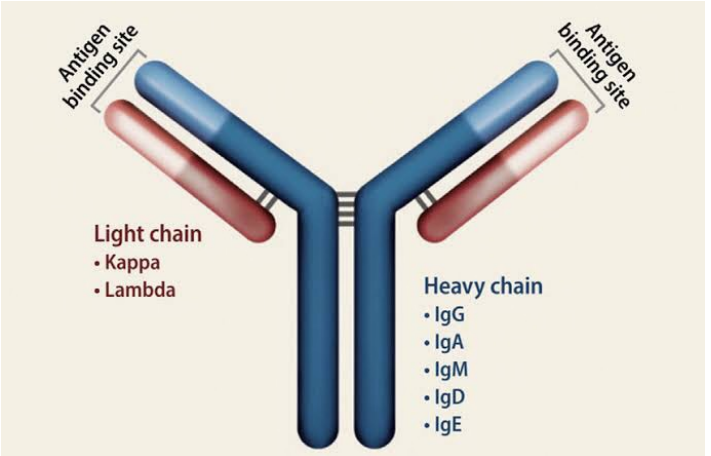
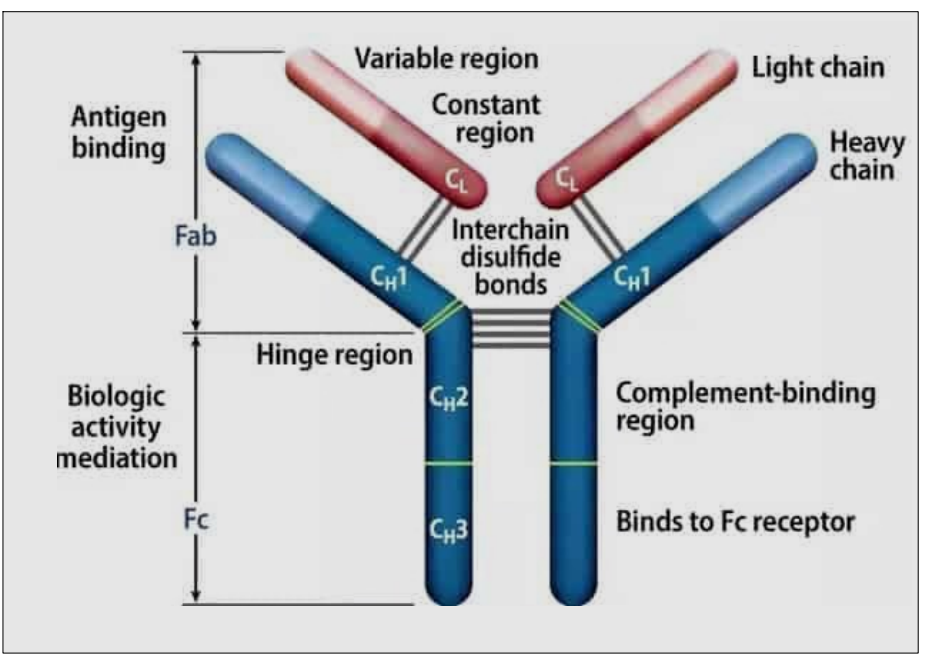
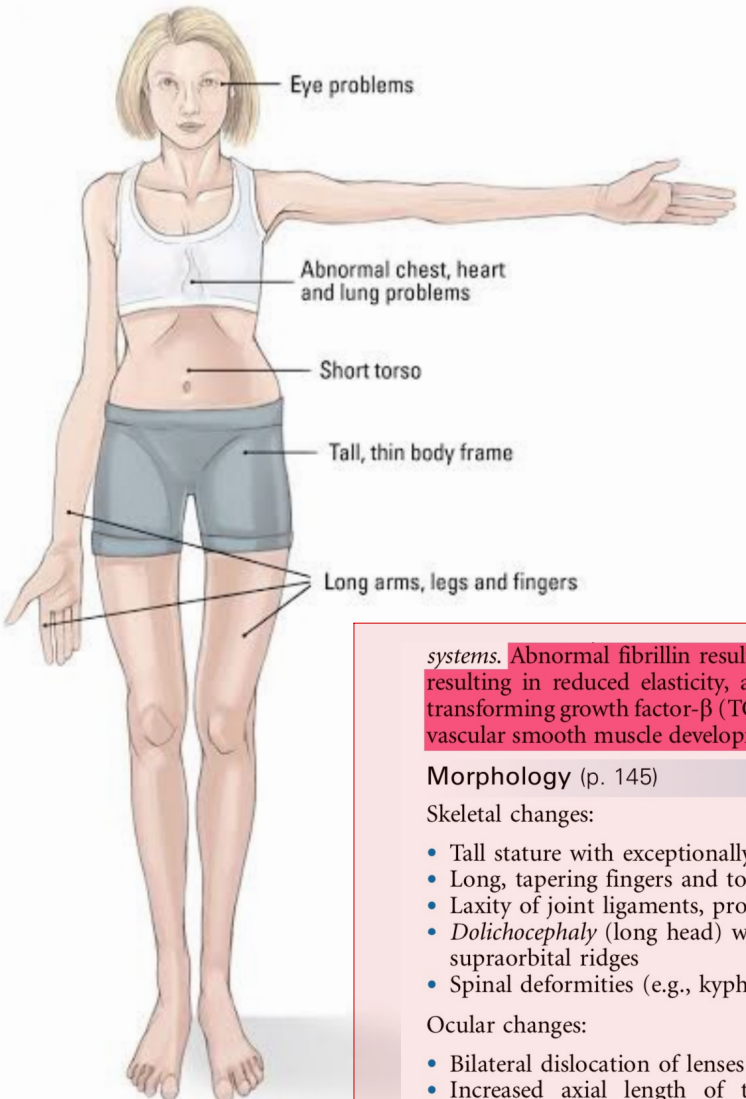
BLOCK H FLASH NOTES BY FATIMA HAIDER KGMC



Immunoglobulin Structure



Marfan syndrome



systems. Abnormal fibrillin results in defective microfibril assembly, resulting in reduced elasticity, as well as reduced sequestration of transforming growth factor-β (TGF-β); excess TGF-β reduces normal vascular smooth muscle development and matrix production.

Morphology (p. 145)

Skeletal changes:

- Tall stature with exceptionally long extremities
- Long, tapering fingers and toes *(arachnodactyly)*
- Laxity of joint ligaments, producing hyperextensibility
- *Dolichocephaly* (long head) with frontal bossing and prominent supraorbital ridges
- Spinal deformities (e.g., kyphosis and scoliosis)

Ocular changes:

- Bilateral dislocation of lenses (ectopia lentis)
- Increased axial length of the globe, giving rise to retinal detachments

Cardiovascular lesions:

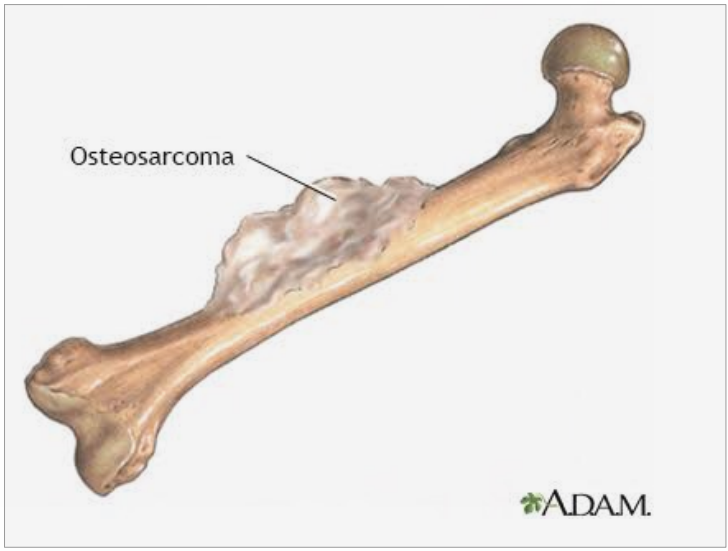
- Mitral valve prolapse
- Aortic cystic medial degeneration causing aortic ring dilation and valvular incompetence. This is likely exacerbated by the excess TGF-β signaling.

Cutaneous changes:

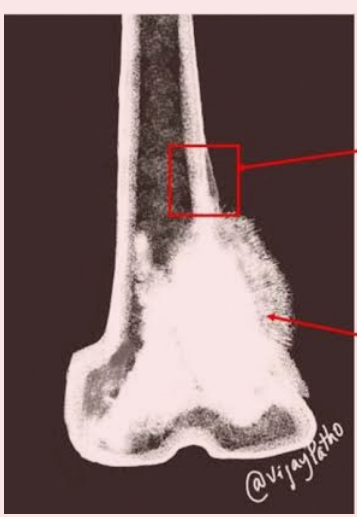
- Striae

Well circumscribed translucent central area, termed nidus

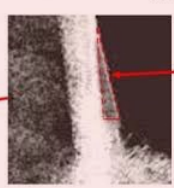
Osteoid osteoma is relieved by aspirin
Osteoblastoma is not relieved by aspirin



Bone forming cells
Sunburst appearance
Codman's triangle



OSTEOSARCOMA

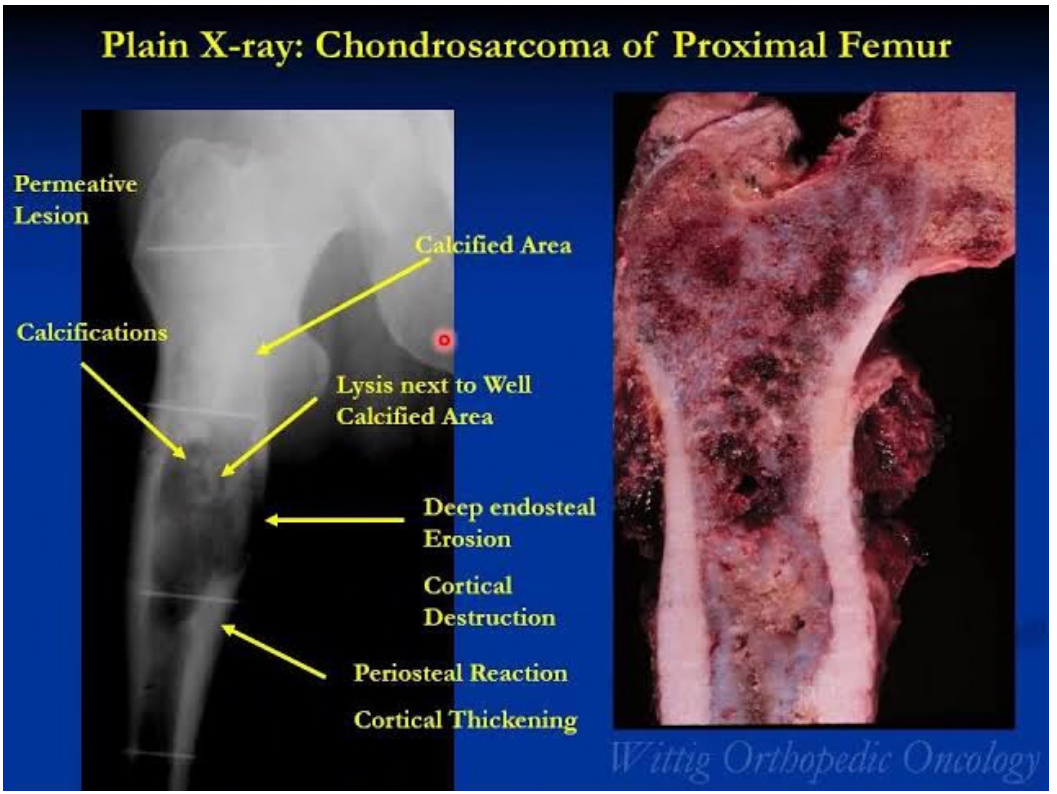


Due to expansion of tumor, elevation of the periosteum may result in formation of triangle of reactive bone

Codman's triangle

Abundant periosteal new bone formation & periosteal reaction

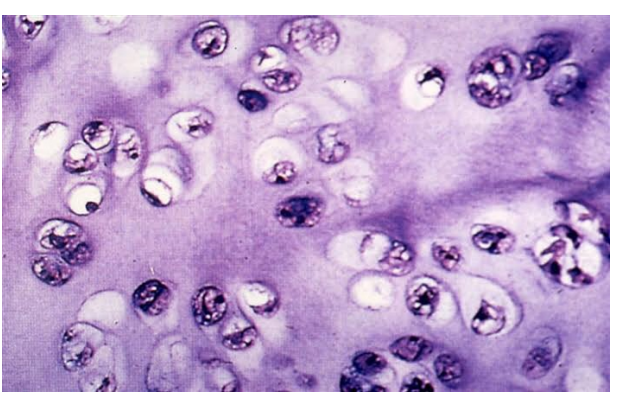
'Sunburst' pattern

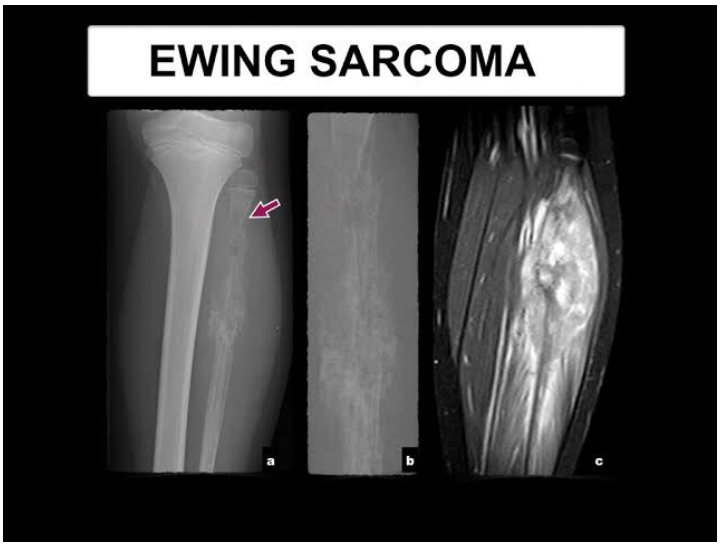


CHONDROSARCOMA

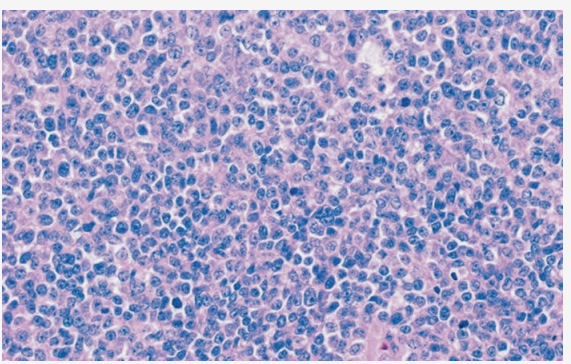
Cartilagenous

Popcorn calcification

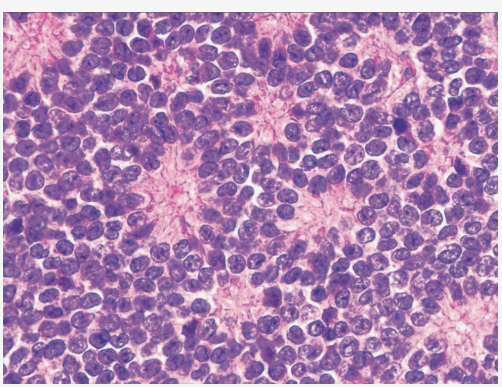




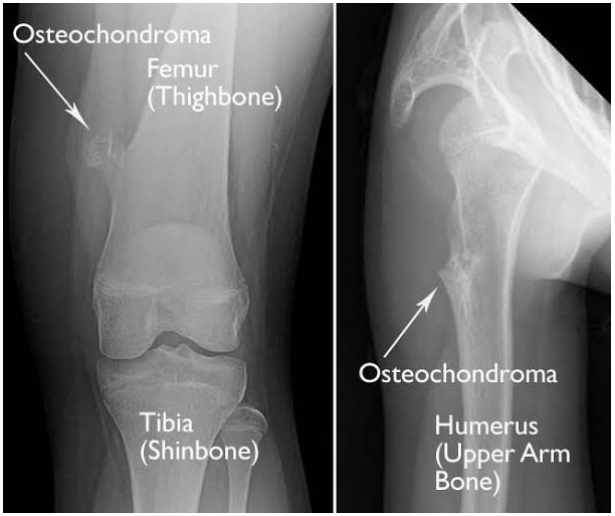
11:22 translocation
Onion skin appearance



Round blue cell tumor



Homer Wright rosettes indicate neural differentiation

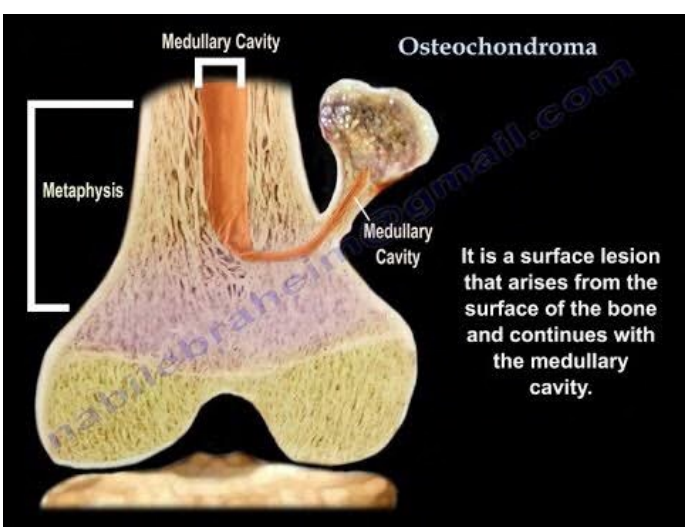


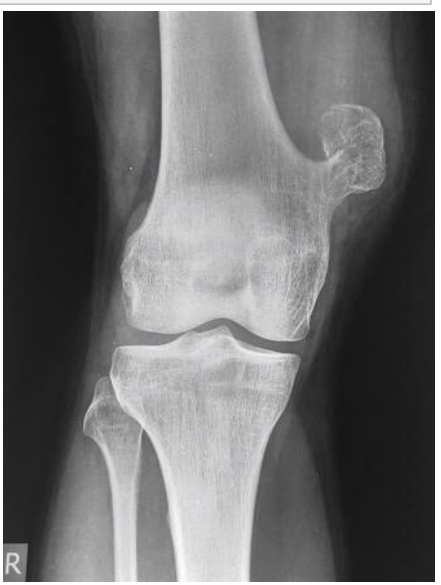
OSTEOCHONDROMA

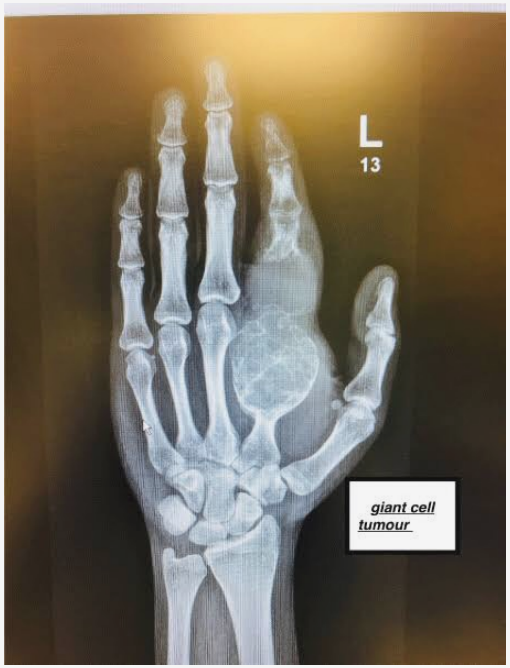
common benign cartilage capped outgrowths attached by a bony stalk to the underlying skeleton

develop only in bones of endochondral origin arising at metaphysis near the growth plate of long tubular bones, esp about the knee

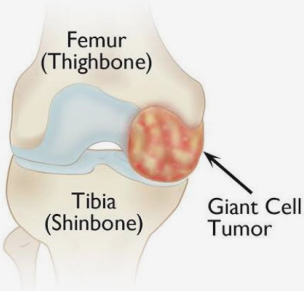
They tend to stop growing once the normal growth of skeleton is completed







Disseminated by multinucleated osteoclast type giant cells, hence the synonym osteoclastoma



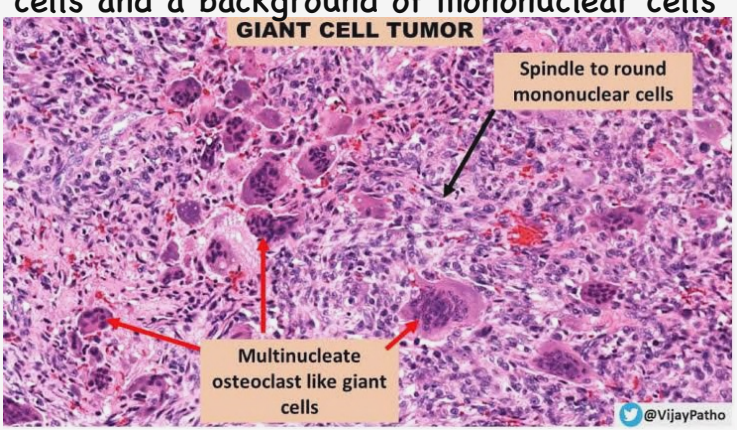
Giant cell tumors involving epiphysis - arthritic

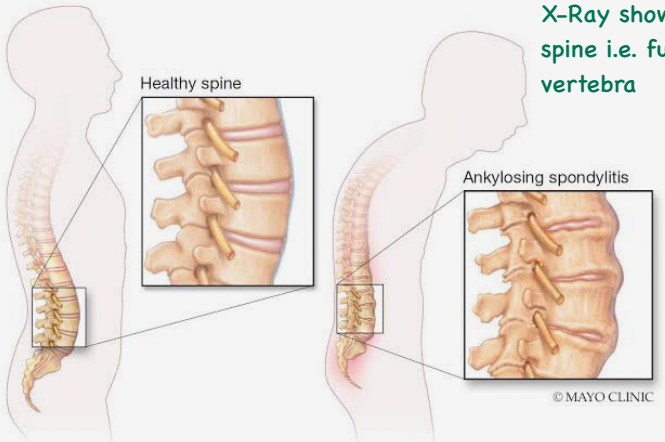
GIANT CELL TUMORS

(Osteoclastoma)

Soap bubble appearance on X Ray

Morphology: Abundant multi nucleated giant cells and a background of mononuclear cells



