Cell injury “1”

Editing File

Objectives

Know the definition of apoptosis , tissue necrosis and its various types with clinical examples.
Differentiate between necrosis and apoptosis.

Color Code:

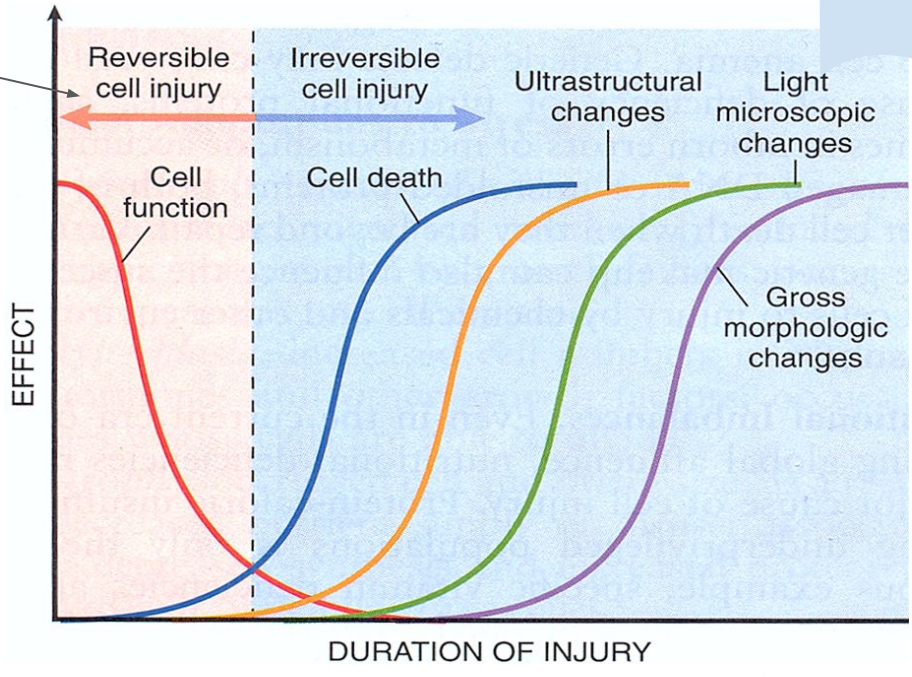
Female’s Notes
Male’s Notes
Important
Extra

Pathology Team 441
MED441 KING SAUD UNIVERSITY
Revised & Reviewed by: Abdulaziz & Bahammam Faye Wael Sendi

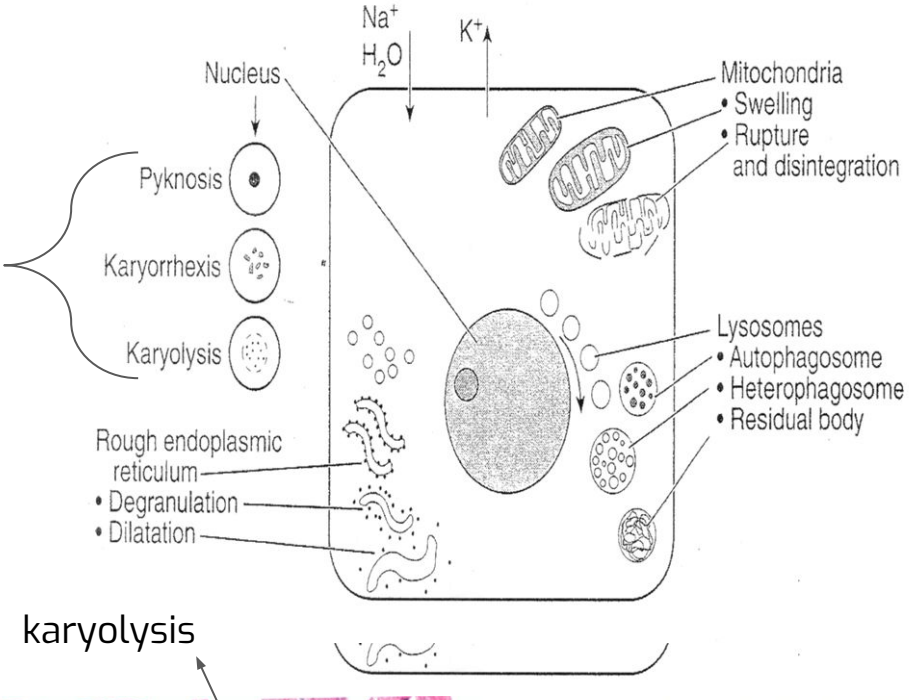
Overview

Boys

Can recover If we remove the cases



irreversible



karyolysis

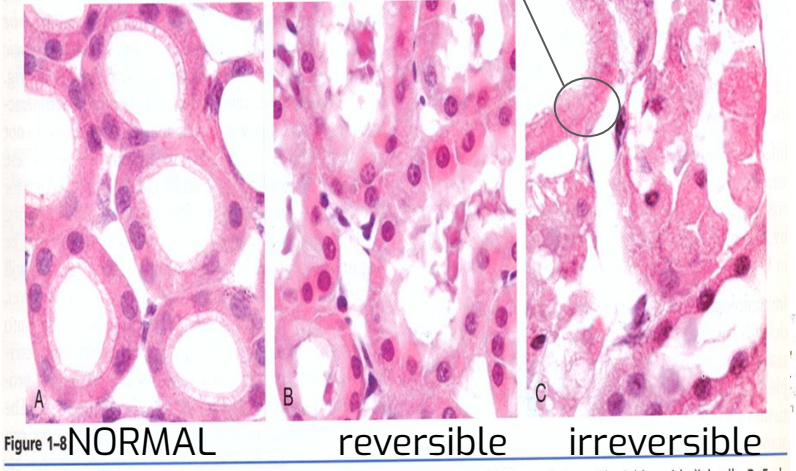
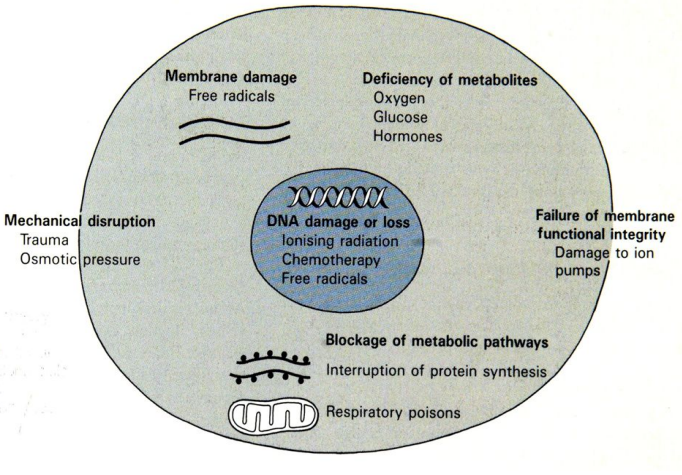


