention*

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Another Question

- *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*

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1. *Anterior Horn Cell*
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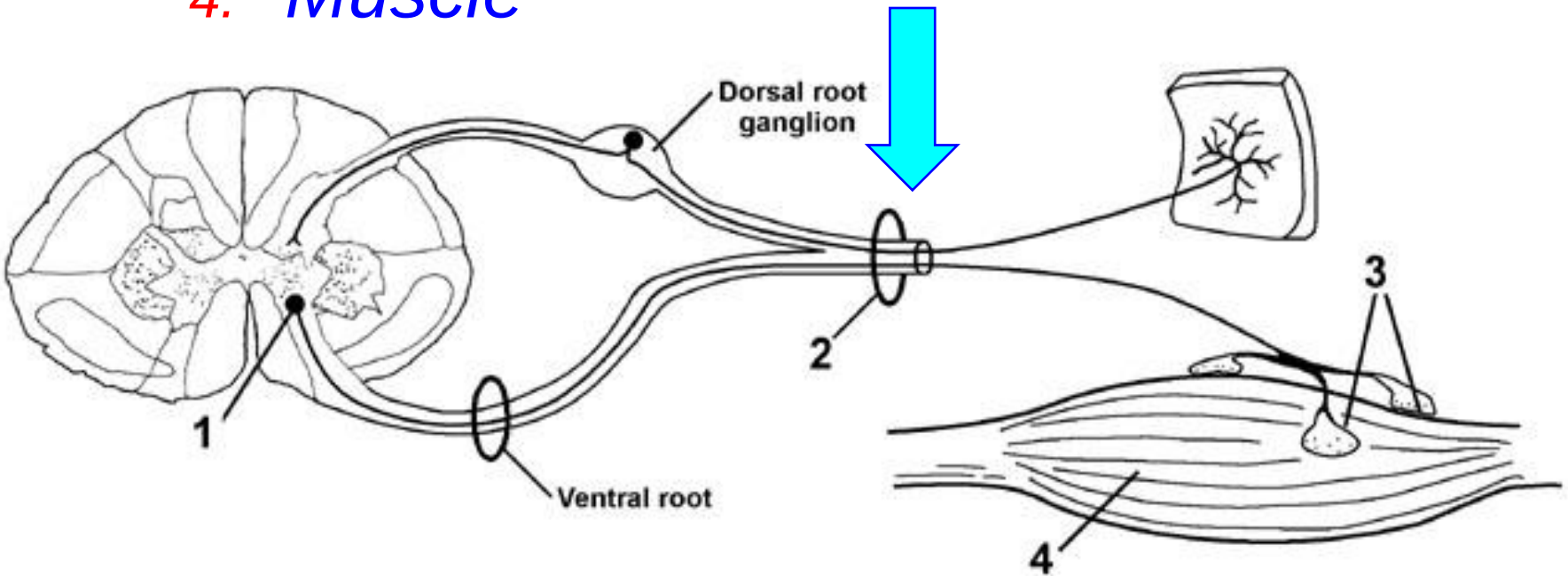