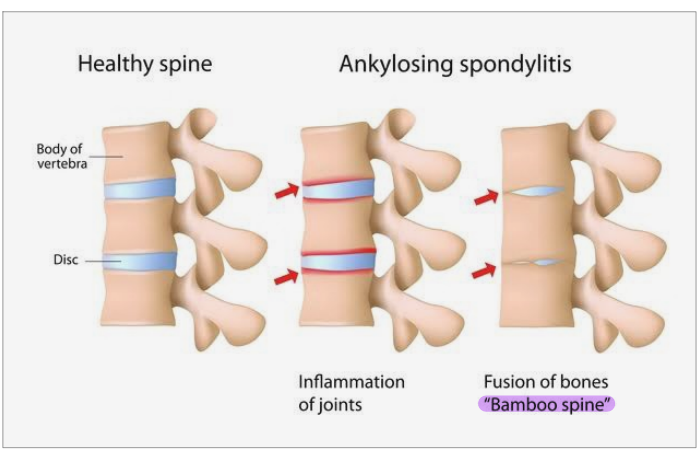


X-Ray shows bamboo spine i.e. fusion of vertebra

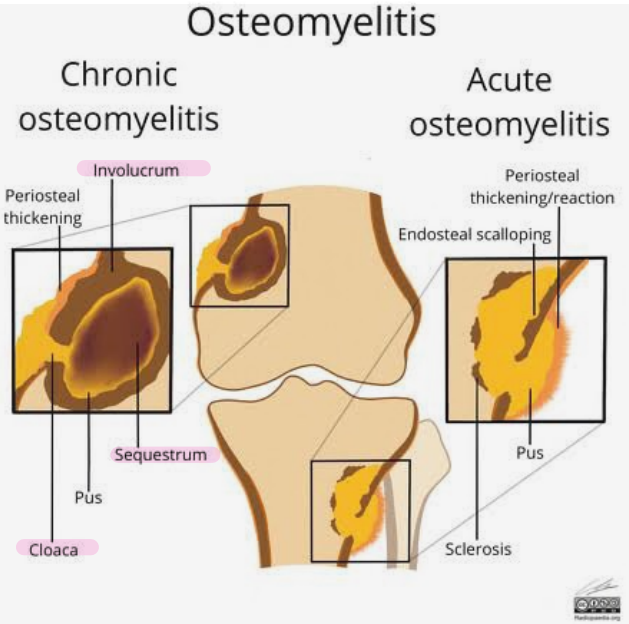
* Inflammation in sacroiliac joints and ligaments of spine
* Autoimmune process associated with HLA-B27

ANKYLOSING SPONDYLITIS

(Ankylosing Spondyloarthritis)



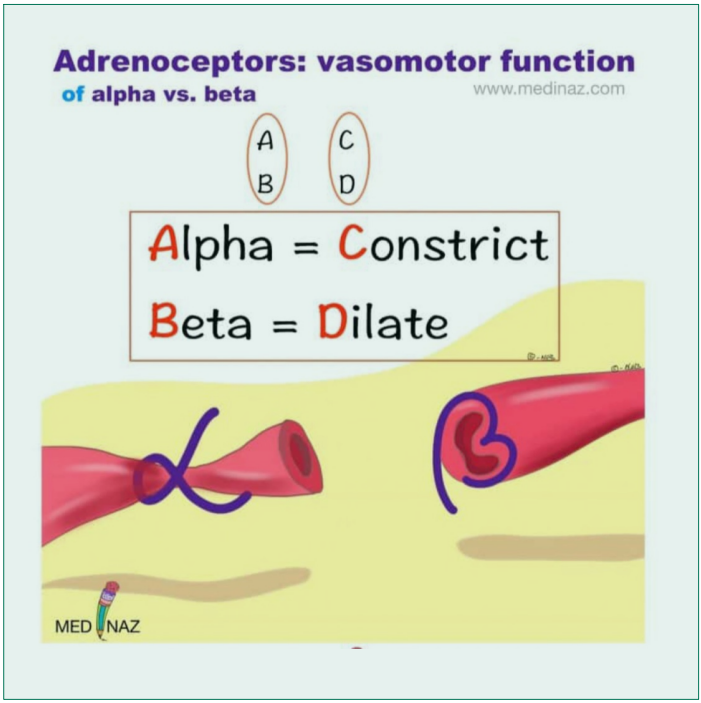
Low back pain due to sacroiliitis characterized by
* Insidious onset
* Pain at night
* Age < 40
* improves with exercise & hot water
* no improvement with rest
* Morning stiffness > 30min
* flattening of normal lumbar curvature and decreased chest expansion

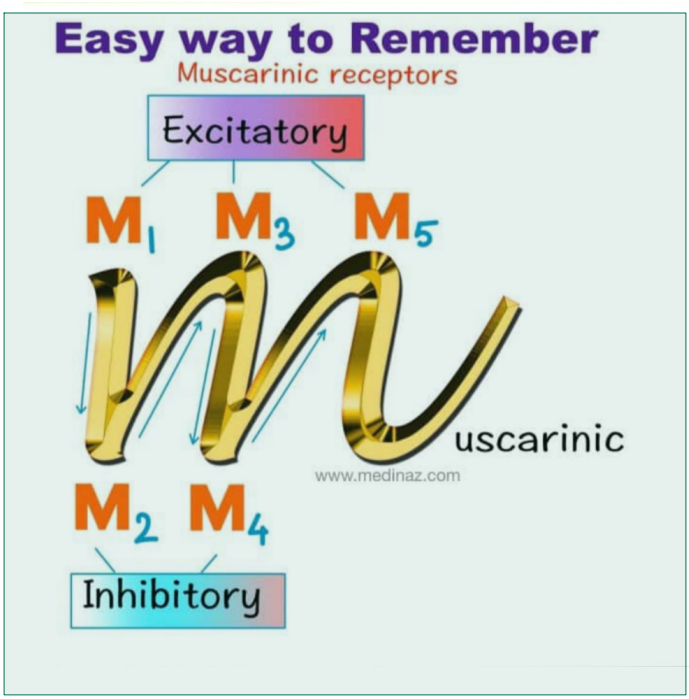


Notice sequestrum, involucrum and cloaca in chronic osteomyelitis

CHRONIC OSTEOMYELITIS

* Sequestrum - Dead bone which is denser than the surrounding bone resulting from cortical and medullary infarcts. It is hallmark of active infectious process.
* Involucrum - Periosteal new bone which is formed in an attempt to wall off infective process
* Cloacae - defects in involucrum which allow the continued discharge (decompression) of inflammatory products from the bone.





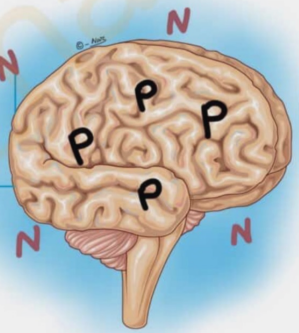
Neostigmine Vs Physostigmine

Neostigmine

Neo CNS = No CNS penetration

Physostigmine:

Phreely (freely) crosses blood-brain



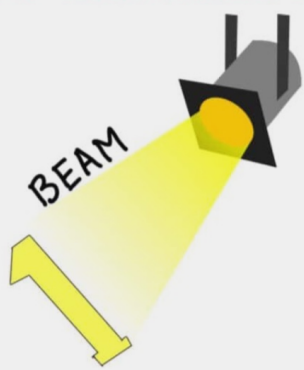
Beta-1 Selective Blockers

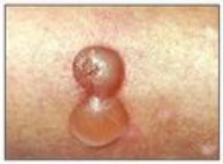
BISOPROLOL

ESMOLOL

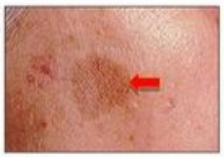
ATENOLOL

METOPROLOL



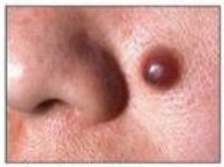


Bulla
Circumscribed collection of free fluid > 1 cm



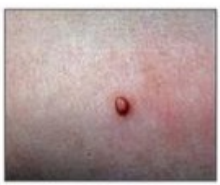
<5mm or 0.5cm

Macule
Circular flat discoloration
< 1cm
brown, blue, red or hypopigmented

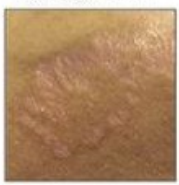


Nodule
Circular, Elevated, Solid Lesion
>1 cm

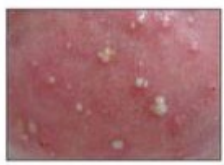
Patch
Circumscribed Flat Discoloration
> 1cm



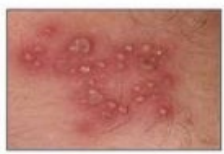
Papule
Superficial solid elevated, ≤ 0.5 cm, color varies



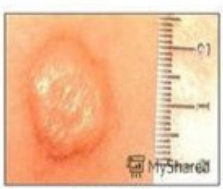
Plaque
Superficial elevated solid flat topped lesion
> 1 cm



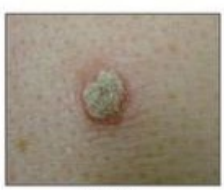
Pustule
Vesicle containing puss (inflammatory cells)



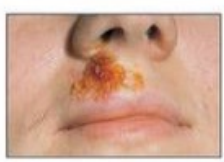
Vesicle
Circular collection of free fluid
≤ 1 cm



Wheal
Edematous, transitory, plauqe, may last few hours

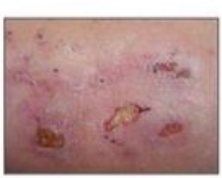


Scale
Epidermal thickening; consists of flakes of plates of compacted desquameted layers of stratum corneum

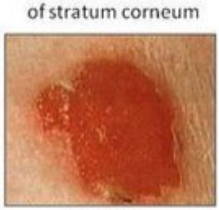


Crust
Dried serum or Eexudate on skin

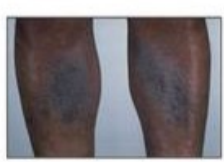
Fissure
Crack or split



Excoriation
Linear erosion

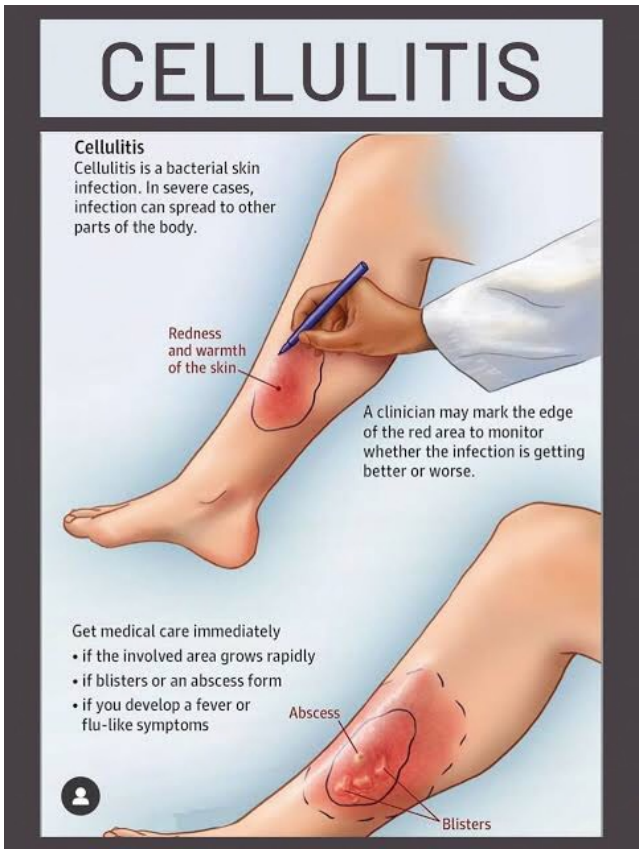


Erosion
Loss of epidermis superficial; part or all of the epidermis has been lost



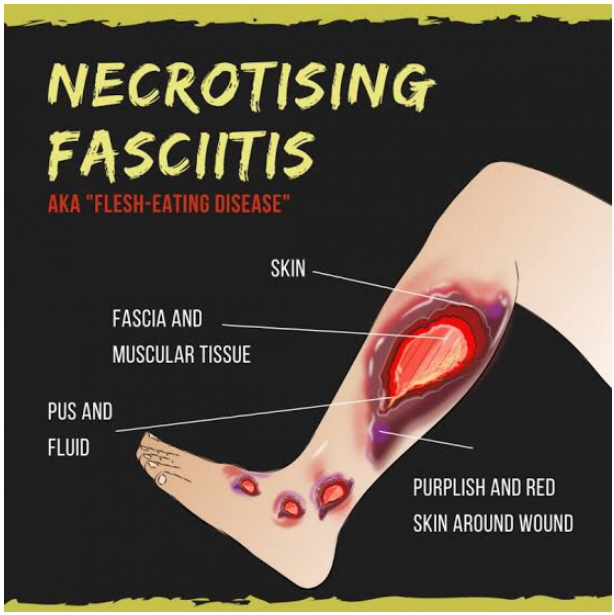
Lichenification
Thickening of the epidemis seen with exaggeration of Normal skin lines

Scar
Thickening; permanent fibrotic changes that occur on the skin following damage of the epidermis



Acute, painful spreading infection of dermis and subcutaneous tissue

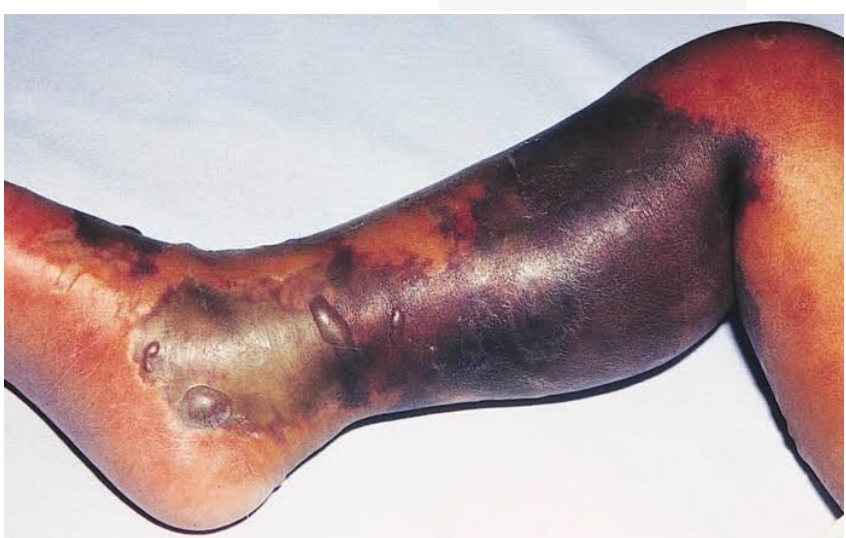
Common cause:
Staph aureus
Streptococcus pyogenes

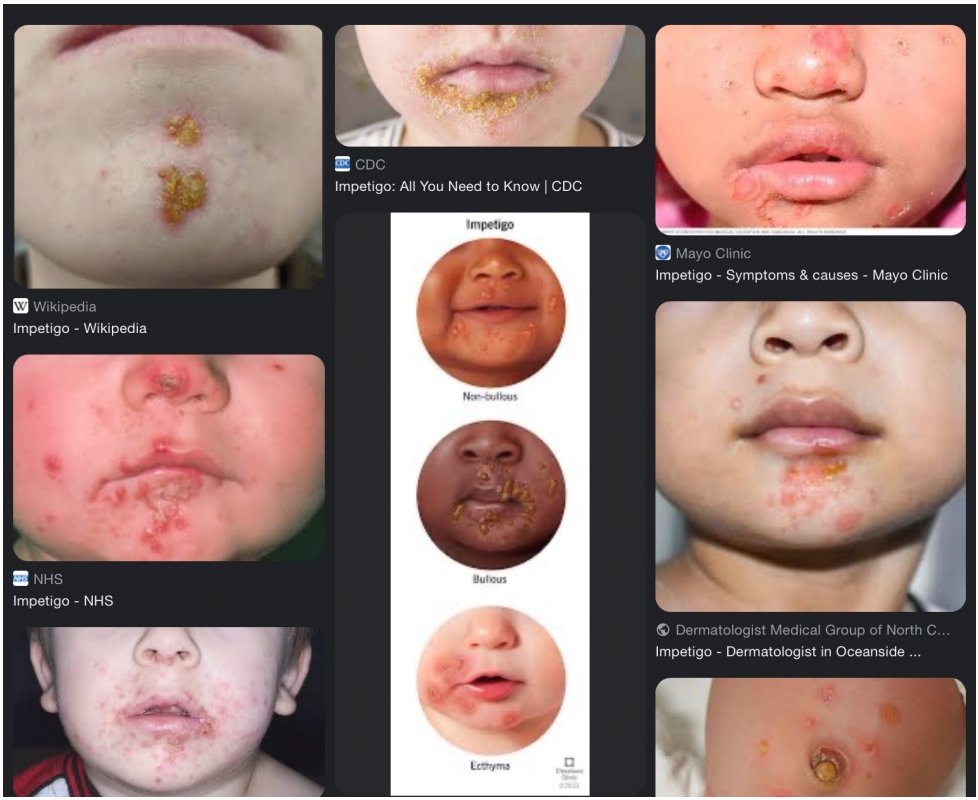


Polymicrobial infection that include:
Staph aureus
E.coli
Clostridium perfringens

Deep infection along fascial planes with severe pain, fever, and leukocytosis

Associated with crepitus due to methane and CO2 production





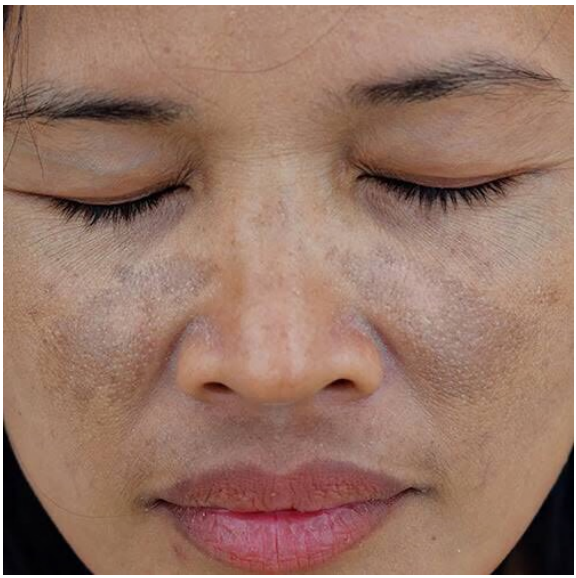
IMPETIGO

* Superficial infection of epidermis
* Characterised by pustules and honey colored crusts on erythematous base

Partial or total loss of melanocytes within epidermis

VITILIGO

Difference from albinism:
In albinism, melanocytes are present but fail to produce pigment due to tyrosine deficiency



MELASMA

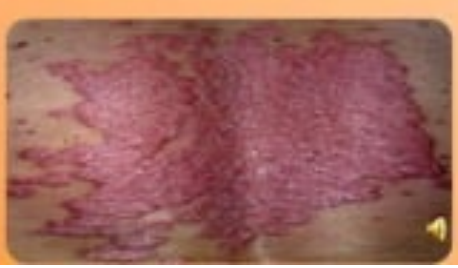
* mask like zone of facial hyperpigmentation
* associated with pregnancy and therefore known as mask of pregnancy

Psoriasis

Clinical features

The hallmark of psoriasis is a well defined scaly red plaque. This may have a "salmon pink" hue. The scale can be waxy or silvery.

Psoriasis is not characteristically itchy, but can be very noticeable and greatly impair patients' quality of life.



Psoriasis

Symptoms by Type

Plaque Psoriasis

inflamed skin and scaly, silvery plaques with a clear border

Nail Psoriasis

nail pitting and nail separation

Guttate Psoriasis

teardrop-shaped bumps

Inverse Psoriasis

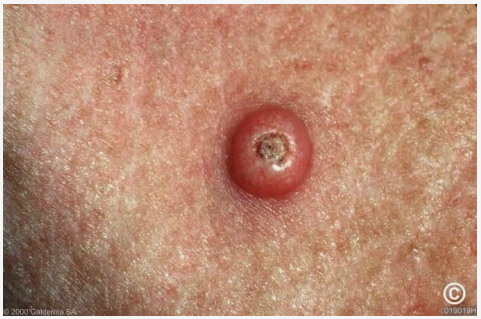
rash appearing in skin folds

Pustular Psoriasis

pus-filled lesions

Erythrodermic Psoriasis

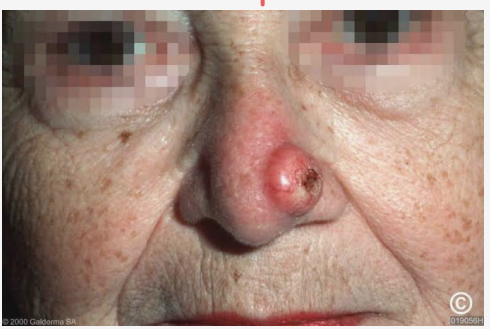
severely inflamed skin shedding in large sheets



KERATOCANTHOMA

Benign tumor that mimics squamous cell carcinoma

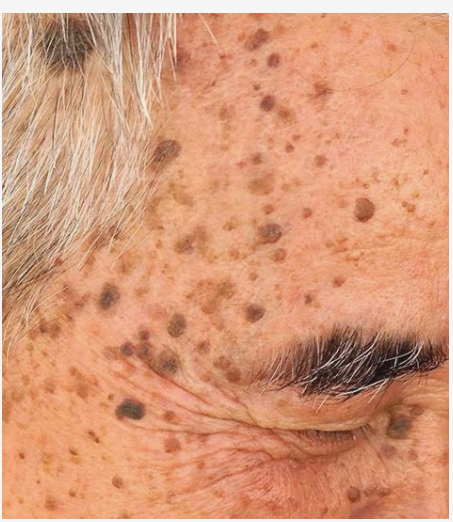
Associated with p53 mutations



Appears as flesh colored, dome shaped nodule with central, keratin filled plug

BENIGN EPITHELIAL TUMORS

SEBORRHEIC KERATOSES

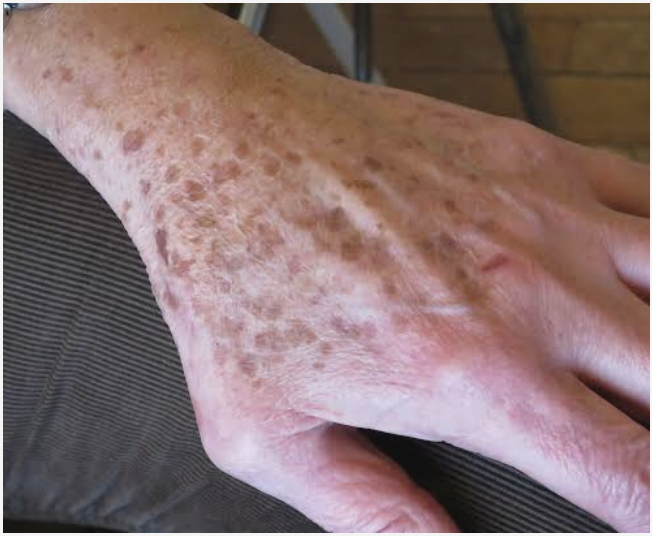


* very common benign skin tumor
* mostly occur after age 40

Waxy brown papules and plaques with prominent follicle openings.

