PATHOLOGY

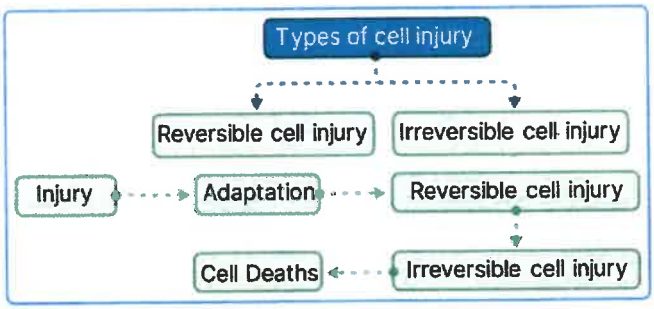
1 CELL INJURY PART 1

Cell Injury

00:00:49

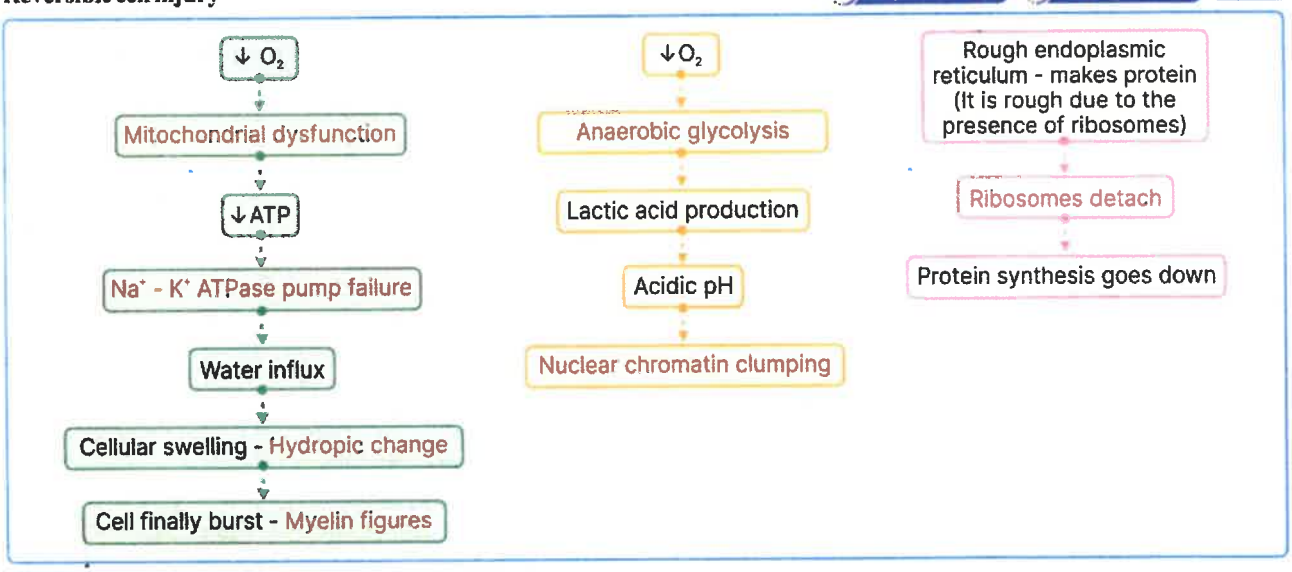
One-liner

- The most common cause of cell injury: Hypoxia
- The most common cause of hypoxia: Ischemia
- Cell most sensitive to hypoxia - Neurons / brain tissue (3-5 mins)
- Cell most resistant to hypoxia - Fibroblasts (can withstand up to 60 minutes of hypoxia)



