SNS COLLEGE OF ALLIED HEALTH SCIENCES
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DEPARTMENT OF OPERATION THEATRE AND ANAESTHESIA TECHNOLOGY

1st YEAR

SUBJECT:PATHOLOGY

TOPIC:CELL DEATH

DEFINITION:

- The body is very good at maintaining a constant number of cells.so there has to exist mechanisms for ensuring other cells in the body are removed when appropriate.

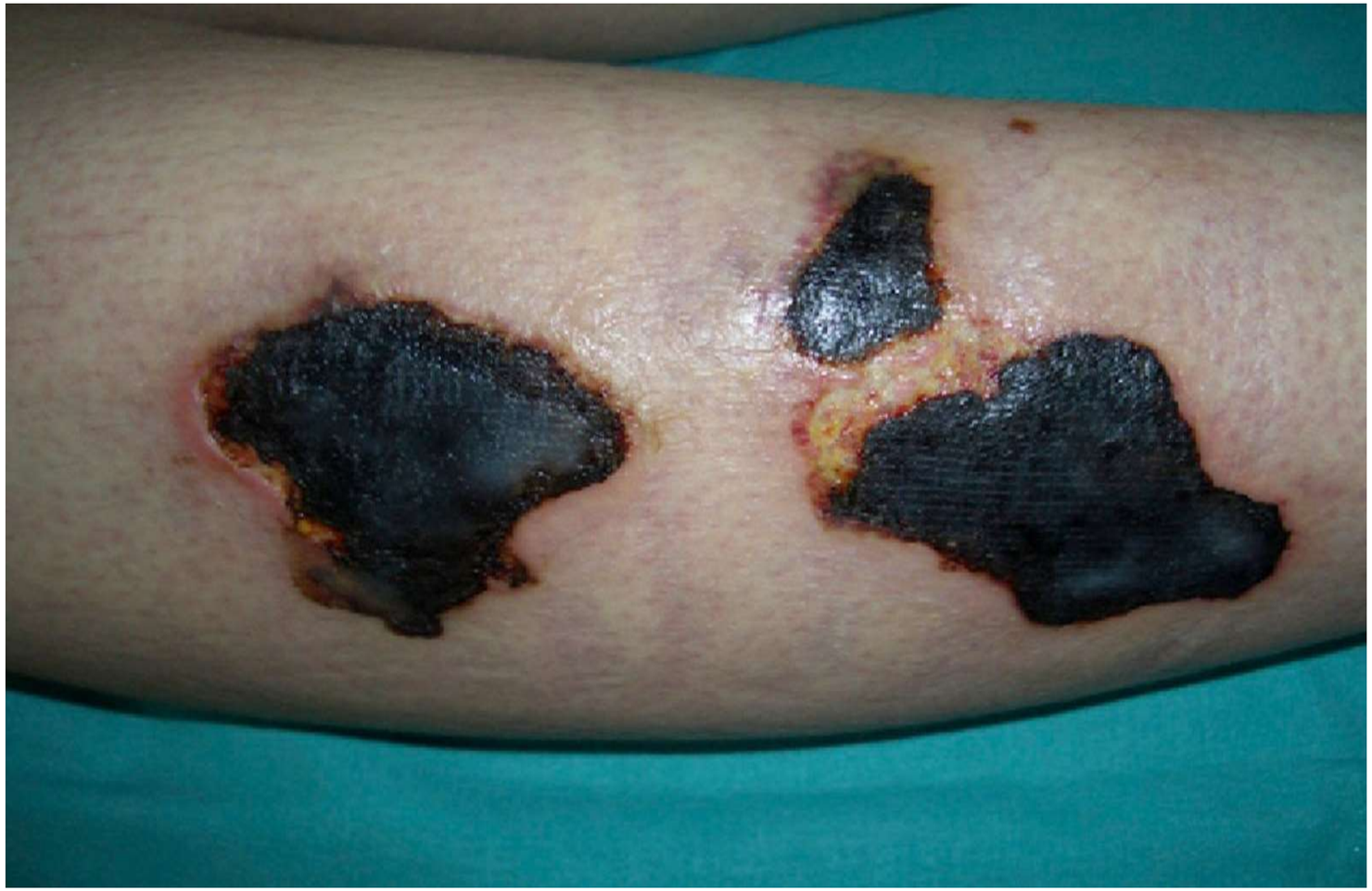
Two Forms:

