Toppersnotes
Unleash the topper in you

NEET-PG

PART-B

VOLUME-II

Pathology

SIERRA INNOVATIONS
Private Limited

PATHOLOGY

Collagen type	localization
I	Skin, Bone, tendon; Maxm tensile strength, most abundant collagen (90%).
II	Cartilage (Hyaline also), Vitreous body.
III	Reticulum-skin, Blood vessels, uterus, fetal tissue, granulation tissue.
IV	Basement membrane
VII	Dermal, Epidermal junction in skin, provide anchoring fibrils within basement membrane beneath stratified squamous epithelium.
VIII	Descement's memb. in eye
IX	Cartilage. It regulates collagen fibril diameters or collagen-collagen interactions by fibril-associated collagen c interrupted triple helices (FACITs)

Cellular Adaptation

- Cells are "completely reversible", coming back to (N) stage
  Cant looking ← Morphology, Physiology, Metabolism

- eg: (1) Atrophy
  (2) Hypertrophy
  (3) Hyperplasia
  (4) Metaplasia

· dysplasia - "pre" partial reversible

(1) Atrophy : • ↓ size, • ↓ No. } Mech = Autophagy (A1 Allows) → by · lysosomes
DNB Ubiquitin - proteasome degradation pathway

(2) Hypertrophy · Size ↑ · No. same

(3) Hyperplasia · Size same, · No. ↑ } a/w = Endometrial Adenocarcinoma { Hyperplasia (A1-014,15 Type-I) ↑ Atrophy ↓ Type-II ↓ Poor prognosis

(4) Metaplasia : In Metaplasia = Mature cell ↓ Replaced by ↓ Another type Mature cell

★ Ubiquitin-Proteasome degradation pathway : - d/t -

Ubiquitin + Target protein ↓ ⊕ Proteasomes → degrade.

(1) Autophagy asso c -
(1) Atrophy
(2) Cancer [dysregulatn,
(3) Infections ↓
Atg1-5-gene → controll of Macrophage function

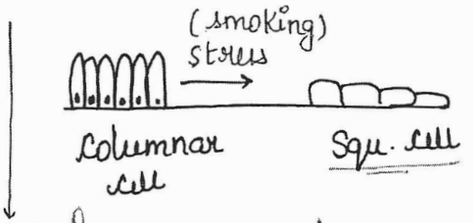
↑ TB infectn. ← degrade of this gene

④ Mitochondrial inheritance.

④. **Metaplasia:**

Mech: "Stem cell reprogramming."

• **MC type:** Sq. metaplasia (eg. respiratory tract).



a/w with Vit-A deficiency or Vit-A excess.

Barrett's oesophagus:

• MCC - "GERD"

↓

Columnar metaplasia

• Mucin fill vacuoles → Blue

↓

AIIMS Alcian Blue stain

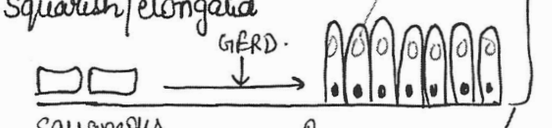
- Barrett's oesophagus — pH = 2.5 (acidic)
- Intestinal goblet cells — pH - 7.5 (alkaline)

future FQ

Alcian Blue Stain

↕

Mucin fill vacuoles



↓

Intestinal metaplasia

↕

Hallmark of Barrett's oesophagus.

↓

Risk factor for Adenocarcinoma of oesophagus.

↓

completely reversible

↓

on removal of stimuli

Cell Injury

↓

MCC - Ischaemia ($\downarrow O_2$)