Reversible cell injury

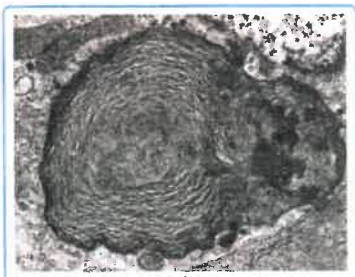
PYQ: FMGE 2023 PYQ: AIIMS 2019 00:02:08

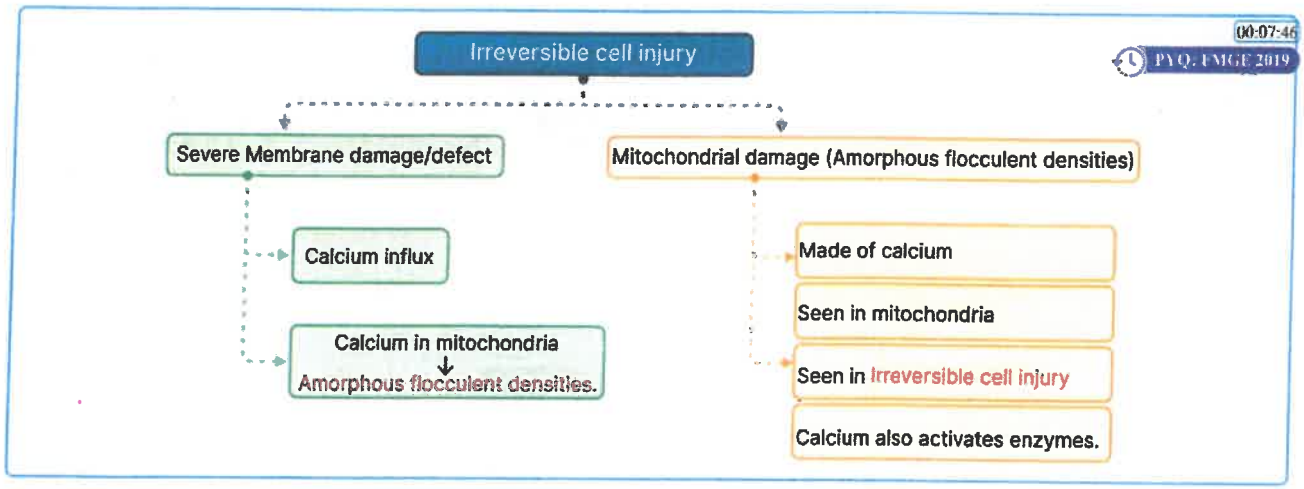


- The first change of cell injury - mitochondrial dysfunction
- Na^+K^+ATPase
  - Normal is NOKIa - Na^+ Out K^+ In
  - 3 sodium ions go out, and 2 potassium ions come in

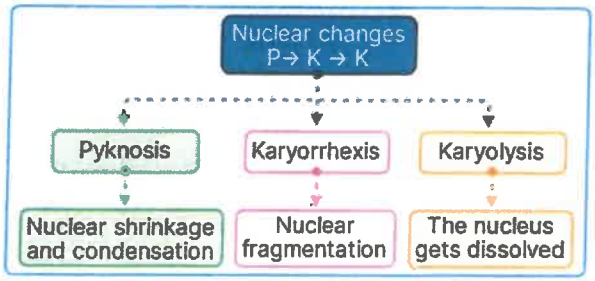
Myelin figures

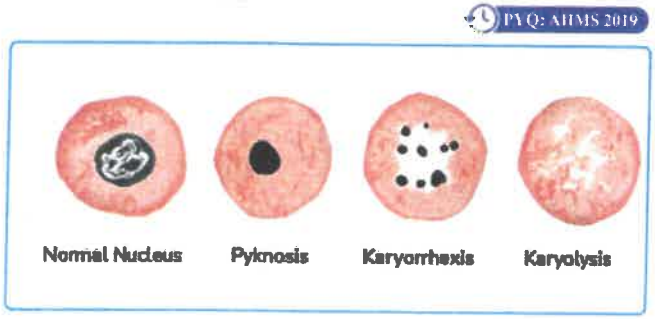
- Myelin figures comprise phospholipid >>> calcium.
- Myelin figures are seen in
  - Reversible cell injury
  - Irreversible cell injury - more enhanced
- Under the microscope - lamellated concretions under electron microscopy


