1. Musculoskeletal System and Integument

Musculoskeletal System and Integument

Basic Human Pathology II, 2008

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2. Skeletal Muscle Diseases

Skeletal Muscle Diseases

• **Skeletal muscle**
  - Histological diagnosis based on evaluation of combination of different types of pathological responses

• **2 main groups**
  - Dystrophic and myopathic
    • Hypertrophy and atrophy of fibers
    • Solitary fiber degeneration, necrosis, phagocytosis
    • Variable fibrosis
  - Neurogenic
    • Atrophy of fibers
    • Groups of fibers with compensatory hypertrophy
    • Fiber type grouping is often seen

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3. Degenerative Skeletal Muscle Diseases - Overview

Degenerative Skeletal Muscle Diseases - Overview

- 3 Groups - weakness, wasting or pain
  - Muscular dystrophies
    - Inherited
    - Result in progressive degeneration
    - Classification – inheritance pattern, clinical pattern of muscle groups, molecular genetic techniques
  - Myopathies
    - Diverse etiologies; 4 main subgroups
      - Inflammatory – primary; very common; treatable
      - Secondary – systemic disease; common; treatable often
      - Metabolic – major impact on function; uncommon
      - Congenital – nonprogressive; rare
    - Neurogenic disease
      - Peripheral nerve and motor neurons - - > atrophy of muscle

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4. Muscular Dystrophies

Muscular Dystrophies

- Genetically determined, progressive degenerative diseases of muscle with profound wasting and weakness
- Destruction of single muscle cells over a prolonged period of time with fiber regeneration and the development of fibrosis
- Increased serum activities of creatine kinase from degenerating muscle fibers
- Biopsy is nonspecific degenerative changes
- Classification – according to muscle group involved, inheritance and age of onset
  - Duchenne
    - Becker type: Limb girdle
    - Fascioscapulohumeral; Scapulohumeral
    - Oculopharyngeal; Myotonic dystrophy

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5. Duchenne Dystrophy

Duchenne Dystrophy

- Most common and severe (skeletal weakness)
- Almost entirely in male children
- Etiology
  - 66% X-linked recessive
  - 33% mutation in gene coding dystrophin protein
    - Helps anchor internal cytoskeleton of muscle fibers through the cell membrane glycoprotein and to the extracellular matrix
    - Lack of dystrophin results in fibers tearing with repeated contraction - - -> free calcium enters muscle cells - - -> cell death and necrosis

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6. Duchenne Dystrophy

Duchenne Dystrophy

- Begins in proximal muscles of extremities - - -> immobilization, wasting, contracture, with death in early teens (pneumonia)
- Cardiac muscle also involved - - -> cardiomyopathy
- Compensatory hypertrophy of distal sites
- Increased serum creatine kinase
- Histology
  - Individual large and small muscle fiber necrosis
  - Phagocytosis of dead fibers
  - Replacement of muscle fibers by fibrofatty tissue
  - Lack or patchy distribution of dystrophin

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7. Duchenne Dystrophy

Duchenne Dystrophy

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Large and small muscle fibers vary considerably in size and shape; interstitial connective tissue increased

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8. Duchenne Dystrophy

Duchenne Dystrophy

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Western blot

Blue = regenerating fibers

Lack of dystrophin in DMD, altered in BMD compared to normal in control

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9. Muscular Dystrophy

Muscular Dystrophy

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Normal uniform distribution of dystrophin

Becker type muscular dystrophy with irregular, weak dystrophin staining

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10. Disorder of Muscle Function

Disorder of Muscle Function

- Myasthenia gravis
  - Effort associated muscle weakness of extremities, extraocular and facial muscles
    - Ptosis, diplopia, difficulty chewing, speaking and/or swallowing
    - Recovery upon rest
  - Autoimmune – lymphocytic aggregates in muscle
    - Antibodies to acetylcholine receptor located in post-synaptic membrane of muscle motor end-plates
    - Prevent synaptic transmission by blocking receptor site

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11. Disorder of Muscle Function

Disorder of Muscle Function

- **Myasthenia gravis (cont’d)**
  - Three times more common in women
  - Diagnosis
    - Therapeutic trial of short acting anticholinesterase drug
      - Increases acetylcholine concentrations in synaptic cleft and allows transmission
  - Treatment
    - Drugs with anticholinesterase
  - Important association
    - 25% of cases have thymoma of thymus gland
    - Some have thymic hyperplasia

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12. Metabolic Bone Disease

Metabolic Bone Disease

- **Osteoporosis**
  - Decrease in bone mass resulting in fragility of bone
    - Decreased amounts of normally formed bone
    - Weight bearing bones such as hips and vertebrae are especially susceptible to fracture
      - Spinal deformities and shortened stature
  - Most commonly occurs in postmenopausal women
  - Primary causes
    - Estrogen deficiency; low density of original bone; lack of exercise
  - Secondary causes
    - Immobilization
    - Endocrinopathies
    - Malnutrition (deficiency of calcium, Vit. D, Vit. C and protein)

