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Session Learning Outcomes

At the end of the session, you should be able to:

- Define Osteoarthritis and discuss its aetiology, pathophysiology, clinical features, investigations and management.
- Describe aetiology, pathophysiology, clinical features, investigations and management of Rheumatoid Arthritis.
- Discuss Seronegative arthritis and describe clinical features, investigations and management of Ankylosing spondylitis, reactive arthritis, and Psoriatic arthropathy.
- Define gout and hyperuricemia. Discuss aetiology, pathophysiology, clinical features, investigations and management of Gout.
Session Plan

- Osteoarthritis
- Inflammatory Joint Disease
  - Rheumatoid arthritis
  - Seronegative Spondarthritis
    - Ankylosing spondylitis
    - Reactive arthritis
    - Psoriatic arthropathy
    - Arthritis associated with IBD
- Gout
Osteoarthritis
Osteoarthritis (OA)

- Definition: OA is characterised by focal loss of articular cartilage, subchondral osteosclerosis, osteophyte formation at the joint margin, and remodelling of joint contour with enlargement of affected joints.

- Risk factors:
  - Constitutional susceptibility
  - Ageing
  - Mechanical factors

Osteoarthritis

**Pathophysiology:**
- Cartilage changes:
  - Severe progressive damage to articular cartilage in a synovial joint
  - Altered balance in synthesis and degradation of cartilage tissue (impaired repair mechanism)
  - Shock absorbent capacity of cartilage decreases
  - Cartilage vulnerable to load bearing injury
  - Fissuring and deep vertical cleft on cartilage, chondrocyte death and severe cartilage loss, decreased cartilage thickness and rough articular surface.
Osteoarthritis

- Pathophysiology:
  - Bone changes:
    → Increase pressure in bone leading to subchondral bone trauma and Attrition of bone
    → Chondral metaplasia
    → New fibrocartilage formation that undergoes endochondral ossification and form osteophytes
    → Osteonecrosis and subchondral cyst formation
  - Other changes:
    → Synovial hyperplasia and inflammation
    → Thickening and contraction of joint capsule
    → Wasting and atrophy of surrounding muscles.
Osteoarthritis

Pathological changes in osteoarthritis seen on radiograph

Osteoarthritis

- Clinical features:
  - Patterns of joint involvement
  - Symptoms and signs of osteoarthritis
  - Generalised OA
  - Knee OA
  - Hip OA
  - Spine OA
  - Early-onset OA

## Osteoarthritis

### Symptoms and signs of osteoarthritis

#### Pain
- Insidious onset over months or years
- Variable or intermittent over time (‘good days, bad days’)
- Mainly related to movement and weight-bearing, relieved by rest
- Only brief (< 15 mins) morning stiffness and brief (< 5 mins) ‘gelling’ after rest
- Usually only one or a few joints painful

#### Clinical signs
- Restricted movement due to capsular thickening, or blocking by osteophyte
- Palpable, sometimes audible, coarse crepitus due to rough articular surfaces
- Bony swelling around joint margins
- Deformity, usually without instability
- Joint-line or periarticular tenderness
- Muscle weakness and wasting
- Synovitis mild or absent
## 25.38 Characteristics of generalised nodal osteoarthritis

- Polyarticular finger interphalangeal joint OA
- Heberden’s (± Bouchard’s) nodes
- Marked female preponderance
- Peak onset in middle age
- Good functional outcome for hands
- Predisposition to OA at other joints, especially knees
- Strong genetic predisposition
Osteoarthritis

Heberden’s nodes and lateral deviation of distal interphalangeal joints, with mild Bouchard’s nodes at the proximal interphalangeal joints.

Marked loss of joint space at all of the distal interphalangeal joints, with osteophyte formation most marked at the first and second DIP joints. The fifth proximal interphalangeal joint also shows loss of joint space with osteophyte formation.

Osteoarthritis

- Clinical features:
  - Knee OA:
    - targets the patello-femoral and medial tibio-femoral compartments
    - Localized discomfort with pain on motion;
    - Limitation of motion: Prolonged walking, rising from a chair, getting in or out of a car, or bending to put on shoes and socks may be difficult.
    - crepitus; joint effusion
    - quadriceps atrophy due to lack of use;
    - Varus or valgus deformity
Osteoarthritis

Typical varus deformity resulting from marked medial tibio-femoral osteoarthritis

Complete loss of joint space affecting the patello-femoral and medial tibio-femoral compartments, and sclerosis of subchondral bone.