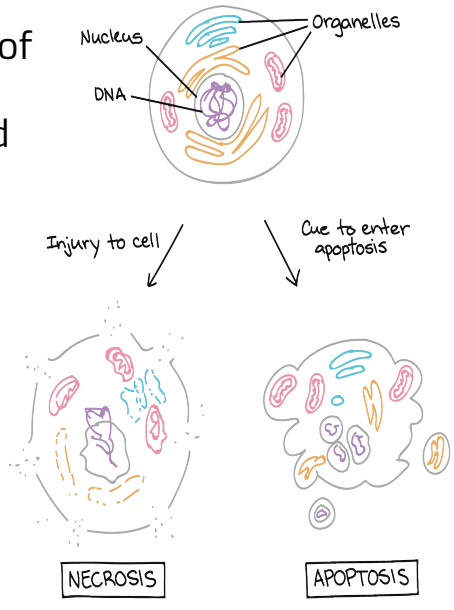
Figure 1–8 NORMAL reversible irreversible

Morphologic changes in reversible and irreversible cell injury (necrosis). **A,** Normal kidney tubules with viable epithelial cells. **B,** Early (reversible) ischemic injury showing surface blebs, increased eosinophilia of cytoplasm, and swelling of occasional cells. **C,** Necrotic (irreversible) injury of epithelial cells, with loss of nuclei and fragmentation of cells and leakage of contents. The ultrastructural features of these stages of cell injury are shown in Fig. 1–9. (Courtesy of Drs. Neal Pinckard and M.A. Venkatachalam, University of Texas Health Sciences Center, San Antonio.)



Necrosis

Necrosis is type of cell death, in which there is enzymatic digestion of the dying cell. Enzymes leak out of lysosomes,enter the cytoplasm and digest the cell.



Always pathologic process, associated with pathologic cell injury. It is usually associated with inflammation in the surrounding tissue.

Occurs in irreversible cell injury. It involves the death of group of cells in one area.

In necrosis :-

There is Loss of function of the involved tissue/organ.

The necrotic cells release certain enzymes, that can be detected in blood tests

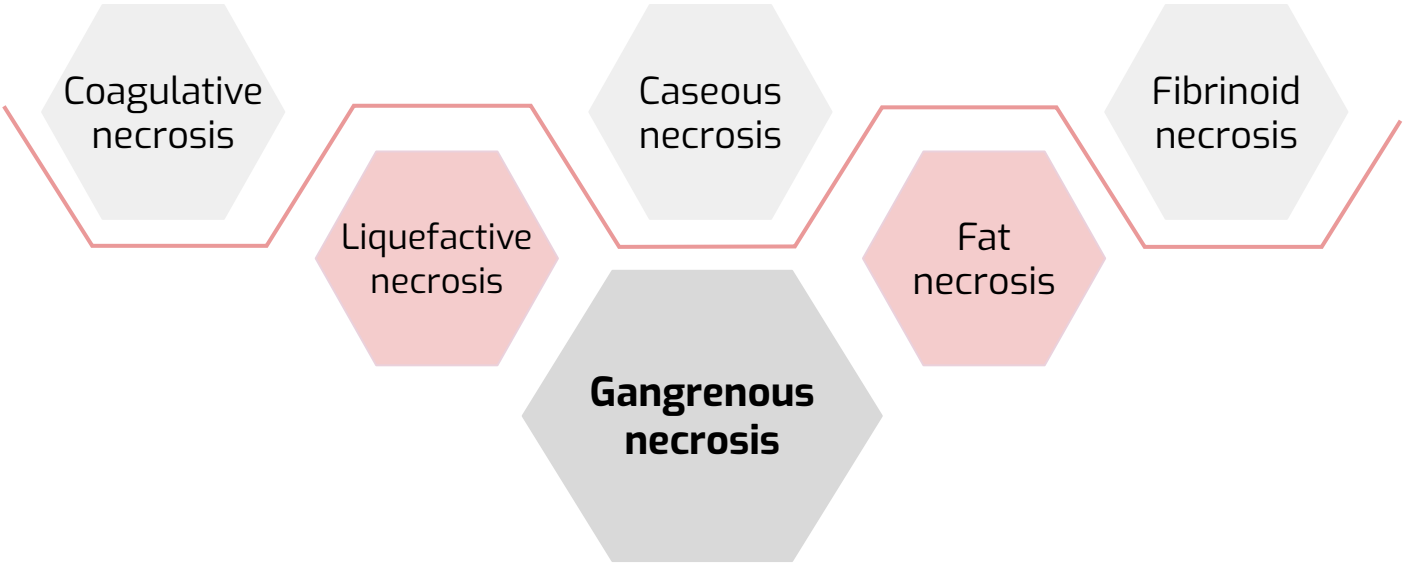
There is an inflammatory response

The level of these enzymes can be used as markers to diagnose and determine the time & the extent of injury, e.g.Detection of cardiac enzymes in myocardial infarction.(heart attack).

The enzymes used in this degradation of cell come from either :

- The lysosomes of the dying cell itself referred to as **autolysis**
- Or from lysosomes of neighboring leukocytes referred to as **heterolysis** . Enzymes of cell A ⟶ cell B
- Autolysis is the death/disintegration of cells or tissues by it's own enzymes. Its seen in cells in necrosis and after death/post Mortem.
- Creatine-Kinase is the most important diagnostic protein when it comes to Cardiac damages.

Types of necrosis



Coagulative necrosis

1. Coagulative necrosis is characteristically seen when blood flow to an organ is affected leading to

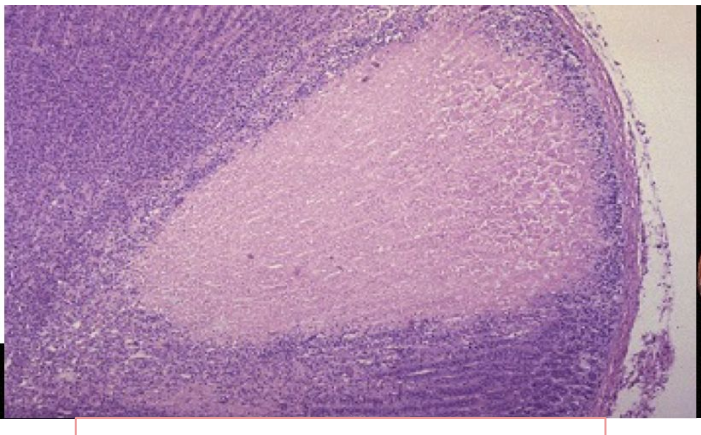
Ischemic → **Hypoxic death** → **Of cells in that organ**

2. Coagulative necrosis is seen in all organs except the brain
- In heart → is called as myocardial infarction
- In kidney → is called as renal cortical necrosis (Renal infarct)
- In spleen. → Spleen infarct
- In liver. → Hepatic infarct etc.