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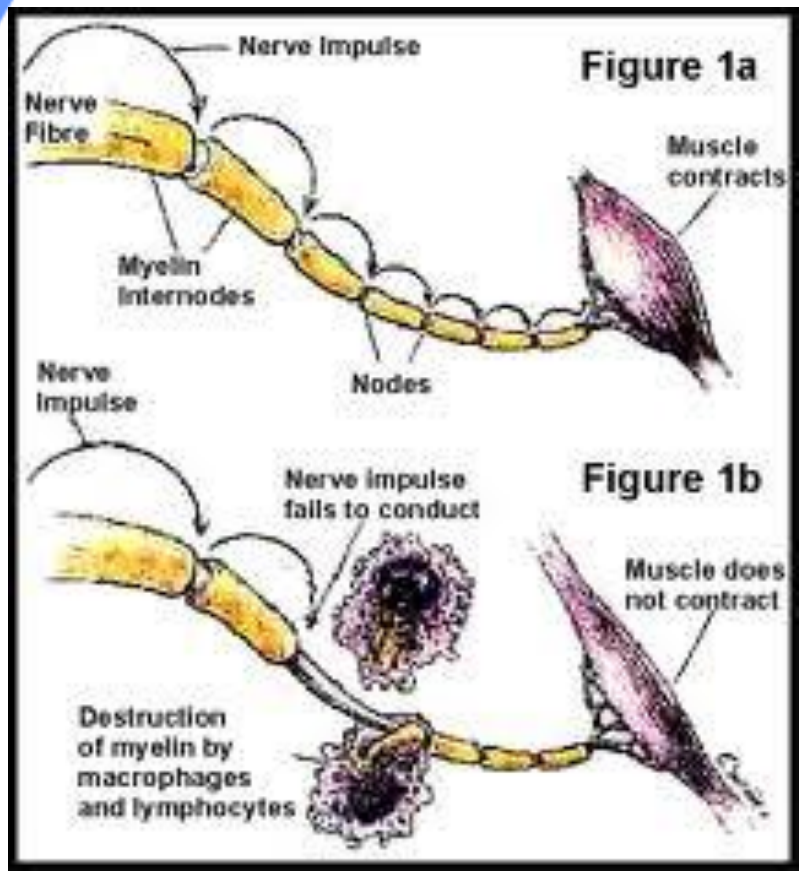
The Nerve !



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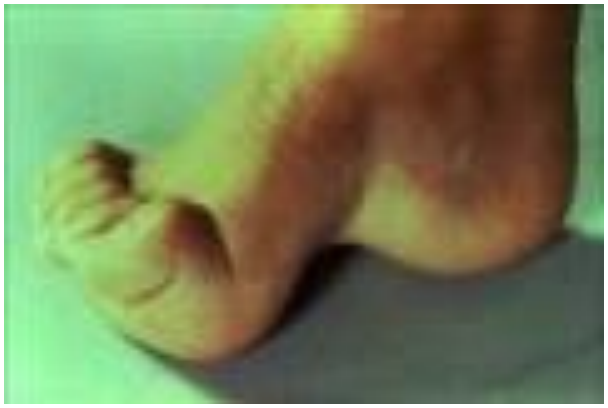
Diseases of the Peripheral Nerve

- *Acute Inflammatory Demyelinating Polyradiculopathy (AIDP) = GBS*
- *Chronic Inflammatory Demyelinating Polyradiculopathy (CIDP)*
- *Hereditary Motor Sensory Neuropathy (HMSN types 1-4)*
- *Toxic Neuropathies*



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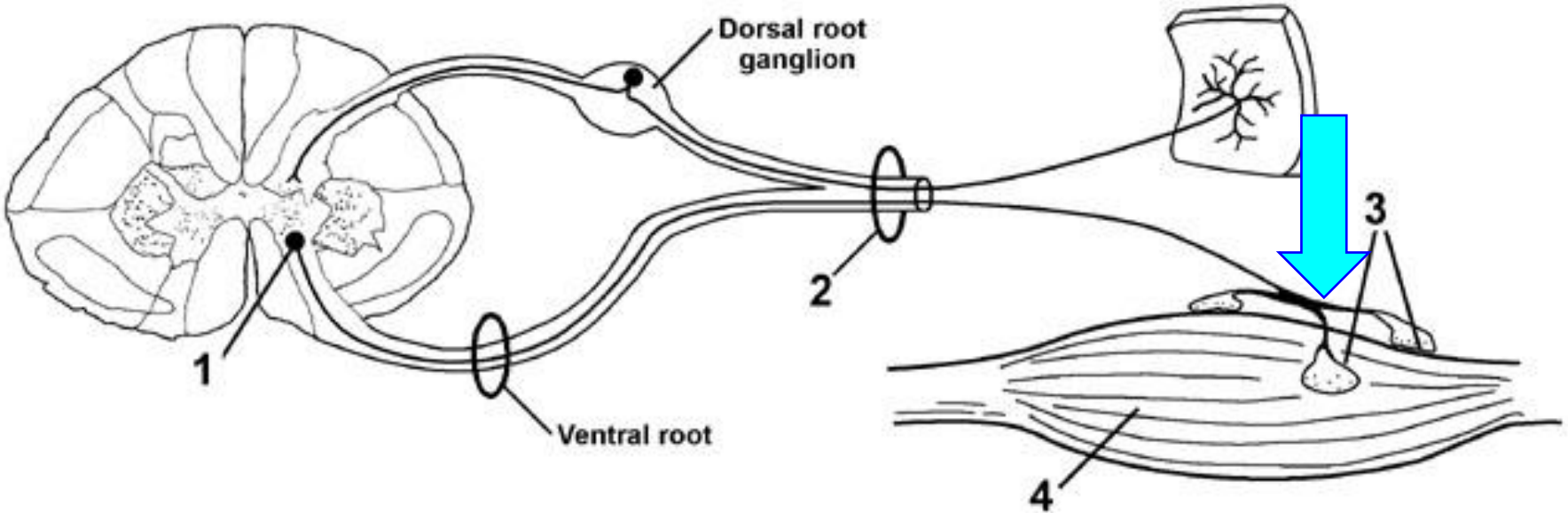