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13. Osteoporosis

Osteoporosis

- All bones are affected
- Thinned cortical bone and enlarged medullary cavity
- Generalized radiolucencies of bone (osteopenia)
- Pain without obvious trauma
- Laboratory findings
  - Normal serum calcium, phosphorous, and alkaline phosphatase
- Histology
  - Normal bone with normal ratio of mineral to organic bony elements

14. Osteoporosis

Osteoporosis

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Normal    Osteoporosis

Normal bone; osteoporotic bone with thinning and wide separation of trabeculae

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15. Osteoporosis

**Osteoporosis**

Thin, widely separated trabeculae

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16. Osteoporosis

**Osteoporosis**

Compression fractures of the vertebrae

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17. Metabolic Bone Diseases

Metabolic Bone Diseases

- Osteomalacia and Rickets
  - Disorders of osteoid mineralization
    - Normal amount of osteoid but not calcified properly
    - When secondary to renal disease called renal osteodystrophy
  - Etiology
    - Both caused by Vitamin D deficiency
      - Chronic renal insufficiency
      - Internal malabsorption
      - Dietary deficiency

18. Metabolic Bone Diseases

Metabolic Bone Diseases

- Rickets
  - Occurs in children prior to closure of the epiphyseal growth plates
  - Decreased calcification and excess accumulation of osteoid -> increased thickness of epiphyseal growth plates and other skeletal deformities
  - Craniotabes
    - Thinning, softening of occipital and parietal bones
  - Late closing of fontanelles
  - Bowing of legs
19. **Metabolic Bone Diseases**

**Metabolic Bone Diseases**

- **Rickets (cont’d)**
  - Harrison groove
    - Depression along line of insertion of the diaphragm into the rib cage
  - Fractures
  - Pigeon breast
    - Caused by protrusion of the sternum
  - Decreased height
    - Caused by spinal deformity
  - Rachitic rosary
    - Swelling at the osteochondral junction of ribs
      - - > deformity of chest wall like a “string of beads”

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20. **Rickets**

**Rickets**

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**Rachitic rosary**

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21. Rickets

Rickets

- Overgrowth of inadequately mineralized epiphyseal cartilage
- Persistence of distorted, irregular masses of cartilage
- Disruption of orderly replacement of cartilage by osteoid matrix with enlargement and lateral expansion

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22. Osteomalacia and Rickets

Osteomalacia and Rickets

- Osteomalacia
  - Adults, after closure of epiphyseal plates
  - Impaired mineralization of osteoid matrix \( \rightarrow \) fractures and bending of bones and widening of osteoid seams (the most characteristic feature)
  - Laboratory tests
    - Low serum calcium and phosphorous
    - High alkaline phosphatase
  - Radiographs
    - Diffuse lucencies of bone

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23. Osteomalacia

Osteomalacia

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24. Congenital Bone Disease

Congenital Bone Disease

- Achondroplasia
  - One of the most common causes of dwarfism
  - Autosomal dominant
  - Abnormal cartilage synthesis → narrow epiphyseal plates and bony sealing off of the area between plate and metaphysis → short, thick bones
  - Short limbs with normal-sized head and trunk
  - Spares cranium and vertebral bones
  - Frontal bossing and saddle nose
Bone Tumors

25. Osteochondroma
   - Bone covered by a cap of cartilage projecting from the surface of the bone
   - Most common benign tumor of bone
   - > Men less than 25 years of age
   - Rarely undergoes transition to chondrosarcoma when solitary
   ⨂ May be seen in Gardner syndrome
     ⨂ Often first diagnosed by a dentist based on panoramic radiographic appearance

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Bone Tumors

26. Osteochondromatosis
   - Hereditary disorder
   ⨂ Formation of multiple exostoses with misdirected growth of growth plate
     ⨂ Bony metaphyseal projections capped with cartilage
     ⨂ Often symmetric and originate from epiphyseal cartilage
   - Asymptomatic or produce deformity and compromise blood supply
   - More often may undergo transition to chondrosarcoma

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27. Osteochondromatosis

Osteochondromatosis

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Cartilaginous cap

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28. Osteochondromatosis

Osteochondromatosis

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Cartilaginous cap

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29. Bone Tumors

Bone Tumors

- **Enchondromatosis (Ollier’s disease)**
  - Nonhereditary syndrome
  - Multiple cartilaginous masses within the medullary cavity of bone
    - Especially hands and feet
    - Pain and fractures
  - May undergo malignant transformation to chondrosarcoma
  - Maffucci’s syndrome
    - Familial association
    - Enchondromas
    - Hemangiomas of skin

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30. Enchondromatosis (Ollier’s Disease)

Enchondromatosis (Ollier’s Disease)

Cartilage encased within bone

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31. Arthritides of Metabolic Origin

