1. Introduction to the Rheumatic Diseases and Joint Physiology...

Introduction to the Rheumatic diseases and Joint physiology

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2. Welcome to musculoskeletal pathophysiology!

Welcome to musculoskeletal pathophysiology!

• Two major themes
  - Disorders of the musculoskeletal system
  - Autoimmune diseases: immunology, pathophysiology and clinical manifestations

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3. What is Rheumatology?

**What is Rheumatology?**

1. **Structural disorders** of the musculoskeletal system 
   *not due to direct trauma*
   - **Anatomy:**
     - Joints – e.g.: osteoarthritis
     - Periarticular structures – tendons, bursas, ligaments
   - **Etiology:** degenerative or related to repeated use

2. **Immune system disorders** leading to autoimmune disease
   - An autoimmune disease is considered “rheumatologic” when involvement is either
     1. predominantly or exclusively of the joints
     2. of more than a single organ system
        - Lupus – rheumatologic
        - primary autoimmune hemolytic anemia – not rheumatologic

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4. What is Rheumatology?

**What is Rheumatology?**

3) Chronic Pain disorders – a subset of these are characterized by musculoskeletal pain though there is no pathology on pathologic examination:

    eg: fibromyalgia – a syndrome of chronic pain and fatigue

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5. Course Lectures and Topics

Course Lectures and Topics

- Chronic Arthritis – Rheumatoid arthritis
- Chronic Arthritis – Spondyloarthropathy and Lyme Arthritis
- Osteoarthritis
- Nonarticular Rheumatism
- Pediatric Rheumatic Diseases
- Crystal Arthritis

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6. Course Lectures and Topics

Course Lectures and Topics

- Connective Tissue Diseases
  - Systemic Lupus Erythematosus
  - Scleroderma
- Vasculitis

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Key Concepts in Musculoskeletal Pathophysiology Course

- What is the primary anatomic structure targeted by the disease process?
  - RA, Juvenile arthritis, Lyme arthritis - Synovial tissue
  - Spondyloarthopathies - Entheses (tendon or ligament insertion into bone)
  - Osteoarthritis - Cartilage
  - Lupus – multiple sites of inflammation
  - Scleroderma – vascular system, fibrosis of skin and other organs, inflammation (autoimmunity) in multiple tissues
  - Vasculitis – blood vessel walls

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Key Concepts

- Genetic Influences
- Mechanism of Immune system dysfunction
- Immune system-environmental interaction
- Clinical applications

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9. Classification of Joints

Classification of Joints

- Synarthrodial joints
  - Juncure of the cranial plates
- Amphiarthrodial (fibrocartilagenous) joints
  - Costosternal joints
- Diarthrodial joints
  - Nearly all familiar moveable joints

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10. Articular cartilage

Articular cartilage

**Composed of**
- Chondrocytes
- Extracellular Matrix
  - Type II collagen meshwork with hydrated proteoglycans
  - Small amount of type IX and XI collagen

**Articular cartilage is**
- avascular
- aneural

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11. Synovium

Synovium

- Lines diarthrodial joints (all parts except articular cartilage), some tendons, bursae
- Composition
  - Matrix layer
    - Thin, loosely constructed and varied by site
    - Features numerous microfibrils and proteoglycans
    - Hyaluronan a major component and filter of protein
  - Synovial cells – simplified:
    - Type A (macrophage-like)
    - Type B (fibroblast-like)

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12. Joint capsule

Joint capsule

- Mainly type I collagen
- Some thin fibrillar type III
- Innervated by mechanoreceptors and free nerve terminals

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13. Physiology – synovial transport

Physiology – synovial transport

- Pathway: synovial capillary → synovial interstitium → synovial fluid → hyaline cartilage
- Features include:
  - Capillaries are fenestrated (small solutes, water)
  - **Glucose** has transport system **into** joint
  - Proteins enter inversely proportional to size
    - Thus albumin > globulin in joint fluid (healthy joint)
    - Hyaluronan plays major filter role for large proteins

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14. Synovial fluid

**Synovial fluid**

- Transudate of plasma
- Hyaluronan: a glycosaminoglycan that is a major matrix element of synovial fluid (made by type B synovial cells)
  - High viscosity
- Cellular content low
  - WBC < 200 cells/mm³

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15. Joint lubrication

**Joint lubrication**

**Lubrication mechanisms**
- **Boundary lubrication** –
  - lubrication at contact points of cartilage on cartilage
  - The glycoprotein lubrican the major element
- **Hydrodynamic lubrication**
  - Lubrication where film of fluid remains between cartilage layers