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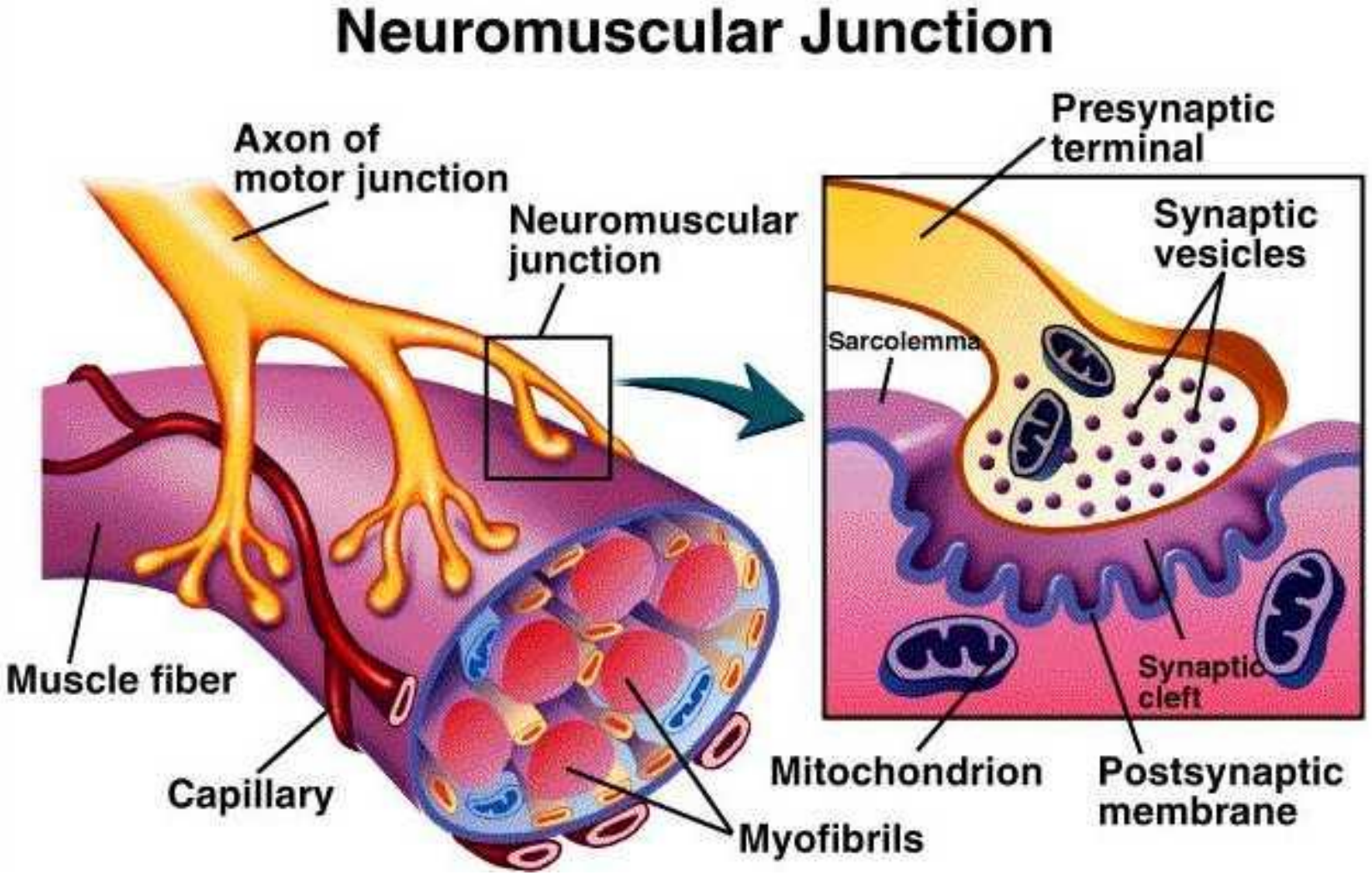
Diseases of the Neuromuscular Junction