↓

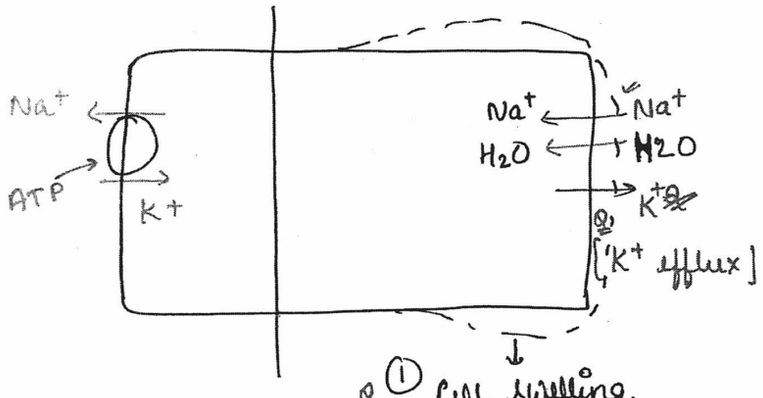
Causes Hypoxia

Ischaemia ($\downarrow O_2$)

- Most susceptible → Neurons (3-4 min)
- Cardiac tissue (20-40 min) DNB (≈ 30 min)
- least susceptible to ischaemia → FQ Fibroblast (hrs to days)

Ischaemia

- Transient → Reversible injury → Ischaemia ($\downarrow O_2$) → ↓ oxidative phosphorylation → ↓ ATP [FQ ↓ 5-10% of N ATP]
- Persistent → Irreversible injury → ↑↑↑ Ca^{+2} (+)
  1. Phospholipases:
     - (i) Myeline figures (↑↑ max)
     - (ii) Mitochondria



- Large amorphous densities.

↓

① Cell swelling. (Earliest sign of cell injury)

- Except for- Apoptosis (cell shrinkage) AIIMS AI.
- eg: Ballooning degeneration of hepatocytes (Acute Hepatitis)

2. Proteases:
   - damage of cyto-skeletal protein → loss of cell architecture.
3. Endonuclease: → Nuclear DNA damage

② Organism [Seen in Electron microscopy / ultrastructurally]

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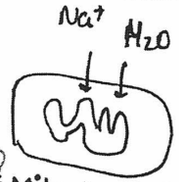
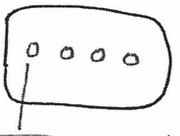


① Mitochondrial swelling.



② Small amorphous density.

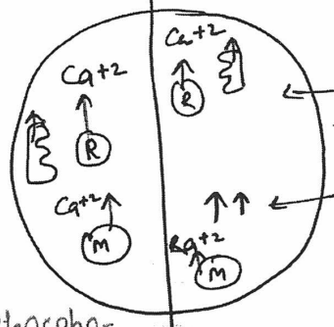
③ Most Imp. factor for cell injury.

DNB 016

[Ca^{+2} > Na^{+}] ⇒ Cytoplasmic / cytosolic Ca^{+2}

Mild ↑ Ca^{+2} → Reversible cell injury.

↑↑↑ Severe Ca^{+2} → Irreversible cell injury



Block the all outlets of Ca^{+2}

(+) ↓

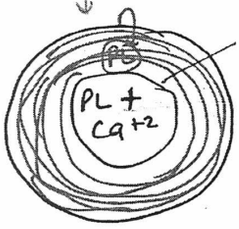
Phospholipase enzyme

↓

memb. [Phospholipid] damage (organelles)

↓

$(PL + Ca^{+2})$



Conc. lamellated whorl like structures.

↓

Myeline figures ⇒ Reversible <<< Irreversible cell inj cell inj.

Seen by Electron microscope

Endonucleases

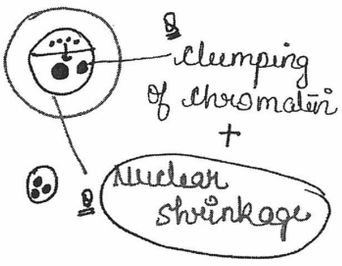
③ Nuclear damage

↓

sequence

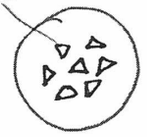
↓

① Pyknosis:

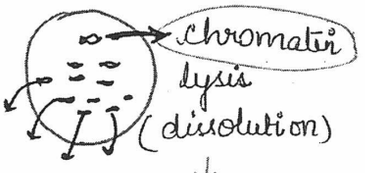


(ii) Karyorrhexis:

Nucleus | Fragmentation



(iii) Karyolysis:



↓

thrown outside of cell

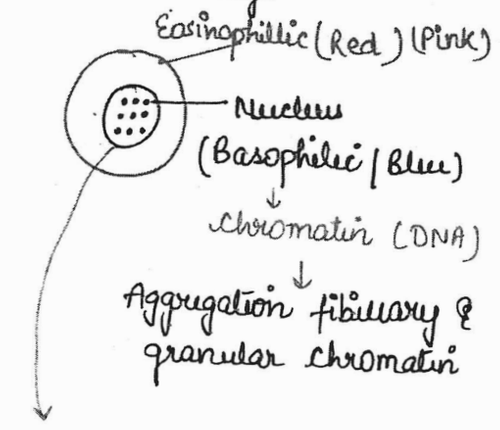
⇓

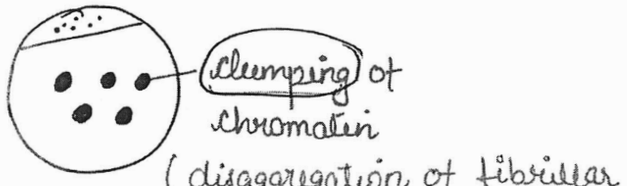
↓ Basophilia of cell

⇓

Cell death.

④ Nuclear damage.





Cell death

① Necrosis ② Apoptosis ③ Necroptosis ④ Pyroptosis

↓

2-patterns

Denaturation of protein

↓

Tissue architecture preserved

↓

[I] & Coagulative Necrosis

↓

eg: Ischaemia / Infarct of solid organs-

- Heart - MC & DNB
- Kidney
- Liver

Solid organ → collagen → forming stromal support

Enzymatic damage

↓

Hydrolytic action

↓

Tissue architecture lost

↓

[II] & Liquefactive Necrosis

↓

Brain infarction

(i) Rich in liquefactive enzyme

(ii) No collagen fibres

↓

No stromal support.

Toppersnotes
Unleash the topper in you

Q: Coagulative Necrosis seen in -

wet gangrene << TB <<

TB → Coagulative Necrosis → Liquefactive necrosis

cheese like → Caseous Necrosis (d/t mycolic acid)

- TB
- Histoplasmosis
- Coccidioidomycosis
- Syphilis

Gangrene (dry) << Zenker's degen necrosis (Proto - coagulative necrosis only)

Lower limb - MC site → Coagulative Necrosis

In DM pt -

Gangrene - (Bladder) → wet

Bact. Infection → Toxin & Enzymes → hydrolytic action → liquefactive Necrosis.

Necrosis

① ↑ lysosomal permeability → Enzymes activate & coming outside from lysosome → cell memb. damage (rupture) → Inflammation

MLE

② Always - pathological

Apoptosis

① • ↑ Mitochondrial permeability
• cell membrane is intact
• Inflammation is absent

② Both < Pathological / Physiological

Apoptosis

[Falling off]

• Most imp. organelle involved - Mitochondria (ATP)

↓

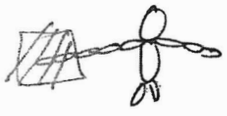
• Active process >>> Programmed cell death
• Energy dependent process

- Programmed cell death
  - Apoptosis
  - Necroptosis
  - Pyroptosis
  - NET (Neutrophilic Extra-cellular Trap)

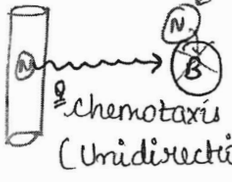
Apoptosis

(A) Physiological

(1) organogenesis :
(Morphology of Embryo)



(2) Killing of cells of Inflammation after completion of function



(3) Killing of Auto-reactive cells ← Bone marrow, Blood, Thymus.
↓
To prevent autoimmunity

(B) Pathological

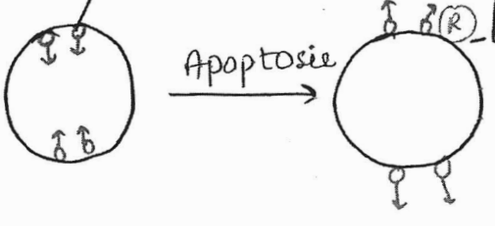
09 AIIMS AI
(1) Chemotherapy & Radiotherapy } Both Apoptosis + Necrosis

CQ (controversial) AIIMS
(2) Glucocorticoids :
Induce Apoptosis.