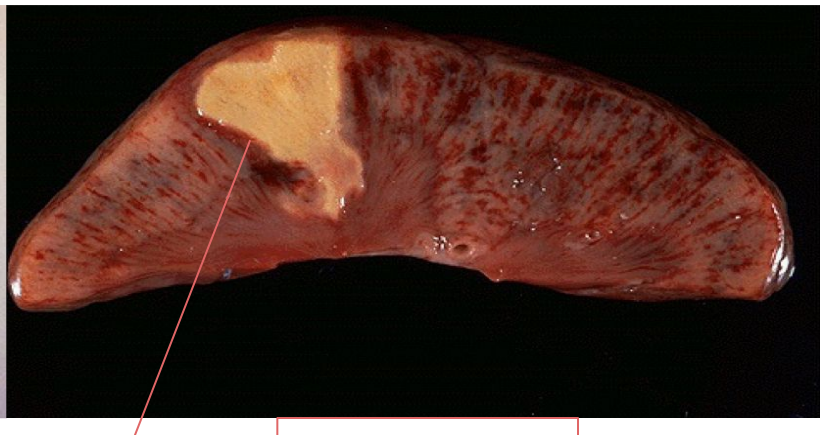
Ischemia: inadequate blood flow to an organ, which leads to decrease oxygen supply to an organ , which leads to Hypoxia.
Team 439

Grossly	Microscopy
• Pale & firm /solid • Like cooked meat or boiled egg • The tissue is firm and architecture is maintained for days after cell death . **NB**: The necrotic tissue appears pale and firm and retains its Normal shape **Because** no enzymatic lysis occurs	In the beginning there's preservation of general tissue architecture. The basic ghost outline of the outline of the affected/coagulated cell remains preserved for a few days but the nucleus is lost. The cell cytoplasm is eosinophilic. Ultimately,the necrotic cells are removed by phagocytosis by the macrophages (they act like vacuum cleaners) and the affected area is replaced by fibrosis (like scars).

Coagulative necrosis

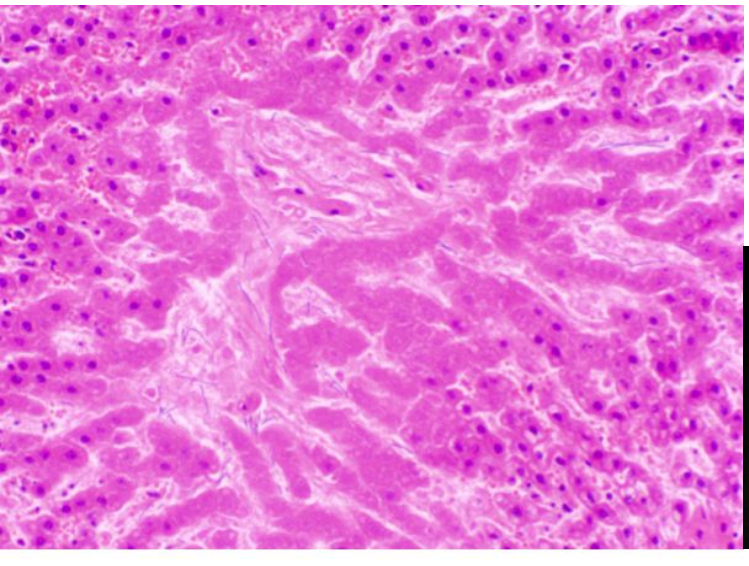


Kidney coagulative necrosis



Tissue is firm

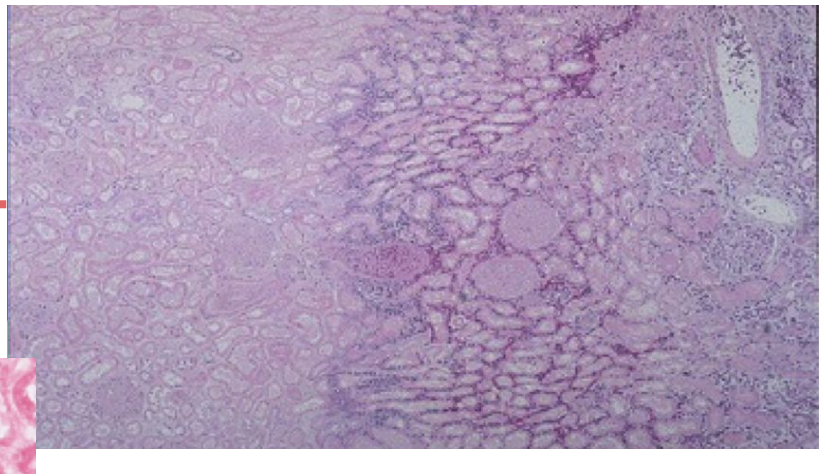
Gross

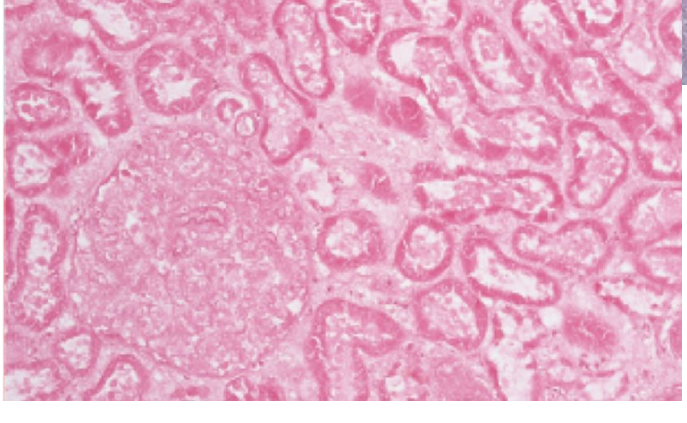


Liver coagulative tissue

Fun hint , The liver coagulative necrosis looks like an alien here

No nucleus





Kidney coagulative necrosis : Micro: cells outlines are preserved (cells look ghostly), and everything looks red

Liquefactive necrosis

1

Type of necrosis which results in transformation of the tissue into a liquid viscous material.

