Introduction

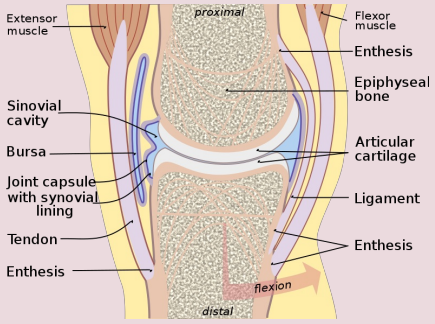
What is pathologic synovial disease?

- Inflammatory
- Infectious
- Degenerative
- Traumatic
- Haemorrhogic
- Neoplastic

=> Leading to irreversible joint destruction

What are arthritides? Inflammation of joints due to infectious, metabolic, or constitutional causes

Synovial joint



Pathophysiology

☐ **Physiology/ function** in abnormal states → specifically the **functional changes** that *accompany* a particular syndrome or disease

☐ It's about disordered function, i.e. there's function but it's abnormal

☐ When you wish to find/define the pathophysiology of a condition it's helpful to ask: **What's not functioning well?**

Mechanisms

☐ Determined by the pathophysiology, i.e. disordered function

☐ They're the **defects** in **systems**, **organs**, **cellular** & **molecules** that constitute the ***triggers*** of specific diseases

☐ They **originate** & **explain** the clinical signs & symptoms

☐ When you wish to find/define the mechanism of disease, it's helpful to ask: **How is the specific *pathophysiology* leading to occurrence of these specific *signs & symptoms*?**

Gout

Signs & symptoms:

- **Acute form:** painful, warm & swollen joint
- **Chronic tophaceous form:** top in tendons, bursae & cartilages

Pathophysiology:

- **Hyperuricaemia** & a ↓ **in urinary excretion of uric acid** → both lead to *deposition* & *crystallisation* of uric acid in joints → followed by an inflammatory response with ***release of enzymes*** in joint space

Mechanism:

- **Deposition** & **crystallisation** occurs in previously traumatised or "-cooler" joints. *Neutrophil disruption* leads to enzyme release & inflammatory cascade

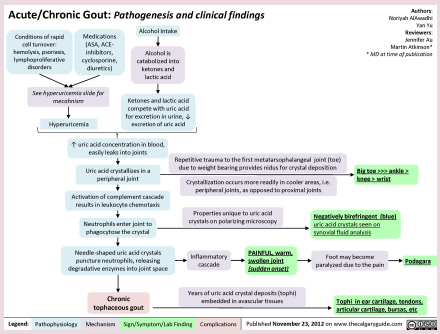
Does the pathophysiology explain/relate to the specific mechanisms of disease, how?

- Yes
- Hyperuricaemia leads to deposition of uric acid
- Previous trauma & location favours crystallisation
- Crystal deposition triggers immune response
- Damage to neutrophils produces the release of enzymes which irritate joints & cause an inflammation, i.e. arthritis

Do the mechanism explain the clinical signs & symptoms, how?

- Yes
- Inflammation causes painful, warm, swollen joints in the acute form
- In chronic tophaceous form: long term deposition of uric acid crystals in avascular tissues cause tophi in tendons, bursae & cartilages

Gout



Rheumatoid Arthritis

Signs & symptoms:

- Poly-articular joint pain, swelling & stiffness
- Most commonly affecting the small joints (wrists, metacarpal-phalangeals)
- Joint involvement is bilaterally symmetrical
- Extra-articular manifestations are often seen

Pathophysiology:

- **Autoimmune activation & proliferation of T-cells** → leading to production of *inflammatory cytokines & B-cells* differentiation into plasma cells → there's an *inflammatory response* which is systemic & *damage of cartilage tissue* in joints

Mechanism:

- The joint damage *recruits* more immune cells into joint spaces
- Immune cells infiltrate synovial membrane causing it to *proliferate & forming* new blood vessels
- Swollen & blood rich synovial (pannus) *invades & enzymatically destroys* joint tissue
- Severe RA will affect the entire body

Does the pathophysiology explain/relate to the specific mechanisms of disease, how?

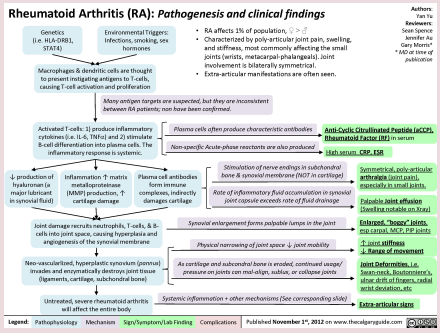
- Yes
- The autoimmune activation of T- & B- cells with consequent inflammation & cartilage damage stimulate nerve endings in subchondraln bone & synovial membrane
- Inflammation of synovial leads to its enlargement with formation of palpable lumps in the affected joints
- Neovascularisation & synovial enlargement cause physical narrowing of joint space & a decrease joint mobility
- Neovascularisation & synovial enlargement erode cartilage & subchondral bone which may cause joint mal-alignment, subluxation or collapse

Rheumatoid Arthritis (cont)

Does the mechanism explain the clinical signs & symptoms, how?

