MSS FINAL 1

EVERYTHING IN ONE FILE

SUMMARY & TESTBANK

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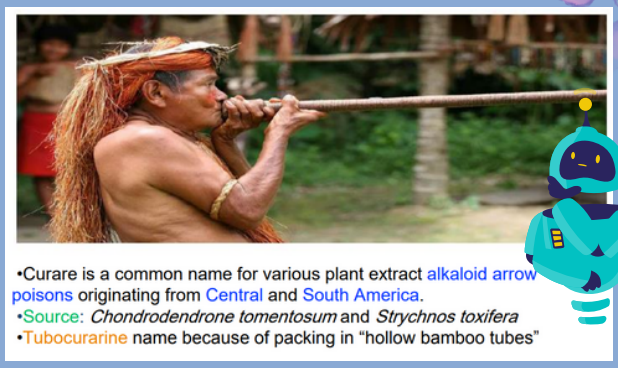
pharmacology

Peripherally Acting Skeletal Muscle Relaxants

In conjugation with General Anesthetics:
- Facilitate intubation of the trachea
- Facilitate mechanical ventilation
- Optimized surgrical working conditions

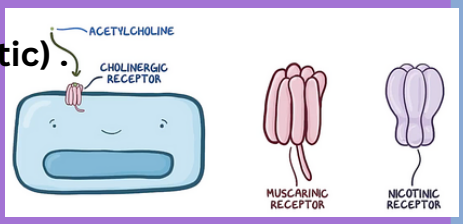


•Curare is a common name for various plant extract alkaloid arrow poisons originating from Central and South America.
•Source: *Chondrodendrone tomentosum* and *Strychnos toxifera*
•Tubocurarine name because of packing in "hollow bamboo tubes"

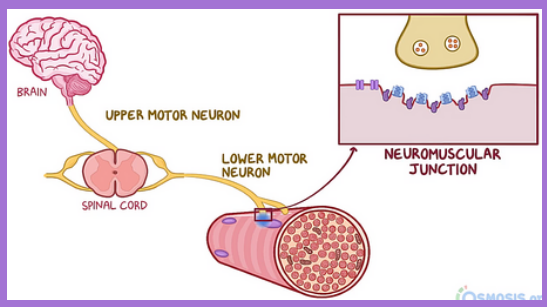
Acetylcholine

Acetylcholine is a major neurohumoral transmitter at autonomic, somatic and central nervous system:

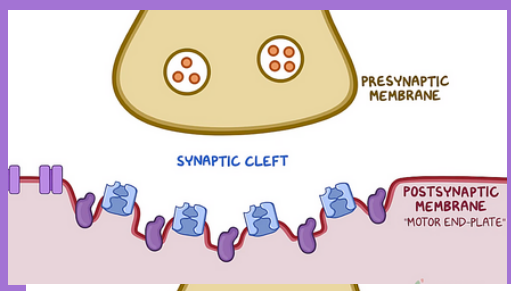
.1All preganglionic sites (Both Parasympathetic and sympathetic) .
2Skeletal Muscles .
3CNS: Cortex Basal ganglia, spinal cord and others

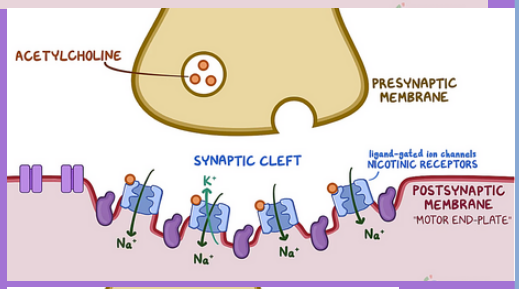


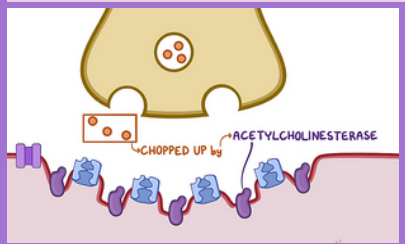
Parasympathetic Stimulation – Acetylcholine (ACh) release at neuroeffector junction – biological effects Sympathetic stimulation – Nonadrenaline (NA) at neuroeffector junction – biological effects .