2

Seen in:

- Ischemic (hypoxic) cell death in the brain/central nervous system.
- Necrosis that results from infections especially suppurative bacterial infection.(pus or abscess producing).

3

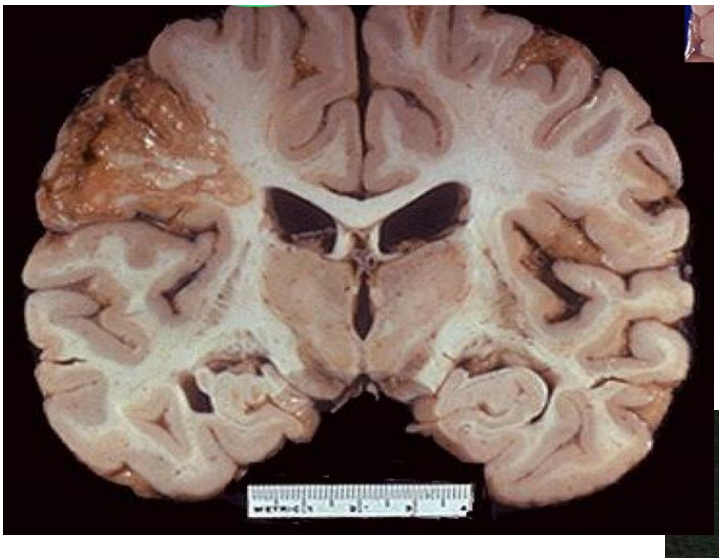
In infections: the affected tissue is softened/liquefied by the action of hydrolytic (digestive) enzymes released from the lysosomes of neutrophils. The affected area becomes soft and liquefied with a creamy yellow center containing necrotic cells and neutrophils and is called (pus/abscess).

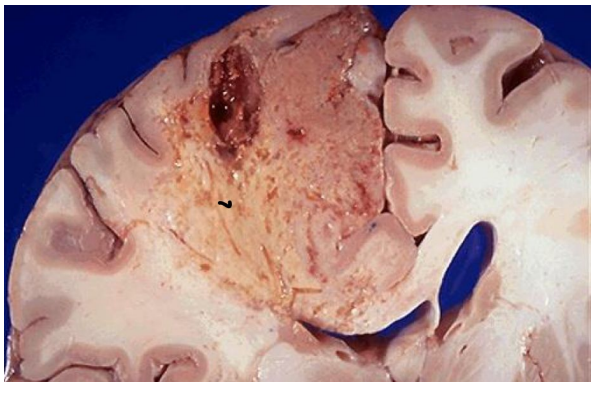
Pus: a thick yellow or green liquid that is produced in a wound as a result of an infection .

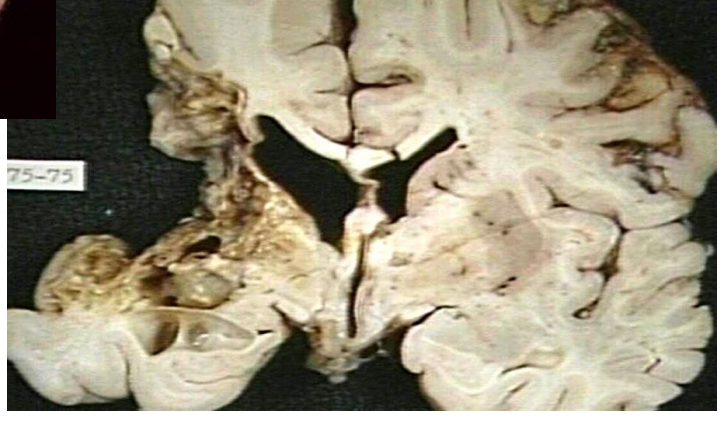
Abscess: a swollen area within body tissue, containing an accumulation of pus .

Note: the reason for liquefactive necrosis following ischemic injury in the brain is poorly understood.

- Ultimately, the necrotic cells are phagocytosed.



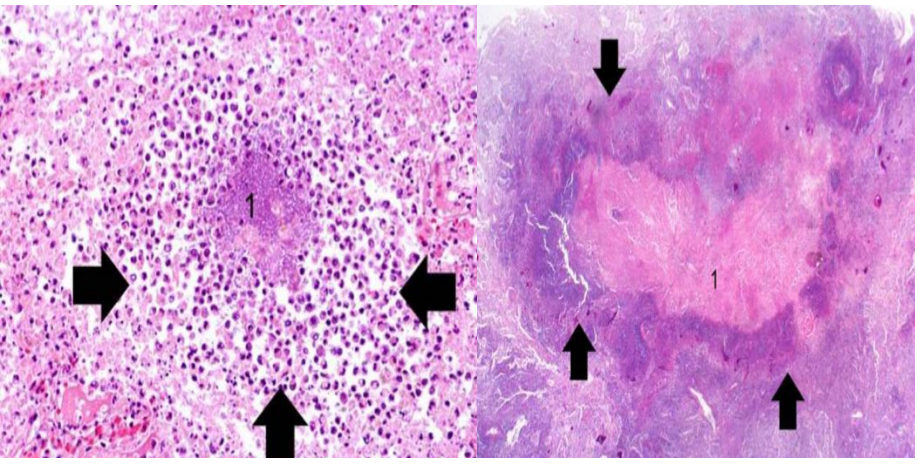


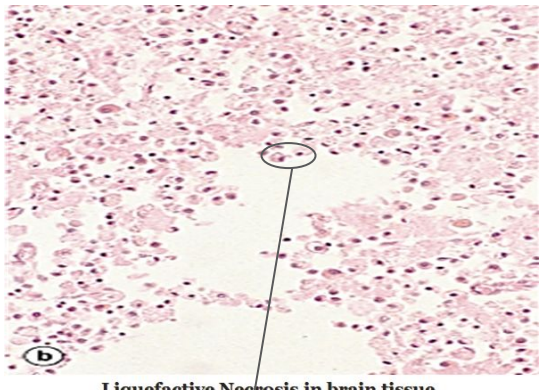


Liquefactive necrosis

Cont..

Infection: Liquefactive necrosis (center labeled one is necrosis and surrounded by neutrophils.