1.Apotosis-Suicide(Programmed cell death)

2.Necrosis-Killing(Decay & destruction)

Necrosis:

- Necrosis is the sum total of morphological changes that follow cell death in a living tissue or organ
- Dead cells usually show changes in both the cytoplasm and in nucleus
- Cytoplasmic changes are:increases eosinophilia,glassy appearence,granular or vascuolated cytoplasm,swollen mitochondria may also show calcification
- Nuclear changes:Karyolysis,Pyknosis and Karyorrhexis & denature.



Causes:(External factors)

- Mechanical trauma
- Damage to blood vessels
- Thermal effects
- Hypoxia
- Ischemia
- Physical agents
- Chemical agents
- Immunology cause
- Ageing
- Idiopathic cause

Internal Factors:

- Trophoneurotic disorders
- Pancreatic enzymes
- Immunological barriers
- Bacterial toxins
- Toxins and pathogens

Symptoms:

- Pain
- Redness
- Blister
- Numbness

Mechanism of necrosis:

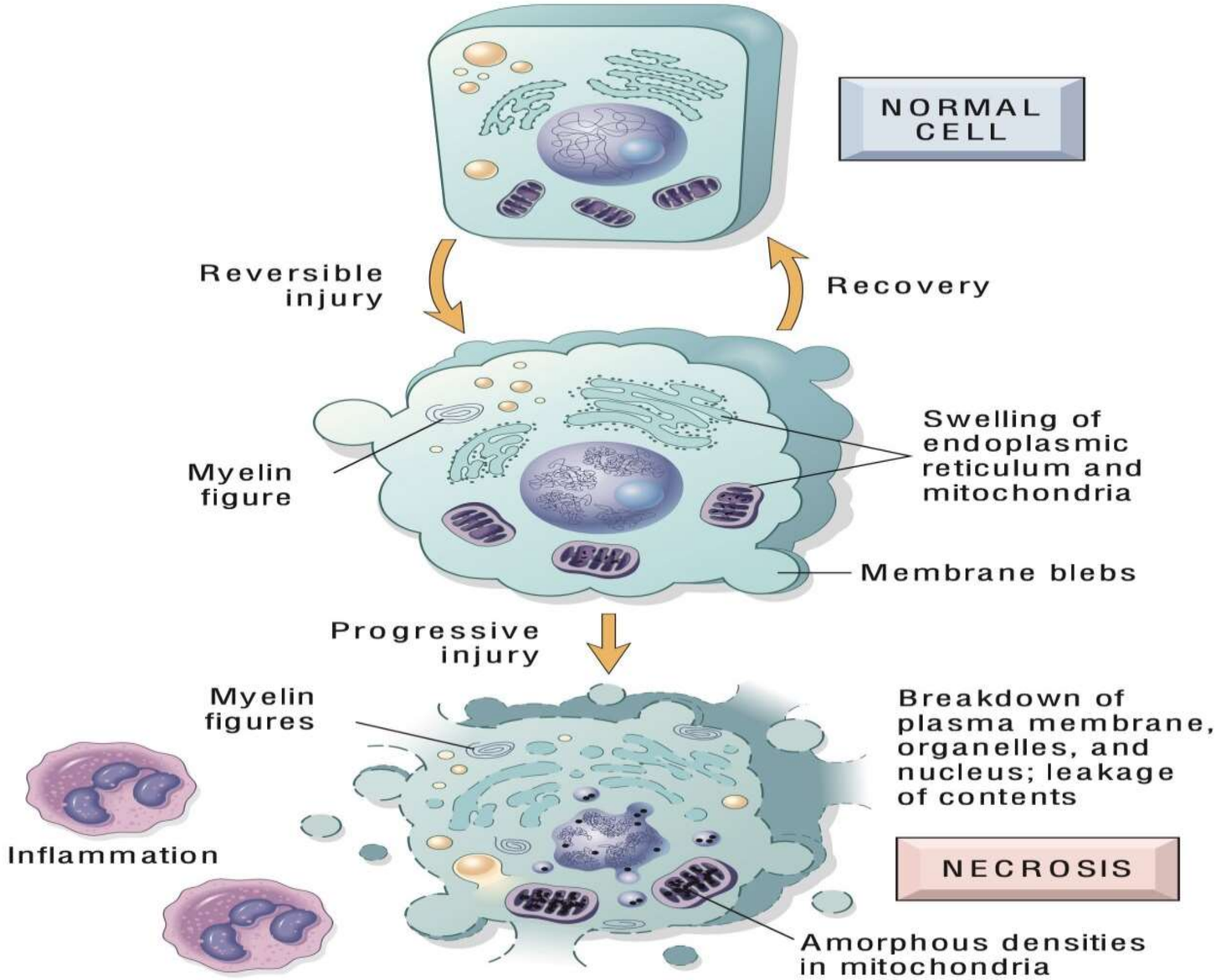
Necrotic cell death:

- Loss of metabolic functions
- Loss of the integrity of the cell membranes
- Cessation of the production of proteins & ATP
- Cells organells sell and become non functional.

1.Depletion of ATP-leads to breakdown of cells ion balance

2.Reduce oxygen level

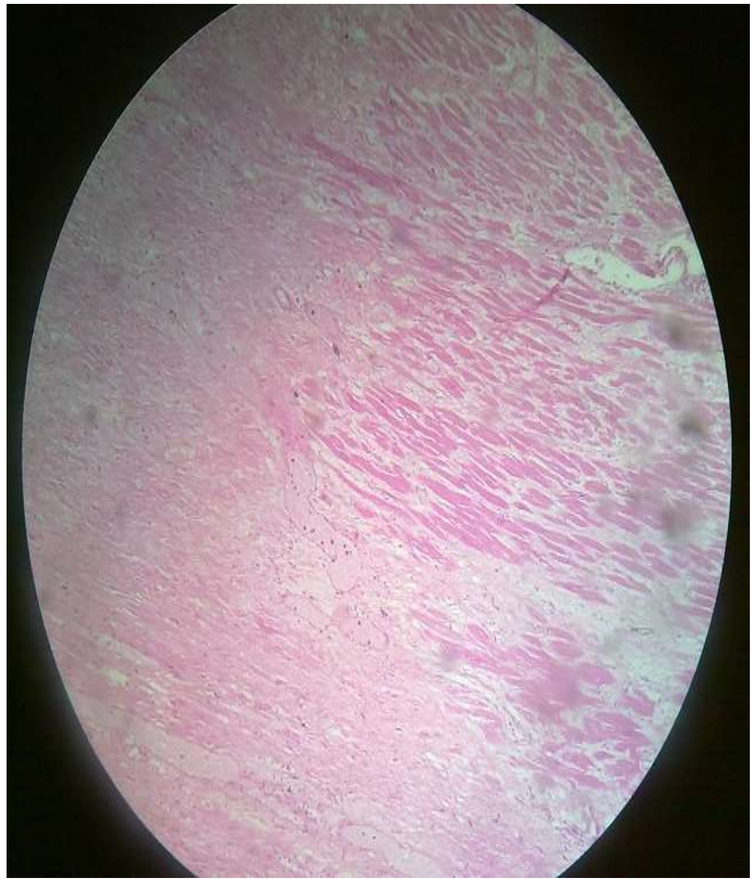
3.Oxidative stress-the presence of excess oxygen radicals