AI 015
(3) Viral Hepatitis
↓
Councilman Bodies

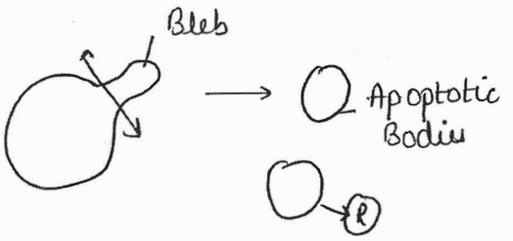
Morphological Examination (M|E) :

(1) Earliest = cell shrinkage
(2) Most characteristic feature = chromatin condensation > Cell membrane intact.
↓
[No inflammation]
(3) Hyper-eosinophilia of cell cytoplasm.
(4) Phosphatidyl serine (R)
AI 014 (lipid)

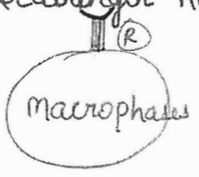


↓
Marker of Apoptosis

(5)



(6) End outcome – Scavanger Receptor

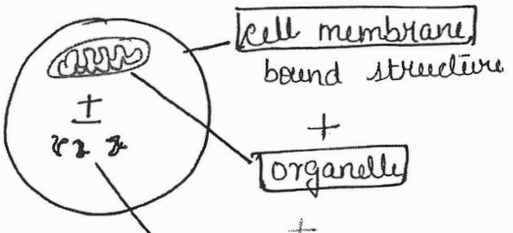


Receptor mediated
⇒ Phagocytosis

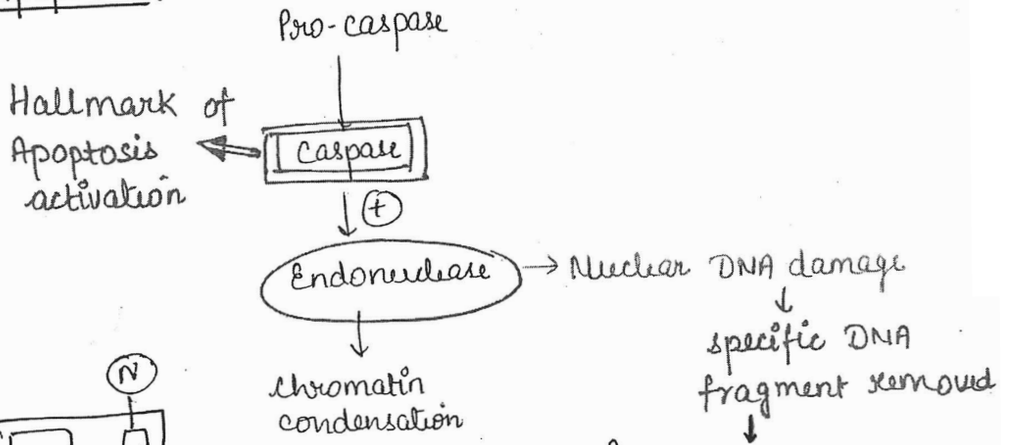
Apoptotic Bodies:

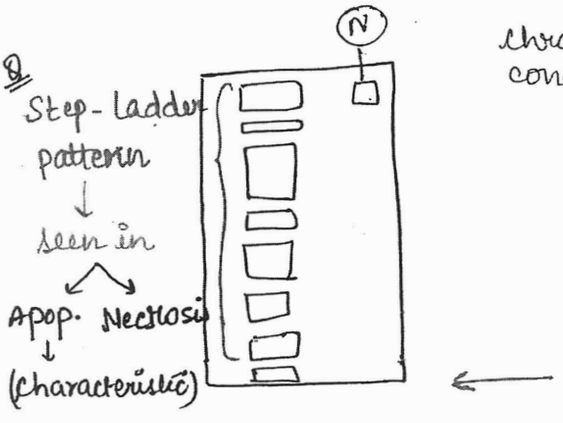
↓

Form through caspase pathway

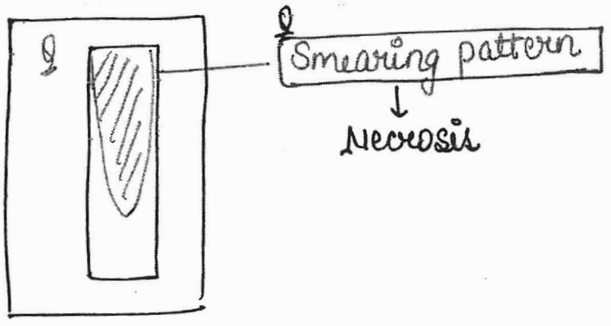


- **Mech. of Apoptosis:**





observed ← Agarose gel electrophoresis



Mechanism of Apoptosis

Initiation → (+) → Execution → Endonuclease → Chromatin condensation

Initiation → Intrinsic pathway / Extrinsic pathway

Execution → C 3, 6, 7

Intrinsic pathway → Caspase-9 (C)

Extrinsic pathway → caspase-8 (animal) / caspase-10 (humans)

Pro-oncogenes

Pro-apoptotic
- Bcl-X_S (↑)

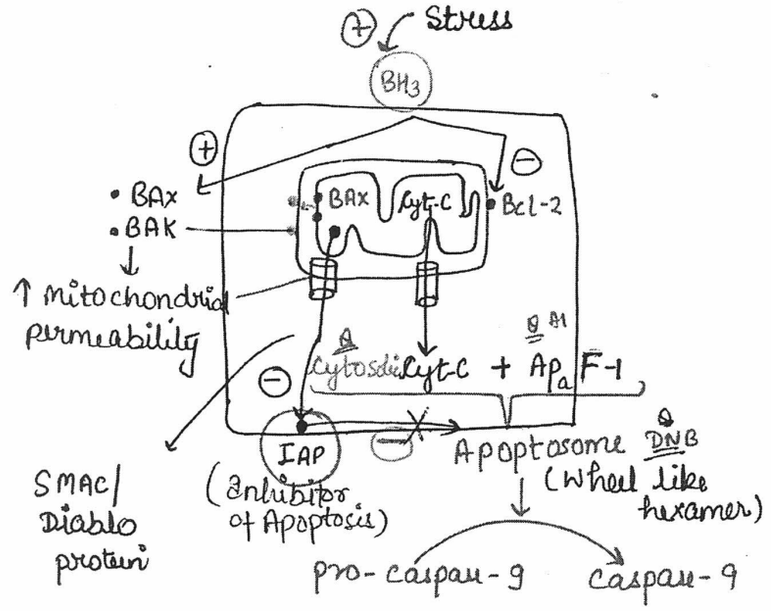
eg: BAX, BAK, BH_3-only protein

present on cell surface [Stress sensors]

- Bim
- Bad
- Bid
- Puma
- Noxa

Anti-Apoptotic
- Bcl-2
- Bcl-X_L (↓)

[I] Intrinsic Pathway (Mitochondrial) (Most imp. & major pathway)

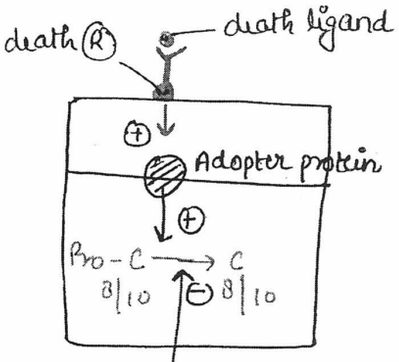


[II] Extrinsic pathway (Death (R) mediated Pathway)

a) TNF-1 = Most well defined death receptor

AIIMS 05

b) Fas = [CD-95] AI-14,15



(N) cell, HIV cell — have ↑ FLIP (Anti-apoptotic protein)