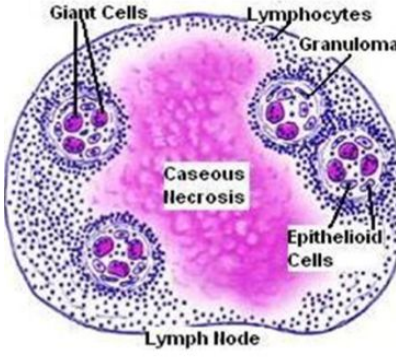
Liquefactive Necrosis in brain tissue.

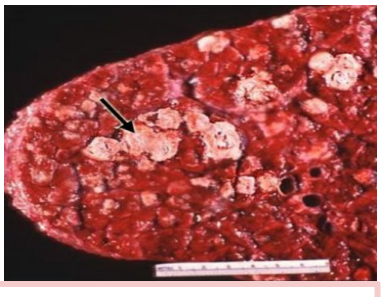
macrophages

Caseous necrosis

1. is a type of coagulative necrosis classically seen in tuberculosis (infection by mycobacterium tuberculi).
2. Grossly: it is white, soft, curdy, cheesy-looking “caseous” material.
3. On microscopic examination, the necrotic area appears as amorphous pink granular debris surrounded by a collar of epitheloid cells (they are modified macrophages), lymphocytes and giant cells. This is known as granuloma.

Here the tissue architecture is completely obliterated





Tuberculous lung with a large area of caseous necrosis. The caseous debris is yellow-white and cheesy

Fat necrosis

1

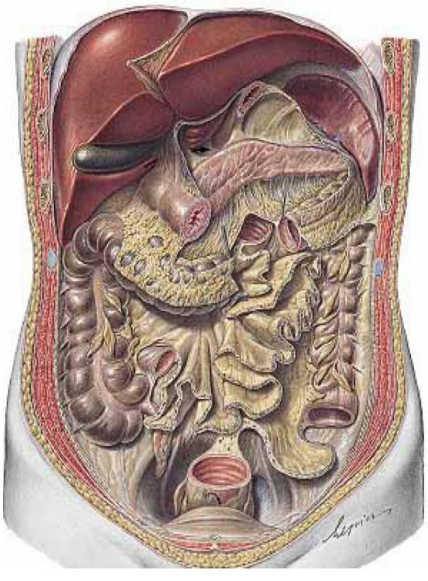
It is necrosis of fat cells

2

it is seen in acute pancreatitis (inflammation of pancreas) in which the injured pancreatic cells release the lipase enzyme into the surrounding fat in the abdominal cavity and cause enzymatic digestion of fat cells.

3

The released lipase breaks down the fat cells into glycerol and free fatty acids. The produced fatty acids combine with calcium circulating in the blood to produce calcium soaps which looks like chalky white spots in the necrotic fat. This process is called as fat saponification



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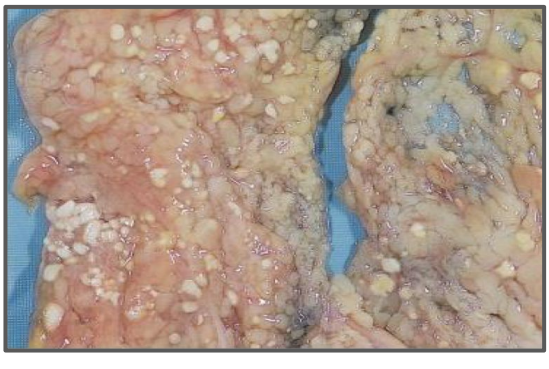
Microscopy: the outlines of necrotic/dead fat cells can be seen. Inflammation is minimal.

5

Fat necrosis can also be seen in breast and abdominal wall fat and other fatty areas due to traumatic injury.



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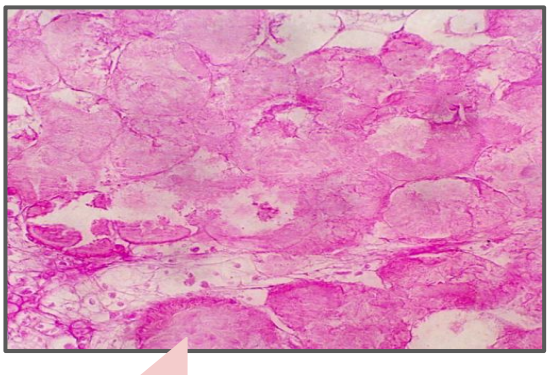
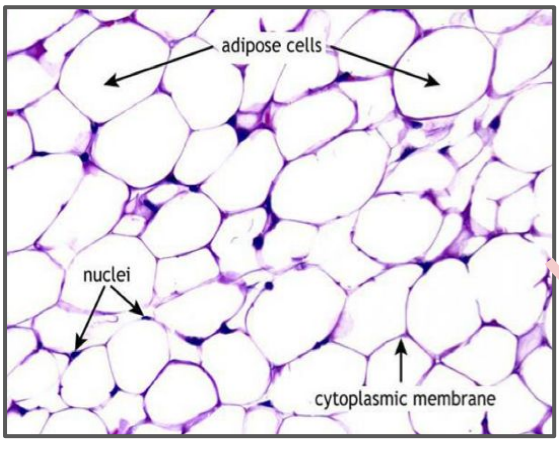
Boys Notes

Drinking alcohol and gallbladder diseases are main reasons for fat necrosis.

Fat Necrosis cells don't show nucleus because the cell degraded





Normal fat (adipose tissue)

2nd fun hint
Fat necrosis looks like orchids

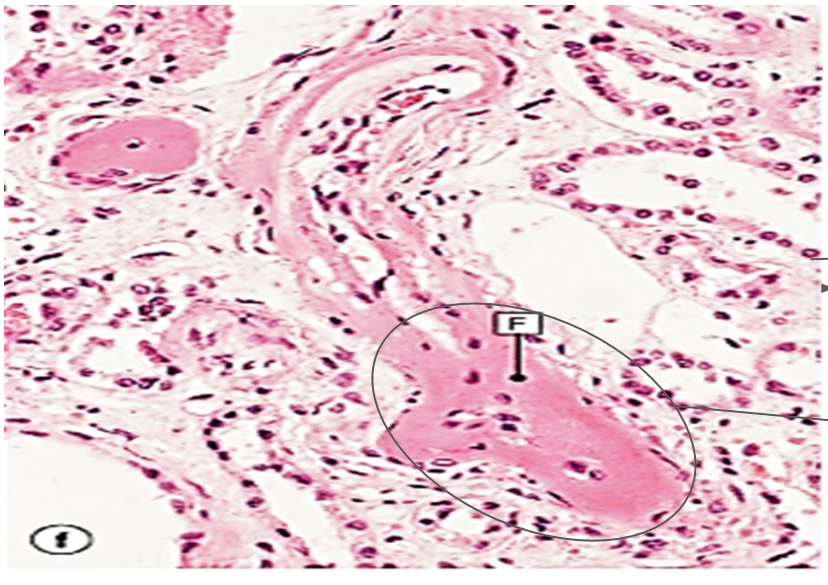
Fibrinoid necrosis

1st Is necrosis in the blood vessels (arteries, arterioles and capillaries)

2nd There is deposition of fibrin material in the arterial walls, which appears smudgy and acidophilic/eosinophilic.