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Diseases of the NMJ

Myasthenia Gravis

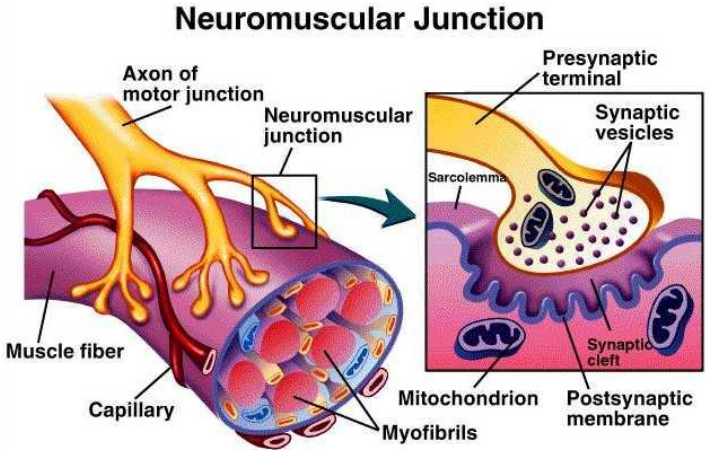
- *Ideopathic*
- *Transient neonatal myasthenia*
- *Congenital myasthenia (GFPT1)*
- *Autoimmune myasthenia*
  - ✓ *(Acetylcholinesterase inhibitors)*
  - ✓ *Immunomodulators*

Botulism

- *Infantile Botulism (75%)*
- *Non-infantile*

(6 weeks-9months)