Lesions have a "stuck on" appearance

Morphology:
Hyperkeratosis
Horn cysts
Invagination cysts



ACTINIC KERATOSIS

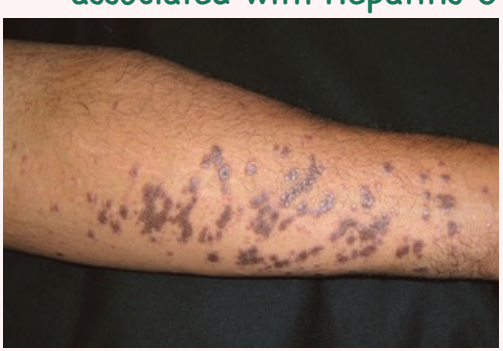
* epidermal dysplastic change that occur due to prolong exposure to UV light
* usually less than 1 cm
* reddish brown
* sandpaper like consistency

Malignant transformation –> squamous cell carcinoma

PRE MALIGNANT TUMORS

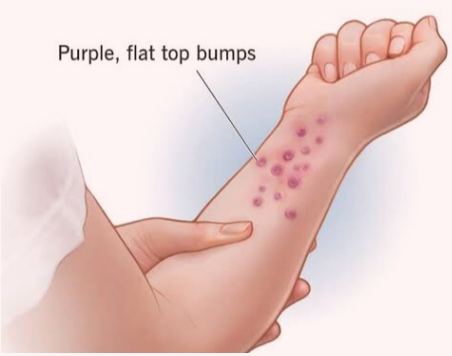
LICHEN PLANUS

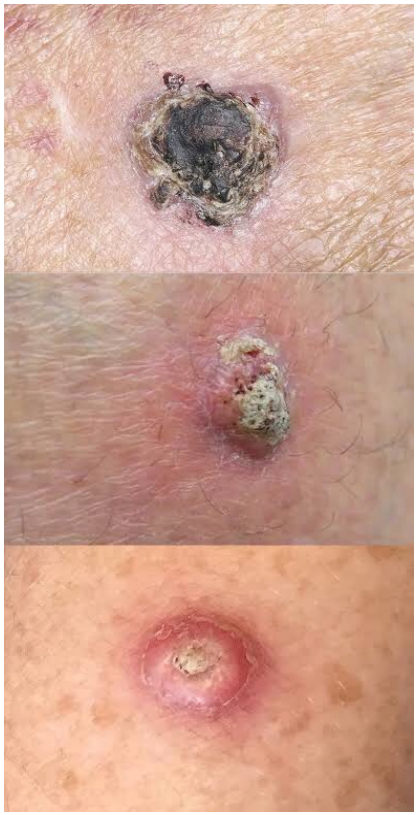
* pruritic, purple, polygonal, flat shaped papule
* generally resolves 1-2 years after onset
* associated with Hepatitis C



Wickham Striae:

- white dots or lines on lesion
- Represent zone of hypergranulosis





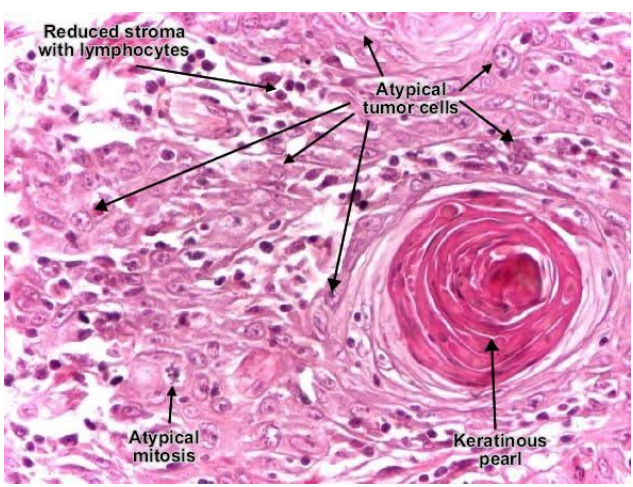
SQUAMOUS CELL CARCINOMA

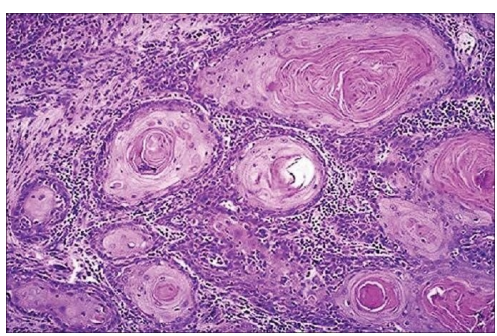
second most common skin malignancy after basal cell carcinoma

Associated with human papilloma virus (HPV-36)

Morphology:

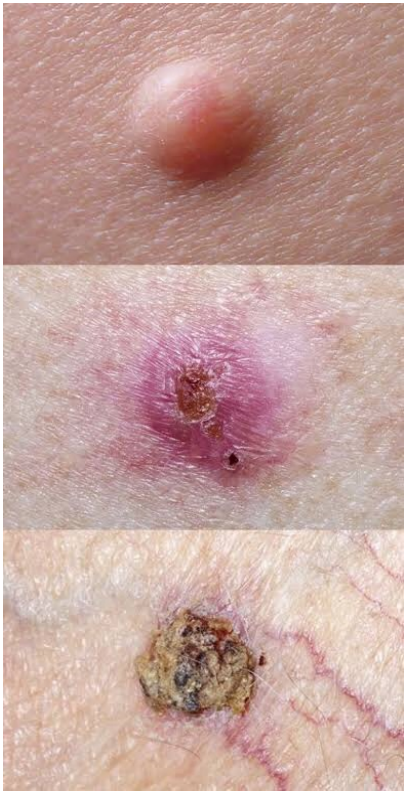
* usually well differentiated
* usually nodular and ulcerated
* tumor cells are enlarged with angulated contours
* Dyskeratosis (single cell keratinization)
* keratin pearls





Notice keratin pearls

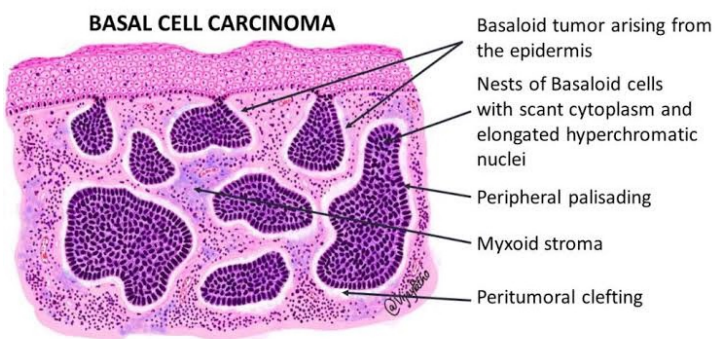
Classically involves lower lip



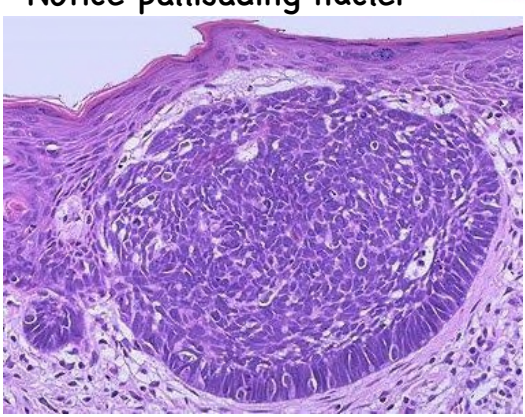
BASAL CELL CARCINOMA

- Most common skin malignancy
- Slow growing tumor
- Rarely metastasize
- Locally aggressive and infiltrative
- Also called Rodent ulcer

Presents as pearly papules containing prominent, dilated subepidermal blood vessels (telengiectasia)



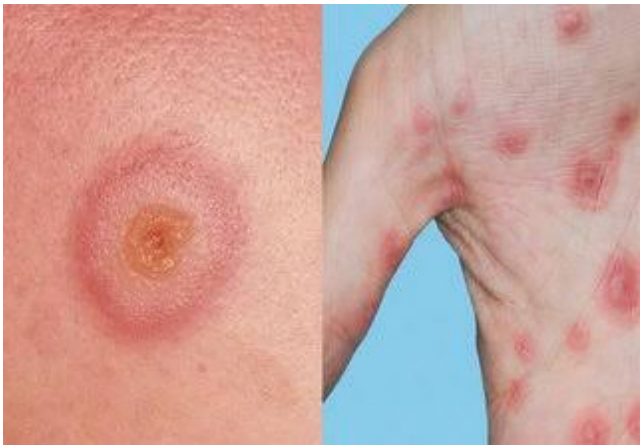
Notice pallisading nuclei



Risk factors:

- Chronic sun exposure
- Lightly pigmented individuals
- Xeroderma pigmentosum
- Immunosuppresion

Classic location is upper lip



ERYTHEMA MULTIFORME

Immunologic (hypersensitivity) reaction of skin

Characterized by diffuse, erythematous target-like lesions in many shapes

ASSOCIATIONS:

HSV

Mycoplasma infections

Histoplasmosis

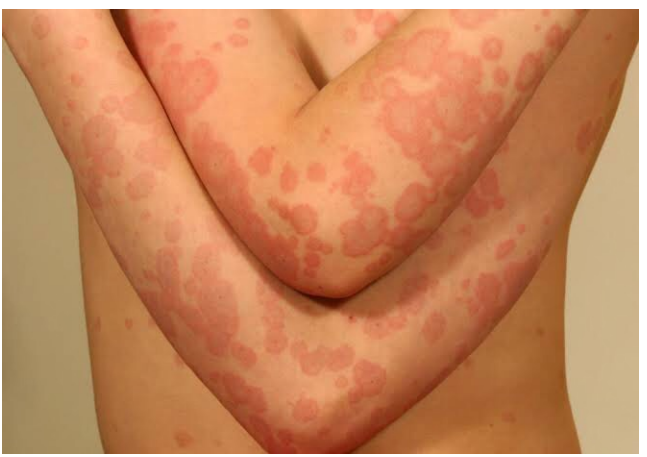
Leprosy

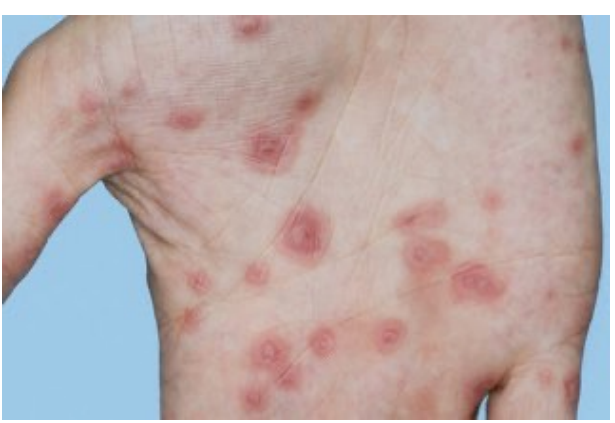
Drugs (penicillins, sulfonamides etc)

Carcinomas and lymphomas

SLE

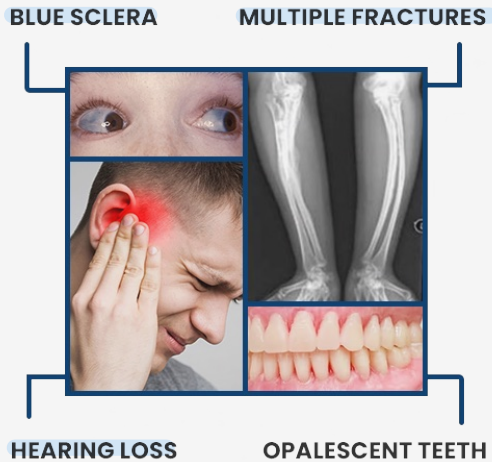
Dermatomyositis





Severe form:

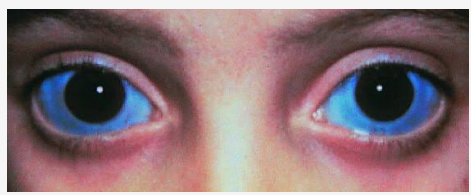
* Stevens-Johnsons syndrome
* Toxic epidermal necrolysis



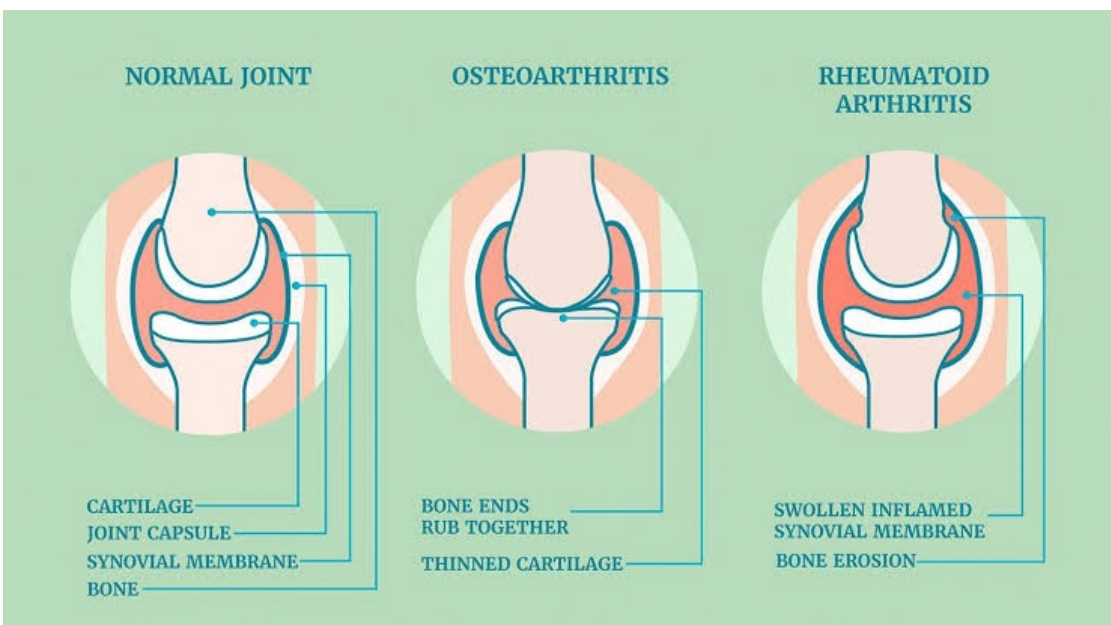
OSTEOGENESIS IMPERFECTA (BRITTLE BONE DISEASE)

Mutations in alpha 1 and alpha 2 chains of Collagen Type 1

Most commonly autosomal dominant



Notice blue sclera in OI

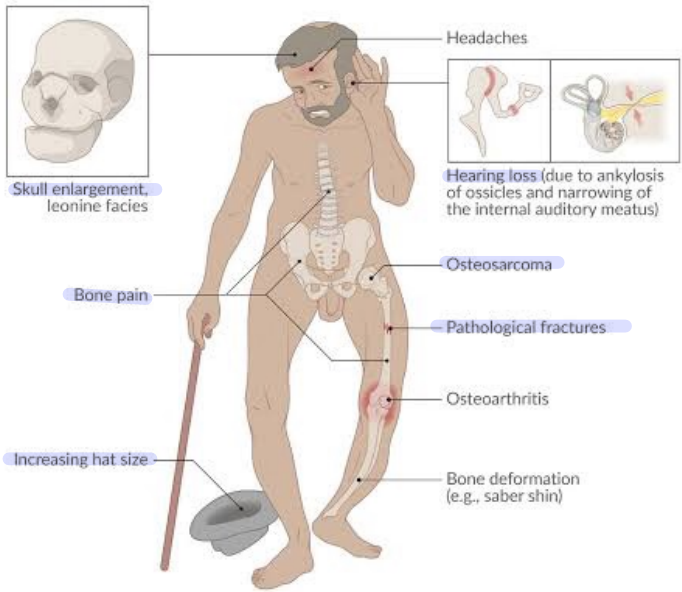


Paget disease of the bone (osteitis deformans)

Pathophysiology
Increased bone remodeling (↑ osteoclastic and osteoblastic activity) → replacement of lamellar bone with weak woven bone

Diagnosis
- Isolated elevation of ALP with normal calcium, phosphate, and PTH
- Urinalysis (markers of collagen degradation)
- X-ray (bone deformation with sclerotic and osteolytic lesions)
- Skeletal scintigraphy (bony lesions)

Treatment
- Indicated in active disease (↑ ALP or active foci on skeletal scintigraphy)
- First-line: bisphosphonates



PAGET DISEASE (OSTEITIS DEFORMANS)

* Localized disorder of bone remodeling due to osteoclast dysfunction
* may be caused by a slow virus infection by paramyxovirus

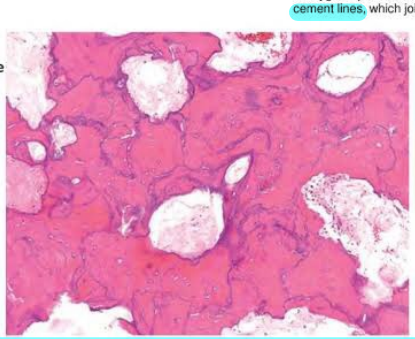
Osteosarcoma is the most dreaded complication of Paget disease

Paget disease, morphology

This jigsaw puzzle-like appearance is produced by unusually prominent cement lines, which join haphazardly oriented units of lamellar bone

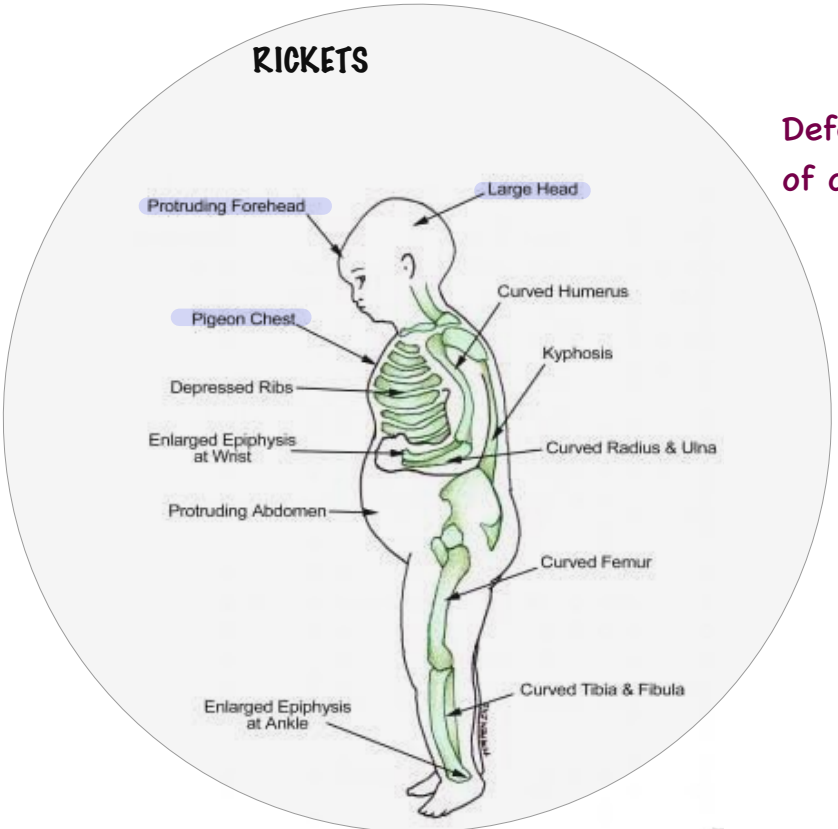
Osteosclerotic phase

...the findings during the other phases are less specific



In the end, the bone is composed of coarsely thickened trabeculae and cortices that are soft and porous and lack structural stability. These aspects make the bone vulnerable to deformation under stress; consequently, it fractures easily.