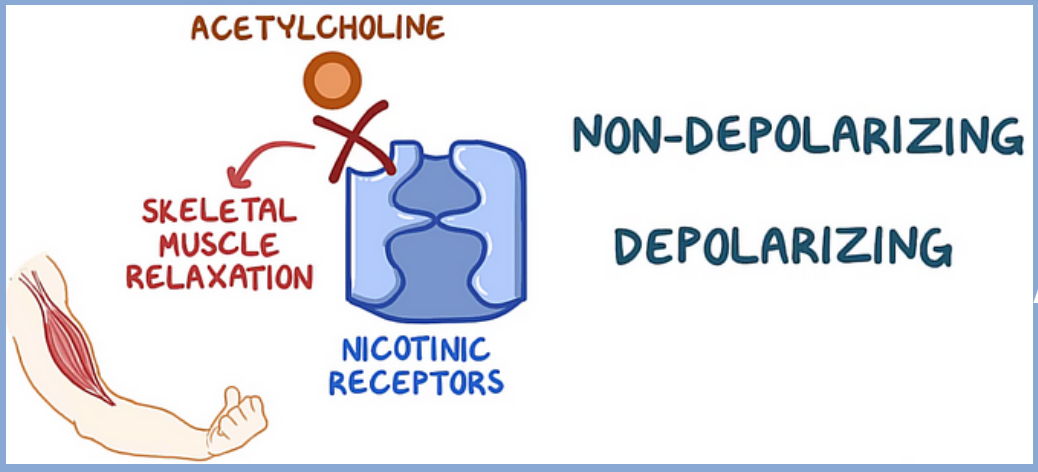


okay, first things first. In order for a skeletal muscle to contract, your brain sends a signal, in the form of an action potential in an upper motor neuron. The upper motor neuron then activates a lower motor neuron in the spinal cord.
From here, the action potential is sent through an axon down to its ending branches, called axon terminals, to muscle fibers which they innervate.
The place where an axon terminal meets the muscle fiber is the neuromuscular junction.
The neuromuscular junction has three main parts: a presynaptic membrane, which is the membrane of an axon terminal; a postsynaptic membrane, which is the membrane of a skeletal muscle fiber and is also called a motor end-plate; and a synaptic cleft, which is the gap between the presynaptic and postsynaptic membranes.
When an action potential reaches the axon terminal, synaptic vesicles that contain neurotransmitters, called acetylcholine, fuse with the cell membrane of the axon terminal, releasing the acetylcholine into the synaptic cleft.
The acetylcholine then diffuses over to the motor end plate on the muscle fiber and binds to ligand-gated ion channels, also called nicotinic receptors.
When that happens, these ligand-gated ion channels open up, letting lots of sodium ions rush into the skeletal muscle fiber, and a few potassium ions leak out of the cell as well. But overall there's an increase in positive charge on the inside of the muscle fiber causing it to depolarize.
This causes the voltage-gated sodium ion channels on the membrane to open up, and there's a huge influx of sodium ions into the muscle fiber.
This leads to a generation of an action potential, which rapidly spreads along the entire membrane, causing the whole muscle fiber to contract.
When the signal sent from the lower motor neuron stops, this causes synaptic vesicles full of acetylcholine to stop fusing with the membrane, while molecules of acetylcholine that are left behind within the synaptic cleft, are chopped up by an enzyme called acetylcholinesterase. And muscle contraction stops.







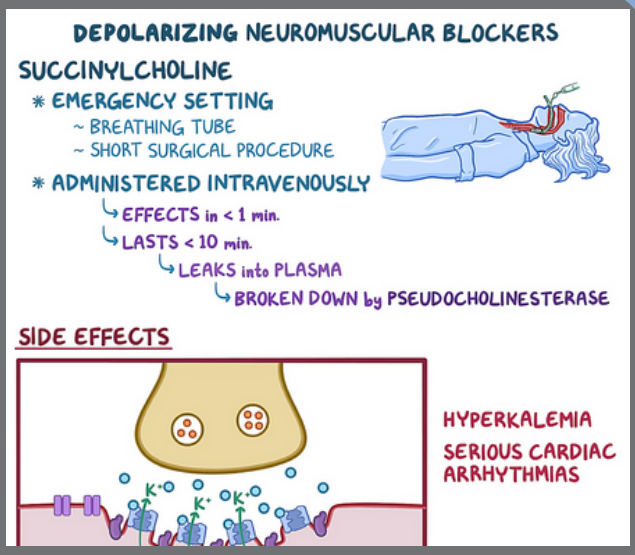


are medications that block the interaction between acetylcholine and nicotinic receptors at the neuromuscular junction. This leads to skeletal muscle relaxation.
And based on their mechanism of action, they're classified into non- depolarizing and depolarizing blockers.