- *Peak 2-3 months*



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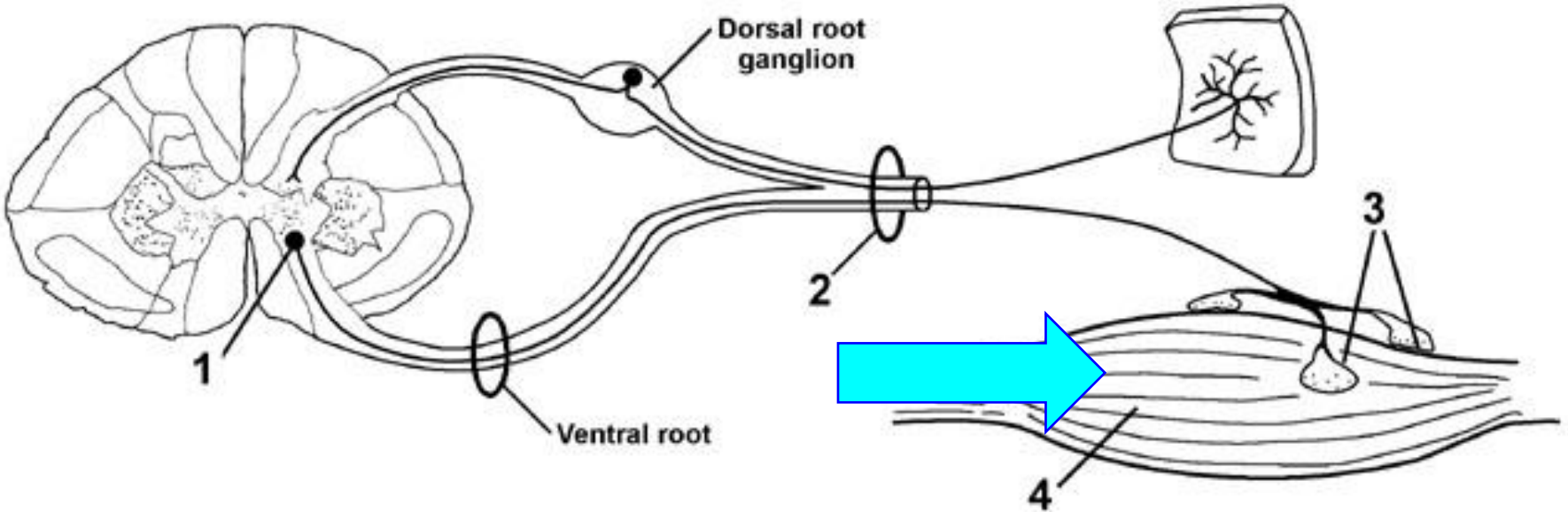

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Muscular Dystrophy

DMD

1:3,500

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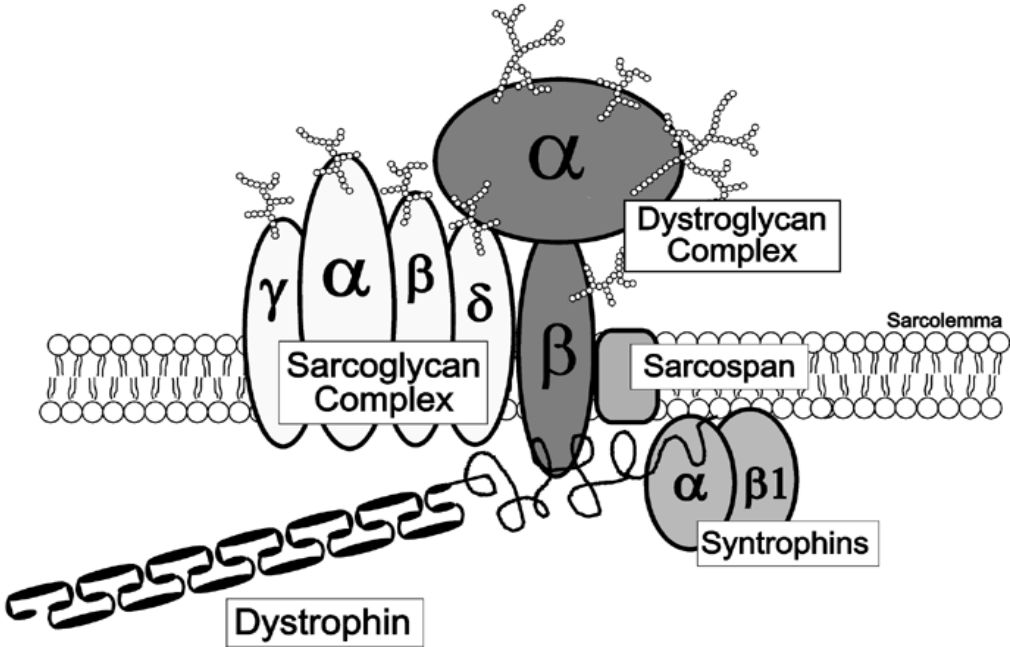
DMD