NORMAL CELL
Reversible injury
Recovery
Myelin figure
Swelling of endoplasmic reticulum and mitochondria
Membrane blebs
Progressive injury
Myelin figures
Breakdown of plasma membrane, organelles, and nucleus; leakage of contents
Inflammation
NECROSIS
Amorphous densities in mitochondria

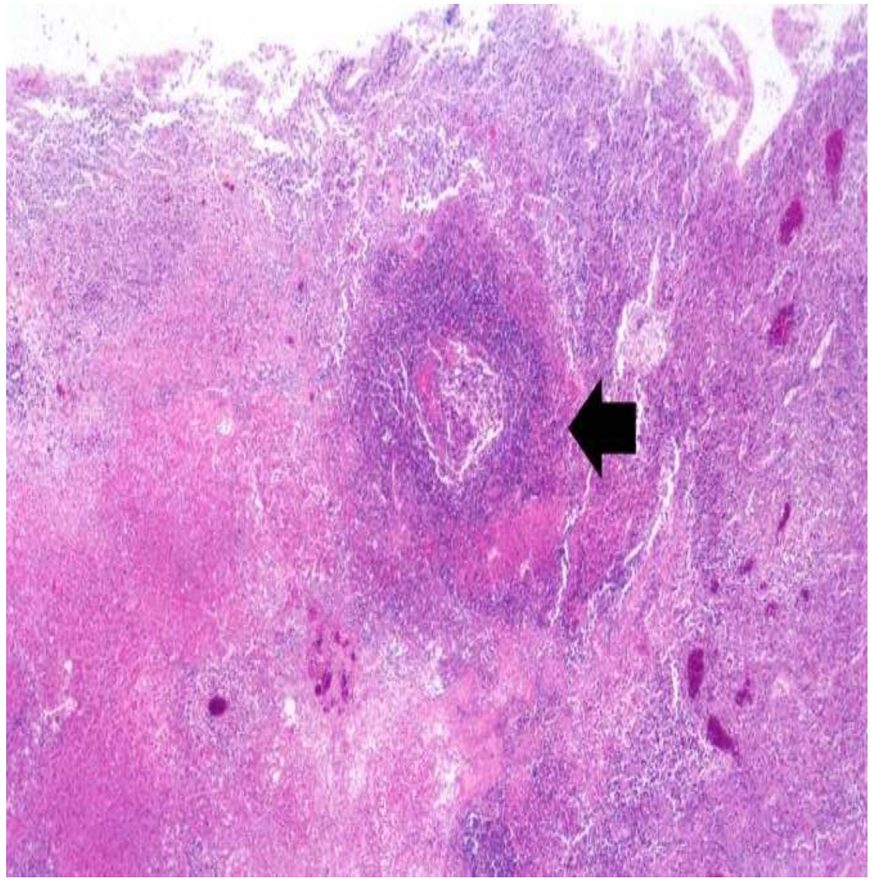
Types:(Classification based on microscopy)

- Coagulative necrosis
- Liquefactive necrosis
- Fat necrosis
- Caseous necrosis
- Gangrenous necrosis
- Fibrinoid necrosis