Electron Microscope



Nucleases: Cause nuclear change





Cell death

1. Necrosis
2. Apoptosis
3. Necroptosis
4. Pyroptosis

Necrosis

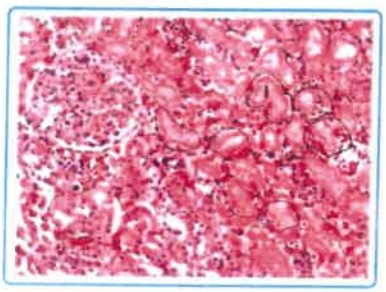
00:12:00

- Pathological cell death
- It is associated with inflammation.

1. Coagulative Necrosis

- The most common type of necrosis
- It occurs in the solid organs - kidney, heart, liver
- The most common organ is - the heart
- Cause infarction in the organs
- **Mechanism of action**: Denaturation of proteins
- **Microscopy**
  - → Ghost cells
    - Tissue architecture is preserved.
    - Details are lost.
  - → Multiple ghost cells: Tombstone Appearance
- Not seen in 2 solid organs
  - → Brain
  - → Pancreas

} They show liquefactive necrosis.

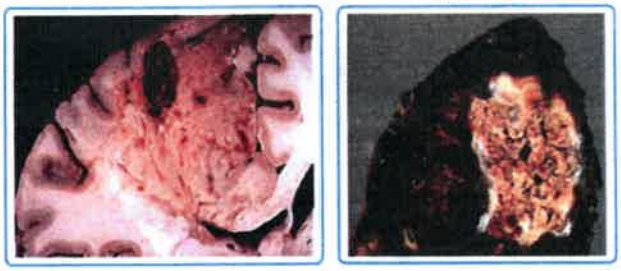


2. Liquefactive Necrosis/ colliquative necrosis

- CNS and Pancreas : They are rich in Hydrolytic Enzymes

- The tissue architecture is not preserved.

PYQ: FMGE 2019



3. Caseous Necrosis

- It is a combination of Coagulative Necrosis + Liquefactive Necrosis
- More Common: Coagulative necrosis
- Caseous = cheesy
- Seen in tuberculosis, fungal infection (histoplasmosis, coccidioidomycosis)

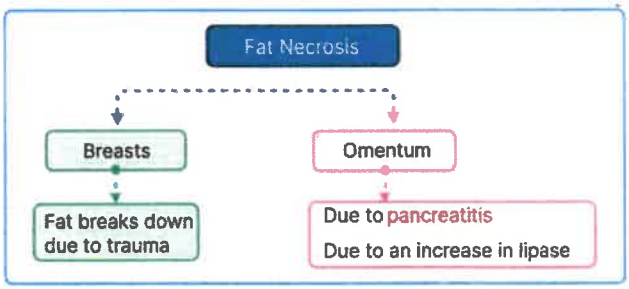
Q. A 61-year-old female patient presents with left-sided chest pain radiating to the left arm and jaw. The patient explains that the pain has increased severely over the past 40 minutes. She was immediately rushed to the hospital. Cardiac enzymes are elevated. The patient was admitted and started on thrombolytic therapy. However, on the fifth day of observation, she suddenly collapses and dies. Which of the following necrosis are you most likely to find in the heart of this patient?

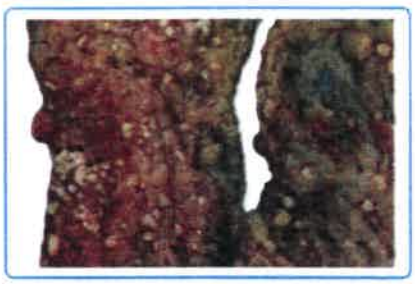
A. Liquefactive Necrosis
B. Coagulative Necrosis
C. Fat Necrosis
D. Fibrinoid Necrosis

Explanation

- This is a case of Myocardial infarction.
- In any solid organ, the type of necrosis is Coagulative Necrosis