Osteoarthritis

- Clinical features:
  - Hip OA:
    - Targets the superior aspect of hip joint
    - Insidious onset of pain, localized to groin region or inner aspect of the thigh; may be referred to buttocks, sciatic region, or knee;
    - Reduced hip motion; leg may be held in external rotation with hip flexed and adducted;
    - Limp or shuffling gait;
    - Difficulty getting in and out of chairs
    - Weakness and wasting of quadriceps and gluteal muscles
Osteoarthritis

X-ray of hip showing changes of osteoarthritis. Note the superior joint space narrowing (N), subchondral sclerosis (S), marginal osteophytes (white arrows) and cysts (C).
Clinical features:

• **Spine OA: Cervical and lumbar spondylosis**
  - Targets the cervical or lumbar spine
  - Pain localised to the low back region or the neck, although radiation of pain to the arms, buttocks and legs may also occur due to nerve root compression
  - Pain is typically relieved by rest and worse on movement
  - Range of movement may be limited and loss of lumbar lordosis
  - Straight leg-raising test may be positive
Osteoarthritis

X-ray of spine showing typical changes of osteoarthritis: Cervical spondylosis showing disc space narrowing between C6 and C7, osteophytes at the anterior vertebral body margins (arrows) and osteosclerosis at the apophyseal joints.

Osteoarthritis

- Clinical features:
  - Early-onset OA:
    - Presentation of typical symptoms and signs of OA at before the age of 45
    - Usually monoarticular with history of previous trauma and localised instability
    - Polyarticular, affecting several joints, especially those not normally targeted by OA
Osteoarthritis

- **Diagnosis:**
  - A plain X-ray of the affected joint
  - MRI
  - Routine biochemistry
  - Haematology
  - Autoantibody tests
  - Synovial fluid analysis
  - Radioisotope bone scans

- **Management:**
  - Weight loss and exercise
  - Analgesics and anti-inflammatory drugs
  - Corticosteroid injections
  - Joint replacement surgery for disabling symptoms.
Osteoarthritis (OA): Focal loss of articular cartilage, subchondral osteosclerosis, osteophyte formation at the joint margin, and remodelling of joint contour with enlargement of affected joints

Constitutional factors: heredity, gender/hormonal status, obesity, high bone mineral density

Ageing

Mechanical factors: Repetitive adverse loading of joints or joint trauma due to: occupation, competitive sports or Congenital abnormalities of the joint

Damage to articular cartilage in a synovial joint

Cartilage changes:
- Fissuring and deep vertical cleft on cartilage
- Chondrocyte death and severe cartilage loss
- Decreased cartilage thickness and rough articular surface

Bone changes:
- Increase pressure in bone leading to subchondral bone trauma and attrition of bone
- Chondral metaplasia
- New fibrocartilage formation that undergoes endochondral ossification- osteophytes formation
- Osteonecrosis and subchondral cyst formation

Other changes:
- Synovial hyperplasia and inflammation
- Thickening and contraction of joint capsule
- Wasting and atrophy of surrounding muscles

Pain related to movement and weight-bearing, relieved by rest
- Restricted movement due to capsular thickening, or blocking by osteophyte
- Palpable, sometimes audible, coarse crepitus due to rough articular surfaces
- Bony swelling around joint margins
- Deformity, usually without instability
- Joint-line or periarticular tenderness
- Muscle weakness and wasting
- Mild synovitis

Diagnosis:
- X-ray
- MRI
- Routine biochemistry
- Haematology
- Autoantibody tests
- Synovial fluid analysis
- Radioisotope bone scans

Management:
- Weight loss and exercise
- Analgesics and anti-inflammatory drugs
- Corticosteroid injections
- Joint replacement surgery
Rheumatoid arthritis
Rheumatoid Arthritis (RA)

- **Definition:** RA is an autoimmune inflammatory joint disease, characterised by persistent cellular activation, autoimmunity and the presence of immune complexes at sites of articular and extra-articular lesions.

