Disorders of Muscle

- Cardinal symptom of diseases of the muscle fiber and neuromuscular junction is weakness
  - Other symptoms
    - Pathologic fatigability
    - Muscular aches and pains
    - Cramping

Muscle Groups Involved in Myopathy

Needle Examination of EMG

Muscle Biopsy

History

- Age of onset
- Onset and tempo
- Distribution of weakness
- Tempo of progression
- Family history
Laboratory Investigations
- Creatine kinase
- Lactic dehydrogenase
- Aldolase

Electrodiagnostic Studies: Needle Exam
- Provides information about the motor unit and muscle
  - Needle is inserted into the muscle and the electrical activity and wave forms of the potentials produced by the muscle at rest and during volitional contraction is recorded

Needle Examination
- Presence of abnormal electrical activity at rest (fibrillations, positive waves, fasciculations) may be seen in many neuropathic disorders
- Fibrillations and positive waves may also be seen in myopathies
- Bizarre, repetitive discharges or myotonic discharges imply muscle membrane instability

Electrodiagnostic Studies: Needle Exam
- Decreased recruitment with volitional activity implies neuropathic disease
- Rapidly firing, large units are also seen in neuromopathies that are chronic
- Rapid recruitment of low complex units suggest myopathic disorders

Disorders of the Muscle Fiber: Myopathies
- Huge spectrum of diseases
- One way classify
  - Muscular dystrophies
  - Inflammatory myopathies
  - Metabolic myopathies
  - Congenital myopathies
Muscle Diseases

Inflammatory Myopathies

- Treatable
- Proximal weakness
  - myalgia
  - occasional arthralgia
  - dysphagia
  - occasional respiratory compromise
- Sporadic, non-familial
- Proximal weakness

Inflammatory Myopathies

- Some patients show signs of skin inflammation
  - rash
- Diagnosis made by:
  - clinical picture
  - elevation of muscle enzymes
  - EMG
  - muscle biopsy
    - foci of inflammation and occasional perivascular inflammation

Inflammatory Myopathies

- Idiopathic polymyositis
- Idiopathic dermatomyositis
  - with skin rash
- Childhood dermatomyositis
  - systemic vasculitis
- Dermatomyositis of adults associated with malignancy
- Polymyositis-dermatomyositis with associated connective tissue disease
- Inclusion body myositis

Polymyositis

- Pathophysiology
  - T-cell mediated muscle injury
  - secondary Ab formation (Jo-1, Mi-2, SRP)
- Clinical Diagnostic Findings
  - symmetric proximal muscle weakness with pain
  - elevated plasma muscle enzymes
  - myopathic changes on electromyography
  - characteristic muscle biopsy abnormalities and the absence of histopathic signs of other myopathies
Polymyositis

- Dermatomyositis
  - Gottron’s papules and heliotrope eyelids
  - humorally mediated vasculitis
  - adult form associated with malignancy
- Therapy
  - steroids
  - cytotoxics
  - plasmapheresis
  - IVIG

Inflammatory Myopathy

- Dermatomyositis
  - unknown cause - likely multifactorial
  - viral connections - coxsackie is main suspect
  - genetic predisposition - HLA-B8/DR3
  - rare before age of 2
    - average onset 8-9 years
  - girls more often affected than boys with a ratio of 3:2

Dermatomyositis

- Clinical findings
  - weakness generally seen first in proximal muscles of extremities and trunk
  - often with a positive Gower’s sign
  - affected muscles are often stiff, indurated, and tender
  - heliotrope rash
    - violaceous in butterfly distribution

Dermatomyositis

Gottron’s papules

Heliotrope eyelids

Myopathy Associated with Statin Therapy

- Myalgia
  - muscle aches, soreness, or weakness
- Myopathy
  - abnormal condition of the muscular tissues characterized by myalgia and CK levels >10,000 U/L
Myopathy Associated with Statin Therapy

- Rhabdomyolysis
  - acute, potentially fatal disease of skeletal muscle
  - entails destruction of skeletal muscle
  - evidenced by myoglobinemia and myoglobinuria
- Risk factors
  - combination lipid lowering therapy
  - CYP 450 mediated drug-drug interactions

Muscular Dystrophies

- Heterogeneous group of muscle disorders
  - progressive muscle weakness, wasting
  - definable pattern of inheritance
  - primary involvement of skeletal muscle

Muscular Dystrophies

- Duchenne’s muscular dystrophy
  - most common and severe of the muscular dystrophies
  - x-linked recessive inheritance
  - unaffected mothers give birth to boys who are normal at birth
  - by age 4 to 6 weakness and pseudohypertrophy evident
  - loss of ambulation by early teens
  - death usually before age 20 of cardiopulmonary complications
  - gene mutation at Xp-21
    - short arm of the X chromosome
    - genetic mutations result in lack of protein Dystrophin