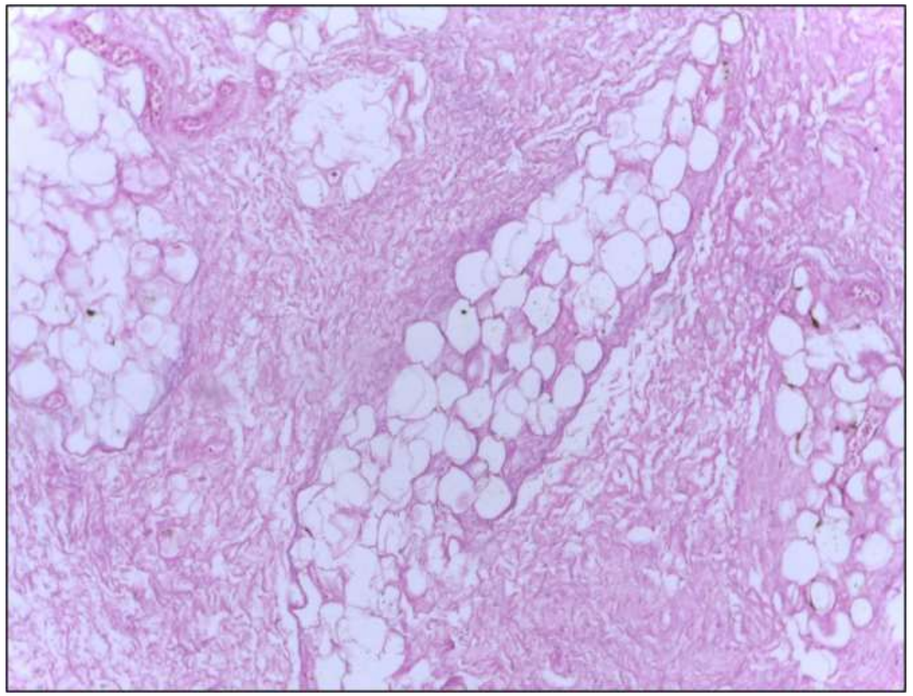
Coagulative Necrosis



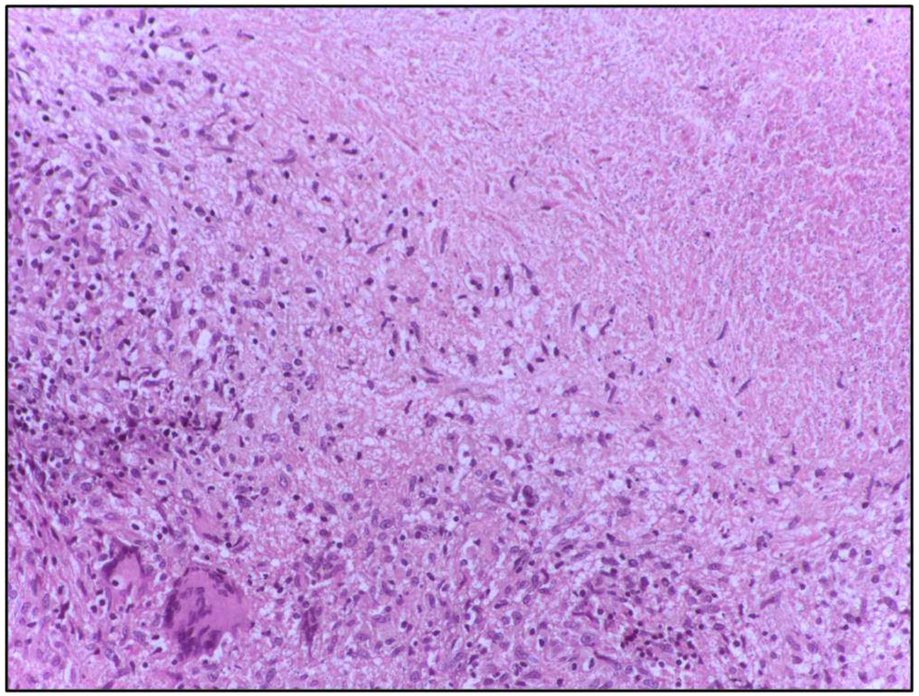
Liquefactive Necrosis



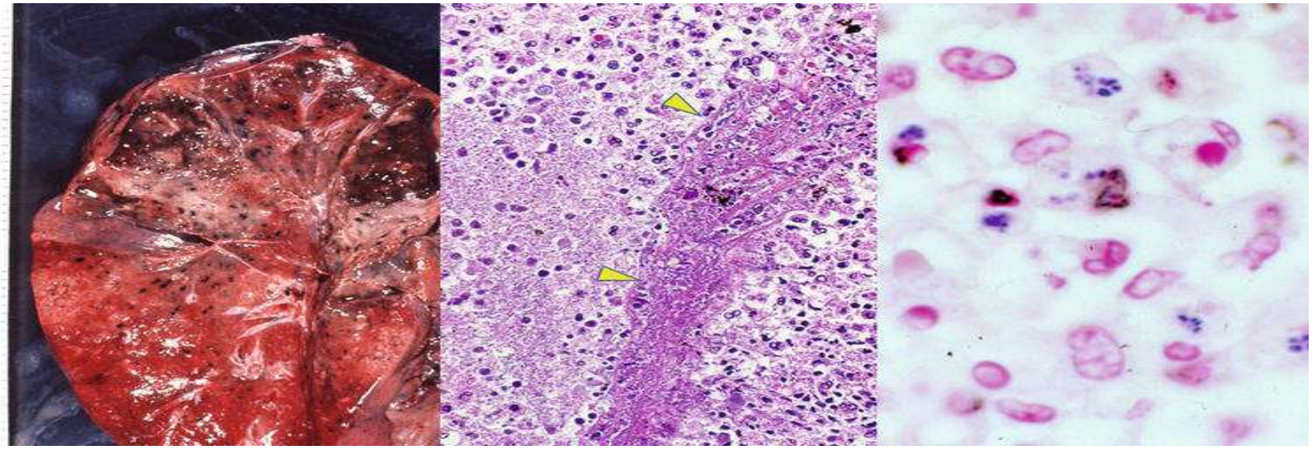
Fat Necrosis



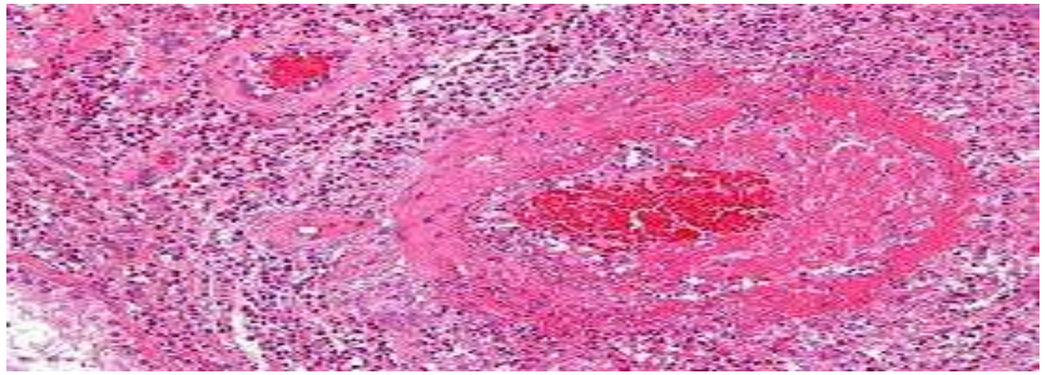
Caseous Necrosis



Gangrene Necrosis



Fibrinoid Necrosis



1.Coagulative Necrosis:

- See this in infracts in any tissue(except brain)
- Due to loss of blood
- Cell outlines are preserved and everything looks red
- Tombstone appearence,swelling,inflammation

2.Liquefactive Necrosis:

- See this in infections in brain infracts
- Due to lots of neutrophils around releasing their toxin contents “liquefying the tissue”
- Tissue is liquidly and creamy yellow
- Lots of neutrophils and cell debris
- Liquifaction,inflammation,proliferation

3.Fat Necrosis:

- Fat necrosis that in which the neutral fats in adiose tissue are spilt into fatty acids and glycerol usually affecting the pancreas
- Shadowy outlines of dead fat cells

5.Caseous Necrosis:

- Cheesy necrosis that in which the tissues is soft,dry and cottage cheese like;most often seen in tuberculosis and syphilis

5.Gangrenous Necrosis:

- See this when an entire limb loses blood supply and dies
- Skin looks black and dead,underlying tissue is in varying stages of decomposition
- Initially there is coagulative necrosis from the loss of blood supply(this stage is called dry gangrene).If bacterial infection is superimposed there is liquefactive necrosis(this stage is called wet gangrene)

6.Fibrinoid Necrosis:

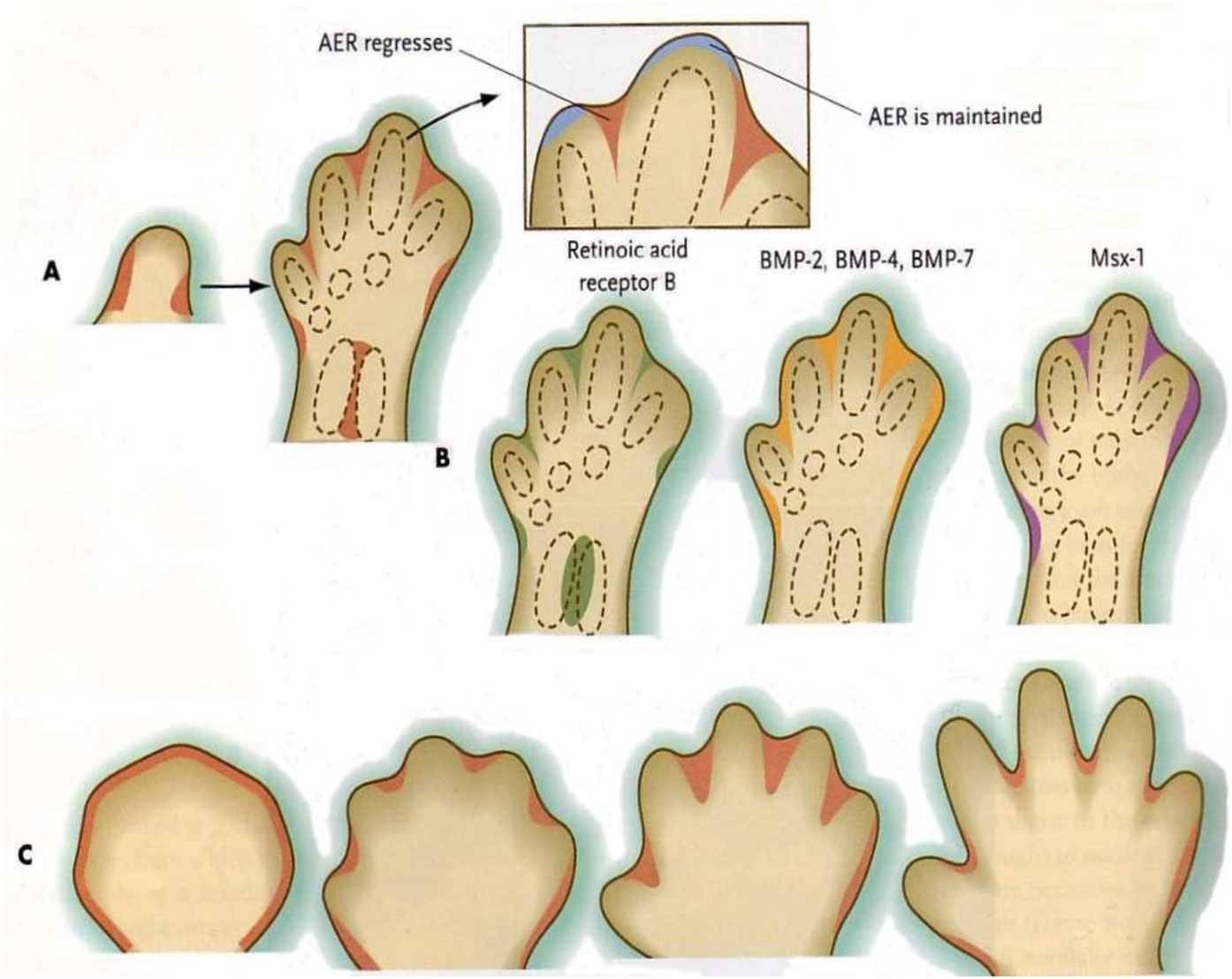
- See this in immune reactions in vessels
- Complexes of antigens and antibodies,combine with fibrin
- Chnges too small to see grossly
- Vessel walls are thickened and pinkish -red called fibrinoid