Succinylcholine

Depolarizing Block , have affinity and sub-maximal/ intrinsic activity at Nm receptor ,acts on sodium channels= open them , does not dissociate rapidly= prolonged depolarisation ,

This process occur in two phases: •Phase I: During Phase I (depolarizing phase), they cause muscular fasciculations while they are depolarizing the muscle fibers. •Phase II: After sufficient depolarization has occurred, phase II (desensitized phase) sets and the muscle is no longer responsive to Ach released by the nerve endings.



Advantages: •Most commonly used for Tracheal intubation •Rapid onset (1-2 min) •Good intubation conditions – relax jaw, separated vocal chords with immobility, no diaphargmatic movements •Short duration of action (5-10 minutes) •Dose 1-1.5mg/kg •Used as continous infusion occasionally

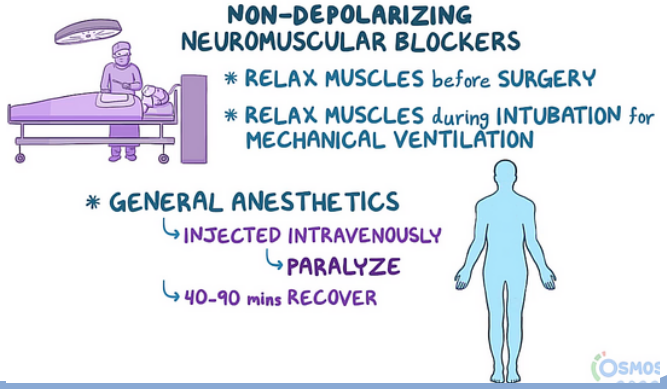
Disadvantages: •Cardiovascular: unpredictable BP, heart rate and arrhythmias •Fasciculation •Muscle pain •Increased intraocular pressure •Increased intracranial pressure •Hyperkelemia: k+ efflux from muscles, life threatening in Cardiac Heart Failure, patient with diuretics etc

Non-Depolarising Drugs

no intrinsic activity

~ ATRACURIUM
~ VECURONIUM
~ ROCURONIUM
~ PANCURONIUM
~ TUBOCURARINE

CUR



•These are of 3 types based on their activity:
–Long Acting : d-TC, Pancuronium, Pipecuronium, Gallamine (Kidney Excretion)
–Intermediate : Vecuronium, Rocuronium, Atracuronium (eliminated by liver)
–Short Acting : Mivacuronium, Ropcacuronium (inactivated by plasma cholinesterase)

• Low Doses: –Competitive antagonists of ACh –Action reversed by ACh ecterase inhibitors
• Large Doses: –Ion Channel is blocked –More weakness of neuromuscular transmission –Action could not be reversed by ACh esterase inhibitors
• Other actions: –Can block pre-junctional Na+ channels and interfere with mobilization of ACh at nerve endings, This process is called fade ofAch

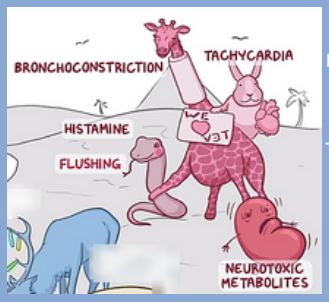
d-Tubocurarine

agent to undergo clinical investigation •purified curare – Chondodendrom tomentosum •ED95= 0.5mg/kg •undergoes minimal metabolism- is excreted %10 -in urine %45 -in bile •excretion impaired in Renal Failure
CVS Effects: • hypotension frequently even at doses < ED95 • histamine released (skin flushing frequently) • autonomic ganglionic blockade- manifests as hypotension Clinical Use: • long duration of action(60 to 120 mins) and CVS effects restricted its use • used as "precurarization" = t's used to reduce side effects of succinylcholine

Gallamine –Less potent than curare –Tachycardia

Atracurium –Rapid recovery –Safe in hepatic & renal impairment –Spontaneous inactivation to laudanosine (seizures)

Dantrolene is a muscle relaxant that reduces Ca release from the sarcoplasmic reticulum.



For side effects, let's have some animals watch the procedure. These animals all love the vet and compete for his attention, which will help you remember that non-depolarizing neuromuscular blockers are competitive inhibitors.
There's a snake going "Hisss" for histamine and it's got red cheeks to represent flushing.
Next is another giraffe with a neck brace for bronchoconstriction, and a bunny holding a heart for tachycardia.
Let's put a kidney having seizures next to the animals to help you remember these medications have neurotoxic metabolites, and should be avoided in people with kidney diseases.