- **Aetiology:**
  - **Genetic factors:**
    - HLA-DR4, DR1 and DW15 genes
  - **Environmental factors:**
    - Periodontal, oral and gastrointestinal organisms,
    - Epstein–Barr and cytomegaloviruses
Rheumatoid Arthritis (RA)

Pathophysiology:
- Infiltration of the synovial membrane with lymphocytes, plasma cells, dendritic cells and macrophages.
- Formation of cytokines and autoantibodies, including RF and ACPA.
- Synovial macrophages act on synovial fibroblasts, to promote swelling of the synovial membrane and damage to soft tissues and cartilage.
- Fibroblasts, drive local tissue damage and remodelling.
- Osteoclasts and chondrocytes drives destruction of bone and cartilage respectively.
Rheumatoid Arthritis (RA)

Pathophysiology: (cont.)

- Joint is hypoxic and neoangiogenesis supporting the recruitment of yet more leucocytes to perpetuate the inflammatory process.
- The inflammatory granulation tissue (pannus) is formed and spreads over and under the articular cartilage, which is progressively eroded and destroyed.
- Maturation of osteoclasts in the synovial membrane and in adjacent bone combine to erode bony structures. May lead to fibrous or bony ankylosis.
- Muscles adjacent to inflamed joints atrophy and may be infiltrated with lymphocytes.
Rheumatoid Arthritis (RA)

- Clinical features:
  - Pain, joint swelling and stiffness of small joints of the hands, feet and wrists.
  - Large joint involvement, systemic symptoms and extra-articular features
  - Proximal muscle stiffness
  - Symmetrical swelling of the MCP and PIP joints.
  - Joints are tender on pressure when actively inflamed and have stress pain on passive movement.
  - Rheumatoid nodules at sites of pressure or friction
  - Characteristic deformities may develop with long-standing uncontrolled disease
Rheumatoid Arthritis (RA)

Articular and extra articular features

Grossman, S, Porth, CM 2013, Porth's pathophysiology, Concepts of Altered Health States, 9th edn, Lippincott Williams & Wilkins
Rheumatoid Arthritis (RA)

Patterns of joint involvement

Rheumatoid Arthritis (RA)

- Diagnosis:
  - Clinical criteria
  - ESR and CRP
  - Ultrasound or MRI
  - Rheumatoid factor
  - Anti-citrullinated peptide antibodies

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Rheumatoid Arthritis (RA)

- Management:
  - Patient education
  - Rest, therapeutic exercises
  - Disease-modifying antirheumatic drugs (DMARDs)
  - Nonsteroidal anti-inflammatory drugs (NSAIDs)
  - Corticosteroid drugs
  - Biologic response modifiers
Rheumatoid arthritis (RA): an autoimmune inflammatory joint disease, characterised by persistent cellular activation, autoimmunity and the presence of immune complexes at sites of articular and extra-articular lesions.

Genetic factors: HLA-DR4, DR1 and DW15 genes

Environmental factors: Periodontal, oral and gastrointestinal organisms, Epstein–Barr and cytomegaloviruses

Triggers inflammatory response

Infiltration of synovial membrane with lymphocytes, plasma cells and macrophages

Activation of helper T cells and B cells stimulation

Immunoglobulin production (autoantibodies: RF, Anti CCP etc)

Immune complex formation

Activation of fibroblast, osteoclasts and chondrocytes

Joint is hypoxic and neoangiogenesis

Inflammatory granulation tissue (pannus) is formed

Synovial membrane swelling and damage to soft tissues and cartilage

local tissue damage and remodelling

Destruction of bone and cartilage

Pain, swelling and stiffness of small joints

Joints are tender on pressure

Rheumatoid nodules at sites of pressure or friction

Characteristic deformities of the small joints

Marked synovitis and vasculitis

Extra articular involvement

Diagnosis:

Clinical criteria

ESR and CRP

Ultrasound or MRI

Rheumatoid factor

Anti-citrullinated peptide antibodies

Management:

Patient education

Rest, therapeutic exercises

DMARDs

NSAIDs

Corticosteroid drugs

Biologic response modifiers

Colour Key:

Definition

Aetiology

Pathophysiology

Clinical features

Diagnosis

Management

Complications
Seronegative Spondarthritis
Seronegative Spondarthritis

- Definition: These comprise a group of related inflammatory joint diseases, which show considerable overlap in their clinical features and a shared immunogenetic association with the HLA-B27 antigen.

