

04-23-09 NMSK - MSK Pathology

****Fracture Healing****

- Hematoma Formation
- Fibrin mesh formed, ingrowth of fibroblasts occurs
- Soft tissue callus
- Bony callus
- Osteoprogenitor cells activated
- Membranous bone formation
- Woven bone – reason why callus is not as strong as surrounding bone!
- Chondroblasts activated
- Fibrocartilage and hyaline cartilage produced
- Cartilage undergoes endochondral ossification
- Eventually primary bony callus is replaced by mature lamellar bone

Avascular Necrosis (AVN)

- AKA osteonecrosis
- Bone necrosis is produced by ischemia

Mechanisms that produce ischemia

- mechanical vascular interruption (fracture)
- corticosteroids
- thrombosis and embolism (nitrogen bubbles in dysbarism)
- vessel injury (secondary to vasculitis, radiation therapy)
- increased intraosseous pressure with vascular compression
- venous hypertension

AVN

- Hip is classic location for AVN
- >10% of joint replacements are due to osteonecrosis
- Gross: wedge-shaped pale-yellow area
- Micro: necrosis with dead trabeculae, fat necrosis, calcium salts deposition



Note the wedge-shaped area of avascular necrosis (osteonecrosis) at the upper right of this femoral head. Avascular necrosis results from bone ischemia, which can be due to many causes, including trauma and corticosteroid administration, though idiopathic cases are

common. There is pain with activity, progressing to pain at rest. Eventually, the necrotic bone collapses, distorting the overlying articular cartilage and producing secondary osteoarthritis. [Image courtesy of John Nicholls MD, Hong Kong University

Osteoporosis

- A disease characterized by increased porosity of the skeleton resulting from reduced bone mass
- The structural changes predispose the bone to fracture – particularly vertebral, hip fractures
- May be localized to a certain bone or region, as in disuse osteoporosis of a limb
- May involve the entire skeleton
- Most common forms are senile and postmenopausal osteoporosis
- Cannot detect reliably on plain X-rays until it is advanced, bone density scans are preferable

Osteoporosis

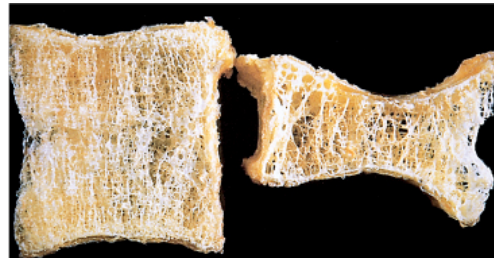


Figure 26-12 Osteoporotic vertebral body (right) shortened by compression fractures, compared with a normal vertebral body. Note that the osteoporotic vertebra has a characteristic loss of horizontal trabeculae and thickened vertical trabeculae.

Osteoarthritis

- Common, slowly progressive condition
- Misleading term since the joint lesions are not basically inflammatory
- AKA Degenerative Joint Disease
- Characterized by progressive erosion of articular cartilage
- Related to aging, mechanical effects, genetic factors
- Chondrocytes that function to maintain the articular cartilage initially proliferate to attempt to repair damage but eventually there is loss of chondrocytes
- Deep achy pain that worsens with use, morning stiffness, crepitus, decreased range of motion
- Hips, knees, lower lumbar and cervical vertebrae, PIP and DIP joints of fingers, 1st carpometacarpal and 1st tarsometatarsal joint

- Heberden's nodes: prominent osteophytes at DIP joints
- Bouchard's nodes: prominent osteophytes at PIP joints
- X-ray: narrowing of joint space, osteophyte formation, sclerosis of subchondral bone, subchondral bone cysts



More advanced osteoarthritis leads to osteophyte formation, seen here as a small protuberance on the proximal interphalangeal joint (Bouchard node). A similar lesion of the distal interphalangeal joint is known as a Heberden node.