4. Fat Necrosis

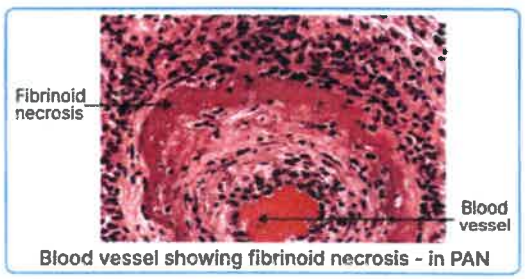




- Fat breaks down into fatty acids and calcium.
- Calcium looks like chalky white areas.

5. Fibrinoid Necrosis

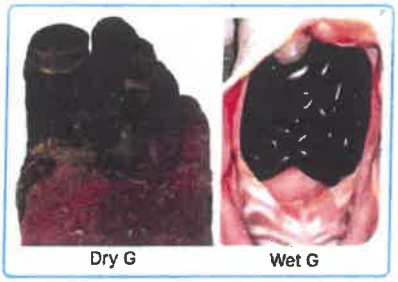
- Associated with antigen-antibody reactions.
- Examples (Mneumonic : All 3 alphabets)
  - Polyarteritis Nodosa (PAN)
  - Rheumatic Heart Disease (RHD)
    → Aschoff body
  - SLE
  - Malignant Hypertension (HTN)



Blood vessel showing fibrinoid necrosis - in PAN

6. Gangrene

- It is a clinical diagnosis.
- Blackish, foul-smelling tissue



Dry gangrene	Coagulative Necrosis
Wet gangrene	Liquefactive Necrosis

7. Zenker's Degeneration

- It is a type of Coagulative Necrosis
- It occurs in typhoid.
- It is a complication seen in the skeletal muscles eg: Rectus Abdominis, Diaphragmatic Muscle

Q. A 45-year-old female patient complained of being hit in the chest by a football while passing by a garden 4 weeks back. Initially, her left breast was tender and swollen. But over the weeks, the tenderness has subsided. However, she now notices a lump in the periareolar region, which is firm and hard in consistency. Radiological investigations reveal calcific deposits. Which of the following best describes the phenomenon above?

A. Liquefactive necrosis
B. Coagulative necrosis
C. Fat necrosis
D. Fibrinoid necrosis

Explanation

- This is a case of traumatic fat necrosis in the breast.

2 CELL INJURY PART-2

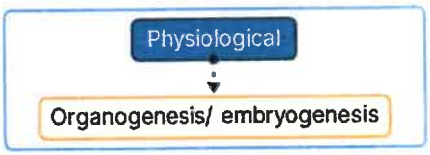
Cell Injury

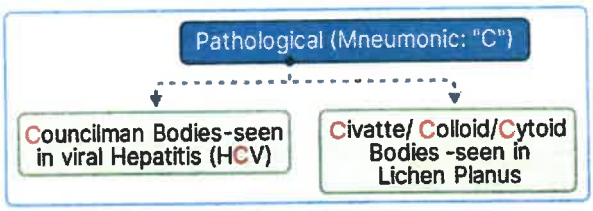
Apoptosis

00:00:15

PYQ: AIIMS 2018, 2019

- Programmed cell death.
- Caspase Dependent Programmed Cell Death
- No inflammation will occur.
- It can be both physiological and pathological.