Intrinsic + Extrinsic

C-9 | C 8|10 → C 3|6|7 → Endonuclease → Chromosomal Condensation

Initiation → Executional

UPSC 014

- Hallmark of Neuronal Apoptosis → No caspase
  - Apoptosis inducing factor activation

Def AIIMS/AI 018

Programmed cell death

↓ Caspase activation → Necroptosis (Necrosis / apoptosis)

Resembles like Extrinsic pathway of Apop. [TNF + TNF-R] → RIP-1|3 (Receptor interacting protein)

↑ Caspase activation → Pyroptosis

- caspase-1 & caspase-11
- Pyrogen induced Apop.
  - IL-1
    - inflammation (+)

2017 (variant of Necrosis)

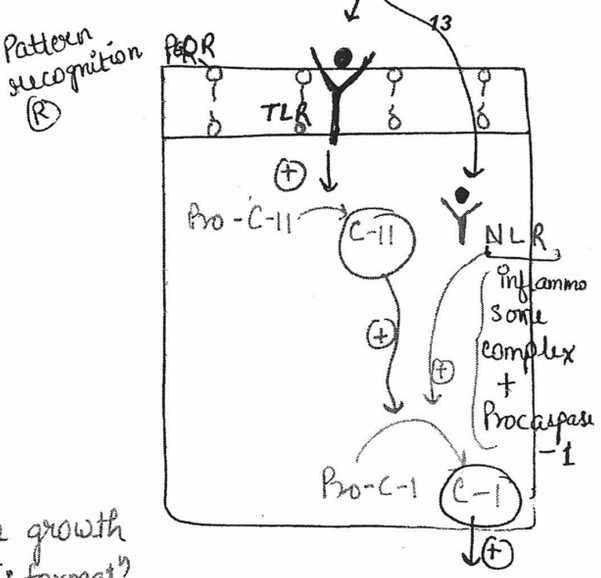
RIP- 1 | 3 (+)

No Caspase-8 → ↑ Free Radical (mitochondria) → M/E: • Cell memb damage • Inflammation (+) → Necroptosis (Variant of Necrosis) → b/c Necroptosis

Caspase-8/10 → Extrinsic Apop.

Necroptosis:
- Physiological -- Bone growth Plate formation
- Pathological →
  1. Neurodegenerative disorder (Parkinson's disease).
  2. Pancreatitis.

• Flagellin - Antigen (Ag)



IL-1 | 18 →
1. Cell memb. damage
2. Inflammat^{n} (+)

• a/w Innate Immunity Response

Free Radicals (oxidants).

• (N) produced in our body → by mito → d/t Incomplete resp.

• definition: Any species ☜ unpaired e^- (in outer orbit)

• MOA: oxidative damage →
- Cell memb.
- Protein.
- Nuclear memb.
- Nuclear DNA.

• oxidants (FR)

1. $O_2^{\cdot}$, $O_2^{2\cdot}$, $OH^{\cdot}$, $HOCl^-$ → $OH^{\cdot}$ Most reactive FR.
2. FR-damaging theory (Most widely accepted theory for aging)

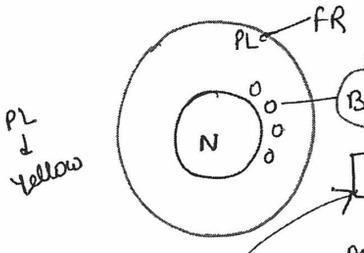
Anti-oxidants
1. Vit-A | C | E
2. Proteins
   - Ceruloplasmin [Cu^{+2}]
   - Transferrin [Fe]
3. Enzymes
   - Catalase
   - Glutathione
   - SOD (Superoxide dismutase)

Peroxisomal

Protect Brain damage

- SOD → Protect from Brain damage
  14
  mut. → Amyotrophic Lateral sclerosis (MND)

- Most potent – Glutathione (FR scavenger)



Brown pigment (Perinuclear)
↓
Lipofuschin – Aging pig.
CA - Cachexia
Malnutrition
↓
Myocardium
↓
Brown atrophy