Rheumatoid Arthritis (RA)

- Autoimmune disease triggered by exposure of a genetically susceptible host to an unknown arthritogenic antigen
- Chronic systemic inflammatory disorder that may affect many tissues and organs-skin, blood vessels, heart, lungs, and muscles-but principally attacks the joints
- Produces a nonsuppurative proliferative and inflammatory synovitis
- Often progresses to destruction of the articular cartilage and ankylosis of the joints
- Pattern of involvement varies but small joints typically affected before large joints
- Involved joints are swollen, warm, painful, and stiff in AM and after inactivity
- Radial deviation of wrist, ulnar deviation of fingers, flexion-hyperextension deformities of fingers
- Course may be slow or rapid
- 20% of pts will have periods of complete or partial remission
- Usually have positive serum rheumatoid factor
- X-ray: juxta-articular osteopenia and bone erosions with narrowing of the joint space from loss of articular cartilage

****Gout****

- Common end point of a group of disorders that produce hyperuricemia
- Transient attacks of acute arthritis initiated by crystallization of urates within and about joints

- Eventually develop chronic gouty arthritis and the deposition of masses of urates in joints and other sites, creating tophi
- Tophi are large collections of urate crystals with a surrounding inflammatory reaction
- Most patients with chronic gout also develop urate nephropathy
- More than 10% of the population of the Western hemisphere has hyperuricemia, but gout develops in less than 0.5% of the population
- A plasma urate level above 7 mg/dL is considered elevated because it exceeds the saturation value for urate at normal body temperature and blood pH
- Most 1st attacks involve one joint (>50% of the time it is the 1st MTP joint)
- Other joints may be involved: insteps, ankles, heels, knees, wrists, fingers, elbows
- Primary Gout (90% of cases)
- Enzyme defects unknown (85%-90% of primary gout)
- Overproduction of uric acid, normal excretion (majority), increased excretion (minority), underexcretion of uric acid with normal production
- Known enzyme defects-e.g., partial HGPRT (hypoxanthine guanine phosphoribosyl transferase) deficiency (rare)
- Overproduction of uric acid

Ankylosing Spondylitis

- Chronic inflammatory joint disease of axial joints, especially the sacroiliac joints
- Pts present in the second and third decades of life with low back pain, which frequently follows a chronic progressive course, M:F=2-3:1
- 90% of pts are HLA-B27 positive
- Like RA → immunogenetic phenotype may predispose to the activation of T cells and antibodies that react with joint elements
- Involvement of peripheral joints, such as the hips, knees, and shoulders, occurs in at least one third of patients

04-23-09 NMSK - NMJ Pathology

Myasthenia Gravis (MG)

- Autoimmune disease
- Prevalence of 3/100,000 people
- Thymic hyperplasia in 65% and thymoma in 15% of MG patients
- Autoantibodies against the acetylcholine receptor (AChR)
- Leads to loss of functional AChRs at neuromuscular junction
- Clinical course
- Weakness begins with extraocular muscles

- Ptosis
- Diplopia
- Weakness fluctuates and may become generalized
- Symptoms respond to administration of acetylcholinesterase inhibitors
- Other tx: prednisone, plasmapheresis, resection of thymoma, azathioprine, cyclophosphamide, cyclosporine
- Mortality due to respiratory compromise

Botulism

- Clostridium botulinum is causative agent
- Gram positive bacillus that grows in anaerobic conditions and produces spores
- Grows in inadequately sterilized canned foods
- Generates a potent neurotoxin that blocks synaptic release of acetylcholine
- Paralysis of respiratory and skeletal muscles
- Therapeutic uses → Botox
- Wrinkles, blepharospasm, hyperhidrosis, migraine headaches, spasmodic torticollis, achalasia

Lambert-Eaton Syndrome

- Typically a paraneoplastic process
- Most commonly (60% of cases) with small cell carcinoma of the lung
- May occur in absence of malignancy
- Patients have muscle weakness and autonomic dysfunction
- Acetylcholine content in neuromuscular junction synaptic vesicles is normal
- Post synaptic membrane is normally responsive
- Fewer synaptic vesicles are released
- Autoimmunity to presynaptic calcium channels

Purpose:

The purpose of this document is to summarize all of the yellow highlighted slides for Dr. Lyons lectures of the NMSK Exam 1 material. Both lectures (NMJ and MSK Pathology) were given on 4-23-09 and are summarized here. Slide content, note content, and non-yellow seeming relevant images are included. Those images that are not yellow in his power points are identified by being in a red colored note. "NOT YELLOW." Everything otherwise not noted is definitely yellow. Hope this is helpful.

Beau Lacefield

leonard.lacefield@Imunet.edu

http://sp.Imunet.edu/personal/leonard_lacefield/fall2008/default.aspx