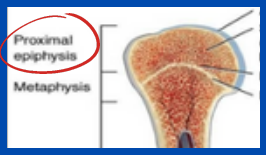
https://quizlet.com/fr/786800869/mss-medicine-pharma-patho-flash-cards/?new

PATHOLOGY

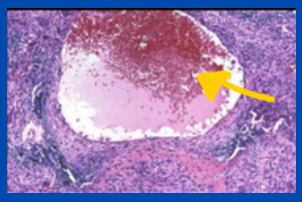
GIANT CELL TUMOR OF BONE:

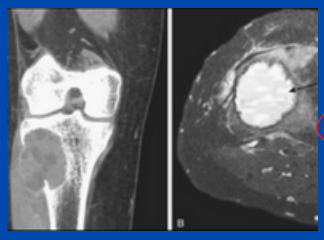
multinucleated, from wall to wall , potentially malignant

Locally aggressive neoplasm of adults.
- Epiphyses of long bones
- Osteoclast-like giant cells
- Rare malignant behavior
- Cells contain high levels of RANKL
- Trx: curetting



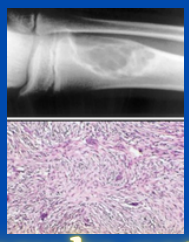
ANEURYSMAL BONE CYST:





- Benign tumor
- Blood filled cyst
- Metaphysis of long bones; adults

NONOSSIFYING FIBROMA:

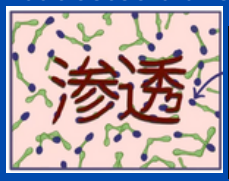


Benign lesion, maybe reactive not a true neoplasm (other names: FCD, MFD)
- Metaphysis لطيف - خفيف
- Histology: bland , fibroblastic proliferation
- May resolve spontaneously

???? (may be not a tumer)

FIBROUS DYSPLASIA (FD):

like paget under CT but osteoid like Chinese letters



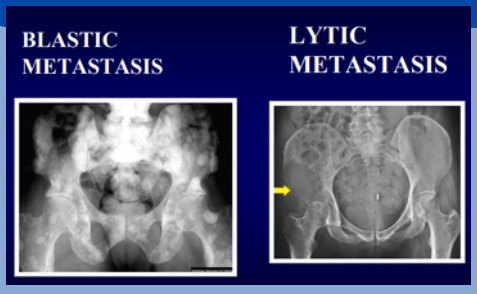
Not a real tumor; rather a developmental abnormality of bone genesis due to mutations in GNAS1 gene (cAMP mediated osteoblast differentiation). • Forms of FD: – Monostotic: affecting one bone – Polystotic: multiple bones – Mazabraud syndrome: FD + soft tissue myxoma – McCune-Albright syndrome: polystotic FD + caféau-lait skin pigmentation + endocrine abnormalities (precocious puberty)

METASTATIC TUMORS TO BONE:

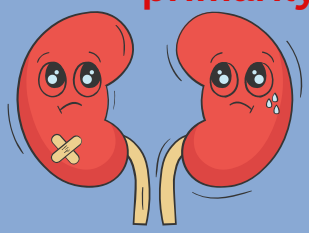
if a male came with bone cancer , we suspect prostate cancer , which metastasis to bone , we use PSA test

more common than primary bone tumors
In adults: most are carcinomas; lung, prostate, breast, kidney, thyroid & liver
In children: Neuroblastoma, Wilms tumor and rhabdomyosarcoma • Usually multiple and axial; mostly hematogenous spread. • Lytic, blastic or mixed (via mediators secretions)

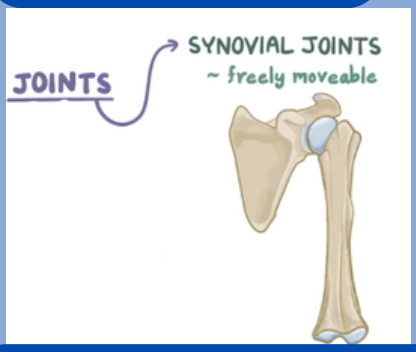
if there is not cancer in it , we test the liver , if there is a cancer in liver , it is dangerous , difficult to tret and life threating



Wilms' tumor is a rare kidney cancer that primarily affects children.