- Yes
- Stimulation of nerve endings in subchondraln bone & synovial membrane, causes joint pain
- Inflammation of synovial leads to its enlargement with formation of palpable lumps in the affected joints
- Physical narrowing of joint space & ↓ in joint mobility causes joint stiffness & a ↓ in the range of movement
- Cartilage & subchondraln bone erosion causes joint mal-alignment, subluxation or collapse, explaining the various types of joint deformities
- The systemic inflammation explains the various extra-articular signs of the disease

Rheumatoid Arthritis



Ankylosing Spondylitis

Signs & symptoms:

- Pain in Lx & gluteal regions
- ↓ in Lx spine flexion
- ↓ in Lx lordosis
- ↑ in Tx kyphosis
- Asymmetric arthritis & enthesitis

Pathophysiology & mechanism:

- *Autoimmunity* causes ***inflammation*** of **axial** joints, **peripheral** joints & **entheses**

Ankylosing Spondylitis (cont)

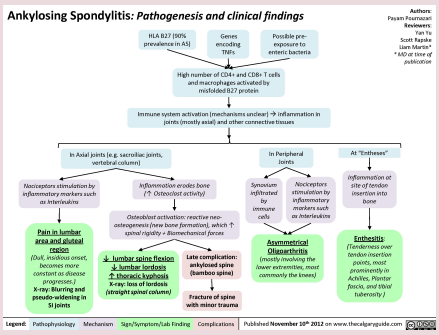
Does the pathophysiology explain/relate to the specific mechanisms of disease, how?

- **Yes**
- Axial joint arthritis (sacroiliac & vertebral column) causes ***release*** of *inflammatory substances* that stimulate ***nociceptors***
- **Inflammation** leads to **osteoclast activation & erosion of bone**, which in turn causes ***osteoblast activation with new bone formation***
- Leads to an ***↑ in spinal rigidity***
- In *peripheral joints*, the arthritis causes ***release of inflammatory substances*** that stimulate ***nociceptors***
- There's ***infiltration*** of the synovium by *inflammatory cells* & *inflammation of the entheses* (places of tendon insertions in bone)

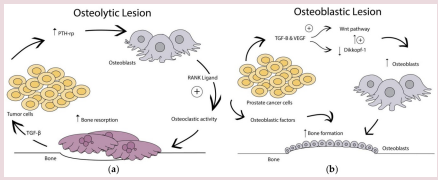
Do the mechanism explain the clinical signs & symptoms, how?

- **Yes**
- ***Stimulation of nociceptors*** causes *pain in axial & peripheral joints*
- ***↑ in spinal rigidity*** causes a *↓ in Lx spine flexion*, *↓ in Lx lordosis* & *↑ in Tx kyphosis*
- Late **complications** include *spinal ankylosis* & *fractures*
- In peripheral joints, ***stimulation of nociceptors*** *causes* pain of lower limb joints *&* knees
- **Enthesitis** *causes* pain in achilles tendon, plantar fascia *&* tibial tuberosity*

Ankylosing Spondylitis



Bone Remodelling Cycle



Osteoarthritis

Signs & symptoms:

- Joint pain with loading & motion
- Palpable bone hypertrophy
- ↓ in ROM
- Crepitus (popping/crackling sound)
- Joint effusion

Pathophysiology & mechanism:

- Joint cartilage ***destruction with inflammation***

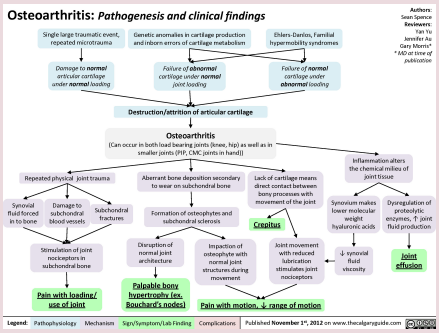
Does the pathophysiology explain/relate to the specific mechanisms of disease, how?

- **Yes**
- Cartilage **inflammation** in weight bearing joints **(knee,hip)** & smaller joints stimulates *nociceptors*
- Joint cartilage loss causes ***wear*** of exposed subchondral bone, which induces **defective new bone formation** leading to the appearance of ***osteophytes*** & *subchondral bone* ***sclerosis*** leading to *changes* in joint architecture
- During movement osteophytes & subchondral sclerosis are firmly pressed against normal joint structures
- Cartilage loss brings joint bones into direct contact between themselves with ***reduction*** in *joint movement* & stimulation of *nociceptors*
- **Joint inflammation** leads to ***chemical changes*** within the joint causing a ↓ in *synovial fluid viscosity* & an ↑ in joint *fluid production*

Do the mechanism explain the clinical signs & symptoms, how?

- **Yes**
- Stimulation of joint *nociceptors* causes ***joint pain*** whether upon **loading** or during **motion**
- Change in *joint architecture* consists of the appearance of *palpable* bone ***hypertrophy***, i.e. **Bouchard's nodes**
- *Osteophytic* & *subchondral sclerosis* impaction against normal joint structures causes ***pain & ↓ joint ROM***
- Joint bones into direct contact causes **friction** & **crepitus**, **pain** & further **↓ in ROM**
- **↓ in synovial fluid viscosity** & an **↑ in joint production** produce joint ***effusions***

Osteoarthritis



Polymyalgia Rheumatica

Signs & symptoms:

- Morning stiffness
- Aching of pectoral & pelvic girdle muscle structures
- Malaise
- Weight loss

Pathophysiology & mechanism:

- Aging combined with systemic (auto) immunologic/inflammatory process targeting structures in the walls of arteries with activation of macrophages

Does the pathophysiology explain/relate to the specific mechanisms of disease, how?

- More challenging to connect pathophysiology & mechanism
- The ***inflammation of arteries*** may lead to their **obstruction** potentially causing ***hypoxia, ischemia & necrosis*** of affected tissues
- This include muscles in the **shoulder girdle** & **pelvic girdle**

Do the mechanism explain the clinical signs & symptoms, how?

- **Yes** but challenging
- It's plausible that the **arteritis** & consequent **hypoxia** & **ischemia** of affected muscles together with the **systemic inflammation** ***lead to*** stiffness, aching, malaise & weight loss*

Polymyalgia Rheumatica