Mosaic pattern of lamellar bone pathognomonic of Paget disease

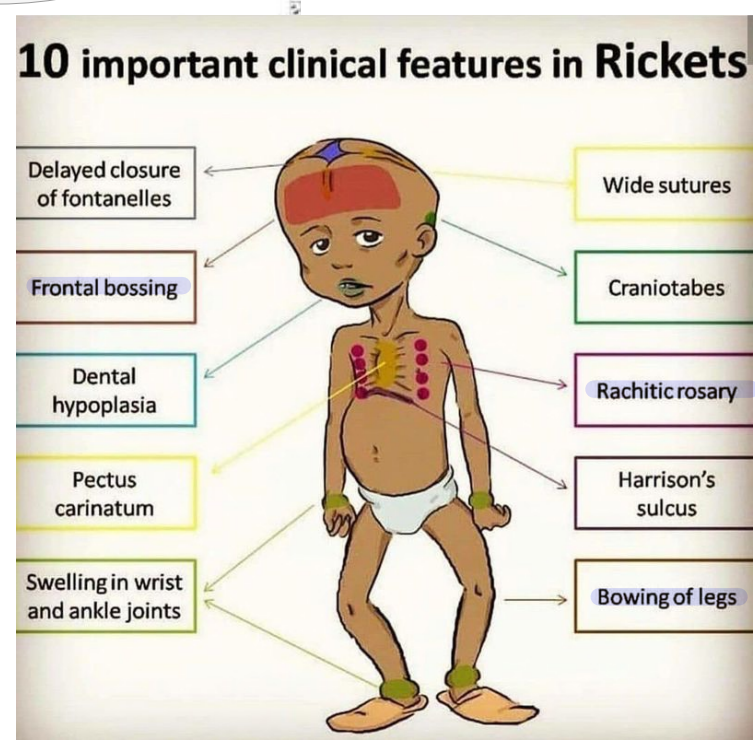


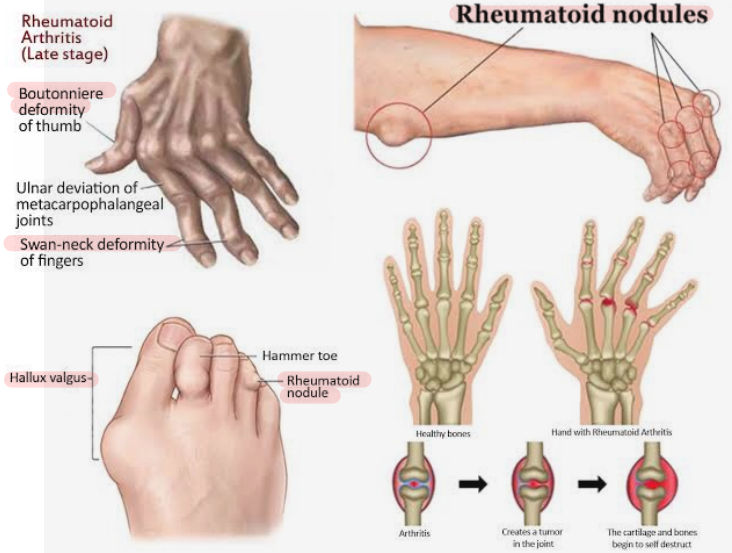
Defective mineralization of osteoid

Vitamin D deficiency

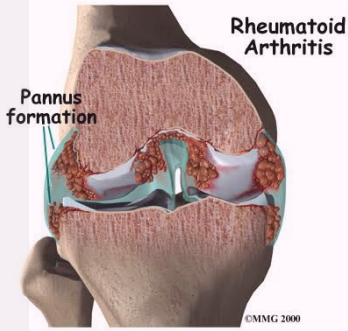
LABS:

* decrease calcium and phosphate
* increase P





Neutrophils and high proteins in synovial fluid

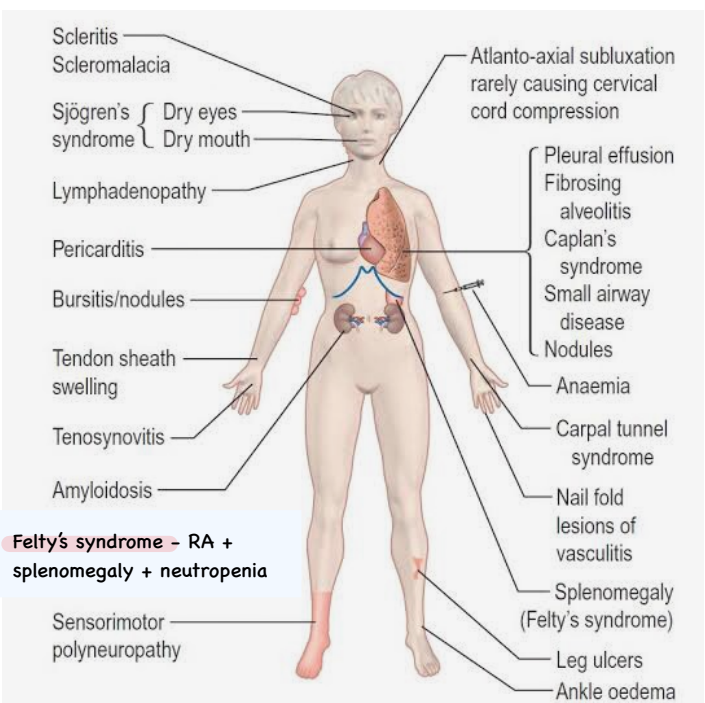


Panus formation
* granulation tissue formed within synovial tissue
* formed by fibroblasts and inflammatory cells
* release cytokines which destroy the articular cartilage
* result in ankylosis i.e. fusion of joint by scar tissue

RHEUMATOID ARTHRITIS

Autoimmune disease

Rheumatoid factor is an IgM autoantibody that has specificity for Fc portion of IgG



Felty's syndrome - RA + splenomegaly + neutropenia

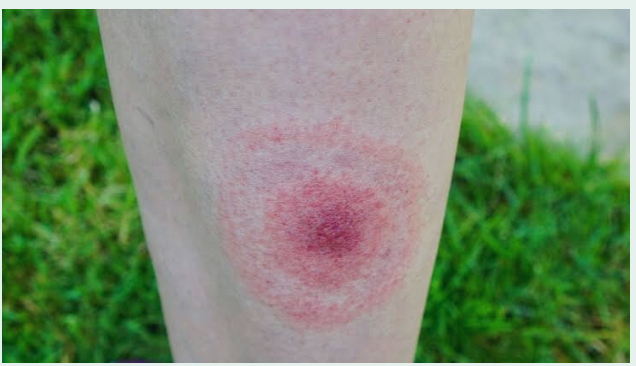
Non-articular manifestations of RA.

Signs:
* radial deviation of wrist and ulnar deviation of fingers
* Swan neck deformity
* Boutonniere deformity
* Cock up toe deformity

Clinical Features:
* symmetric involvement of joints
* polyarticular (5 or more joints)
* small joints affected first
* morning stiffness (more than 1 hr) improves with activity

LYME ARTHRITIS

Caused by spirochete "borrelia burgdorferi"

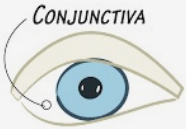


Bull's eye lesion - pathognomonic of Lyme disease

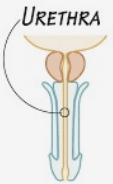
REACTIVE ARTHRITIS (REITER'S SYNDROME)

CLASSIC TRIAD

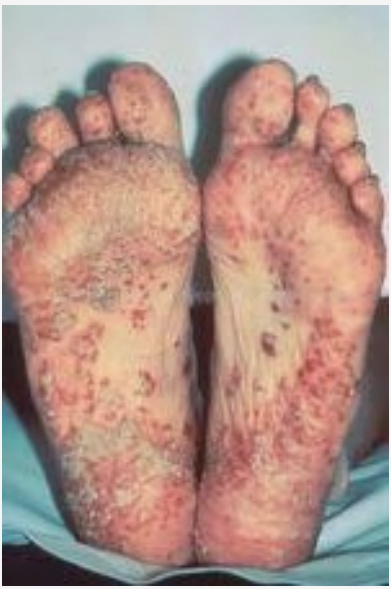
Conjunctivitis
(CAN'T SEE)



Urethritis
(CAN'T PEE)

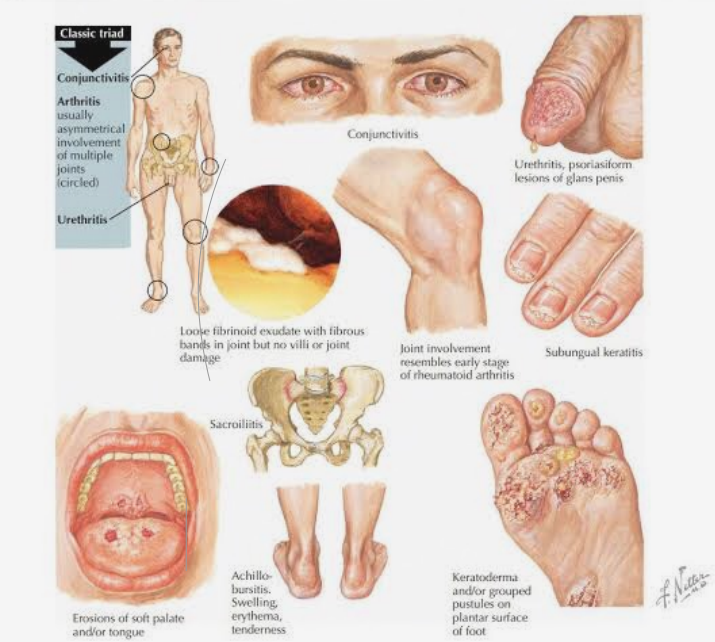


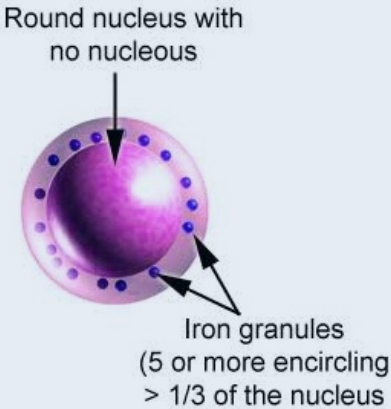
Arthritis
(CAN'T BEND THE KNEE)



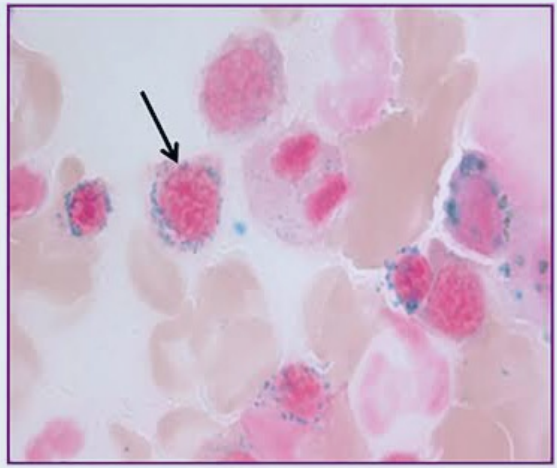
Keratoderma Blenorrhagica

REACTIVE ARTHRITIS



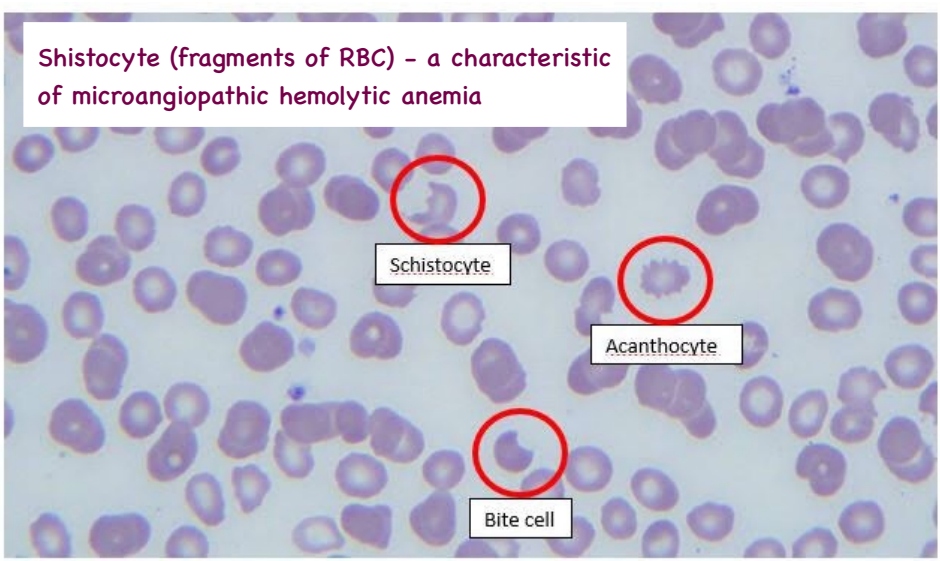


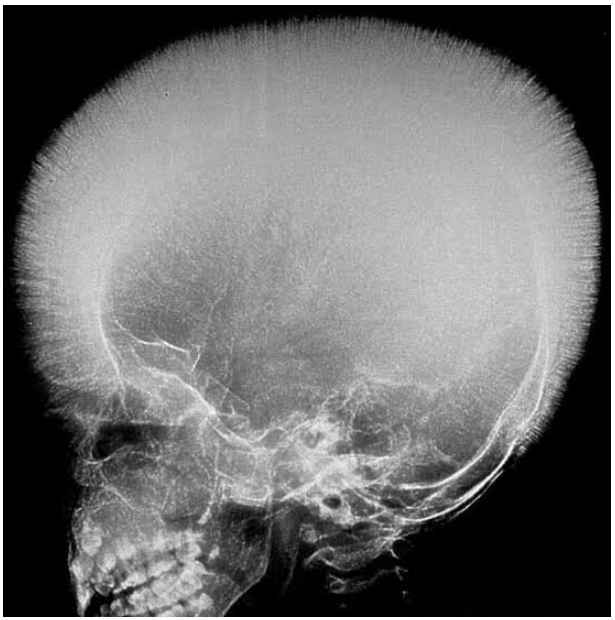
Iron laden mitochondria form a ring around the nucleus of erythroid precursors. These cells are called ringed sideroblasts.



Prussian blue stain demonstrating ring sideroblasts (arrow).

Shistocyte (fragments of RBC) – a characteristic of microangiopathic hemolytic anemia

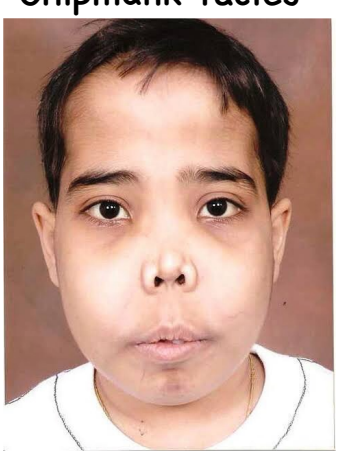




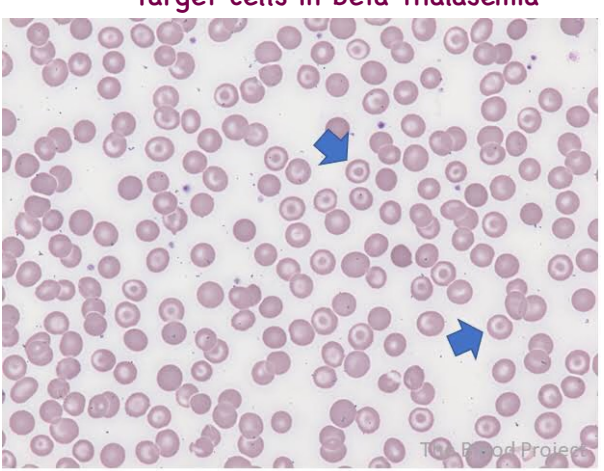
BETA THALASEMMIA

Crew cut appearance of skull seen on X-Ray in beta thalassemia major patients

Chipmunk facies

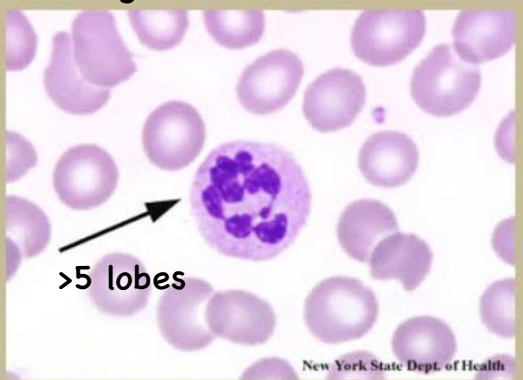


Target cells in beta thalasemia

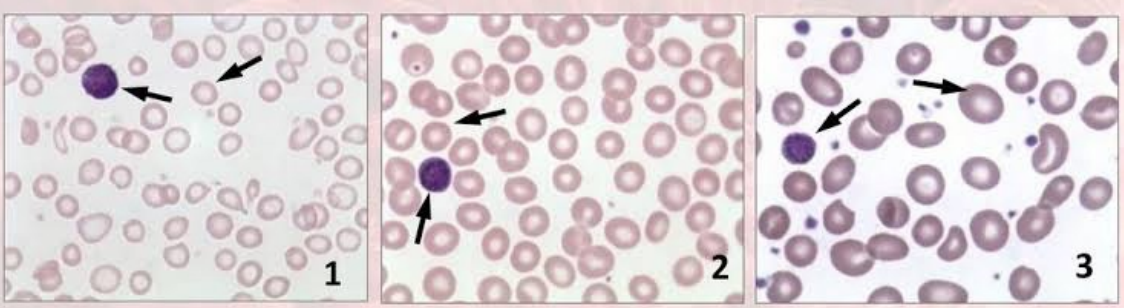


Hypersegmented Neutrophils

Seen in megaloblastic anemia

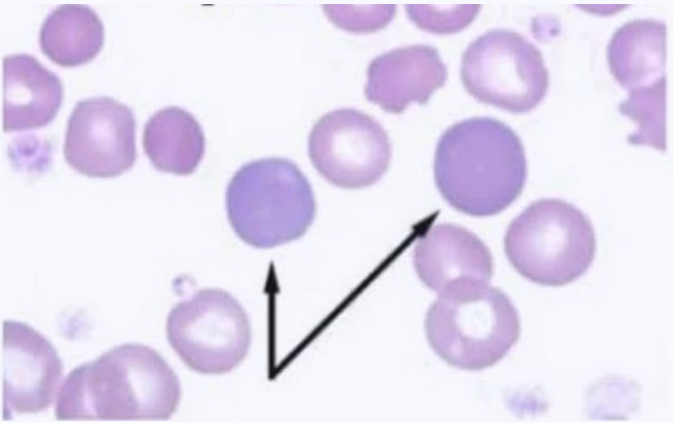


Morphologic Categories of Anemia



1 Microcytic/hypochromic 2 Normocytic/Normochromic 3 Macrocytic/Normochromic

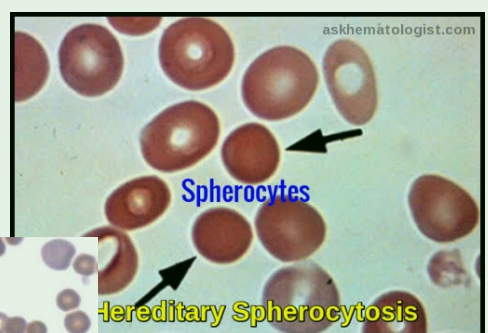
N.B. The nucleus of a small lymphocyte (shown by the arrow) is used as a reference to a normal red cell size

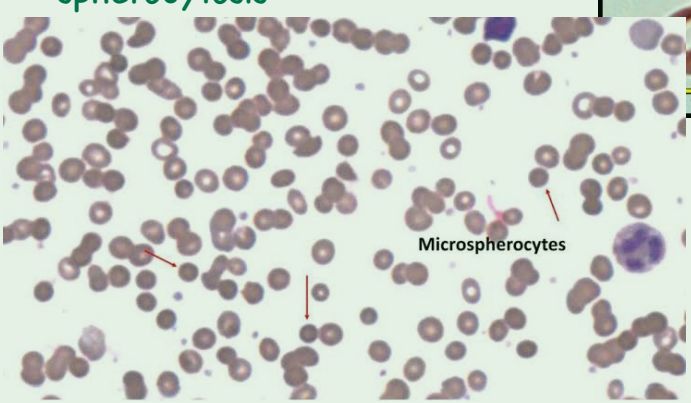


Reticulocytes identified on blood smear as larger cells with bluish cytoplasm (due to residual RNA)

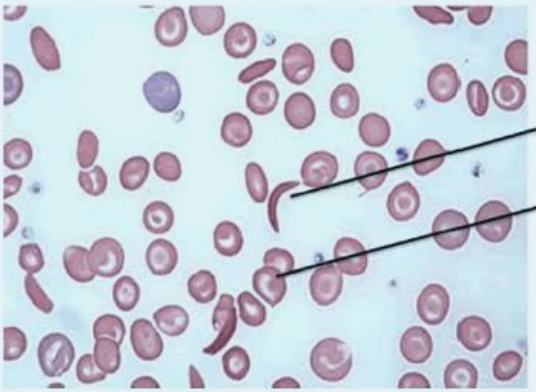
HEREDITARY SPHEROCYTOSIS

Spherocytes with loss of central pallor seen in hereditory spherocytosis





* splenomegaly
* jaundice with unconjugated bilirubin
* risk for bilirubin gallstones
* increased risk for aplastic crisis with parvovirus B19 infection of erythroid precursors

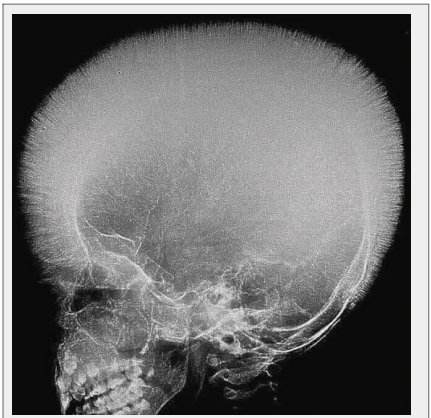


* sickle cells
* target cells
* Howell jolly bodies

Figure 1: A peripheral blood smear demonstrating irreversibly sickled cells, and red blood cells (RBCs).

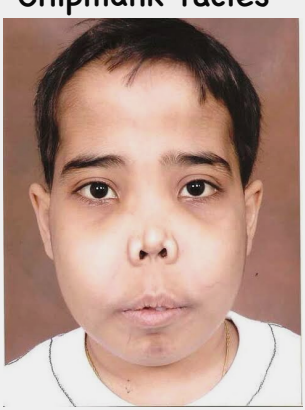
SICKLE CELL ANEMIA

Autosomal recessive disorder in beta chain of Hb. Glutamic acid is replaced by valine.



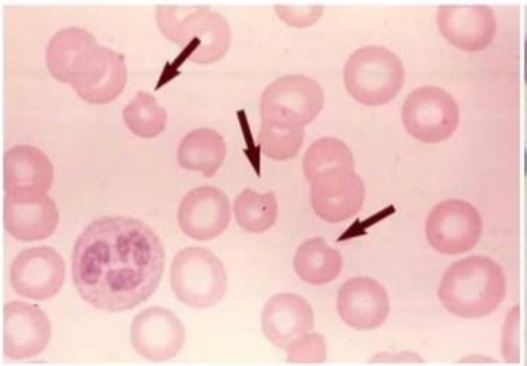
Crew cut appearance due to massive erythroid hyperplasia

Chipmunk facies

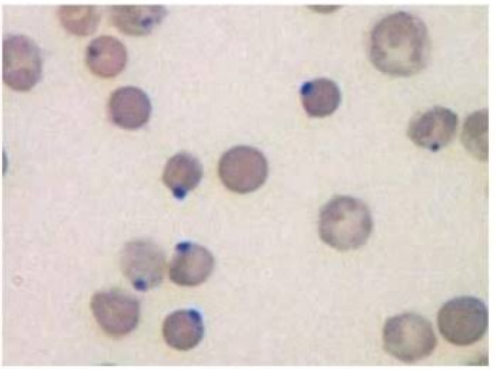


Increased risk of sickling occurs in hypoxemia, dehydration and acidosis.