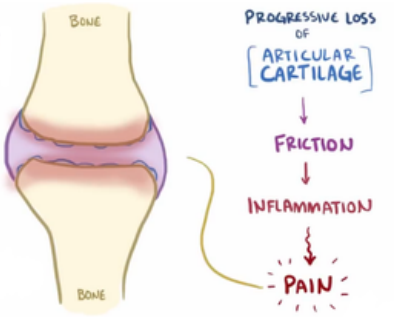


JOINTS



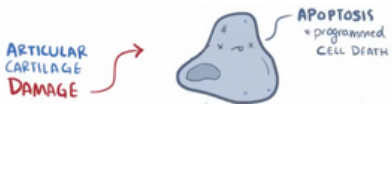
Synovial joints covered by hyaline cartilage (70% water, 10% type II collagen, 8% proteoglycans + chondrocytes • Synovial membrane contains: A synoviocytes (diff. macrophages), and B synoviocytes fibroblast-like • Synov membrane lacks basement membrane • Hyaline cartilage: no blood supply, no nerves, no lymphatics (shock absorber)

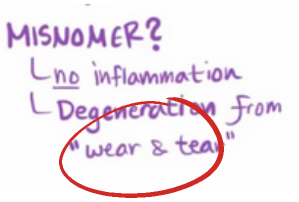
OSTEOARTHRITIS

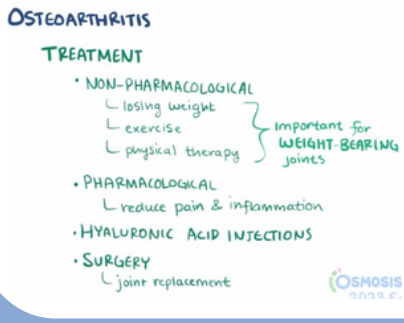


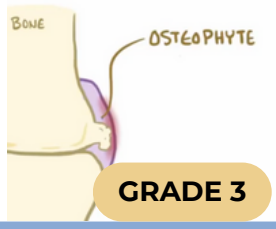
Degeneration of cartilage, not true – ITIS • Primary or idiopathic: aging process; few joints • Secondary: due to pre existing diseases • Insidious; increase with age (>50 yr); 40% of people > 70 years are affected • Degeneration of cartilage >> repair and proliferation

apoptosis of chondrocytes: aging: wear and tear







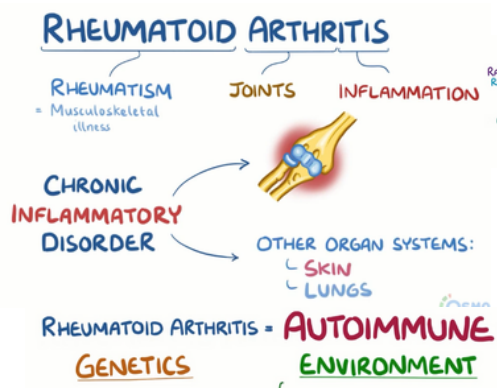


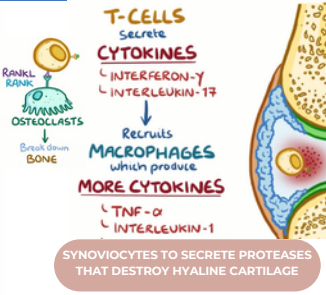
GRADE 3

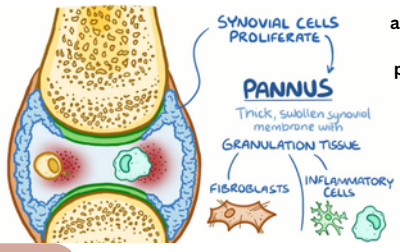
Joint pain worsens with use, morning stiffness, crepitus & range limitation, radicular pain, osteophytes impingement on vertebrae, muscle spasm & atrophy • No magic preventive strategies (weight loss?) • Trx: pain control, decrease inflammation (NSAIDs), intra-articular steroids, or joint replacement for severe cases • Large health cost on countries

preventive but not a cure , there is no final treatment for it

RHEUMATOID ARTHRITIS

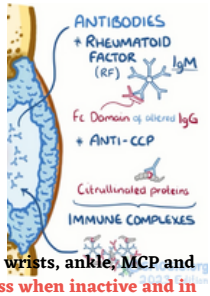






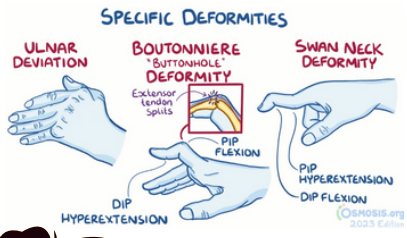
80% of patients with RA have autoantibodies IgG & IgM against the Fc portion of their own IgG [Rheumatoid factor]