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16. The diseased joint

**The diseased joint**

**Categorization:**
- By initiating mechanism: mechanical vs. inflammatory
- By synovial fluid white cell count:
  - WBC<2,000 – noninflammatory
  - WBC>2,000 - inflammatory

The above two categorizations are usually but not always in accord. The latter is the more true pathogenic differentiator

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17. The diseased joint – gross pathology in acute inflammation

The diseased joint – gross pathology in acute inflammation

- Must differentiate clinically from involvement of skin, veins and periarticular structures (tendons, ligaments, bursae)

- Joint takes position of least intrasynovial pressure

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18. Physiology of acute joint inflammation

Physiology of acute joint inflammation

- Vasodilatation
- Edema
- Neutrophilic infiltration
- Depolymerization of hyaluronic acid
  - Reactive oxygen species do this
  - Loss of viscosity in joint results
- Synovial fluid volume increases massively
- Synovial ischemia

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19. Transfer of solutes in the acutely inflamed joint

Transfer of solutes in the acutely inflamed joint

Contrasting effects on protein and glucose

- Protein – the normal structural and cellular blocks to diffusion are disrupted
- Glucose
  - Transport system from capillary into joint fails
  - Consumption is increased
    - Increase in anaerobic metabolism (glycolysis turned on)
    - Increased cell mass devouring glucose

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20. Clinical implications of acute synovitis

Clinical implications of acute synovitis

Joint damage varies:
- Bacterial arthritis – rapid cartilage loss
- Crystal arthritis – attacks are severe but self-limited so damage slow over time
- Rheumatoid arthritis – Synovial tissue turns from Jimmy Buffet gentle tropical to "Katrina-like" destructive pannus and gradually erodes cartilage and bone
- Lupus – Immune complex deposition in synovium does not elicit destructive synovitis

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21. Mechanism of joint damage in acute arthritis

Mechanism of joint damage in acute arthritis

- Reactive oxygen species released by neutrophils are damaging
  - Hyaluronan depolymerized
- Proteolytic enzymes are released
- Prostaglandins and leukotrienes

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22. Synovial fluid analysis

Synovial fluid analysis

- WBC cells – very useful in diagnosis
- Crystal content
  - Gout (monosodium urate)
  - Pseudogout (calcium pyrophosphate)
- Glucose
  - low in infection, rheumatoid arthritis
- Culture

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23. Synovial fluid analysis

Synovial fluid analysis

<table>
<thead>
<tr>
<th>Arthritis Type</th>
<th>White Cell Count</th>
<th>Crystal analysis</th>
<th>Glucose</th>
<th>Culture/Gram Stain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Septic Arthritis</td>
<td>&gt;100,000</td>
<td>none</td>
<td>low</td>
<td>protein/positive</td>
</tr>
<tr>
<td>Inflammatory Arthritis</td>
<td>&gt;10,000</td>
<td>none</td>
<td>low</td>
<td>none</td>
</tr>
<tr>
<td>R.A.</td>
<td>&gt;1,000</td>
<td>none</td>
<td>low</td>
<td>none</td>
</tr>
<tr>
<td>Osteoarthritis</td>
<td>&lt;1,000</td>
<td>none</td>
<td>normal</td>
<td>none</td>
</tr>
<tr>
<td>Lyme</td>
<td>&lt;2,000</td>
<td>none</td>
<td>normal</td>
<td>none</td>
</tr>
<tr>
<td>Lupus</td>
<td>&lt;5,000</td>
<td>none</td>
<td>normal</td>
<td>none</td>
</tr>
<tr>
<td>Psoriatic Arthritis</td>
<td>&gt;2,000</td>
<td>positively birefringent</td>
<td>normal</td>
<td>none</td>
</tr>
<tr>
<td>Reactive Arthritis</td>
<td>&gt;2,000</td>
<td>negatively birefringent</td>
<td>normal</td>
<td>none</td>
</tr>
</tbody>
</table>

*routine bacteriologic techniques cannot easily detect Borrelia Burgdorferi

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24. Diagnosis and treatment of acute arthritis

Diagnosis and treatment of acute arthritis

- ALWAYS consider bacterial infection
- Use joint aspiration to help diagnose
- Immobilize, then mobilize
- Infection
  - Must be drained effectively
  - Appropriate antibiotics immediately

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