3rd It is seen in immune mediated diseases (autoimmune diseases) and also seen in malignant hypertension.

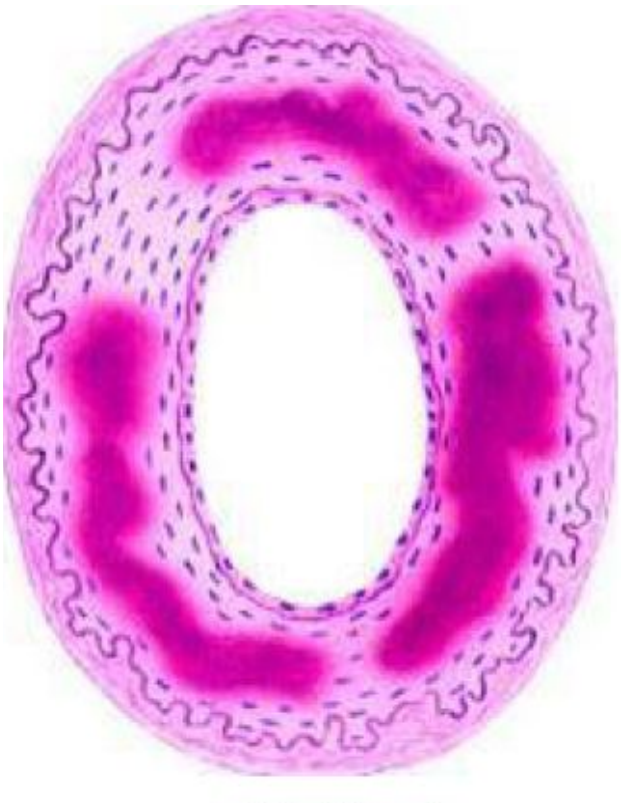
Because of the High Demand on heart in hypertension patients they may show Heart Hypertrophy in X-ray

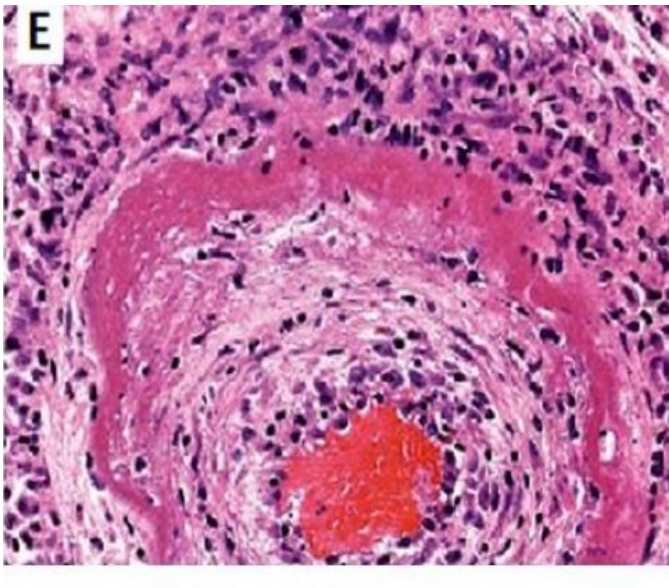


Boys

More in BV usually immune mediated and we know diagnosis from it which called **vasculitis**

Antigen precipitation (eosinophilic homogeneous material)





Fibrinoid necrosis in an artery. The wall of the artery is bright pink with dark neutrophils

Gangrenous necrosis

Dry gangrene/ mummification

It is coagulative necrosis typically seen in a limb with inadequate blood supply (ischemia of that limb).

Dry gangrene is non-infected ischemic coagulative necrosis of tissue.

It is without superadded infection. It is seen as a complication of peripheral artery disease e.g. atherosclerosis, and diabetes mellitus due to ROS (Free Radicals).

The affected part is dry, shrunken and dark reddish-black.

Common Disease

It is a term commonly used in clinical practice by surgeons. It can be dry or wet

Wet /infected gangrene

Very Rare Disease

it is dry gangrene (coagulative necrosis) with superadded bacterial (putrefactive) infection resulting in liquefactive necrosis. So, initially there is coagulative necrosis and then there is superadded infection associated liquefactive necrosis. Wet gangrene usually develops rapidly. The bacteria is usually saprogenic (i.e. it lives in the gut or the soil and it can thrive in low oxygen states) e.g. gram-positive Clostridia or Bacillus fusiformis. It has a poor prognosis compared to dry gangrene because the infection can spread to the rest of the body (septicemia) and be life threatening (death). The limb becomes foul smelling and black and starts decomposing.

Treatment of gangrene: amputation

NOTE : Diabetes mellitus is a risk-factor for dry gangrene and for wet gangrene (as elevated serum glucose creates a favorable environment for bacterial infection).

Apoptosis

Apoptosis or *"Falling Off"*: programmed *planned* cell death (cell suicide) resulting from activation of 'death pathway genes'.
A pathway of cell death in which cells destined to die activate their own enzymes to degrade their own nuclear DNA and proteins

Damage of cell's DNA or proteins
OR
Cell deprivation of growth factors

Leads to

Apoptosis

Can be

- Pathologic
- Physiological or Adaptive

Characteristics of Apoptosis

- Nuclear dissolution *separation* without loss of membrane integrity
- Active, energy-dependant, tightly regulated