IMPMER
Carcinoid is Brown in colour b/c of Lipofuschin

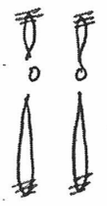
Also Wear & Tear Pigment

Brown pigment
- Lipofuschin
  - FQ special stain
    1. Oil-Red-O-staining
    2. Sudan-Black-B "
  - Best stain – for Oil / Lipid for Frozen section
- Haemosiderin
  - FQ Perl's prussian Blue staining
  - Fe^{+3} = stored form
    ALWAYS

- Lipofuschin (Lipochrome)
  - Lipid polymer + PL + protein

Aging

1. Most imp. = FR damage theory for aging.
2. ↑ cross linking of collagen. ∝ ↑ Aging.
3. Cellular Aging
   - Telomerase shortening (Attrition)
     - T → short end of DNA stretch. (Non-coding area)
     - Fusion of DNA prevented by Telomerase
       or
       degradation of chromosome.



cell division
↓
Telomerase shortening
↓
Telomerase (over | finished)
↓
Fusion | degradation of chromosome
↓
Cellular Aging

(N) human cell
↓
60 – 70 times ← divides
(all Telomerase used up)
↓
Hayflick limit or Hayflick phenomenon.

- Most important factor to prolong life span: Calorie restriction
  - ↓
  - Red Wine (+) → Sirtuin protein
    - ↓
    - MOA
      - ↓ FR damage
      - ↓ Apoptosis
      - ↓ overall metabolism
      - ↑ Glucose metabolism → ↑ Insulin sensitivity

- Werner syndrome
  - ↓
  - Pre-mature aging
  - ↓
  - d/t defect in DNA-Helicase enzyme
  - ↓
  - Repair → defective

Wermore syndrome
MEN-1. Syndrome.

Calcification
↓
alkaline pH
↓
Starts → in Mitochondria
Except - Kidney
(Basement membrane)

Calcification

① tissue ab(N) ← dead, degeneration, damage

② Ca^{+2} (N)

↓

Dystrophic calcificat^{n}

eg:- 1° TB – LN

2° RHD (Valvular damage)

3° Psammoma bodies

① tissue (N)

② Ca^{+2} ↑↑

↓

Metastatic calcification

eg:- MCC – 1° Hyperparathyroidism

↓

MCC

Parathyroid adenoma

2. Renal failure

3. ↑ Vit – D & A

↑↑ Vit-A

↓

Retinoic-A

↓(+)

osteoclasts

↓

Bone eating

↓

↑ Ca^{+2}

• Metastatic calcif^{n}

↓

Ca^{+2} deposition – MC seen → Lungs (Alveoli)

↳ least common site

↓

Parathyroid gland

H|E : Ca^{+2} = dense Amorphic Basophilic deposition

↓

sp. stain = ① Von-Kossa (MC Best) → Kala

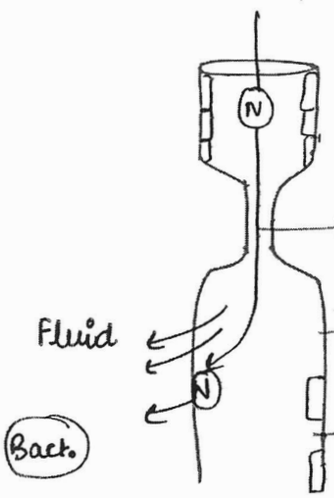
FA AIIMS ② Alizarin Red = Most specific

Inflammation

Acute Inflammation

Vascular Events ⟷ Cellular events

[I] Vascular Events



Inflammation

I Vasoconstriction (Earliest)

↓

II Vasodilation

↓

III ↑ Vascular permeability [Hallmark of Acute inflammation]

↓

IV Stasis

↑ Vascular permeability

Endothelial gap

↓

- Immediate
- Transient response

↓

Usually involves

Venules

↓

Except-lungs

↓

(Capillaries)

direct endothelium damage

↓

- Immediate
- Prolonged response

- Mild endothelial injury (Sun Burn)

↓

- delayed
- Prolonged response

Leukocyte mediated injury

↓

- delayed & Prolonged response