Complications of vaso occlusion:
* Dactylitis
* Autosplenectomy
* Acute chest syndrome
* Pain crisis
* Renal papillary necrosis



Bite cells

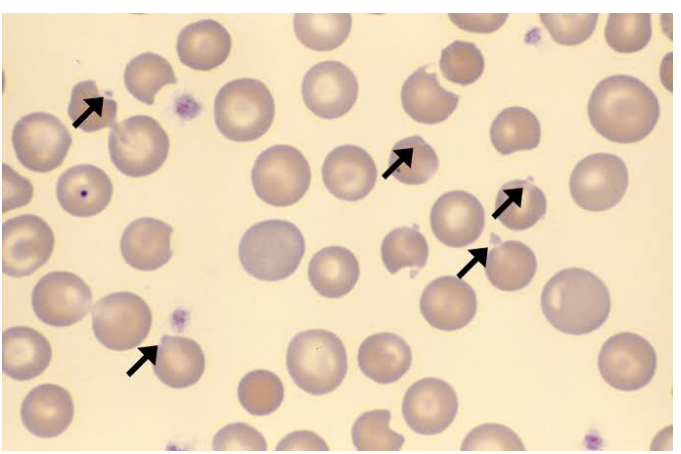


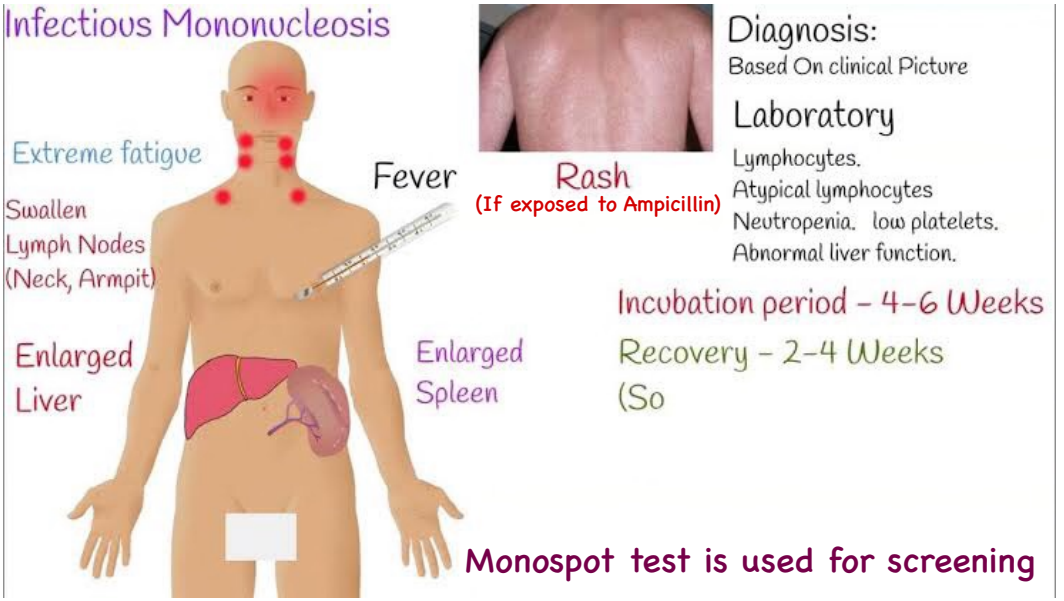
Heinz bodies

HEINZ BODIES AND BITE CELLS SEEN IN G6PD DEFICIENCY

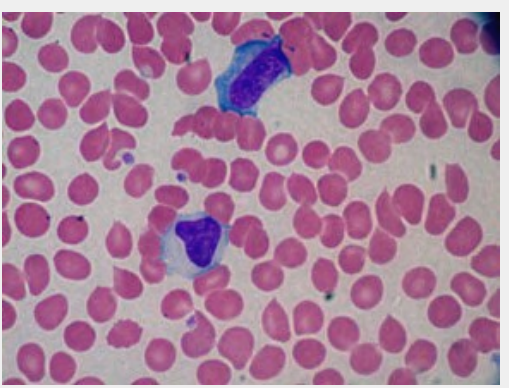
X linked recessives disorder resulting in reduced half life of G6PD. Renders cells susceptible to oxidative stress.

Protective role against falciparum malaria

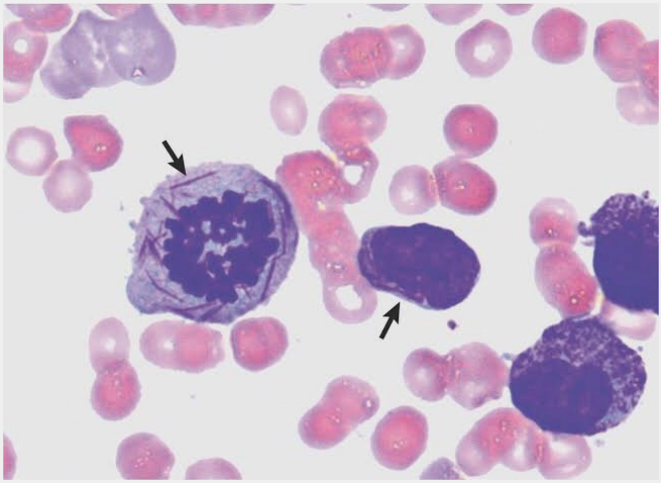




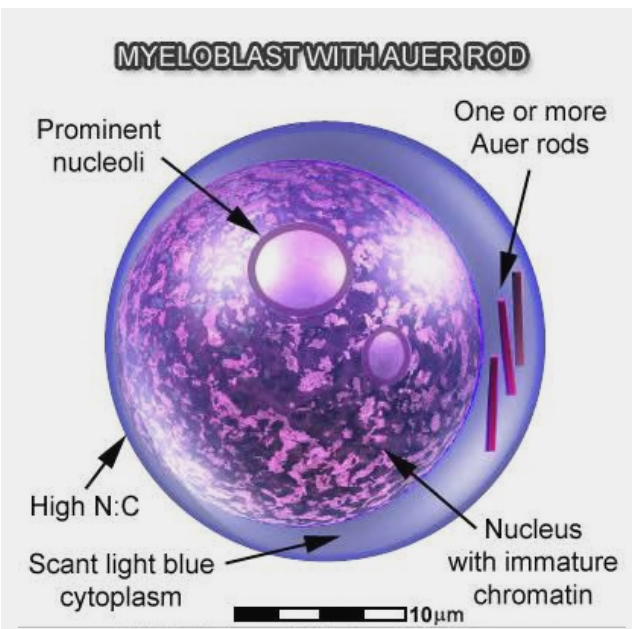
Most common cause - EBV
Less common cause - CMV

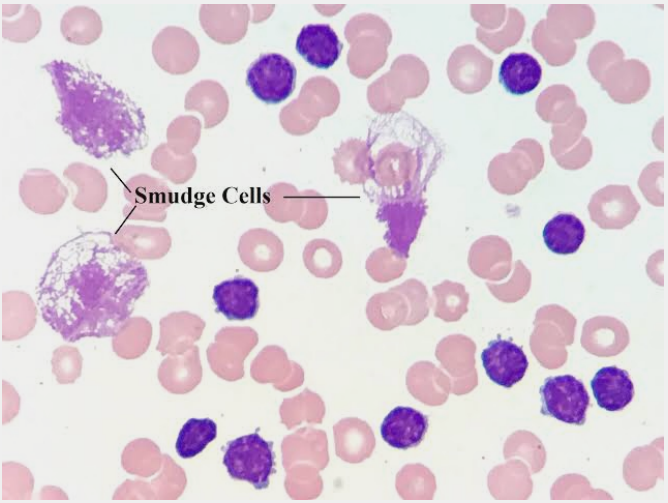


Atypical lymphocytes in Infectious Mononucleosis



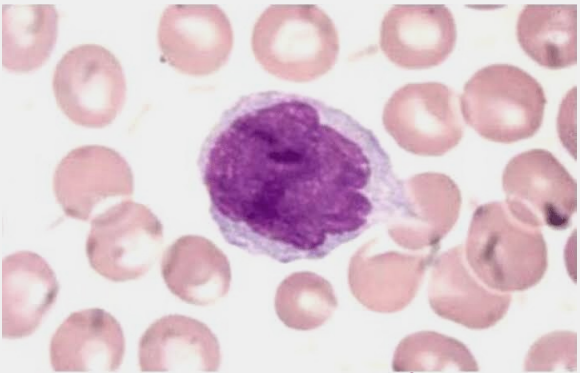
Myeloblasts are usually characterised by positive cytoplasmic staining for myeloperoxidase (MPO). Crystal aggregates of MPO may be seen as Auer rods



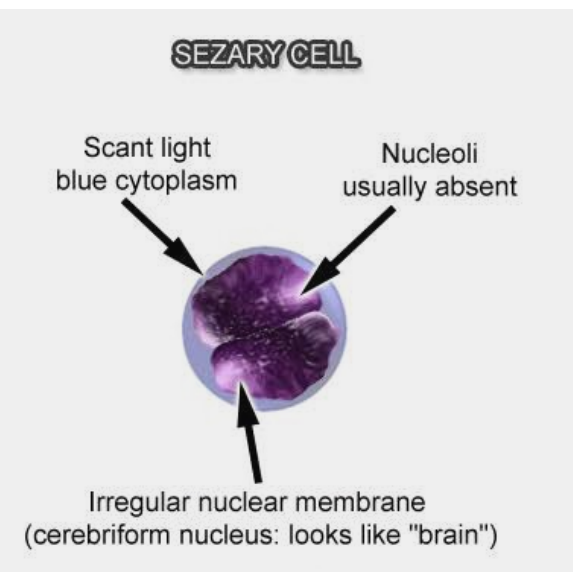


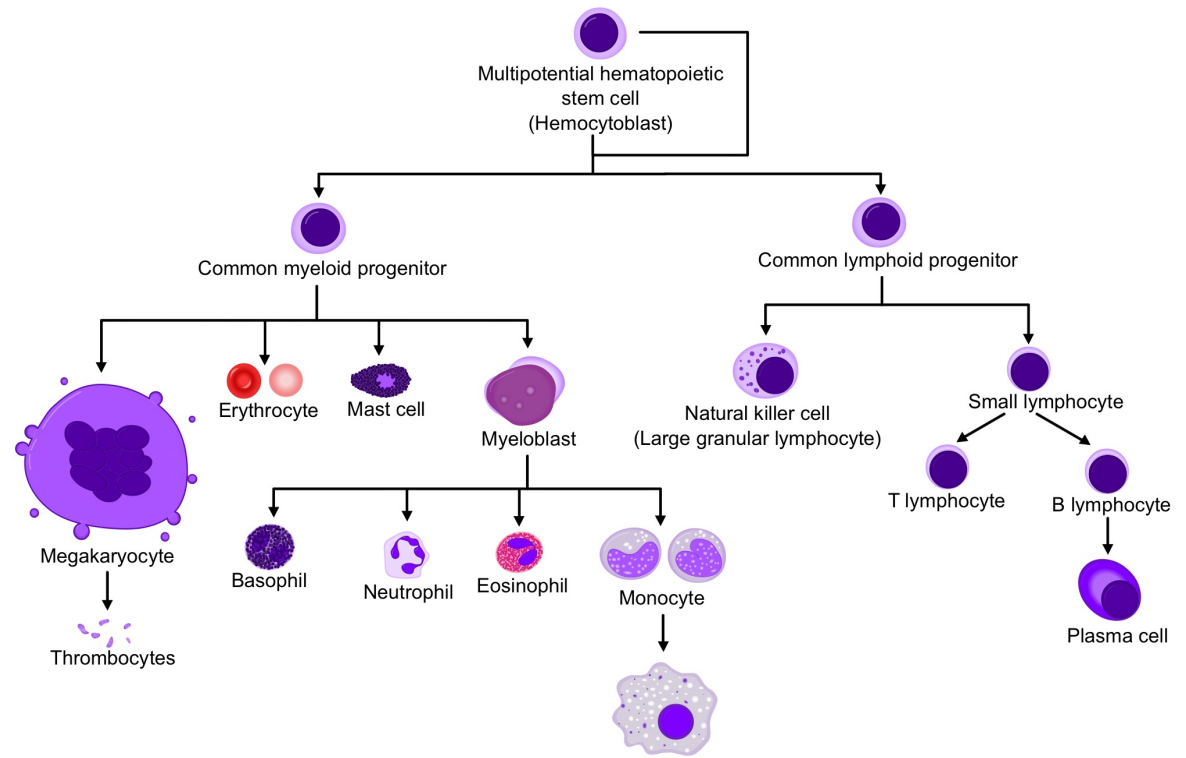
Smudge cells seen in Chronic Lymphocytic leukemia

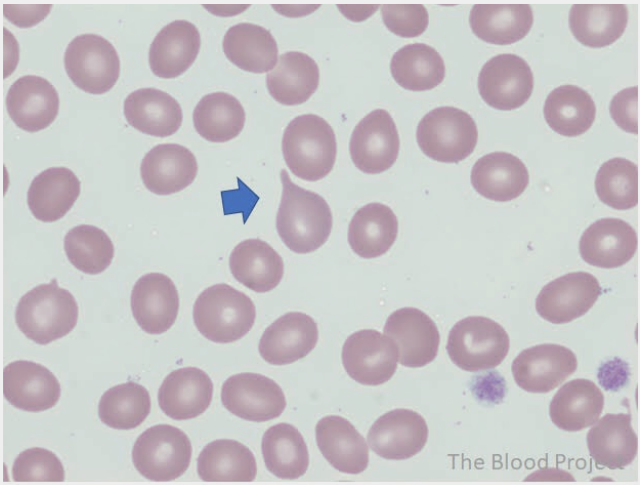
Among B cell lymphomas, only CLL/SLL and mantle cell lymphoma commonly express CD5. So it is a helful diagnostic clue.



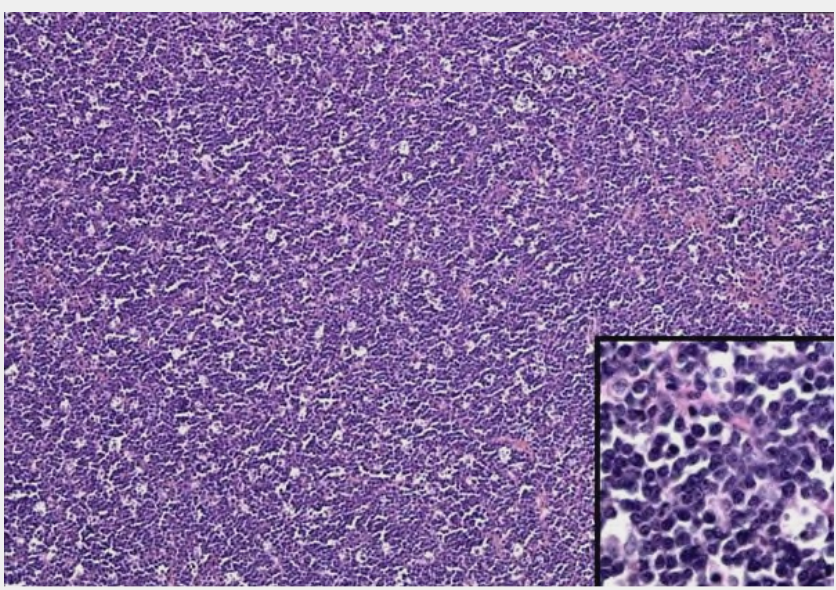
Sezary cells seen in Mycoses fungoides. Sezary cells are characteristic lymphocytes with cerebriform nuclei.



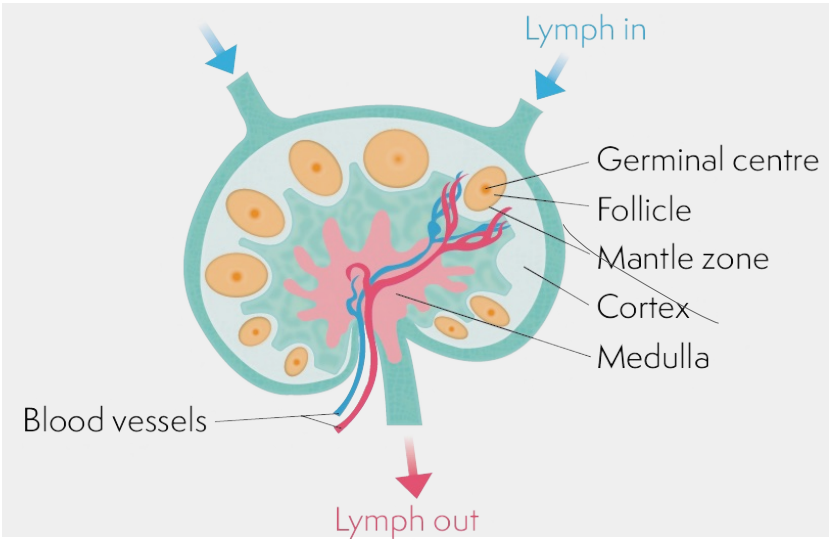




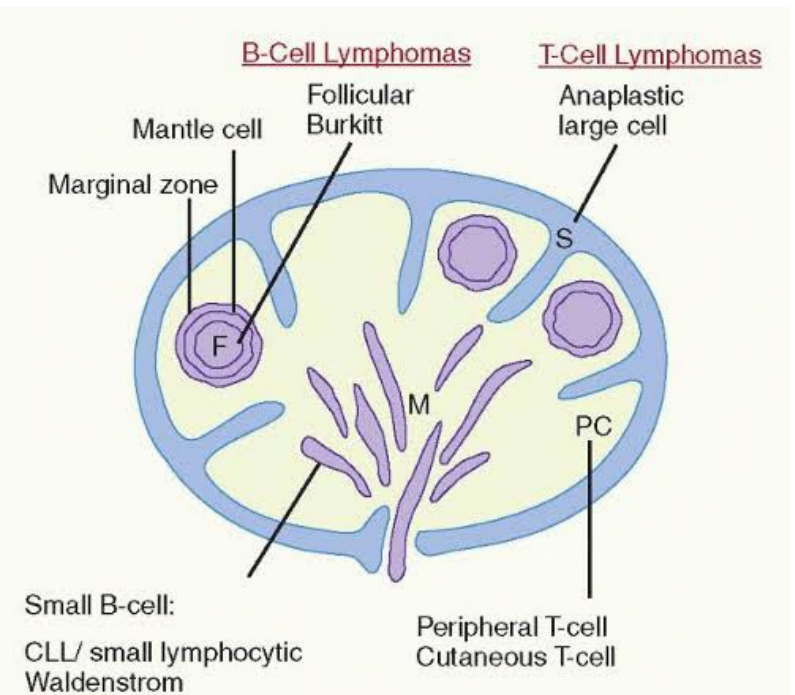
Teardrop RBCs, nucleated RBCs and immature granulocytes seen in Myelofibrosis

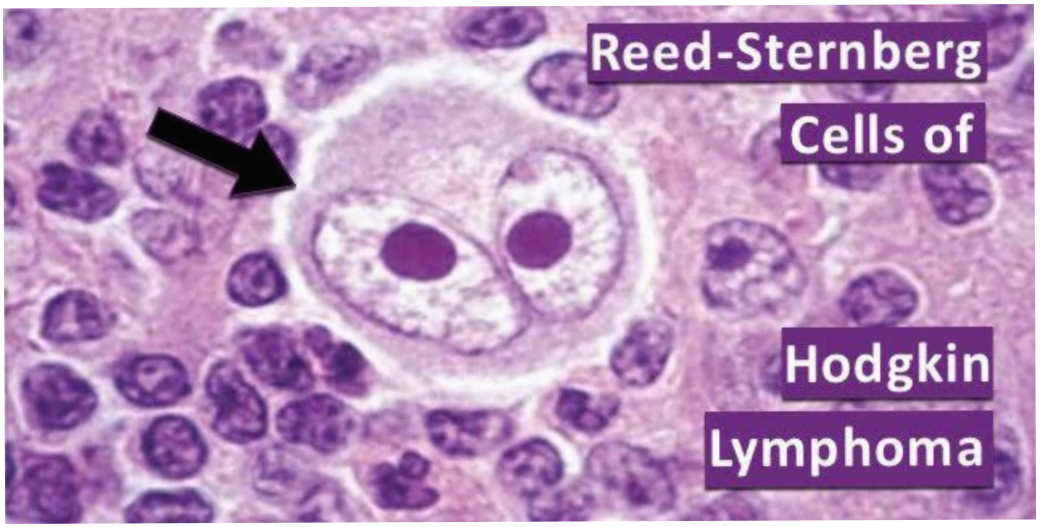


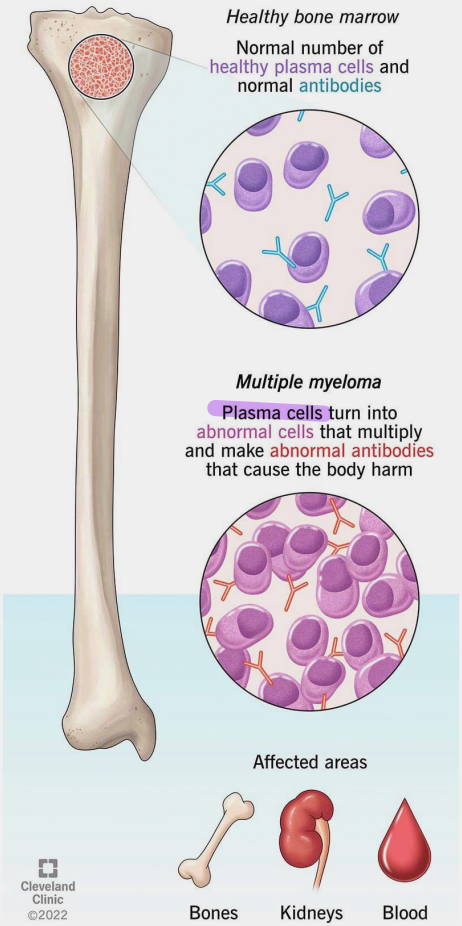
Starry sky pattern seen in Burkitt lymphoma