Mechanism of apoptosis

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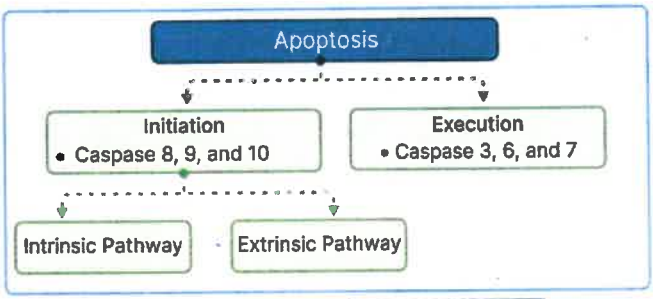


Extrinsic Pathway

PYQ: AIIMS 2019 00:06:11

- Caspase 8, 10
- It happens outside the cell
- The cell has CD95 / Fas
- T cell has CD95 Ligand / Fas Ligand
- Binding leads to Trimerization of CD95/ Fas
- The FADD will activate Procaspase 8, 10 into Caspase 8,10
- The process is inhibited by FLIP (anti-apoptotic molecule)

Execution

- The cells go off in bits and pieces as membrane-bound organelles.
- May go with a piece of a nucleus or without it.
- These are called apoptotic bodies.
- Apoptotic bodies send signals to macrophages by flipping of phosphatidylserine.
- This process is called eat me signal or efferocytosis
- Macrophages then phagocytose the cells.

Intrinsic Pathway

PYQ: AIIMS 2019 00:08:31

- Caspase 9
- It occurs when the cells are under stress.
  - Like UV ray
- Stress sensors
  - BIM, BID, BAD, NOXA and PUMA
- The sensor increases the pro-apoptotic factor and decreases the anti-apoptotic factors.
- They send a signal to mitochondria.
- Mitochondria release SMAC/DIABLO and cyt C
- Cyt C combines with Apaf 1 and together they form the apoptosome
- The Apoptosome activates Procaspase 9 into Caspase 9

00:09:43

Pro-Apoptotic	Anti-Apoptotic L - Lower apoptosis
• P53 • BAK • BAX • BCLXS	• BCL2 • MCL1 • BCLXL

Important Information

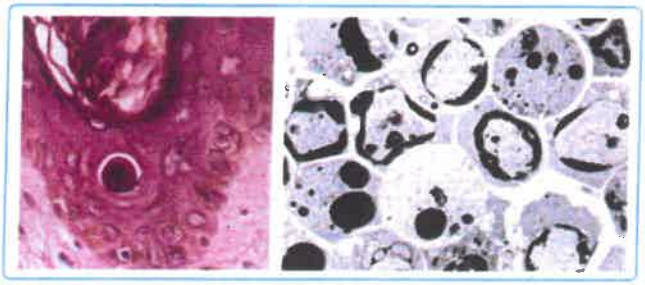
Caspase

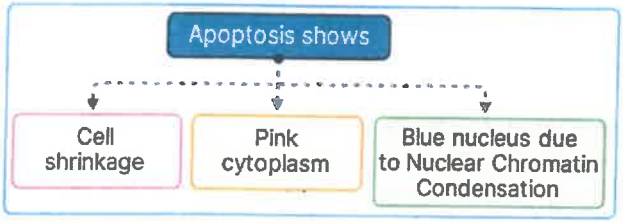
- C- cysteine residues
- ASP - aspartic acid
  - Breaks after aspartic acid
- Ase - for enzyme

Diagnosis of Apoptosis

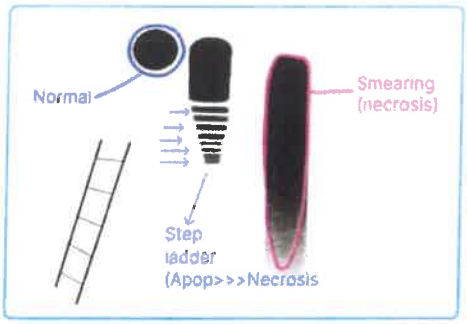
- **The hallmark of apoptosis:** Nuclear Chromatin Condensation

1. **Marker:** Annexin V (Apoptosis- Annexin Penta)
   - Annexin a1 is seen in hairy cell leukemia
2. **Molecular Marker:** CD95/ Fas
3. **Microscopy**





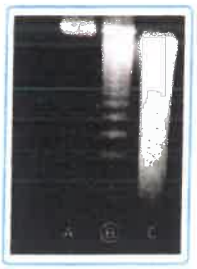
4. **Stain:** Tunel Stain
   - Positive - apoptosis
   - Negative - necrosis
5. **Gel Electrophoresis**



- DNA gel electrophoresis
  - Step Ladder pattern can be seen in apoptosis and necrosis.
  - Smearing pattern in necrosis and apoptosis.