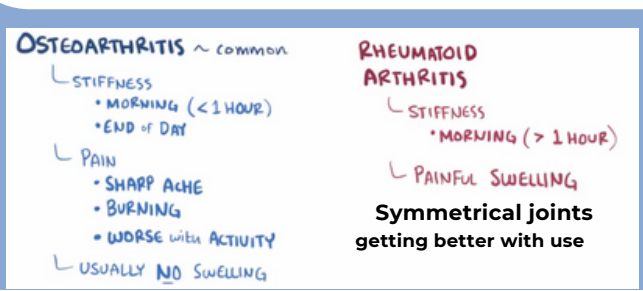
70% of patients with RA have Anti-Citrullinated Protein Antibodies (ACPA)



• Chronic inflammatory disease; autoimmune in nature; attacks joints with nonsuppurative proliferative and inflammatory synovitis; leading to destruction of joints and adhesions (ankylosis); systemic disease (skin, heart, vessels & lungs). • 1% prevalence in USA; F:M = 3:1; 4 th -5 th decade • Genetic predisposition + environmental factors plays a role in the development, progression and chronocity of the diseas

Begins slowly and insidiously, polyarthritis • Symmetrical joints: hands, feet, wrists, ankle, MCP and proximal IPJ are commonly affected • Joints: warm, swollen & painful • Stiffness when inactive and in the morning • Waxing and waning chronic • Ulnar deviation • Trx: Steroids, MTX, Anti-TN





FROM FLASH CARD NUM7
https://quizlet.com/fr/786800869/mss-medicine-pharma-patho-flash-cards/

JUVENILE IDIOPATHIC ARTHRITIS (JIA):

• Heterogeneous group; arthritis of unknown cause ; <16 years for at least 6 weeks • Pathogenesis is similar to adult RA • Prognosis variable; only 10% will have serious functional disability .

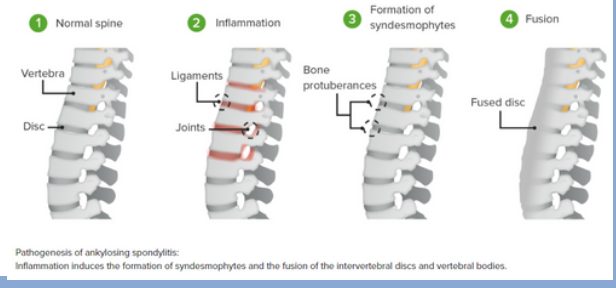
IN CONTRAST TO ADULTS RA; JIA IS CHARACTERIZED BY:
Oligoarthritis is more common
Systemic disease is more common
Large joints are affected more than small joints
Rheumatoid nodules and Rheum Factor are usually absent
Anti Nuclear Antibody seropositivity is common

SERONEGATIVE :

Autoimmune T cell response to unidentified antigen (possibly infectious agent) that cross react with self musculoskeletal antigens. Ankylosing spondylitis: most common prototype. - Destructive arthritis and bony damage and ankylosis of sacroiliac joint, main joint involved. - 90% HLA-B27 - Anti IL-17 has shown some efficacy as treatment

HETEROGENOUS GROUP THAT SHARE THE FOLLOWING FEATURES:
Absence of rheumatoid factor
Ligaments pathology rather than synovium
Sacroiliac joints mainly
Association with HLA-B27
Bony ankylosis (fusion)

- **Ankylosing Spondylitis:**
  - Adolescent boys, HLA B27, axial joints (sacroiliac)
- **Reiter Syndrome:**
  - Triad of arthritis, urethritis/cervicits & conjuctivitis
  - Autoimmune but initiated by bacterial infection.
- **Enteropathic Arthritis:**
  - Secondary to bowel infections (salmonella, shigella)
  - HLA B27 positive
- **Psoriatic Arthritis:**
  - 5% of patients, starts in DIP joints, similar to RA.



Pathogenesis of ankylosing spondylitis: Inflammation induces the formation of syndesmophytes and the fusion of the intervertebral discs and vertebral bodies.