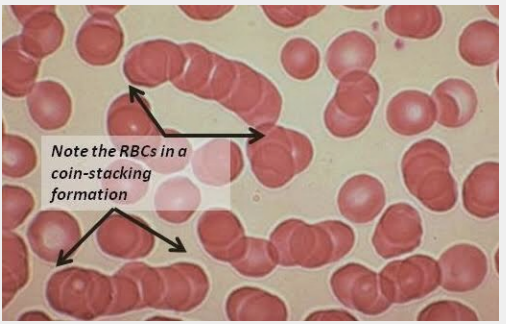


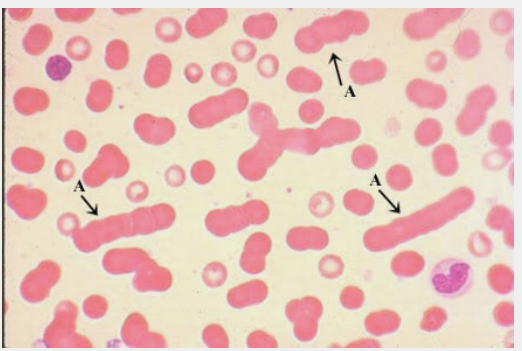
LYMPHOMAS CORRESPONDING TO LYMPH NODE REGIONS











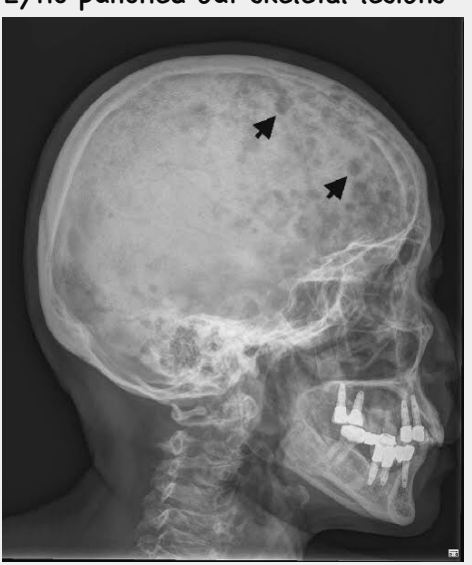
Rouleaux formation

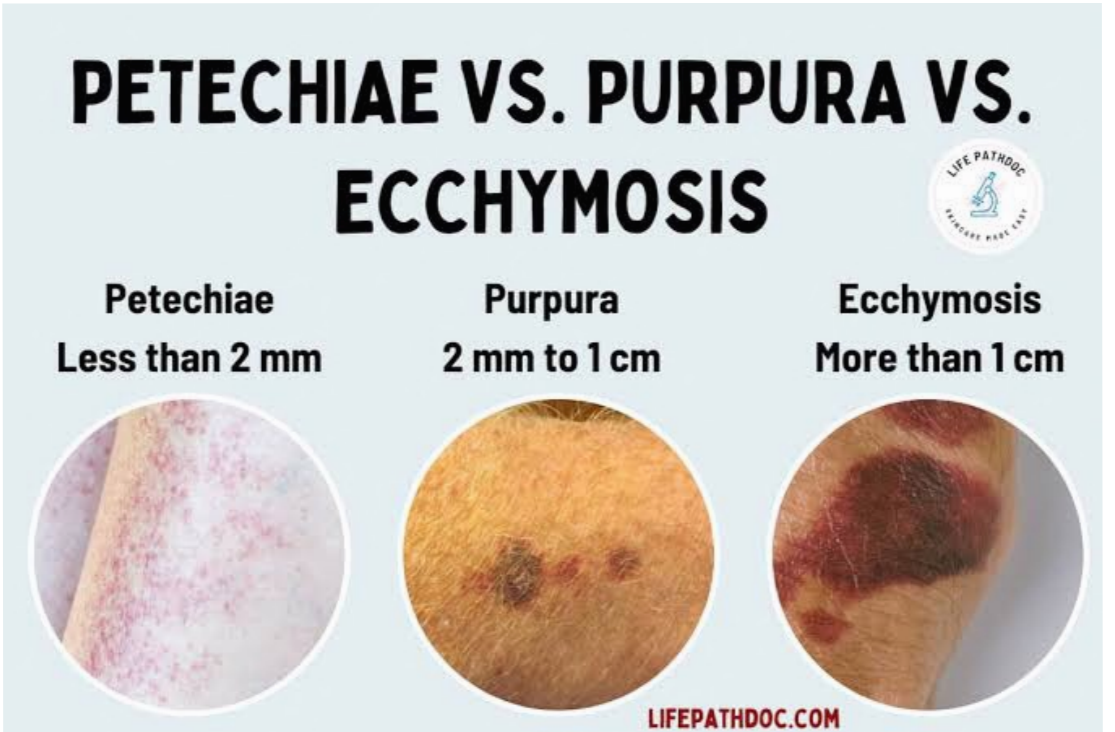
MULTIPLE MYELOMA

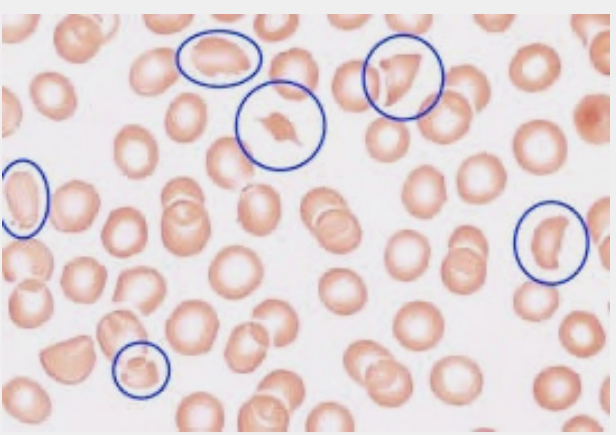
Presence of Bence Jones proteins

M spike is present on serum electrophoresis, most commonly due to IgG or IgA

Lytic punched out skeletal lesions



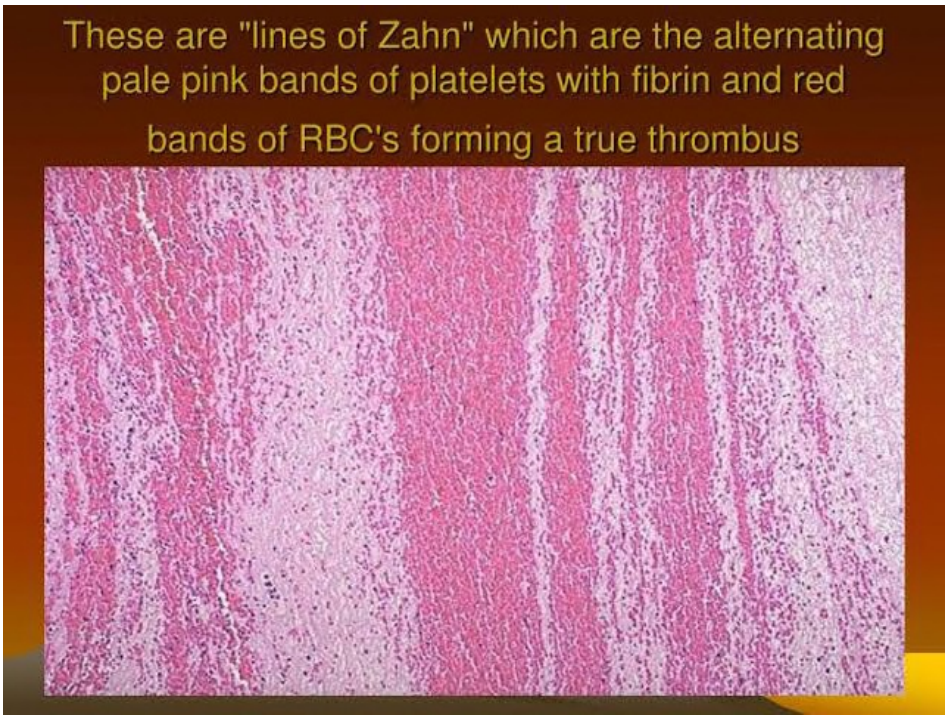




Shistocytes seen in microangiopathic hemolytic anemia

Microangiopathic hemolytic anemia seen in:

* TTP
* HUS



Lines of Zahns indicating thrombus formation

CHARACTERISTIC FINDINGS

* Sideroblastic anemia - Ringed sideroblasts
* Vitamin B12 Deficiency - increased urine methylmalonic acid
* Sickle cell disease - Howel Jolly bodies
* G6PD Deficiency- Heinz bodies and bite cells
* Autoimmune hemolytic anemia - Positive Coomb's test
(negative Coomb test in Cold Agglutinin disease)
* Microangiopathic Hemolytic anemia - Schistocytes
* Hodgkin Lymphoma - Reed Sternberg cells
Nodular sclerosis Hodgkin Lymphoma - Lacunar cells
Lymphocyte predominant Hodgkin Lymphoma - popcorn cells
* Follicular Lymphoma - Centrocytes, buttock cells, centroblasts
* Burkitt Lymphoma - Starry sky patterns
* Multiple Myeloma - M spike, Reuleaux formation, Bence Joes protein, Flame cells, Mott cells, Russel bodies, Dutcher bodies
* Waldenstrom's Macroglobulinemia - Russel bodies, Dutcher bodies
* Acute Myelogenous Leukemia (AML) - Auer rods
* CML - Sea blue histiocytes
* Primary Myelofibrosis - Tear drop cells
* Mycosis fungoides - Sezary cells (characteristic lymphocytes with ceribriform nuclei)
* Langerhans cell histiocytosis - Birbeck (tennis racket) granules
* Gout - mono sodium urate crystals
* Pesudo Gout - calcium pyrophosphate dihydrate crystals
* Thrombus - Lines of Zahn

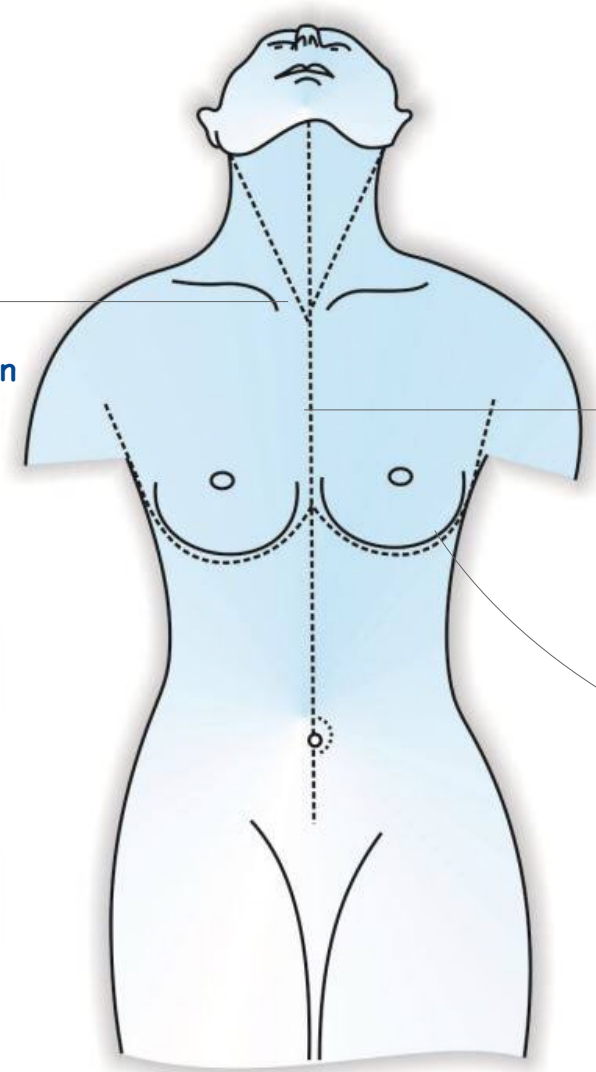
DIAGNOSTIC TESTS

* Paroxysmal nocturnal hemoglobinuria - Ham's test
* Leukomoid reaction is LAP positive
* Hairy cell leukemia are positive for tartrate - resistant acid phosphatase (TRAP)
* Tingible body macrophages are present in follicular hyperplasia but absent in follicular lymphoma

CHROMOSOMAL TRANSLOCATIONS

* Philadelphia chromosome - t(9:22) - CML
* Follicular Lymphoma - t(14:18)
* Burkitt Lymphoma - t(8:14)
* Acute promyelocytic leukemia - t(15:17)
* Ewing sarcoma - t(11:22)
* Mantle cell lymphoma - t(11:14)

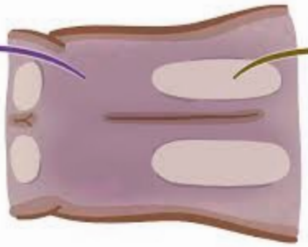
* bcl1 overexpression due to - t(11:14) - mantle cell lymphoma
* bcl2 overexpression due to - t(14:18) - Follicular lymphoma



LIVIDITY

BLUISH-PURPLE DISCOLORATION of SKIN AFTER DEATH

↳ CAUSED by BLOOD POOLING at LOWEST POINT



BLANCHING

WHITISH DISCOLORATION of SKIN

↳ CAUSED by APPLIED PRESSURE

WHAT IT TELLS FORENSIC SCIENTISTS

* TIME of DEATH
* POSITION in which INDIVIDUAL DIED

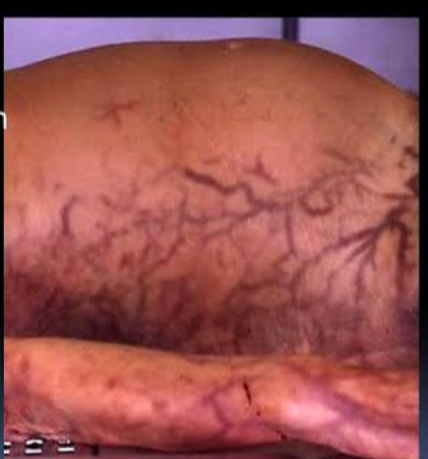
WHAT IT TELLS PATHOLOGISTS

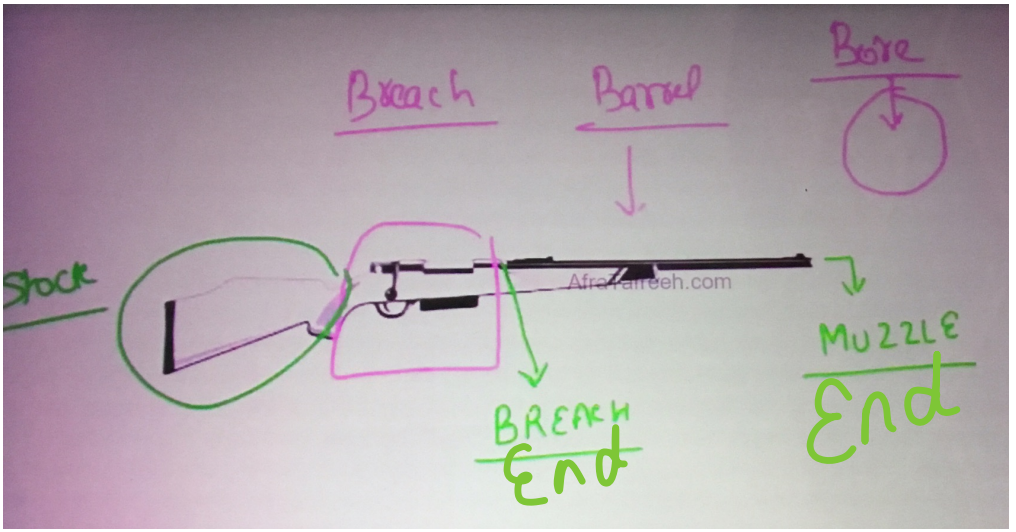
* CAUSE of DEATH
  ↳ BASED on COLOR of LIVIDITY

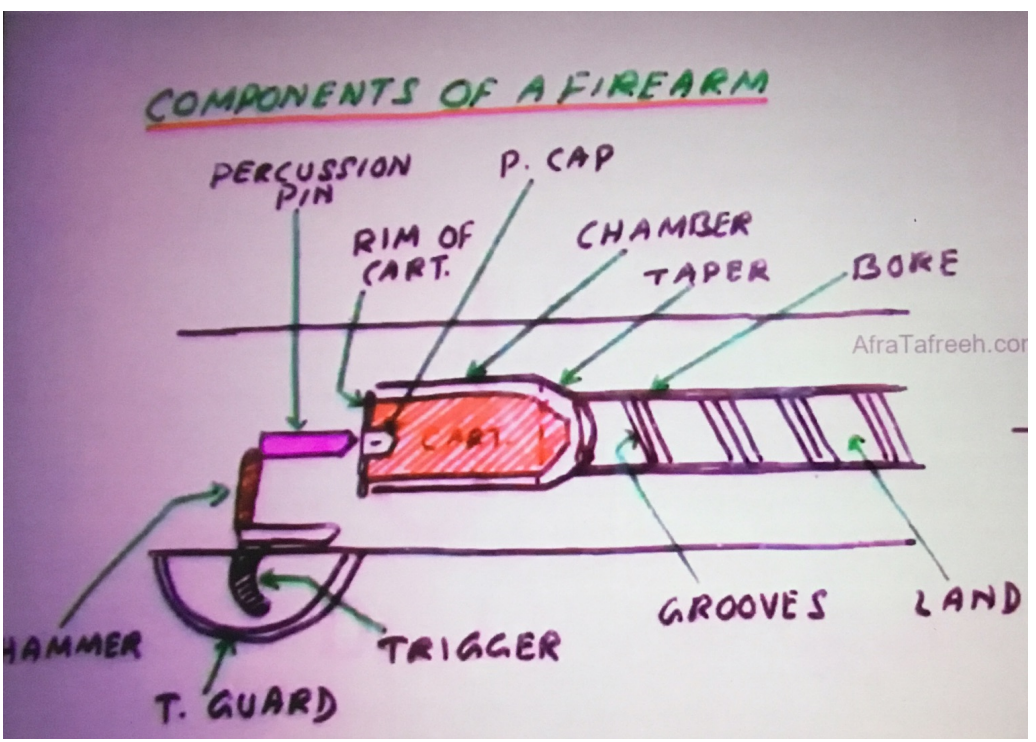
OSMOSIS.org

Putrefaction

Marbling is caused by the reaction of hydrogen sulfide, produced by bacteria, with hemoglobin remaining in the vasculature.







Parts of a Bolt-Action Rifle

Rifles, shotguns, and handguns have many similar parts. Shown here are the parts of a commonly used rifle—the bolt-action rifle.

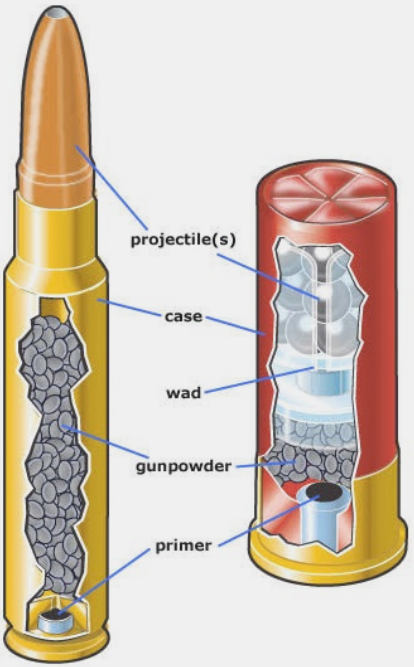
Other Firearm Parts

bore:
Inside of the firearm barrel through which the projectile travels when fired

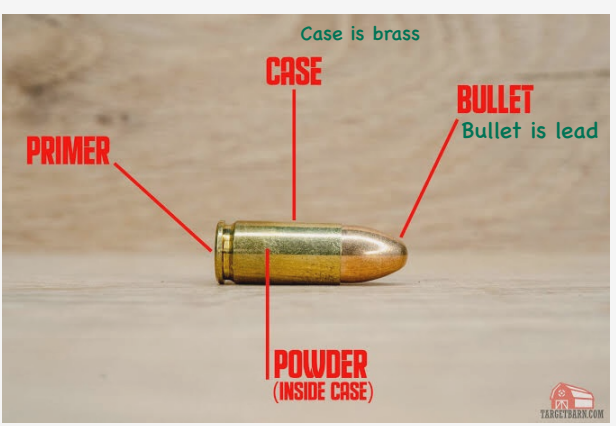
breech:
Rear end of the barrel

firing pin:
A pin that strikes the primer of the cartridge, causing ignition

receiver:
Metal housing for the working parts of the action

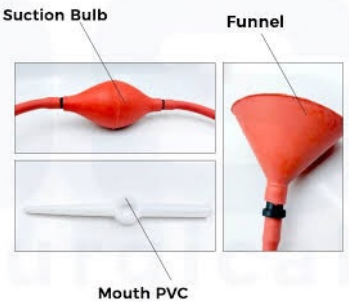


Shotgun cartridge



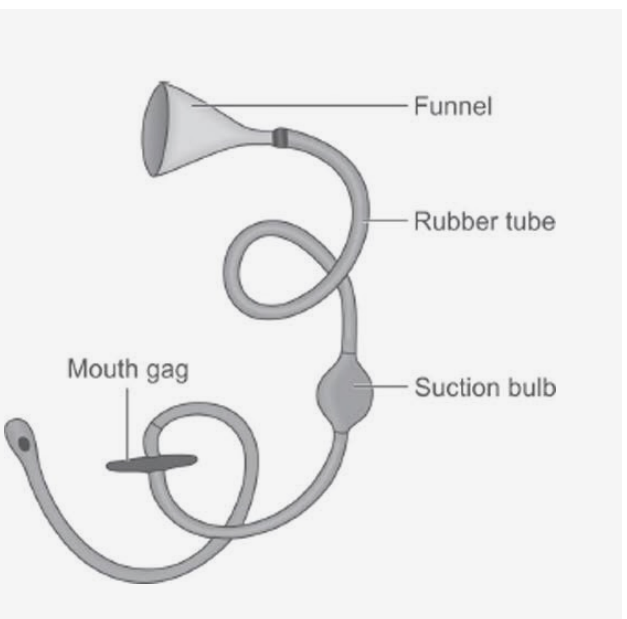
Rifle bullet

Stomach Wash Tub

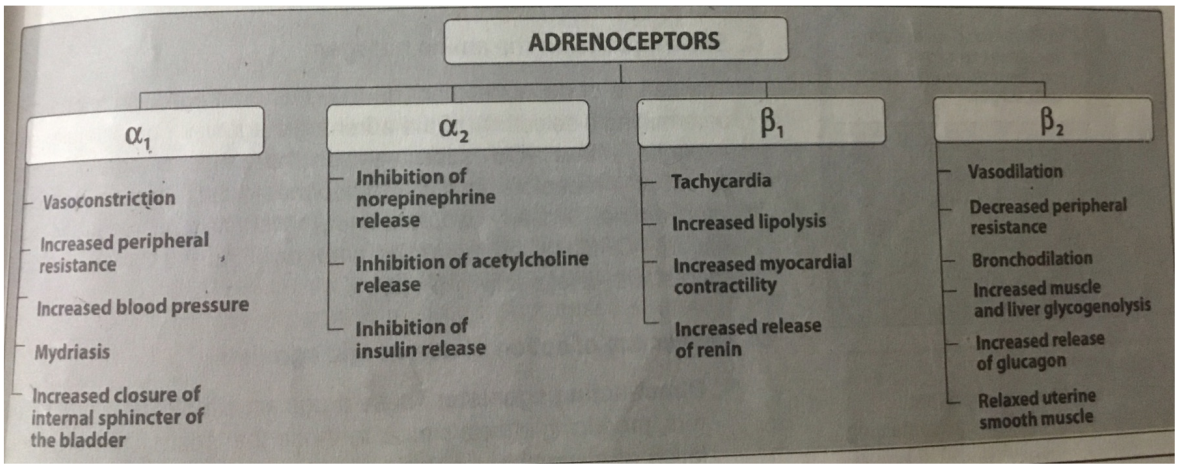


50 inch in length
Half inch in diamter

Ryle's tube used in children



* Maceration is an important example of Aseptic autolysis
* First overall site of discolouration in Putrefaction - reddish brown discolouration at aortic intima
* First external site of color change - greenish discolouration at Right iliac fossa (cecum is in RIF)



TISSUE	RECEPTOR TYPE	ACTION	OPPOSING ACTIONS
Heart			
• Sinus and AV	β_1	↑ Automaticity	Cholinergic receptors
• Conduction pathway	β_1	↑ Conduction velocity, automaticity	Cholinergic receptors
• Myofibrils	β_1	↑ Contractility, automaticity	
Vascular smooth muscle	β_2	Vasodilation	α-Adrenergic receptors
Bronchial smooth muscle	β_2	Bronchodilation	Cholinergic receptors
Kidneys	β_1	↑ Renin release	α_1-Adrenergic receptors
Liver	β_2, α_1	↑ Glycogenolysis and gluconeogenesis	—
Adipose tissue	β_1, β_3	↑ Lipolysis	α_2-Adrenergic receptors
Skeletal muscle	β_2	↑ Increased contractility Potassium uptake; glycogenolysis Dilates arteries to skeletal muscle Tremor	—
Eye-ciliary muscle	β_2	Relaxation	Cholinergic receptors
GI tract	β_2	↓ Motility	Cholinergic receptors
Gall bladder	β_2	Relaxation	Cholinergic receptors
Urinary bladder detrusor muscle	β_2, β_3	Relaxation	Cholinergic receptors
Uterus	β_2	Relaxation	Oxytocin

Figure 6.16
Summary of β-adrenergic receptors. AV = atrioventricular; GI = gastrointestinal.