- *Xp21*
- *Lack of Dystrophin = sarcolemmal membrane instability*
- *Muscle Breakdown*



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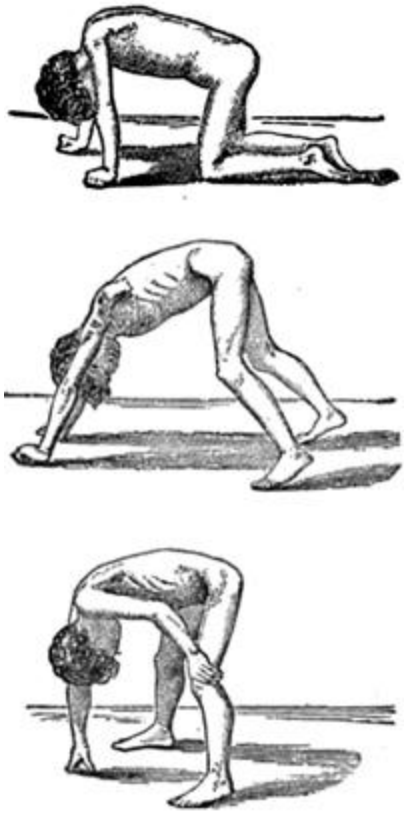
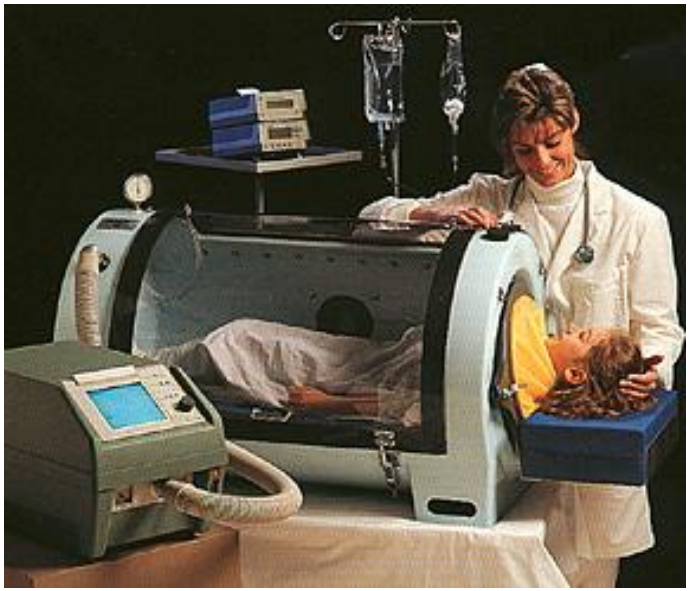
The Story





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- *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)*

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(reverse) 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*

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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)*

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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*

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Another Board Question

- *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*

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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*

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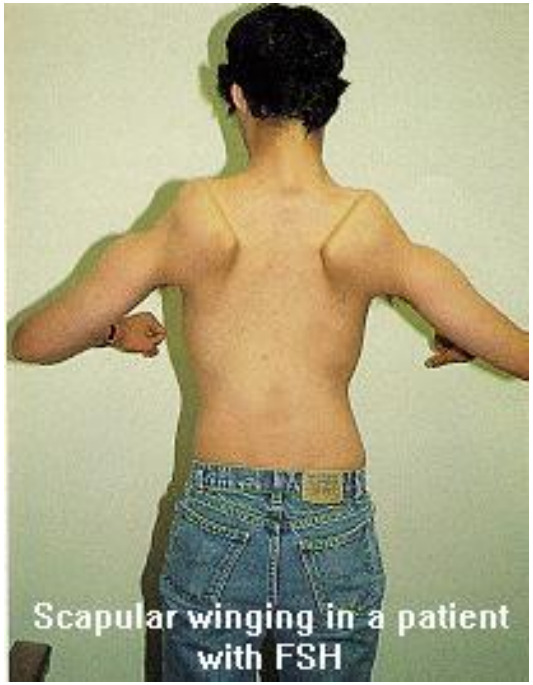
FSH MD