- Include:
  - Ankylosing spondylitis
  - Reactive arthritis, including Reiter’s syndrome
  - Psoriatic arthritis
  - Arthropathy associated with inflammatory bowel disease (Enteropathic arthritis)
Seronegative Spondarthritis

- **Aetiology:**
  - Genetic factors:
    - HLA-B27
  - Environmental triggers:
    - Varies in the four seronegative arthritis

- **Pathophysiology:**
  Genetic and environmental triggers → inflammatory cytokine release by macrophages and dendritic cells → increased levels of circulating cytokines → activate enthesial or synovial T cells → Inflammatory disease
Seronegative Spondarthritides

<table>
<thead>
<tr>
<th>25.64 Clinical features common to seronegative spondyloarthritis</th>
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<tbody>
<tr>
<td>• Asymmetrical inflammatory oligoarthritis (lower &gt; upper limb)</td>
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<tr>
<td>• Sacroiliitis and inflammatory spondylitis</td>
</tr>
<tr>
<td>• Inflammatory enthesitis</td>
</tr>
<tr>
<td>• Tendency for familial aggregation</td>
</tr>
<tr>
<td>• RF and ACPA negative</td>
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<tr>
<td>• Absence of nodules and other extra-articular features of RA</td>
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<tr>
<td>• Typical overlapping extra-articular features:</td>
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<tr>
<td>Mucosal inflammation: conjunctivitis, buccal ulceration,</td>
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<td>urethritis, prostatitis, bowel ulceration</td>
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<tr>
<td>Pustular skin lesions and nail dystrophy</td>
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<tr>
<td>Anterior uveitis</td>
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<td>Aortic root fibrosis (aortic incompetence, conduction</td>
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<tr>
<td>defects)</td>
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<tr>
<td>Erythema nodosum</td>
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</tbody>
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Ankylosing Spondylitis (AS)

- Definition: AS is characterised by a chronic inflammatory arthritis predominantly affecting the sacroiliac joints and spine, which can progress to bony fusion of the spine.

- Aetiology:
  - Genetic factors:
    - HLA-B27
  - Environmental factors:
    - Klebsiella aerogenes
    - Wider alterations in the human gut microbial environment
Ankylosing Spondylitis (AS)

- Clinical features:
  - Low back pain and early morning stiffness with radiation to the buttocks or posterior thighs.
  - Symptoms are exacerbated by inactivity and relieved by movement.
  - The disease tends to ascend slowly, ultimately involving the whole spine.
  - The spine becomes increasingly rigid as ankylosis occurs.
  - Secondary osteoporosis of the vertebral bodies.
  - Increased risk of vertebral fracture.
  - Extra articular features: Acute anterior uveitis.
Ankylosing Spondylitis (AS)

Grossman, S, Porth, CM 2013, Porth’s pathophysiology, Concepts of Altered Health States, 9th edn, Lippincott Williams & Wilkins
Ankylosing Spondylitis (AS)

- Diagnosis:
  - X-rays
  - MRI
  - ESR and CRP
  - HLA-B27
  - Autoantibodies such as RF, ACPA and ANA

‘Bamboo’ spine of severe late ankylosing spondylitis

Ankylosing Spondylitis (AS)

- Management:
  - Patient education
  - Appropriate physical activity
  - NSAIDs and analgesics
  - Anti-TNF therapy
  - Local corticosteroid injections
  - Oral corticosteroids
  - Surgery
Reactive Arthritis (ReA)

- Definition: ReA is a sterile inflammatory joint disorders that are distant in time and place from the initial inciting infective process. It predominantly affects young men, aged 16–35.

- Aetiology:
  - Genetic factors:
    - HLA-B27
  - Environmental factors:
    - Bacterial dysentery, mainly Salmonella, Shigella, Campylobacter or Yersinia
    - Sexually acquired infection with Chlamydia
Reactive Arthritis (ReA)

- Clinical features:
  - Acute onset, with an inflammatory oligoarthritis
  - Asymmetrical involvement of lower limb joints, such as the knees, ankles, midtarsal and MTP joints
  - Fever and weight loss
  - Achilles tendinitis or plantar fasciitis
  - Low back pain, stiffness and sacroiliitis
- Extra-articular features:
  - Non-specific urethritis
  - Conjunctivitis
  - Circinate balanitis
  - Keratoderma blennorrhagica
  - Nail dystrophy
  - Buccal erosions
Reactive Arthritis (ReA)