Adrenergic Agonists

CATECHOLAMINES

- Rapid onset of action
- Brief duration of action
- Not administered orally
- Do not penetrate the blood-brain barrier

NONCATECHOLAMINES

Compared to catecholamines:

- Longer duration of action
- All can be administered orally or via inhalation

DRUG	RECEPTOR SPECIFICITY	THERAPEUTIC USES
Epinephrine	α_1, α_2 β_1, β_2	Anaphylactic shock Cardiac arrest In local anesthetics to increase duration of action
Norepinephrine	α_1, α_2 β_1	Treatment of shock
Isoproterenol	β_1, β_2	As a cardiac stimulant
Dopamine	Dopaminergic α_1, β_1	Treatment of shock Treatment of congestive heart failure Raise blood pressure
Dobutamine	β_1	Treatment of acute heart failure
Oxymetazoline	α_1	As a nasal decongestant For relief of eye redness
Phenylephrine	α_1	As a nasal decongestant Raise blood pressure Treatment of paroxysmal supraventricular tachycardia
Clonidine	α_2	Treatment of hypertension
Albuterol *Metaproterenol* *Terbutaline*	β_2	Treatment of bronchospasm (short-acting)
Arformoterol *Formoterol* *Indacaterol* *Salmeterol*	β_2	Treatment of bronchospasm (long-acting)
Amphetamine	α, β, CNS	As a CNS stimulant in treatment of children with ADHD, narcolepsy, and for appetite control
Ephedrine *Pseudoephedrine*	α, β, CNS	Raise blood pressure As a nasal decongestant

Figure 6.17
Summary of the therapeutic uses of adrenergic agonists. ADHD = attention deficit hyperactivity disorder; CNS = central nervous system.

CLASS OF DRUG	DRUG NAMES	MECHANISM OF ACTION	SIDE EFFECTS
β-Adrenergic antagonists (topical)	*Betaxolol, carteolol, levobunolol, metipranolol, timolol*	Decrease of aqueous humor production	Ocular irritation; contraindicated in patients with asthma, obstructive airway disease, bradycardia, and congestive heart failure.
α-Adrenergic agonists (topical)	*Apraclonidine, brimonidine*	Decrease of aqueous humor production and increase of aqueous outflow	Red eye and ocular irritation, allergic reactions, malaise, and headache.
Cholinergic agonists (topical)	*Pilocarpine, carbachol*	Increase of aqueous outflow	Eye or brow pain, increased myopia, and decreased vision.
Prostaglandin-like analogues (topical)	*Latanoprost, travoprost, bimatoprost*	Increase of aqueous humor outflow	Red eye and ocular irritation, increased iris pigmentation, and excessive hair growth of eye lashes.
Carbonic anhydrase inhibitors (topical and systemic)	*Dorzolamide* and *brinzolamide* (topical), *acetazolamide*, and *methazolamide* (oral)	Decrease of aqueous humor production	Transient myopia, nausea, diarrhea, loss of appetite and taste, and renal stones (oral drugs).

Figure 7.8
Classes of drugs used to treat glaucoma.

Adrenergic Antagonists

DRUG	RECEPTOR SPECIFICITY	THERAPEUTIC USES
Propranolol	β_1, β_2	Hypertension Migraine Hyperthyroidism Angina pectoris Myocardial infarction
Nadolol *Pindolol*[1]	β_1, β_2	Hypertension
Timolol	β_1, β_2	Glaucoma, hypertension
Atenolol *Bisoprolol*[2] *Esmolol* *Metoprolol*[2]	β_1	Hypertension Angina Myocardial infarction Atrial fibrillation
Acebutolol[1]	β_1	Hypertension
Nebivolol	β_1, NO ↑	Hypertension
Carvedilol[2] *Labetalol*	$\alpha_1, \beta_1, \beta_2$	Hypertension

* Drugs that possess membrane stabilizing or local anesthetic properties:

Propranolol

Metoprolol

Labetolol

Acebutolol

Pindolol

Cardvedilol is:

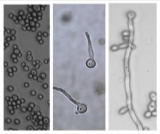
Alpha blocker

Beta blocker

Calcium channel blocker

Anti oxidant

Candida albicans

Microscope	Features	Epidemiology	Diseases	Treatment
 Yeast GermTube P-hyphae	• Oval yeast with single bud in mucous membranes • Germ tubes in serum • Forms **pseudohyphae and true hyphae when invading tissues**	• Part of the normal flora of skin, mucous membranes and GI tract • Immunocompromised patients, IVDA, overuse of antibiotics	• **Oral/esophageal thrush** (neonates, AIDS, steroids, antibiotic overuse)—white patches easily scraped off • **Yeast vaginitis** (↓pH; diabetic women, antibiotic overuse) • **Endocarditis** (IVDA) • Cutaneous infections (obesity, infants—diaper rash) Nystatin—swish and swallow for oral thrush (topical for diaper rash or vaginitis)	DOC • **Miconazole;** Clotrimazole • Nystatin • Fluconazole, Amphotericin B (disseminated)

Cestodes (tapeworms)

Ingestion

Organism	Acquisition	IH	DH	Disease progression	Diagnosis	Treatment
Taenia saginata (beef tapeworm)	**Rare beef** (containing cysticerci)	Cattle	Humans	Intestinal tapeworm (sm intestine) • Asymptomatic or vague abdominal pains	Proglottids or eggs in feces	Praziquantel (surgery for some T. solium cysts)
Taenia solium (pork tapeworm)	**Raw pork** (containing cysticerci)	Swine	Humans	Intestinal tapeworm (same symptoms as saginata)	Proglottids or eggs in feces	
	Water, vegetation (contaminated with eggs)	**Humans**	—	Cysticercosis • Larvae develop in brain **(brain cysts) "swiss cheese brain"** eye, heart, lung→ **adult onset epilepsy, seizures** • **"Immigrant with new onset seizures"**	Biopsy	
Diphyllobothrium latum (fish tapeworm)	**Raw pickled fish** (with sparganum/larvae)	Crustacean → fish	Humans	Intestinal tapeworm • Competes for B12 in intestine (megaloblastic anemia)	Proglottids or eggs in feces	
	Drinking pond water (contaminated by copepods carrying larvae)	Humans	—	Sparganosis • Larvae penetrate/encyst intestinal wall	Biopsy	
Echinococcus granulosus	**Ingestion of eggs from dog feces**	**Humans; Sheep**	**Herding dog**	Hyatid cyst disease • **Liver cysts with brood capsules** (and/or lung cysts)	Imaging; serology	Surgery; albendazole

Larvae develop in **Intermediate hosts** (IH)… Adult tapeworms develop in **Definitive hosts** (DH)… Cysticerci= encysted larvae found in Intermediate host

Retroviridae (+ssRNA; enveloped; contain **reverse transcriptase**)

Viruses	HIV genes/functions	HIV associated conditions	HIV labs/prophylaxis
HTLV (Human T-cell Leukemia Virus)—Oncovirus group • **Adult T-cell Leukemia**; Japan, Caribbean • C-type particle (central, electron-dense nucleocapsid) **HIV** (Human Immunodeficiency Virus)—Lentivirus group • Diploid genome **(2 copies of ssRNA)** • Sexual contact, blood (needles), vertical transmission • Homosexual males, IVDA, sexually active adults • Infects macrophages and T-cells; progresses to AIDS Progression followed by declining CD4 count -Early flu-like, generalized lymphadenopathy -Later progresses to AIDS-defining conditions -Homozygous CCR5 mutation= immune -Heterozygous CCR5 mutation= slow course	Gag genes • **p24** (capsid protein; early marker) Pol genes • **Reverse transcriptase** • **Integrase** (DNA integration to host DNA) • **Protease** (cleaves viral polyprotein) Env genes • **gp120** (binds CD4 & coreceptors CCR5:macrophages; CXCR4: T-cells) • **gp41** (fusion to host cell) Regulatory genes • LTR (integration), Tat (transcription) Rev (transport), **Nef** (Virulence; when defective= won't progress to AIDS)	Early symptomatic period • Bacillary angiomatosis (disseminated bartonella) • Candidiasis, Hairy leukoplakia, Listeriosis • PID, Cervical dysplasia, Peripheral neuropathy AIDS associated conditions • **Recurrent pneumonia (MCC death)** P. jiroveci • Candidiasis of esophagus/upper airway, Coccidioidomycosis, Cryptococcosis, Histoplasmosis • Malignancies—Cervical carcinoma, Kaposi sarcoma, Burkitt's lymphoma (immunoblastic or primary CNS) • CMV, HSV, PML (JC virus), wasting due to TNF-α • Cryptosporidiosis, toxoplasmosis (brain lesions) • TB (>200 CD4), M. avium (<200), salmonella	Screening—ELISA Confirmation—Western blot Viral load—RT-PCR Newborns—PCR Early marker—p24 antigen Progression—CD4:CD8 ratio P. jiroveci < 200 CD4 Toxoplasma < 100 Histoplasma < 100 M. avium <50 CMV <50 Cryptococcus < 50

Herpes

- Large dsDNA (linear)
- Envelope derived from nuclear membrane
- **Virus assembly in nucleus** *(others assemble in cytoplasm)*
- Establishes latency

①HSV-1 [Latent in **trigeminal ganglia**]

- Human mucosa→ direct contact
- Gingivostomatitis/ Herpes labialis **(cold sores)** vesicular blisters of mouth, lips
- Esophagitis—punched out lesions
- Keratoconjunctivitis (dendritic ulcers)
- MCC sporadic **encephalitis** in U.S. (focal fronto-temporal lesions, necrotizing, high fatality)
- Herpetic whitlow (dentists- vesicles on finger)

②HSV-2 [Latent in **sacral nerve ganglia**]

- Human mucosa→ sexual contact
- Painful **genital vesicles**, (encephalitis is mild)
- Neonatal herpes (at birth; encephalitis)

③VZV [Latent in **dorsal root ganglia**]

- Human mucosa→ respiratory (also touch)
- **Chickenpox** (fever, pharyngitis, asynchronous rash-macules, vesicles, scabs not same stage)
- **Shingles** (Stress→ reactivation of latent infection in 5th or 6th decade of life; pain & vesicles restricted to 1 dermatome (unilateral)

Tzanck smear—intranuclear **Cowdry type A** (All 3)

④EBV [Latent in **B-cells**]

- **Heterophile** ⊕ mononucleosis (kissing disease; teens- fever, exudative sore throat, lymphadenopathy, splenomegaly)
- Hairy oral leukoplakia (AIDS)
- Malignancies (**Burkitt lymphoma**, Hodgkins, nasopharyngeal carcinoma)
- **Downey cells** (atypical reactive T-cells)

⑤CMV [Latent in **mononuclear cells**]

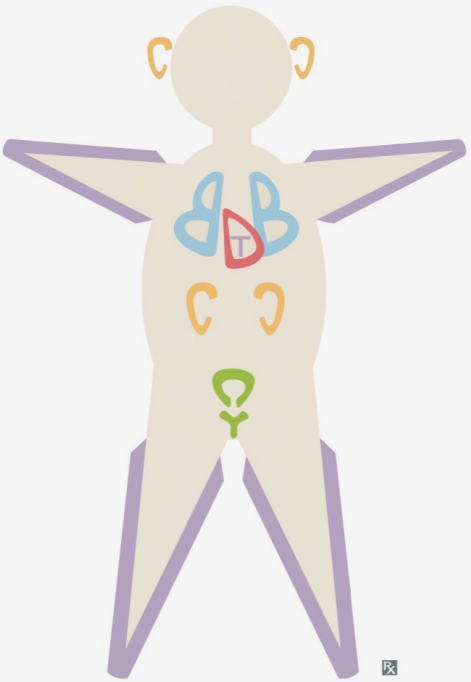
- MCC in utero infection U.S. (blueberry muffin baby- thrombocytic purpura, MR, jaundice, pneumonitis, periventricular calcifications)
- **Heterophile neg** mononucleosis
- AIDS= retinitis + ulcerations of GI tract
- **Owl's eye inclusion bodies**

⑥HHV-6 [Transmitted by saliva]

- **Roseola** (infants— 3 day fever, seizures; lacy body rash when fever breaks)

⑧HHV-8 [AIDS patients]

- **Kaposi sarcoma** (↑VEGF expression causes purple splotches)



Cisplatin, Carboplatin → ototoxicity

Vincristine → peripheral neuropathy
Bleomycin, Busulfan → pulmonary fibrosis
Doxorubicin, Daunorubicin → cardiotoxicity
Trastuzumab → cardiotoxicity
Cisplatin, Carboplatin → nephrotoxicity

CYclophosphamide → hemorrhagic cystitis

Nonspecific common toxicities of nearly all cytotoxic chemotherapies include myelosuppression (neutropenia, anemia, thrombocytopenia), GI toxicity (nausea, vomiting, mucositis), alopecia.

SIDE EFFECTS OF ANTI CANCER DRUGS

The Hematopoietic and Lymphoreticular System

Most Common . . .	
Cancer—leukemia—14-year-old	**Acute lymphoblastic leukemia (ALL)**
Cancer—leukemia—15–39-year-old	**Acute myeloid leukemia (AML)**
Cancer—leukemia—40–60-year-old	**Chronic myelogenous leukemia (CML)**
Cancer—leukemia—>60-year-old	**Chronic lymphocytic leukemia (CLL)**
Cancer in infancy	**Hemangioma**
Cancer in children	1. **Leukemia** 2. Medulloblastoma of cerebellum
Cancer; genetic alteration	**p53**
Cancer; malignant lymphoma in children	**Burkitt lymphoma**
Cancer; site of metastasis	**Regional lymph nodes**
Cancer; site of metastasis (second most common)	**Liver**
Hereditary bleeding disorder	**von Willebrand disease**
Single-gene disorder	**Thalassemia**
Type of Hodgkin lymphoma	**Nodular sclerosis Hodgkin lymphoma**
Type of non-Hodgkin lymphoma	**Diffuse large B-cell lymphoma**

Genetics

Quick List: Inherited Diseases

Mode of Inheritance	Diseases
Autosomal dominant diseases	Adult polycystic kidney disease, familial hypercholesterolemia, Marfan syndrome, neurofibromatosis type 1, neurofibromatosis type 2, tuberous sclerosis, von Hippel–Lindau disease, Huntington disease, familial adenomatous polyposis, hereditary spherocytosis, achondroplasia
Autosomal recessive diseases	Cystic fibrosis, albinism, α_1-antitrypsin deficiency, phenylketonuria, thalassemias, sickle cell anemia, glycogen storage disease, mucopolysaccharidoses (except Hunter syndrome), sphingolipidoses (except Fabry disease), infant polycystic kidney disease, hemochromatosis
X-linked dominant diseases	Hypophosphatemic rickets
X-linked recessive diseases	Bruton agammaglobulinemia, Wiskott–Aldrich syndrome, fragile X syndrome, G6PD deficiency, ocular albinism, Lesch–Nyhan syndrome, Duchenne muscular dystrophy, hemophilia A and B, Fabry disease, Hunter syndrome
Mitochondrial diseases	Leber hereditary optic neuropathy, mitochondrial myopathies
Trisomies	Down syndrome (chromosome 21), Edward syndrome (chromosome 18), Patau syndrome (chromosome 13)
Trinucleotide repeat diseases	Huntington disease, myotonic dystrophy, Friedreich ataxia, fragile X syndrome

G6PD, glucose-6-phosphate dehydrogenase.

TABLE 9-19 Skin Disorders

Disorder	Description
Keloid scarring	• **Excessive scarring** that occurs after minor trauma • Results in raised, firm lesions on the skin • Occurs more frequently in Blacks • Genetic predisposition is a factor
Xanthomas	• Accumulation of foam-filled histiocytes within the dermis • Often associated with **hyperlipidemia** or lymphoproliferative disorders • Often found on the Achilles tendon, the extensor tendons of the fingers, and the eyelids
Verrucae	• "Warts" • Histology: epidermal hyperplasia, hyperkeratosis, koilocytosis
Seborrheic keratosis	• Common **benign neoplasm** in the elderly • Raised papules and plaques that appear to be "pasted on"; often dark, and can be large
Actinic keratosis	• A series of dysplastic changes that occur before the onset of **squamous cell carcinoma** • A buildup of keratin caused by excessive exposure to sunlight leads to a **"warty"** appearance • Higher incidence in lightly pigmented individuals
Albinism	• **Lack of melanin pigment** production • Ocular type limited to eyes; X linked • Oculocutaneous type involves the skin, eyes, and hair; autosomal recessive; lack of tyrosinase, which converts tyrosine to DOPA (3,4-dihydroxyphenylalanine)
Vitiligo	• Irregular areas of depigmentation due to **decreased number of melanocytes**
Melasma	• Pregnancy-associated hyperpigmentation
Acanthosis nigricans	• Velvety thickening and **hyperpigmentation** of the axilla, neck, and groin region • Associated with insulin resistance (type 2 diabetes mellitus) and sometimes with occult visceral malignancy
Hemangiomas	• Large-vessel malformation composed of masses of blood-filled channels • **Port-wine stain** birthmarks are the most common manifestation • Cavernous hemangiomas are a subset with large cavernous vascular spaces that can occur in von Hippel–Lindau disease
Psoriasis	• Plaques with **silvery scale**; plaque bleed when scraped (**Auspitz sign**) • Often affects elbows, knees, scalp, hands • Autoimmune etiology; may be associated with psoriatic arthritis • Histology: parakeratotic scaling, increased thickness of the stratum spinosum, decreased thickness of the stratum granulosum
Atopic dermatitis (eczema)	• Dry skin with pruritic inflammatory lesions that become lichenified with chronic scratching, especially in flexural areas • Commonly seen in infants and children • Associated with other atopic diseases (allergic rhinitis, asthma)

TABLE 9-2 Metabolic and Infectious Bone Disease

Disease	Etiology	Clinical Features
Osteoporosis	**Primary:** ***Type I:*** postmenopausal, with excess loss of trabecular bone ***Type II:*** men and women >70 years of age, with loss of trabecular and cortical bone **Secondary:** Physical inactivity, increased parathyroid levels, hypercortisolism, hyperthyroidism, vitamin D deficiency, hypocalcemia	**Bone mineral density** is 2.5 or more standard deviations **below** normal; **decrease in bone mass** leads to fractures (especially of the weight-bearing bones of the spine); radiolucent bone seen on radiograph; DEXA scan positive
Scurvy	Lack of vitamin C intake; defective **proline and lysine hydroxylation** in collagen synthesis	Impaired bone formation and lesions result; painful subperiosteal hemorrhage; osteoporosis; bleeding gums; poor wound healing
Rickets (children); osteomalacia (adults)	Impaired calcification of bone because of deficiency of vitamin D; if caused by renal disease, termed "renal osteodystrophy"	**Children:** Skeletal malformations Craniotabes (thinned and softened bones of the skull) Late fontanelle closure Decreased height Rachitic rosary (costochondral junction thickening resembling string of beads) Pigeon breast owing to a protruding sternum **Adults:** Fractures Radiolucency on radiography
Avascular necrosis	Death of osteocytes and fat necrosis via the following mechanisms: vascular compression, vascular interruption (fracture), thrombosis (sickle cell disease, caisson disease), vessel injury	Joint pain; osteoarthritis; sites include head of the femur, shoulder, knee
Pyogenic osteomyelitis	Infection of bone most often caused by ***Staphylococcus aureus***; routes of infection include hematogenous extension from adjacent infection, open fracture, or surgery	Acute febrile illness; pain; tenderness; usually affects metaphysis of distal femur, proximal tibia, and proximal humerus; forms sequestrum and involucrum
Tuberculous osteomyelitis	Tuberculous infection spreads to bone from elsewhere in body	Seen in hips, long bones, hands, feet, and vertebrae **(Pott disease)**

DEXA, dual energy x-ray absorptiometry.