Apoptosis:

- In humans the rate of cell growth and cell death is balenced to maintain the weight of the body

Two main mechanism of cell death:

- Apoptosis-Programmed cell death
- Necrosis-Ordinary cell death


AER regresses
AER is maintained
A
Retinoic acid receptor B
BMP-2, BMP-4, BMP-7
Msx-1
B
C

- The word apoptosis comes from the ancient greek meaning:The falling of petals from a flower
- The term apoptosis was first used in a now classic paper by Kerel at 1972 to describe a morphologically distinct form of cell death.

Definition:

- Apoptosis or programmed cell death is a made of cell death that occurs under normal physiological condition and the cell is an active participant in its own demise.
- It is important for the development of multicellular organism and homeostatsis of their tissues.

Importance:

1.Apoptosis is a beneficial and important phenomenon:

- In embryo development-cellular homeostasis-maintaining normal internal environment of the body
- During embryonic development it help to digit formation
- Lack of apoptosis in humans can lead to webbed fingers called syndactly.

2.Normal event in development of nervous system:

- Normal cell turn over
- Tissue homeostatis
- Induction and maintenance
- Development of nervous system
- Endocrine-dependent tissue atrophy
- ELimination of activated damaged and abnormal cells

Apoptosis vs Necrosis:

- Apoptosis is the physiological cell death which unwanted or useless cells are elimiated during development and other normal bilogical processes
- Necrosis is the pathological cell death which occurs when cells are exposed to a serious physical or chemical insult (hypoxia,hyperthermia,ischemia)

Difference between apoptosis and necrosis:

Morphological features:

Necrotic:

- Volume enlargement
- Swelling of cytoplasm &mitochondria
- Loss of membrane integrity
- No vescile formation

Apoptic:

- Volume reduction
- Shrinking of cytoplasm
- No loss of membrane integrity
- Formation of apoptotic bodies
- Condensation of chromatin & DNA fragmentation

Biochemical features:

Necrotic cells:

- Loss of regulation of ion homeostasis
- No energy requirement (passive process also occurs at 4’c

Apoptic cells:

- Extrinsic Pathway(death receptor-mediated events)
- Intrinsic Pathway(mitochondria-mediated events)

Extrinsic Pathway:(stimulation comes from outside)

Components:

- Death receptors
- Death ligands
- Adaptos proteins
- Caspases

Caspases:

- Cysteinly aspartate specific proteases
- A family of intracellular cysteine proteases that play a pivotal role in the initiation and execution od apoptosis.
- At least 14 different members of caspase in mammalian

cells have been identified

- All are synthesized as inactive proenzymes.

Caspases subgroups:

- To date ten major caspases have been identified and broadly categorized into:
- Signaling
- Effector
- Inflammatory caspases

Extrinsic Pathway:

- Death receptors that are members of the tumor necrosis factor receptors superfamily
- Death receptors have a cytoplasmic domain of about 80 amino acids called the death domain
- This death domain plays a critical role in transmitting the death signal from the cell surface to the intracellular signaling pathways

Intrinsic Pathway:

- Stimulation starts from inside the cell
- Cell(unrepair) gets damaged it activates mitochondria
- Mitochondria release 2 protein:

1.Cytochrome C

2.Second mitochondria-derived activator of caspases

- Normal stage-Apoptosis-Inhibition
- If mitochondria activates-2 protein-inhibitor-inhibit
- 2 protein factor directly activte caspases

Process:

- Caspases activation
- Cell shrinkage - contact looser
- Nucleus degradation - DNA fragments
- DNA fragments - Phagocytes

THANK YOU