SUPPURATIVE ARTHRITIS:

• Bacterial infection • Hematogenous spread • < 2 years: H. influenza; older children & adults S. aureus; gonococcus young adults • Sickle cell disease: salmonella • Clinically: sudden acute pain, swollen and warm joints, mainly knee with systemic manifestation (fever, leukocytosis, elevated ESR) • Dx & Rx: aspiration of joint; antibiotics

CRYSTAL-INDUCED ARTHRITIS:

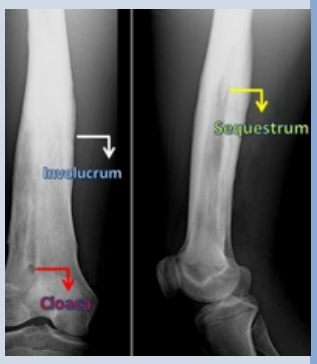
• Crystals deposited in joints causing disease • Crystals triggers inflammatory reaction that destroys cartilage • Endogenous crystals: – Monosodium urate, MSU (GOUT) – Calcium pyrophosphate dehydrogenase, CPPD (PSEUDOGOUT)

LYME ARTHRITIS :

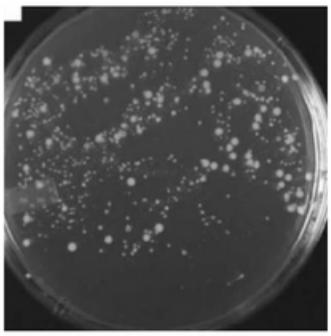
ausative organism: Spirochete, (gram-negative bacterium) , Most common species :Borrelia burgdorferi Spirochetes
then spread to the blood and regional lymph nodes Eventual spread to multiple organs : joints , T-cell–mediated immune response IgM ---IgG , Symptoms develop in months to years in untreated patients .
Migratory polyarthritis (60% of patients)
Large joints, particularly the knee
Intermittent joint swelling and pain .

microbiology

Osteomyelitis :



is an infection involving bone, (hematogenous versus nonhematogenous) , (acute versus chronic) , The hallmark of chronic osteomyelitis is the presence of dead bone (sequestrum).
Nonhematogenous osteomyelitis can occur via direct inoculation of infection into the bone (as a result of trauma or surgery).
Risk factors for nonhematogenous osteomyelitis include poorly healing soft tissue wounds (including decubitus ulcers), presence of orthopedic hardware, diabetes, peripheral vascular disease, and peripheral neuropathy .
Nonhematogenous osteomyelitis may be polymicrobial or monomicrobial. Staphylococcus aureus (including methicillin-resistant S. aureus), coagulase-negative staphylococci, and aerobic gram-negative bacilli are the most common organisms.
Hematogenous osteomyelitis is the most common form of osteomyelitis in infants and children. • In adults, vertebral osteomyelitis is the most common form of hematogenous osteomyelitis. Most cases occur in patients >50 years.
Tuberculous osteomyelitis usually occurs from reactivation of tuberculous bacilli lodged in bone during the mycobacteremia occurring at the time of the primary infection.
large inoculation of organisms, presence of bone damage, and/or presence of hardware or other foreign material.
Adherence appears to play a central role in the early stages of S. aureus-induced osteomyelitor arthritis.
S. aureus can survive intracellularly in cultured osteoblasts.



after more than 48 hours

small colony variants

Acute osteomyelitis typically presents with gradual onset of symptoms over several days. Patients usually present with a dull pain at the involved site, with or without movement. Local findings (tenderness, warmth, erythema, and swelling) and systemic symptoms (fever, rigors) may also be present.
Chronic osteomyelitis may also present with intermittent flares of pain and swelling. The presence of a sinus tract is pathognomonic of chronic osteomyelitis.
the diagnosis of osteomyelitis is established via culture obtained from biopsy of the involved bone.
Bone histopathology consistent with osteomyelitis in the absence of positive culture data

Clinical and radiographic findings typical of osteomyelitis and positive blood cultures with a likely pathogen (such as Staphylococcus aureus); in such cases, bone biopsy is not required
Complications of osteomyelitis include: ●Sinus tract formation ●Contiguous soft tissue infection ●Abscess ●Septic arthritis ●Systemic infection ●Bony deformity and Fracture ●Malignancy

- In adults, **vertebral osteomyelitis** is the most common form of hematogenous osteomyelitis. Most cases occur **in patients >50 years**. (when there is bone deformation (because of aging, fractures,..) there will be a higher chance for bacteria to enter bone and cause infection)
- **Acute osteomyelitis** evolves **over several days to weeks** and can progress to a chronic infection. (bone infections are tricky, sometimes it's hard for antibiotics to reach the site so it acute infection becomes chronic)