- **Diagnosis:**
  - Clinical features
  - Synovial fluid
  - HLA-B27
  - High vaginal swabs
  - Serum agglutinin tests
  - Autoantibodies such as RF, ACPA and ANA
  - X-rays

- **Management:**
  - Rest, oral NSAIDs and analgesics
  - Intra-articular steroids
  - Antibiotics
  - DMARDs
  - Topical, subconjunctival or systemic corticosteroids
Psoriatic Arthropathy

- **Definition:** It is a seronegative inflammatory arthropathy that occurs in 7% of people with psoriasis with features of the spondyloarthropathies or, RA or both coexisting.

- **Aetiology:**
  - Genetic factors:
    - HLA-B27
  - Environmental factors:
    - infectious agents and physical trauma
Psoriatic Arthropathy

- Clinical features:
  - Pain and swelling affecting the joints and entheses
  - Nail changes
  - Rash of psoriasis
  - Conjunctivitis, uveitis
  - Several patterns of joint involvement:
    - Asymmetrical inflammatory oligoarthritis
    - Symmetrical polyarthritis
    - Distal IPJ arthritis
    - Psoriatic spondylitis
    - Arthritis mutilans

Psoriatic Arthropathy

- **Diagnosis:**
  - Clinical features
  - Autoantibodies such as RF, ACPA and ANA
  - ESR and CRP
  - X-rays
  - MRI and ultrasound with power Doppler

- **Management:**
  - NSAIDs and analgesics
  - Intra-articular steroids injections
  - DMARDs
  - Anti-TNF treatment
Enteropathic Arthritis

- **Definition:** An acute inflammatory oligoarthritis that occurs in around 10% of patients with ulcerative colitis and 20% of those with Crohn’s disease.

- **Clinical features:**
  - Predominantly affects the large lower limb joints (knees, ankles, hips) but wrists and small joints of the hands and feet can be involved
  - May also develop sacroiliitis (16%) and AS (6%)
  - Coincides with exacerbations of the underlying bowel disease,
  - Sometimes accompanied by aphthous mouth ulcers, iritis and erythema nodosum.
Gout
Gout

- Definition: Gout is an inflammatory disease caused by deposition of monosodium urate monohydrate crystals in and around synovial joints.

- Pathophysiology:
  High serum uric acid → Formation of monosodium urate crystals that precipitate in the joint → Initiate an inflammatory response.

Gout

- Clinical features:
  - an acute monoarthritis, affects the first MTP joint
  - Other common sites are the ankle, midfoot, knee, small joints of hands, wrist and elbow.
  - rapid onset, reaching maximum severity in 2–6 hours, and often waking up in the early morning severe pain, often described as the ‘worst pain ever’
  - Extreme tenderness, unable to wear a sock or to let bedding rest on the joint
  - Marked swelling with overlying red, shiny skin
  - Self-limiting over 5–14 days, with complete resolution.
  - Formation of irregular firm nodules called tophi
Gout

Podagra. Acute gout causing swelling, erythema and extreme pain and tenderness of the first metatarsophalangeal joint

Tophus with white monosodium urate monohydrate crystals visible beneath the skin
Punched-out erosions are visible (arrows), in association with a destructive arthritis affecting the first metatarsophalangeal joint.
Gout

**Diagnosis:**
- Aspirate from a joint, bursa or tophus
- Synovial fluid analysis
- Renal function, uric acid, glucose and lipid profile
- ESR and CRP
- X-rays

**Management:**
- Oral NSAIDs
- Local ice packs
- Oral colchicine
- Joint aspiration with an intra articular steroid injection
- Oral or intramuscular corticosteroids
- Urate-lowering therapy- Allopurinol
Reading and Resources

- Crowley LV, 2012, *An Introduction to Human Diseases – Pathology and Pathophysiology Correlations*, 9th edn, Jones and Bartlett Learning
Reading and Resources

- Mosby’s dictionary of medicine, nursing and health professions 2013, 9th edn, Elsevier, St. Louis, MO.
- VanMeter, KC & Hubert, RJ 2014, *Gould's pathophysiology for the health professions*, 5th edn, Elsevier, St Louis, MO.
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