- *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)*

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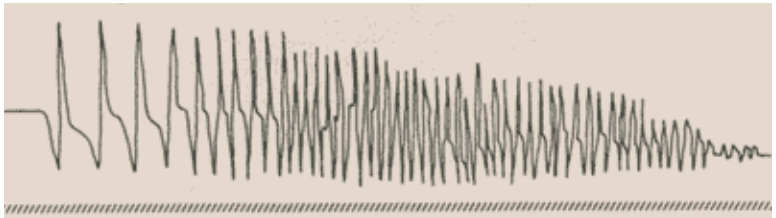
MYOTONIC DYSTROPHY

- *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*



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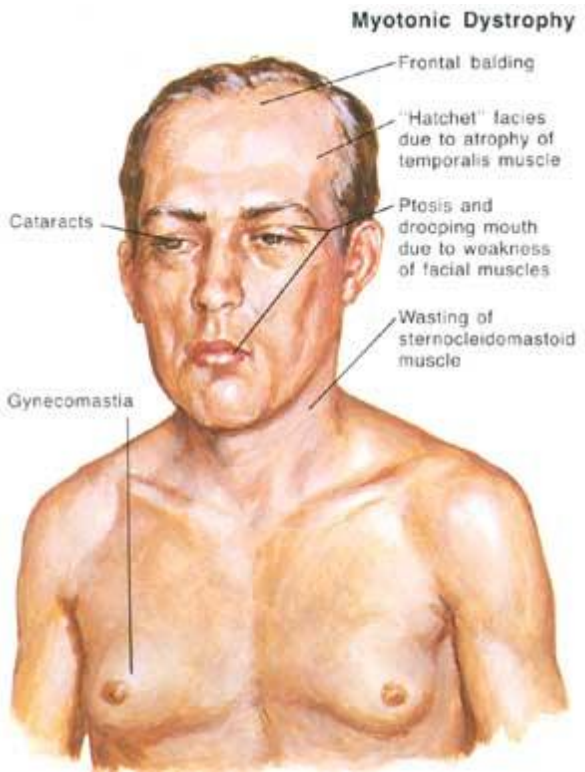
MYOTONIC DYSTROPHY

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



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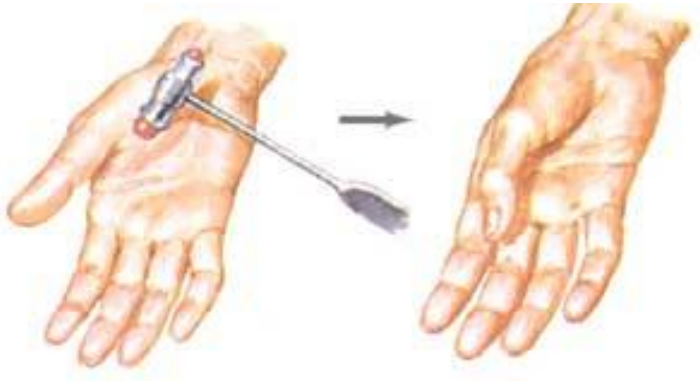
Myotonia

- *Delayed relaxation or Sustained Contraction of Skeletal Muscles*
- *Worsens with cold, stress*
- *Grip myotonia*
- *Percussion myotonia*



- *Difficulty releasing objects*

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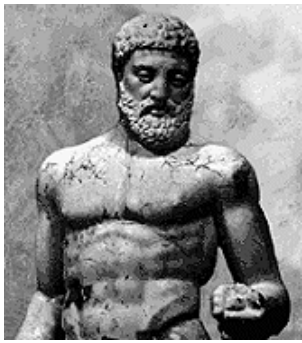
Other Forms



Myotonia Congenita (autosomal dominant)

- *Herculean appearence*
- *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*

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Care of the Child with Neuromuscular Disease

- *Help Identify the Condition*
- *Optimize Function*
- *Prevent Secondary Complications*
- *Provide Appropriate Resources*