Q. The following gel electrophoresis pattern of the patient is seen in

A. Necrosis
B. Apoptosis
C. Both
D. None



Cell injury - newer cell deaths

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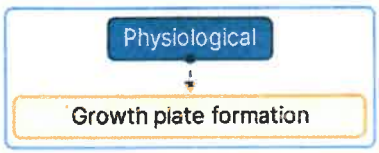
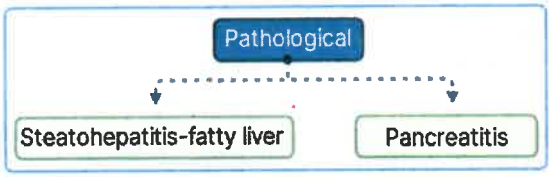
- Necroptosis
- Pyroptosis

Necroptosis

00:20:58

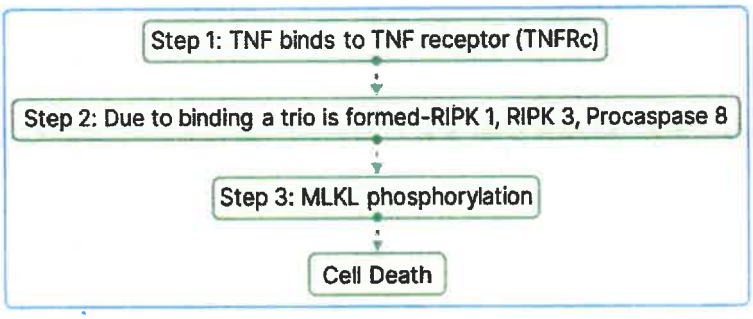
- Necrosis + Apoptosis
- Caspase-independent programmed cell death
- Physiological or pathological





Mechanism

- Mneumonic: 1-2-3 death



Pyroptosis

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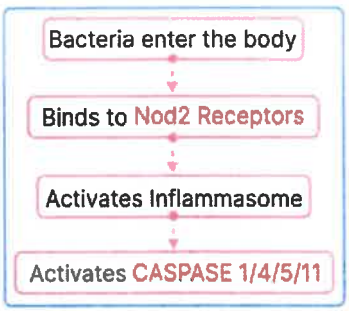
- Pyro means Fever + Apoptosis means cell death.
- Associated with bacteria like Shigella and salmonella.
- Caspase 1 activates Interleukin 1 (IL-1) - causing fever.



Q. Choose the incorrect statement about Necroptosis.

A. It is a caspase-independent cell death
B. RIP 1&3 complex is formed.
C. **Caspase 8 is formed.**
D. Growth plate formation follows necroptosis.

Explanation

- Procaspase 8 is used
- It is caspase-independent programmed cell death.

Q. Choose the incorrect statement about pyroptosis

A. Seen in response to Shigella.
B. TLR is used.
C. Caspase 1 is required.
D. IL1 activated.

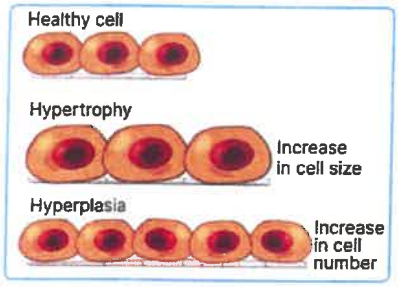
Explanation

- It uses NOD 2 receptor

3 CELL INJURY PART 3

Cell Injury - Cellular Adaptations

- Hypertrophy
- Hyperplasia
- Atrophy
- Metaplasia



00:00:05

00:01:16

Hypertrophy	Hyperplasia

• Increase in the Size of cells
• Increase in - Transcription Factors
  ○ GATA
  ○ NFAT
  ○ MEF 2
	• Increase in the number of cells
	• Increase in mitosis