NOTE: Apoptosis and necrosis can sometimes coexist
eg. tumors/cancer

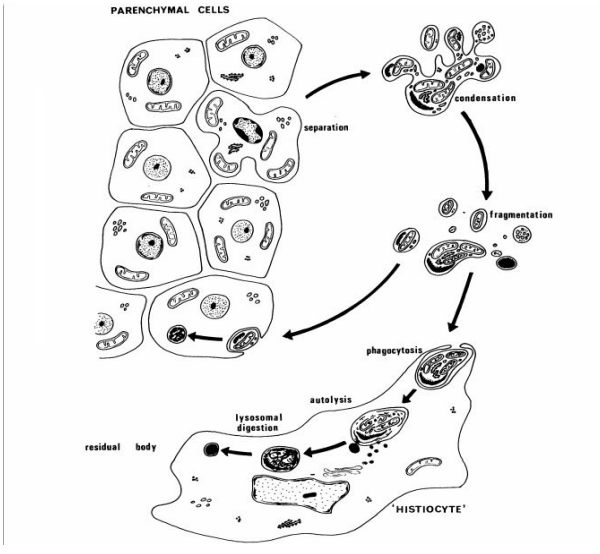
Apoptosis in physiological conditions

- Embryogenesis *formation of a fetus*
- Hormone-dependant e.g. endometrial cell breakdown during the menstrual cycle, the regression of the lactating breast after weaning, and prostatic atrophy after castration
- Proliferating cells تجدد e.g. constant replacement of the intestinal epithelial lining
- Cells that undergo apoptosis after performing their functions e.g. lymphocytes and neutrophils in inflammation
- Harmful lymphocytes that are produced by the body

Apoptosis in pathological conditions

- Injury e.g. radiation
- Diseases e.g. viral hepatitis infected hepatocytes undergo apoptosis (acidophilic bodies), injury of skin epidermal cells leads to apoptosis of keratinocytes (Civatte bodies)
- Pathologic atrophy in organs e.g. pancreas, parotid gland, and kidney.
- Corticosteroid induced atrophy of the neonatal thymus.
- Cell death in tumors (usually accompanied by necrosis)

Mechanism of Apoptosis

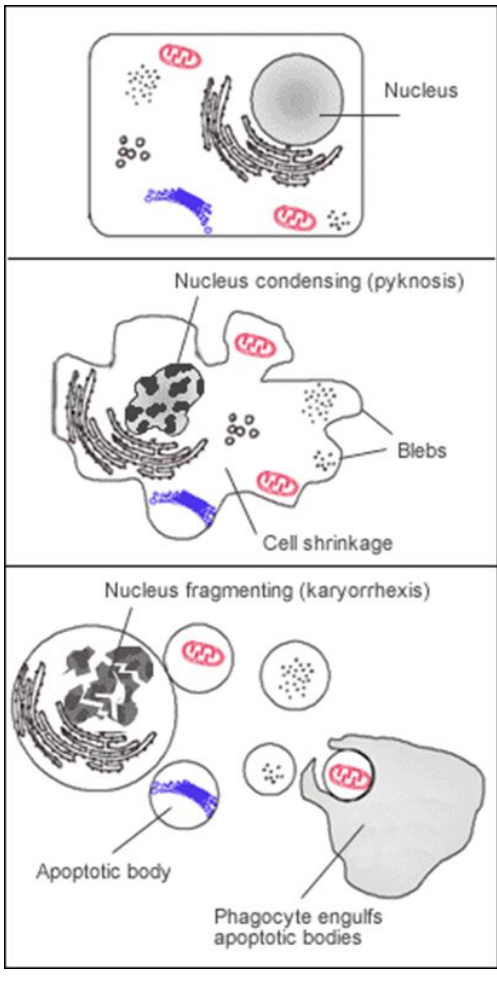


Death pathway genes are activated

Cell Shrinkage

Chromatin Condensation in the nucleus

The most characteristic feature of apoptosis. The nucleus may break up into fragments.



Formation of cytoplasmic blebs and apoptotic bodies

Cell shows surface blebbing then fragments into membrane-bound apoptotic bodies.Apoptotic bodies contain cytoplasmic content with or without nuclear material.

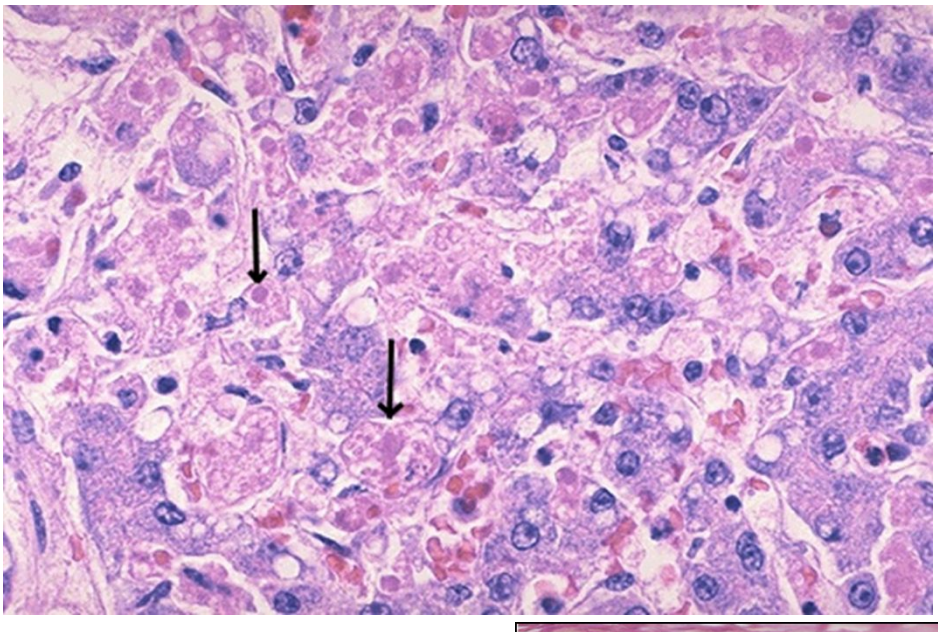
Cell's plasma membrane remains INTACT unchanged

Phagocytosis of apoptotic bodies by the macrophages

Plasma membrane sends signals to macrophages for phagocytosis.

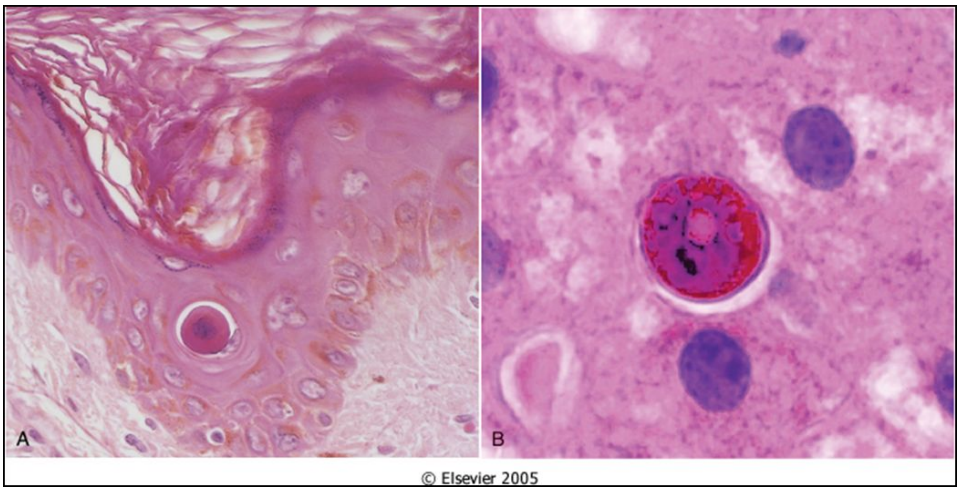
Because the apoptotic body is bound by a plasma membrane , cytoplasmic content is not released, so there is no inflammation. Some fragments degenerate extracellularly,while others are ingested by local phagocytic cells .