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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*

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History

- *Prenatal*
- *After delivery*
- *Developmental milestones*

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Clinical History

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

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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?*

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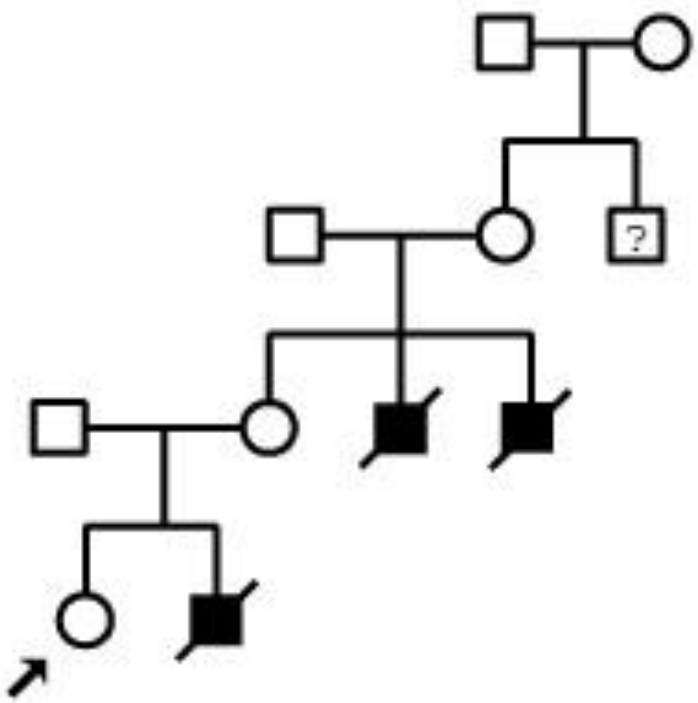
Family History

- *Detailed*
  - ✓*Autosomal dominant*
  - ✓*Autosomal Recessive*
  - ✓*X-linked Dominant*
  - ✓*X-linked Recessive*



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Rigorous History before Anesthesia

- *MALIGNANT HYPERTHERMIA*
  - ✓*Central core myopathy*
  - ✓*DMD*
  - ✓*BMD*
  - ✓*Also*
    - *LGMD*
    - *FSHMD*

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Physical Exam

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

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Functional Exam

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

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Functional Exam

- *Difficulty whistling*
- *Scapular Winging*
- *Gower's sign*
- *Gait exam*
  - ✓*Lordosis, Trendelenburg, Toe walking*
  - ✓*Foot slap, circumduction, hip hike*

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Optimize Function and Prevent Secondary Conditions

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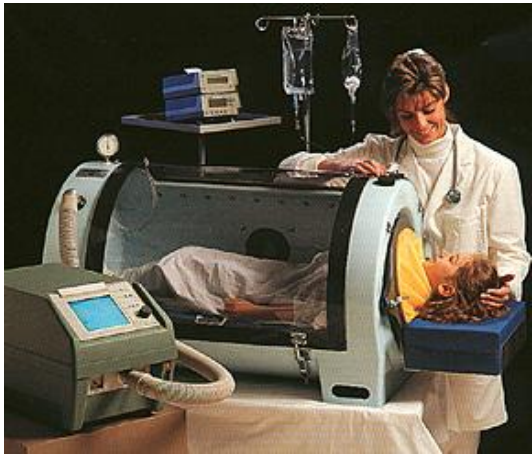
Challenges to Address

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



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Treatment Plan

- *Exercise?*
- *Manage Contractures*
- *Braces*
- *Wheelchairs*
- *Adaptive Equipment*
- *Spinal Arthrodesis*
- *Positive and Negative Pressure Ventilation*

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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*

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Resources

- *Muscular Dystrophy Association*
  http://www.mdausa.org
- *Muscular Dystrophy Family Association*
  http://www.mdff.org
- *Families of Spinal Muscular Atrophy*
  http://www.fsma.org

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Clinics

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Questions / Discussion