PYQ: FMGE 2021

Both hypertrophy and hyperplasia are seen in

- Gravid Uterus - Pregnant uterus
  - Hypertrophy>>> Hyperplasia
- Breast
  - Puberty
  - Pregnancy
    → Hyperplasia >>> Hypertrophy

Hypertrophy alone

- Bodybuilders - skeletal muscle hypertrophy
- Proximal to obstruction
  - Obstruction in the urinary bladder due to stone
    → remaining tissue adapts by hypertrophy.

Hyperplasia alone

- **Females**
  - Endometrial hyperplasia - Estrogen
  - Lead to endometrial cancer type 1
- **Males**
  - Nodular hyperplasia prostate

Testosterone $\xrightarrow[\text{reductase type 2}]{5\alpha}$ Dihydrotestosterone (DHT) → Nodular hyperplasia prostate

↑ inhibits

Finasteride (treatment)

00:06:04

Atrophy

- Decrease in size and number of cells
- UPP: Ubiquitin Proteasome Pathway (mechanism)

a. Disuse Atrophy
   - Muscle atrophy following a fracture.

b. Malnutrition

c. Ischemic Atrophy

d. Denervation Atrophy

e. Endometrial Atrophy
   - Postmenopausal
   - Can cause Endometrial Cancer Type 2

Important Information

- Endometrial hyperplasia → Endometrial Cancer Type 1
- Endometrial atrophy → Endometrial Cancer Type 2
  - Worse prognosis

Metaplasia 00:08:56

- One epithelium to another epithelium
- One mesenchymal tissue to another mesenchymal tissue
- 100% reversible phenomena

Mechanism

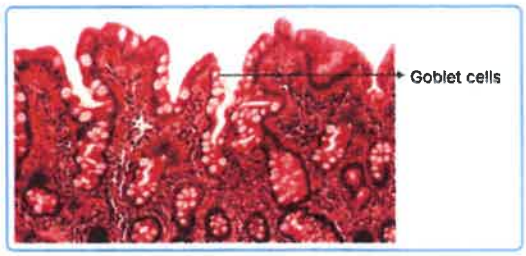
- Reprogramming of stem cells

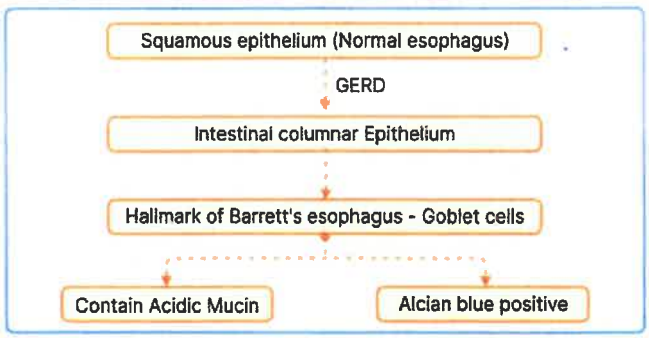
Eg. 1 Most common metaplasia - Squamous metaplasia

- Terminology based on the end result.
- In Chronic Smokers or Vitamin A (deficiency/excess)
  → Pseudostratified ciliated columnar epithelium changes to squamous epithelium

Eg. 2 Barrett's Esophagus

PYQ: NEET PG 2020





Eg. 3 Mesenchymal metaplasia - Myositis ossificans

- Muscle changes to bone
- Occurs due to trauma.

Q. What is the histopathological difference between Barrett's epithelium and gastric mucosa?

A. Barrett's mucosa is acidic and stains alcian blue positive.
B. Barrett's is alkaline and stains Prussian blue positive.
C. Barrett's alcian blue negative because it's negative.
D. The gastric mucosa is alkaline and stains alcian blue positive.

Intracellular accumulations 00:16:20

- Pigments
- Lipid
- Protein
- Glycogen
- Calcium