Dog and Cat Bites

Dog and cat bites can cause superficial and deep tissue destruction, as well as serious wound infections. Dog bites occur more frequently in men and children and often cause crushing or tearing trauma. Cat bites are more frequent in adult women and result in puncture wounds. Because puncture wounds allow inoculation of bacteria into the deep tissues, cat bites are more frequently associated with infection. The diagnosis is clinical, and cultures should be obtained if the wound appears infected. Management requires fastidious wound care and antibiotics for high-risk or infected wounds.
. Cat bites usually occur on the extremities and tend to penetrate deeply, with higher risk of deep infection (abscess, septic arthritis, osteomyelitis, tenosynovitis, bacteremia, or necrotizing soft tissue infection) than dog bites.
The physical examination should ensure that the patient is hemodynamically stable and should assess for injuries to adjacent structures.
Bite wound infection may be superficial (eg, cellulitis, with or without abscess) or deep (abscess, septic arthritis, osteomyelitis, tenosynovitis, or necrotizing soft tissue infection). • Clinical manifestations of superficial infection include fever, erythema, swelling, and warmth, purulent drainage, and/or lymphangitis. An associated superficial abscess may present as a tender, erythematous, fluctuant nodule..
Pasteurella species are isolated from 50 percent of dog bite wounds and 75 percent of cat bite wounds.
The average bite wound culture yields five types of bacterial isolates. Mixed aerobic and anaerobic bacteria are observed in 60 percent of cases; skin flora are isolated in about 40 percent of cases

Table: Common bacteria involved in bite wounds

Dog bites	Cat bites	Both
• *Capnocytophaga canimorsus*	• *Bartonella henselae*	• *Staphylococcus*
• *Eikenella*	• *Actinomyces*	• *Streptococcus*
• *Proteus*	• *Propionibacterium*	• *Pasteurella multocida*
• *Klebsiella*	• *Clostridium*	• *Bacteroides*
• *Haemophilus*	• *Wolinella*	• *Fusobacterium*
• *Enterobacter*	• *Peptostreptococcus*	
• *Moraxella*		
• *Corynebacterium*		
• *Neisseria*		
• *Prevotella*		
• *Porphyromonas*		

Human Bites

Like dog and cat bites, human bites can carry a significant risk for infection.

Bartonella :

gram-negative, coccobacillary or bacillary rods with fastidious growth.
Bartonella species are transmitted by vectors such as ticks, fleas, sand flies, and mosquitoes.
B. henselae is responsible for a disease acquired after exposure to cats : cat-scratch disease .
Symptoms typically include a non-painful bump or blister at the site of injury and painful and swollen lymph nodes.

Septic arthritis :
infection in a joint.
usually caused by bacteria but can also be caused by other microorganisms.
hematogenous seeding. Bacteremia is more likely to localize in a joint
with pre-existing arthritis .
usually monomicrobial. S. aureus.
a single swollen and painful joint (ie, monoarticular arthrit is).
Most patients with septic arthritis are febrile (fever).
Septic arthritis classically presents with acute onset monoarticular joint pain, fever, swelling, and a reluctance or refusal to move the affected joint.
The knee is involved in more than 50 percent of cases .
• The diagnosis of septic arthritis is made based on synovial fluid analysis and culture.
Collection of synovial fluid and blood cultures should be performed prior to administration of antibiotics.
• Management of acute bacterial arthritis consists of joint drainage and antibiotic therapy. empiric treatment with vancomycin.
In one study including 121 adults with septic arthritis, a poor joint outcome (as defined by the need for amputation, arthrodesis, prosthetic surgery, or severe functional deterioration) occurred in one-third of the patients; adverse prognostic factors included older age and preexisting joint disease

risk factors

- Aging population
- Resistance to antibiotics
- Orthopedic procedures
- Immunosuppressive agents
- Diabetes, leukemia, cancer, hypogammaglobulinemia, cirrhosis, HIV, granulomatous diseases, intravenous drug users

Organism
Staphylococcus aureus ★
Streptococcal species ★
Neisseria gonorrhoeae ★
Aerobic gram-negative bacteria
Anaerobic gram-negative bacteria
Brucellosis
Mycobacterial species ★
Fungal species (*Candida* species, sporotrichosis, *Cryptococcus*, blastomycosis, coccidioidomycosis)
Spirochete (*Borellia burgdorferi*) ★

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