**Arthritides of Metabolic Origin**

- **Gout**
  - Hyperuricemia associated with recurrent bouts of acute painful arthritis resulting from monosodium urate crystals deposited in joint tissues
    - Types
      - Primary (90%)
        - Inborn error of purine metabolism
          » Only 10% a known defect
        - Some familial; middle-aged men
      - Secondary (10%)
        - Hyperuricemia resulting from disorders unrelated to purine metabolism (e.g., leukemia and polycythemia - - - - > excessive cell breakdown)

32. Arthritides of Metabolic Origin

**Arthritides of Metabolic Origin**

- **Gout**
  - Most cases are in men; occasionally post-menopausal women
    - Often precipitated by large meal or alcohol intake which may lead to hyperuricemia
  - Hyperuricemia
    - Underexcretion of uric acid (90%) or overproduction of uric acid (10%)
      - Asymptomatic hyperuricemia - - - - > acute episodes of joint pain and swelling - - - - > ~10 years later - - - - > chronic, decreased range of motion and joint deformities
      - Uric acid kidney stones in ~ 25% of patients
33. Arthritides of Metabolic Origin

Arthritides of Metabolic Origin

- **Gout**
  - Precipitation of urate crystals in joint fluid causes the acute inflammatory synovitis with edema and WBC infiltrate
  - Affects lower extremity joints, esp. large toe
  - Tophus (tophi)
    - Pathognomonic – monosodium urate crystal deposits in a protein matrix surrounded by inflammatory cells in fibrous connective tissue
    - Form in helix of ear, bursae, ligaments, Achilles tendon, and kidney (urate nephropathy)

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34. Muskuloskeletal System: Slide 34

Gout

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35. Gout

Gout

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36. Gout

Gout

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Gouty tophus (above) with crystals seen following light polarization (right)

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37. **Skin – Superficial Fungal Infections**

- May be caused by
  - Trichophyton spp.,
  - Microsporum spp., and
  - Malassezia spp.
- Confined to the epidermis
  - Tinea capitis
    - Scalp in children
  - Tinea corporis (“ring worm”)
    - Trunk and extremities of children
- Tinea versicolor
  - Hypo- or hyper-pigmented macules
- Tinea pedis (“athlete’s foot”)
- Tinea curis (“jock itch”)
- Tinea unguium (onychomycosis)
  - Thickening and discoloration of the nail bed

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38. **Normal Skin**

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39. Tineas

Tineas

H & E stain

PAS stain

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40. Tineas

Tineas

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PAS stain

Potassium hydroxide preparation

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41. Tinea Capitis

Tinea Capitis

42. Tinea Corporis

Tinea Corporis
43. Tinea Versicolor

Tinea Versicolor

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44. Tinea Pedis (“Athlete’s Foot”)

Tinea Pedis (“Athlete’s Foot”)

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45. Skin – Miscellaneous Infectious Disease

Skin – Miscellaneous Infectious Disease

- **Scalded skin syndrome**
  - Pediatric condition
  - Caused by exfoliative toxin produced by *Staph. aureus*
    - Toxin splits epidermis at level of stratum granulosum - - - -> global denudation

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46. Scalded Skin Syndrome

Scalded Skin Syndrome

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47. Skin – Hypersensitivity Reactions

Skin – Hypersensitivity Reactions

- Urticaria ("hives")
  - Transient, raised, pruritic, pink wheals with dermal edema
- Eczema
  - Class of very common, pruritic skin disorders
  - Atopic dermatitis
    - Variable, unknown etiology
    - Usually family history of atopy (allergy)

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48. Skin - Hypersensitivity Reactions

Skin - Hypersensitivity Reactions

Eczema pathologic types

- Acute eczema (contact dermatitis)
  - Edematous, oozing red plaques often with vesicles and dermal inflammation
- Subacute eczema (childhood atopic dermatitis)
  - Moist red papules and plaques with epithelial hyperplasia and dermal inflammation
- Chronic eczema
  - Dry scaly plaques present for months

- Treatment
  - Moisturizers to control itching
  - Oral antihistamine and topical steroid

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49. **Urticaria**

![Image of Urticaria](image)

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50. **Acute Eczema (Contact Dermatitis)**

![Image of Acute Eczema](image)

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Balsam of Peru  Shoe glue

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51. **Subacute Eczema (Childhood Atopic Dermatitis)**

![Image of Subacute Eczema](image)

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52. **Skin - Inflammatory Conditions**

- **Pityriasis rosea**
  - Common in ages 10-40 years old
  - Possible viral etiology
  - **Herald patch**
    - 4 cm red, scaling patch followed within days by eruption in a "turtle neck-short sleeve" distribution
  - Small, pink, oval patches along flexural lines (fur tree pattern), appearing in crops
  - Usually self-limited
    - 1-4 months

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53. **Pityriasis Rosea**

![Pityriasis Rosea Image](image)

*Herald patch*

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