Gower’s Maneuver

Duchenne’s Dystrophy
Muscular Dystrophies

- Myotonias
  - muscle membrane disorders share phenomenon of myotonia or delay in muscle relaxation in response to volitional contraction, muscle percussion, or electrical stimulation of nerve or muscle
  - dive bomber sound on EMG
  - myotonic dystrophy is most common

Muscular Dystrophies

- Myotonic dystrophy
  - systemic disease
  - autosomal dominant presenting with distal weakness and atrophy in the teens or early adulthood
  - cataracts, baldness, endocrine and immunologic disturbances occur
  - cardiac conduction defects occur

Myotonias

- Myotonia
  - delay in muscle relaxation in response to volitional contraction, muscle percussion or electrical stimulation
  - needle EMG dive bomber

Myotonic Dystrophy

- Myotonic dystrophy most common
  - autosomal dominant
  - distal weakness and atrophy presenting in teens
  - cardiac conduction defects occur, cataracts
  - due to trinucleotide expansion on chromosome 19
Myotonia

Becker’s Muscular Dystrophy
- Same locus as Duchenne but a much milder, more protracted course
- Usually remain ambulatory until late adolescence
- Death often postponed until the late 20’s

Metabolic Myopathies
- Muscle weakness and fatigability may be presenting complaint in patients with:
  - hyper- or hypothyroidism
  - hyper- or hypoparathyroidism
  - hyper- or hypoadrenocortical dysfunction

Metabolic Myopathies
- Electrolyte imbalance especially hypokalemia and hyperkalemia may be associated with acute or subacute weakness
- Dyskalemic paralysis may occur as autosomal dominant “periodic paralysis syndromes”

Metabolic Myopathies
- patients are subject to recurrent episodes of weakness often provoked by exercise, high carbohydrate intake, especially the hypokalemic form, or high sodium intake
  - most common form is iatrogenic hypokalemia due to:
    - diuretic therapy
    - chronic laxative abuse
    - other forms which induce potassium wasting
Disorders of Energy Metabolism

- In resting state
  - muscles rely on beta oxidation of fatty acids as its main fuel source
  - during periods of brief intense exercise: muscles shift to anaerobic metabolism of glycogen
  - with more prolonged exercise, system reverts back to beta oxidation of fatty acids

Myophosphorylase deficiency:
- McArdle disease
  - characterized by myalgias, cramps and myoglobinuria in response to brief intense exercise

Acid maltase disease:
- Pompe’s disease
  - rapidly progressive hypotonic weakness with cardiomegaly, and hepatomegaly in infancy

Disorders of Energy Metabolism

- Carnitine deficiency:
  - may present as a skeletal muscle disorder which mimics early onset limb girdle muscular dystrophy
    - systemic form affects muscle and liver
  - Carnitine palmitoyl transferase deficiency (CPT):
    - this enzyme is necessary to carry carnitine-fatty acid moiety into the mitochondria of muscle for beta oxidation
    - sustained moderate to intense physical activity results in cramps and myoglobinuria

Congenital Myopathies

- Rare
- Inherited diseases
- Identified by muscle biopsy
- Usually apparent shortly after birth
- Examples:
  - central core disease
  - nemaline myopathy
  - congenital fiber type disproportion

Malignant Hyperthermia

- Usually without clinical expression unless patient is exposed to certain anesthetic agents such as succinylcholine or halogenated anesthetics
- When exposed:
  - muscular rigidity
  - hypercarbia
  - lactic acidosis
  - hyperthermia
- Medical emergency due to inability of sarcoplasmic reticulum to re-uptake calcium ions
- Autosomal dominant

Take Home Messages

- Symptoms of neuromuscular disease:
  - weakness
  - fatigue
  - sometimes pain
  - myoglobinuria
- Laboratory investigations of neuromuscular disorders
  - creatine kinase determination
  - electromyography (EMG)
  - muscle and or nerve biopsy where indicated
  - genetic testing to define some metabolic myopathies and muscular dystrophies
Take Home Messages

• Inflammatory myopathies may be treatable
• Iatrogenic and toxic myopathies may be treatable
• Adults with dermatomyositis need careful evaluation for an associated carcinoma or connective tissue disease

Take Home Messages

• Metabolic myopathies include disorders of glycogen, lipid and mitochondrial metabolism
• Congenital myopathies are defined by clinical, genetic and morphological abnormalities and muscle biopsy
• Malignant hyperthermia is multifactorial due to defective Ca++ re-uptake by the sarcoplasmic reticulum
  – dangerous or fatal reactions may occur

Take Home Messages

• Muscular dystrophies are genetic disorders
  – X-linked
    • Duchenne – Becker muscular dystrophy
      – Xp-21 = Dystrophin
  – Autosomal dominant
    • myotonic dystrophy 19.13.3
      – unstable DNA
    – facioscapulohumeral chromosome 4
    – some forms of Limb girdle dystrophy
    – oculopharyngeal muscular dystrophy
  – Autosomal recessive
    • most limb girdle muscular dystrophies