Morphology of Apoptosis



Apoptosis in liver cells

Apoptosis in epidermis



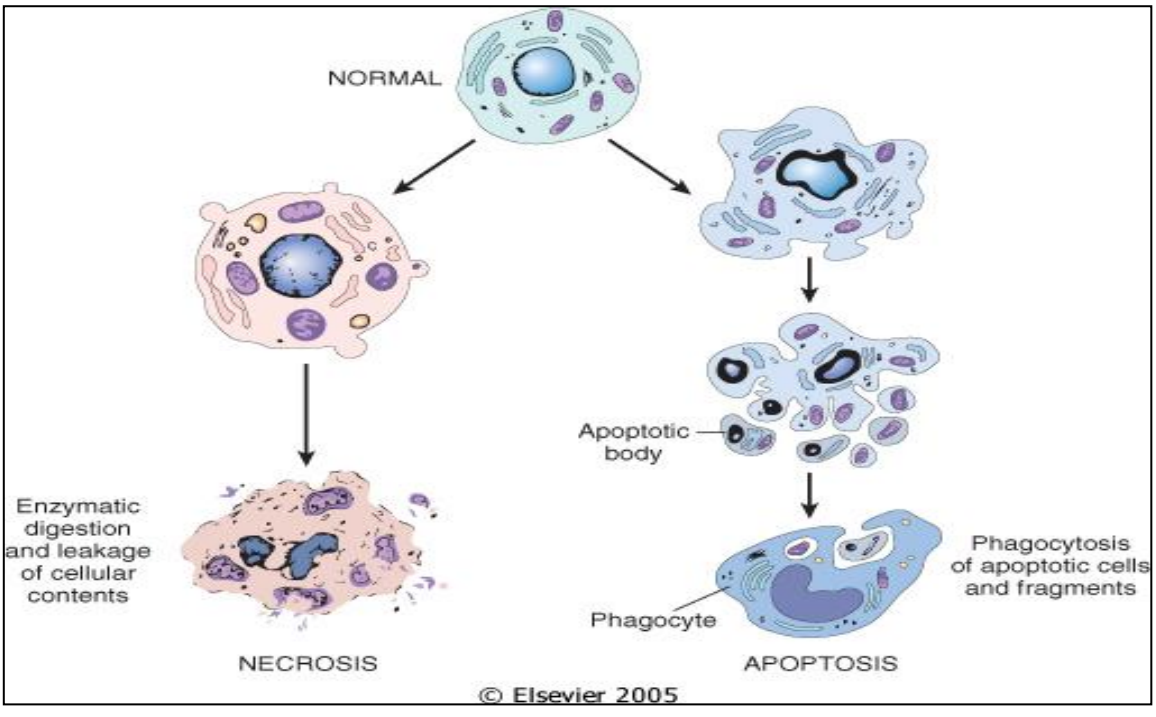
- On histology apoptosis involves single cells or small clusters of cells *ONLY. (Necrosis affects a large group of cells).*
- The apoptotic cell appears as a round or oval mass of intensely eosinophilic *pink* cytoplasm with dense nucleus. There is no inflammation.

Important enzymes of Apoptosis

- Cysteine proteases called *caspases*
- Ca2+ dependant endonucleases
- Mg2+ dependant endonucleases

Regulation of Apoptosis

- Bcl-2 gene inhibits *stops* apoptosis
- Bax gene facilitates *promotes* apoptosis
- P53 facilitates apoptosis by inhibiting bcl2 and promoting bax genes



In necrosis there is loss of membrane integrity, enzymatic digestion of cells, and frequently an inflammatory reaction.

Apoptosis and necrosis sometimes coexist

Feature	Necrosis	Apoptosis
Cell Size	Enlarged (swelling)	Reduced (shrinkage)
Nucleus	Pyknosis *shrinkage* Karyorrhexis *fragmentation* Karyolysis *dissolution*	Fragmentation into nucleosome size fragments Karyorrhexis
Plasma Membrane	Disrupted *inflammation*	Intact; altered structure, especially orientation of lipids *No inflammation*
Cellular Contents	Enzymatic digestion; may leak out of cell	Intact; may be released in apoptotic bodies
Adjacent Inflammation	Frequent	No
Physiologic or pathologic role	Invariably pathologic (culmination of irreversible cell injury)	Often physiologic, means of eliminating unwanted cells; may be pathologic after some forms of cell injury, especially DNA damage

MCQs

Q1: Necrosis that transfer the tissue into liquid viscous material			
A: coagulative necrosis	B: liquefactive necrosis	C: Fat necrosis	D: caseous necrosis
Q2: Coagulative necrosis is seen in all organs except			
A: Kidney	B: Heart	C: Brain	D: Spleen
Q3: The type of necrosis that starts as coagulative necrosis then turns into liquefactive necrosis after getting infected , is			
A: Liquefactive necrosis	B: Fat necrosis	C: Dry gangrene	D: Wet gangrene
Q4: Type of necrosis which is seen in immune mediated diseases			
A: Fibrinoid necrosis	B: Dry gangrene	C: liquefactive necrosis	D: Caseous necrosis
Q5:What could be a cause of Apoptosis?			
A: Viral hepatitis	B: Menstrual Cycle	C: Injury of skin epidermal cells	D: All of the above
Q6:Release of cytoplasmic contents occurs in which of the following?			
A: Necrosis	B: Atrophy	C: Metaplasia	D: Apoptosis
Q7:What gene/s facilitate apoptosis?			
A: bcl-2	B: bax	C: p53	D: B&C
Q8::What does an apoptotic cell look like?			
A: Round mass of an intensely basophilic cytoplasm	B: Round mass of an intensely eosinophilic cytoplasm	C: Round mass of a neutrophilic cytoplasm	D: Round mass of an acidic cytoplasm

Q1:B Q2:C Q3:D Q4:A Q5:D Q6:A Q7:D Q8:B

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