TABLE 9-3 Tumors of Bone and Cartilage

Tumor	Morphology	Clinical Features
Osteochondroma	Benign bone tumor; **most common benign tumor**; originates in metaphysis of long bones; growth of mature bone (exostosis) with a cartilaginous cap	Most common in men younger than 25 years of age; usually occurs on the lower end of the femur or upper end of the tibia
Giant cell tumor	Benign bone tumor; spindle-shaped cells with multinuclear giant cells; most commonly occur in the epiphysis of the distal femur or proximal tibia	Most common in women 20–55 years of age; has **"soap bubble"** appearance on radiograph; usually occurs on the lower end of the femur or upper end of the tibia
Osteoma	Benign bone tumor; mature bone (dense tissue)	Most common in men; affects skull or facial bones; protrudes from surface; associated with Gardner syndrome
Osteoid osteoma	Benign bone tumor; **nidus** rimmed by osteoblasts and surrounded by vascular, spindled stroma; <2 cm in diameter	Most common in men 20–30 years of age; occurs near the ends of the tibia and femur; painful due to excess prostaglandin E_2 production; radiolucent **nidus** is seen on radiograph
Osteosarcoma	Malignant mesenchymal bone tumor; malignant cells produce bone matrix; origin usually in metaphyseal long bones; destructive masses with hemorrhage and necrosis; retinoblastoma, Paget disease, radiation exposure are risk factors	Bimodal distribution, most common in boys in their teenage years and in elderly; usually occurs in tibia or femur near the knee; local pain; tenderness; swelling; metastasizes to lung first; growth under bone results in the **Codman triangle and a "sunburst" appearance** on radiograph
Chondrosarcoma	Malignant cartilage tumor; lobulated translucent tumors; necrosis; calcification	Most common in men usually 40 years of age or older; central skeleton is affected such as the pelvis, ribs, shoulders, spine; radiograph shows localized area of bone destruction
Ewing sarcoma	Malignant small round cell tumors of bone and soft tissue; **t(11;22)**; sheets of small round cells producing **Homer-Wright pseudorosettes**; histologically similar to lymphoma, small cell carcinoma, rhabdomyosarcoma	Most common in boys 10–15 years of age; occurs in long bones, ribs, pelvis, scapula; early metastasis; responds to chemotherapy; painful, warm, swollen mass; "onion skin" appearance on radiograph
Fibrous dysplasia	Benign; bone replaced haphazardly by fibrous tissue	**"Chinese figures"** configuration on radiograph. Three types: Single bone involvement Several bones involved Several bones involved, along with precocious puberty and café au lait spots
Metastasis	Malignant; usually lytic lesions unless arising from prostate or breast	Originate from prostate, breast, kidney, lung; ectopic hormone production **(parathyroid hormone-related protein [PTHrP])**

TABLE 9-4 Arthritic Joint Disease

Disease	Etiology	Clinical Features
Osteoarthritis (degenerative joint disease)	Degeneration of joint articular cartilage followed by growth of surrounding bone; the **most common type of arthritis**; primary type has no specific risk factor; secondary type related to trauma, metabolic disorder, or inflammatory arthropathy; knee is the most common site	Pain in joint after use, improves with rest, stiffness in the morning or after a period of immobility; **"Joint mice"** form from pieces of torn and frayed joint cartilage and broken pieces of osteophytes; erosion of cartilage results in **eburnation** (polishing) of the underlying bone; cysts visible in bone on radiograph; Heberden nodes are osteophytes at the DIP joint; Bouchard nodes are osteophytes of the PIP joints
Rheumatoid arthritis	Symmetrical, chronic inflammation of the synovium with edema and cellular infiltrate, leading to the destruction of articular cartilage of joints, most likely because of autoimmune reaction; synovial hypertrophy and hyperplasia; granulation tissue **(pannus)** over articular cartilage; **rheumatoid factor**—IgM autoantibody against the Fc receptor located on IgG; more common in women; associated with **HLA-DR4**	Ulnar deviation of MCP joints, **swan-neck**, and **boutonnière** deformity develop owing to inflammation, muscle atrophy, and contracture; **DIP joints are spared**; morning stiffness that improves throughout the day; subcutaneous rheumatoid nodules; systemic symptoms such as fever, weight loss, fatigue
Ankylosing spondylitis	Unknown cause; high association with **HLA-B27**; negative rheumatoid factor; males are more commonly affected	Bilateral sacroiliitis (inflammation of the sacroiliac joint) noted; chronic low back pain and stiffness; improves with movement; calcification of spinal ligaments and fusion of the facet joints produces a **"bamboo spine"**; may produce extraskeletal manifestations of **apical lung fibrosis, aortic insufficiency**, or **cauda equina syndrome**
Psoriatic arthritis	Unknown cause; may present similar to rheumatoid arthritis; HLA-B27 association; **no rheumatoid factor**; no male or female preponderance	**Asymmetric** involvement of **DIP joints**, PIP joints, feet, ankles, and knees; **"pencil-in-a-cup"** deformity of the proximal phalanges
Reiter syndrome	Caused by reaction to systemic illness that originated either enteropathically or urogenitally; HLA-B27 association; most common in males, usually 20–40 years of age	Classic triad of genitourinary inflammation **(urethritis)**, ocular inflammation **(conjunctivitis)**, and acute asymmetric **arthritis**

TABLE 9-4 Arthritic Joint Disease *(Continued)*

Disease	Etiology	Clinical Features
Gout	Inflammatory reaction in joints caused by monosodium **urate crystal** deposition; IgG opsonization of the crystals followed by phagocytosis stimulates inflammation; pathogenesis includes increased uric acid production such as Lesch–Nyhan syndrome (hypoxanthine-guanine phosphoribosyltransferase deficiency), increased activity of phosphoribosyl pyrophosphate (PRPP) synthetase, and decreased uric acid secretion such as diuretics; acidosis; often precipitated by a large, high-protein meal or by drinking excessive amounts of alcohol	First MTP joint involvement is called **podagra**; **tophi** (nodules of fibrous tissue and crystals) occur near the joints, on the ear, and on the Achilles tendon; renal damage may occur when crystals deposit in collecting tubules; urate crystals have **strong negative birefringence** under polarized light and are **needle shaped**. For treatment, see Table 9-5.

DIP, distal interphalangeal; HLA, human leukocyte antigen; Ig, immunoglobulin; MCP, metacarpophalangeal; MTP, metatarsophalangeal; PIP, proximal interphalangeal.

TABLE 9-12 Therapeutic Agents for Pain

Therapeutic Agent (common name, if relevant) [trade name, where appropriate]	Class—Pharmacology and Pharmacokinetics	Indications	Side Effects or Adverse Effects	Contraindications or Precautions to Consider; Notes
Acetaminophen [Tylenol]	Analgesic, antipyretic—reversibly inhibits COX centrally (inactivated peripherally); prostaglandin inhibitor, **not anti-inflammatory**	Pain, fever	Liver toxicity in high doses **(high levels deplete glutathione)**	**Overdose treated with** *N*-acetylcysteine (regenerates glutathione); unlike aspirin, **can be used in children**, **gout**, **peptic ulcer**, **and patients with platelet dysfunction**
Acetylsalicylic acid (aspirin)	**Anti-inflammatory, antipyretic, analgesic**—acetylates COX irreversibly	Articular, musculoskeletal pain; chronic pain; **maintenance therapy for preventing clot formation**	GI distress, **GI ulcers**, **inhibits platelet aggregation**; causes **hypersensitivity reactions (rash)**; reversible hepatic dysfunction	**Contraindicated for children** with the flu or chicken pox (leads to **Reye syndrome**), **patients with gout**
Ibuprofen [Advil, Motrin]	**NSAID—reversibly inhibits COX** (both COX-1 and COX-2) → decreases prostaglandin synthesis	**Inflammation**, **pain**	GI distress, **GI ulcers**, coagulation disorders, aplastic anemia, metabolic abnormalities, hypersensitivity, renal damage	

TABLE 9-12 **Therapeutic Agents for Pain** *(Continued)*

Therapeutic Agent (common name, if relevant) [trade name, where appropriate]	Class—Pharmacology and Pharmacokinetics	Indications	Side Effects or Adverse Effects	Contraindications or Precautions to Consider; Notes
Naproxen [Naprosyn, Aleve]	**NSAID—reversibly inhibits COX** (both COX-1 and COX-2) → decreases prostaglandin synthesis	Inflammation, pain	GI distress, **GI ulcers**, coagulation disorders, aplastic anemia, metabolic abnormalities, hypersensitivity, renal damage	
Indomethacin [Indocin]	**NSAID—reversibly inhibits COX** (both COX-1 and COX-2) → decreases prostaglandin synthesis	Acute gout; closes patent ductus arteriosus	GI distress, **GI ulcers**, coagulation disorders, aplastic anemia, metabolic abnormalities, hypersensitivity, renal damage	
Ketorolac [Toradol]	**NSAID—reversibly inhibits COX** (both COX-1 and COX-2) → decreases prostaglandin synthesis; relieves pain and reduces swelling	**Postoperative pain**, severe pain	GI distress, **GI ulcers**, coagulation disorders, aplastic anemia, metabolic abnormalities, hypersensitivity, renal damage	
Celecoxib [Celebrex]	**NSAID—selectively inhibits COX-2**	Rheumatoid arthritis, osteoarthritis; pain, inflammation	**Increased risk of thrombosis; sulfa allergy; less toxic to GI mucosa**	COX-2 selectivity reduces inflammation while minimizing GI adverse effects (ulcers)
Morphine [MS Contin, MSIR, Roxanol]	**Opioid agonist**—converted to more potent morphine-6-glucose	Severe pain; general anesthetic; antitussive; antidiarrheal	Respiratory depression; histamine release; constipation; nausea; miosis	
Meperidine [Demerol]	**Opioid agonist**	**Pain**, acute migraine attacks	**CNS excitation at high doses**; histamine release	**Contraindicated in patients with MAOI** (results in hyperpyrexia)
Fentanyl	**Opioid agonist**	**Pain**; general anesthetic	Prolonged recovery; nausea	
Codeine	**Opioid agonist**	**Pain**; antitussive	**Constipation**	
Oxycodone [Roxicodone]	**Opioid agonist**	Severe pain; general anesthetic	Respiratory depression, constipation, nausea	
Hydromorphone [Dilaudid]	Opioid agonist	**Pain**; antitussive	Respiratory depression, constipation, nausea	
Methadone	**Opioid agonist**—synthetic	Maintenance therapy for **heroin addiction**	Respiratory depression; histamine release; constipation; nausea; miosis	
Tramadol [Ultram]	Analgesic—similar to opioid agonist	Chronic pain of **osteoarthritis**	Nausea, vomiting, constipation, drowsiness	

CNS, central nervous system; COX, cyclooxygenase; GI, gastrointestinal; MAOI, monoamine oxydase inhibitor; MSIR, morphine sulfate instant release; NSAID, nonsteroidal anti-inflammatory drug.

TABLE 9-20 Skin Cancers

Disorder	Description
Squamous cell carcinoma	• Malignant tumor of the skin associated with excessive exposure to sunlight (UV rays) leading to DNA damage, immunosuppresion, or xeroderma pigmentosum • Rarely metastasizes • Characterized by ulcerated, scaling nodules • Appears microscopically as islands of neoplastic cells with **whorls of keratin** ("pearls") and cells with atypical nuclei at all levels of the epidermis
Basal cell carcinoma	• **Most common skin tumor** • Appears grossly as a pearl-like papule on sun-exposed areas • Appears histologically as a dark cluster with **palisading peripheral cells** • Almost never metastasizes but can cause local invasive tissue destruction

Malignant melanoma	• Aggressive tumor that arises from melanocytes (neural crest origin)
	• Associated with excess exposure to sunlight, immunosuppression, and xeroderma pigmentosum
	• Associated with the S-100 tumor marker
	• Two growth patterns:
	  • **Benign radial manner** (growth within skin layer)
	  • **Aggressive vertical manner** (growth through deeper layers)

UV, ultraviolet.

TABLE 9-5 Drugs Used to Treat Gout

Therapeutic Agent	Mechanism of Action	Indications	Side Effects	Notes
Allopurinol	Inhibition of uric acid production—**competitive inhibitor of xanthine oxidase**, decreases conversion of **xanthine to uric acid**	Chronic gout therapy; lymphoma, leukemia (prevents tumor lysis associated urate nephropathy), uric acid stones	Rash, fever, diarrhea, occasional peripheral neuritis; enhances effect of azathioprine	Should not be used to treat acute gout
Probenecid	Increased secretion of uric acid (uricosuric)—small dose inhibits uric acid secretion; large dose inhibits uric acid reabsorption (i.e., promotes excretion)	Chronic gout therapy	**Caution: should not be used in patients with sulfa allergies**	Should not be used to treat acute gout or patients with uric acid stones
Colchicine	Anti-inflammatory—interrupts **microtubule formation**, thereby interfering with normal mitosis and inhibiting WBC migration and phagocytosis	Acute gout therapy	Diarrhea (common)	

TABLE 9-5 Drugs Used to Treat Gout *(Continued)*

Therapeutic Agent	Mechanism of Action	Indications	Side Effects	Notes
NSAIDs (e.g., indomethacin)	Decrease **prostaglandin** production, thereby interrupting the inflammatory process	Acute therapy	Bone marrow suppression and renal damage (indomethacin); GI distress and ulceration	
Celecoxib	Selectively inhibits cyclooxygenase-2 (COX-2)	Acute therapy	Sulfa allergy; renal damage	Less toxic to GI mucosa than NSAIDs
Glucocorticoids (prednisone)	Suppresses prostaglandin and leukotriene synthesis	Acute therapy	Osteoporosis, Cushingoid reaction, psychosis, glucose intolerance, infection, hypertension, cataracts	

GI, gastrointestinal; NSAID, nonsteroidal anti-inflammatory drug; WBC, white blood cell.

MNEMONICS

* Muscarinic Effects - SLUDGE
* Nicotinic effects - MTWTF
* Organophosphate (ecothiophate) poisoning - SLUDGE + MTWTF
* Drugs for bradycardia and low BP - IDEA
* Selective beta 1 blockers - MAN BABE
* Drugs with partial agonist activity - PAL

* Transferrin - transports iron in the blood and delivers it to liver and bone marrow macrophages for storage
* Ferritin - binds stored iron
* Hepcidin - sequesters iron in storage sites

VALUES

* Hb in males = 13.5 - 17.5
* Hb in females = 12.5 - 16.0
* MCV = 80 - 100
* Microcytic < 80
* Macrocytic > 100
* % saturation = 33%
* TIBC =300
* Serum iron = 100
* Retic count = 1-2%
* RBC Life span = 120 days
* Life span of platelet in blood = 8-12 days
* HbS < 50% is sickle cell trait

HbS > 50% is sickle cell disease

* WBC count = 5000-10000
* Normal PLT count = 150,000-400,000
* Thrombocytopenia - PLT < 50,000
* Thrombocytosis - PLT > 750,000
* Normal bleeding time = 2-7 minutes
* Neutrophilia > 7000
* Neutropenia < 1500
* Eosinophilia > 700
* Basophilia > 110
* Monocytosis > 800
* Lymphocytosis in children > 4000

Lymphocytosis in adults > 8000

* Lymphocytopenia in children < 1500

Lymphocytopenia in adults < 3000

* Lymphoblasts are TdT positive
* Myeloblasts are MPO positive
* B cell surface markers - CD10, 19, 20
* T cell surface markers - CD3,4,5,6,7,8
* Among B cell lymphomas, only CLL/SLL and mantle cell lymphoma commonly express CD5. So it is a helpful diagnostic tool
* Hairy cell leukemia - Tartrate resistant acid phosphatase (TRAP) positive
* Leukemoid reaction is LAP positive
* Gout - Synovial fluid shows needle shaped crystals with negative birefringement under polarized light
* Pseudo Gout - Synovial fluid shows rhomboid shaped crystals with weakly positive birefringement under polarized light
* Dermatomyositis - positive ANA and anti-Jo-1 antibodies
* Rhabdomyosarcoma is desmin positive
* SLE - anti dsDNA antibodies
* S-100 positive in Melanoma, Schwannoma and Langerhans cell histiocytosis
* Elevated D-dimer is the best screening test for DIC

TREATMENT

* Sickle cell anemia - Hydroxyurea
* Hemophilia A - Recombinant Factor 8
* Von Willebrand disease - Desmopressin

Chemotherapeutic agents
- Cyclophosphamide
- Hydroxyurea
- Methotrexate
- Azathioprine
- Mercaptopurine
- Cladribine
- Cytosine arabinoside
- 5-Fluouracil

Antiretroviral
- Zidovudine
- Stavudine

Hypoglycemic
- Metformin

Antimicrobials
- Pyrimethamine
- Sulfamethoxazole
- Trimethoprim
- Valacyclovir

Diuretics
- Triamterene

Anticonvulsant agents
- Phenytoin
- Primidone
- Valproic acid

Anti-inflammatory
- Sulfasalazine

Other
- Nitrous oxide

DRUG INDUCED MACROCYTIC ANEMIA

Paroxysmal Nocturnal Hemoglobinuria

- PNH is a rare X-linked disease with RBC membrane defect resulting in chronic, complement-induced intravascular hemolysis, intermittent **dark urine** (morning), and venous thrombosis.

- The defect in phosphatidyl inositol glycan A (PIG-A gene) allows increased binding of complement to RBCs and hemolysis, more susceptible in an acid environment and at night (hypoventilation).

- Essentials of diagnosis :

1. Anemic symptoms, jaundice, morning dark urine (Hb urine) after sleep, venous thrombosis
2. Lab tests: Flow cytometry (CD55/CD59) is the most specific diagnostic test

- Treatment :

1. Eculizumab (a complement inhibitor) is the mainstay of therapy.
2. In addition, all patients with ongoing hemolysis are recommended for :
    a) RBC transfusions for severe anemia,
    b) supplemental iron for iron deficiency
    c) supplemental folic acid.

Definitions White Cell Numbers

- **Leukocytosis**: increase in the numbers of circulating white cells: >12,000/uL
- **Leukopenia**: decrease in the numbers of circulating white cells: < 4,000/uL
- **Left Shift** – increased circulating numbers of immature neutrophils
- **Leukoerythroblastic Reaction** – leukocytosis with a left shift accompanied by nucleated red cells: seen in malignancy.
- **Leukemoid Reaction** – benign excessive leukocytosis accompanied by an exaggerated neutrophilia and a left shift in response to an **infection; the WBC > 50 x 109**

Interleukin (cytokine)	Source	Target cell	Effect
IL-1	Macrophage, lymphocytes, endothelium, fibroblasts, astrocytes	T-cells, B-cells macrophage, endothelium, tissue cells	Lymphocyte activation, leukocyte-endothelial adhesion, fever, regulates sleep
IL-2	T-cells	T-cells	T-cell growth factor
IL-3	T-cells	Bone marrow cells	Stimulates bone marrow growth
IL-4	T-cells	B- and T-cells	B-cell growth factor
IL-5	T-cells	B-cells	B-cell growth factor
IL-6	T- and B-cells, macrophages, fibroblasts	B-cells and hepatocytes	B-cell differentiation and synthesis of acute phase reactants
IL-7	Lymphocytes	B- and T-cells	Stimulates proliferation of immature cells
IL-8	T-cells, macrophages	Granulocytes, endothelium	Stimulates the activity of neutrophils, acts as chemotaxin, inhibitor of endothelial cell-leukocyte adhesion
IL-9	T-cells	T-cell	T-cell and mast cell growth enhancement
IL-10	T-cells	Macrophage	Suppresses the development of T-cell subpopulations (TH_1) by inhibition of macrophage IL-12 production
IL-11	Bone marrow stromal cells	Hepatocyte	Induces synthesis of acute phase proteins
IL-12	Macrophage	T-cells	Enhances the B-cells expression of IFN-γ during T-cell activation; also stimulates a lymphocyte subpopulation (NK cells)

Color of hypostasis can determine the cause of death:

Cherry-pink	CO poisoning
Dark blue-pink	Cyanide poisoning
Brown	Methemoglobinemia
Grayish Brown	septic abortion caused by Clostridium perfringes.
Pallor	anemia, hemorrhage (or normal in extremes of age)
Purple	Asphyxia
Chocolate brown	Potassium chlorate poisoning
Dark brown	Phosphorus poisoning
Bluish green	Hydrogen sulphide
Black	Opium poisoning

C3 def : staph & other GPB infection

MAC complex or MBL def: Neisserial inf

C2C4 def : SLE

Psoriasis: **Munro microabscess + Auspitz Sign**

Lichen Planus: **Wickhamm striae + sawtooth appearance**

Pemphigus Vulgaris: **tombstone appearance, Positive Nikolsky sign, Fishnet pattern**

Bullous Pemphigoid: **Negative Nikolsky sign, linear pattern**

Seborrheic Keratosis: **Leser Trelat sign, coin like stuck on appearance**

Acanthosis Nigricans: **velvet like skin**

Basal Cell Carcinoma: **Pink pearl like papule**

Keratoacanthoma: **Cup shaped tumor**

(1) onion like skin Ewing sarcoma
(2) auto splenectomy sickle cell anemia
3) mosaic pattern Paget disease
4) marble bone osteoptrosis
5) skull defect multiple myeloma
6) vertebrae defect osteoporosis
(7) codman triangle osteosarcoma
8) blue cell Ewing sarcoma
9) blue sclera osteogenesis imperfecta
(10) soap bubbles gaint cell tumor
11) Lion like face Paget disease
(12) pigeon and frontal bossing rickets..

Thalassemia: **Target Cells**

Thalassemia major: **Crewcut + Chipmunk facie**

Hereditary spherocytosis: **Howell Jolly bodies**

Sickle Cell Anemia: **Crewcut + Chipmunk facie + Howell Jolly bodies**

G6PD Deficiency: **Heinz bodies + Bite cells**

Microangiopathic hemolytic Anemia: **Schistocytes**

AML: **Auer rods**

CLL: **Smudge Cells**

Mycosis Fungoids: **Sezary Cells**

Myelofibrosis: **Tear drop RBCs**

Hodgkin's: **Owl eyed RS cells**

Nodular Sclerosis: **Lacunar Cells**

Langerhans Cell Histiocytosis: **Birbeck Granules**

7:07 pm

PEMPHIGUS VULGARIS VS BULLOUS PEMPHIGOID

Two rare, autoimmune, blistering conditions of the skin

	PEMPHIGUS VULGARIS	BULLOUS PEMPHIGOID
Age at presentation	40-60	70+
Histology	Intraepidermal	Subepidermal
Blister features	Flaccid	Tense
Blister distribution	Oral mucosa common, but anywhere on skin/mucosa	Flexor surfaces and abdomen
Blister symptoms	Painful	Itchy
1st line treatment	Oral steroids	Oral/topical steroids
Mortality	Upto 10-15% (!)	Generally self limiting

Important cytokines	Acute (IL-1, IL-6, TNF-α), then recruit (IL-8, IL-12).	
Secreted by macrophages		
Interleukin-1	Causes fever, acute inflammation. Activates endothelium to express adhesion molecules. Induces chemokine secretion to recruit WBCs. Also called osteoclast-activating factor.	"Hot T-bone stEAK": IL-1: fever (hot). IL-2: stimulates T cells. IL-3: stimulates bone marrow. IL-4: stimulates IgE production. IL-5: stimulates IgA production. IL-6: stimulates aKute-phase protein production.
Interleukin-6	Causes fever and stimulates production of acute-phase proteins.	
Tumor necrosis factor-α	Activates endothelium. Causes WBC recruitment, vascular leak.	Causes cachexia in malignancy. Maintains granulomas in TB. IL-1, IL-6, TNF-α can mediate fever and sepsis.
Interleukin-8	Major chemotactic factor for neutrophils.	"Clean up on aisle 8." Neutrophils are recruited by IL-8 to clear infections.
Interleukin-12	Induces differentiation of T cells into Th1 cells. Activates NK cells.	Facilitates granuloma formation in TB.
Secreted by T cells		
Interleukin-2	Stimulates growth of helper, cytotoxic, and regulatory T cells, and NK cells.	
Interleukin-3	Supports growth and differentiation of bone marrow stem cells. Functions like GM-CSF.	
From Th1 cells		
Interferon-γ	Secreted by NK cells and T cells in response to antigen or IL-12 from macrophages; stimulates macrophages to kill phagocytosed pathogens. Inhibits differentiation of Th2 cells. Induces IgG isotype switching in B cells.	Increases MHC expression and antigen presentation by all cells. Activates macrophages to induce granuloma formation.
From Th2 cells		
Interleukin-4	Induces differentiation of T cells into Th (helper) 2 cells. Promotes growth of B cells. Enhances class switching to IgE and IgG.	Ain't too proud 2 BEG 4 help.
Interleukin-5	Promotes growth and differentiation of B cells. Enhances class switching to IgA. Stimulates growth and differentiation of Eosinophils.	I have 5 BAEs.
Interleukin-10	Attenuates inflammatory response. Decreases expression of MHC class II and Th1 cytokines. Inhibits activated macrophages and dendritic cells. Also secreted by regulatory T cells.	TGF-β and IL-10 both attenuate the immune response.
Interleukin-13	Promotes IgE production by B cells. Induces alternative macrophage activation.	Interleukin thirtEEn promotes IgE.

- Misoprostol → prevention of NSAID induced ulcers
- Alprostadil → maintain the patency of ductus arteriosus before surgery
- Epoprostenol → Tx of pulmonary hypertension
- PGI_2 → useful during hemodialysis to prevent platelet aggregation
- PGE_2, $PGF_{2\alpha}$ → induce labour at term
- Carboprost and Misoprostol → control post partum hemorrhage
- Alprostadil → Tx of erectile dysfunction