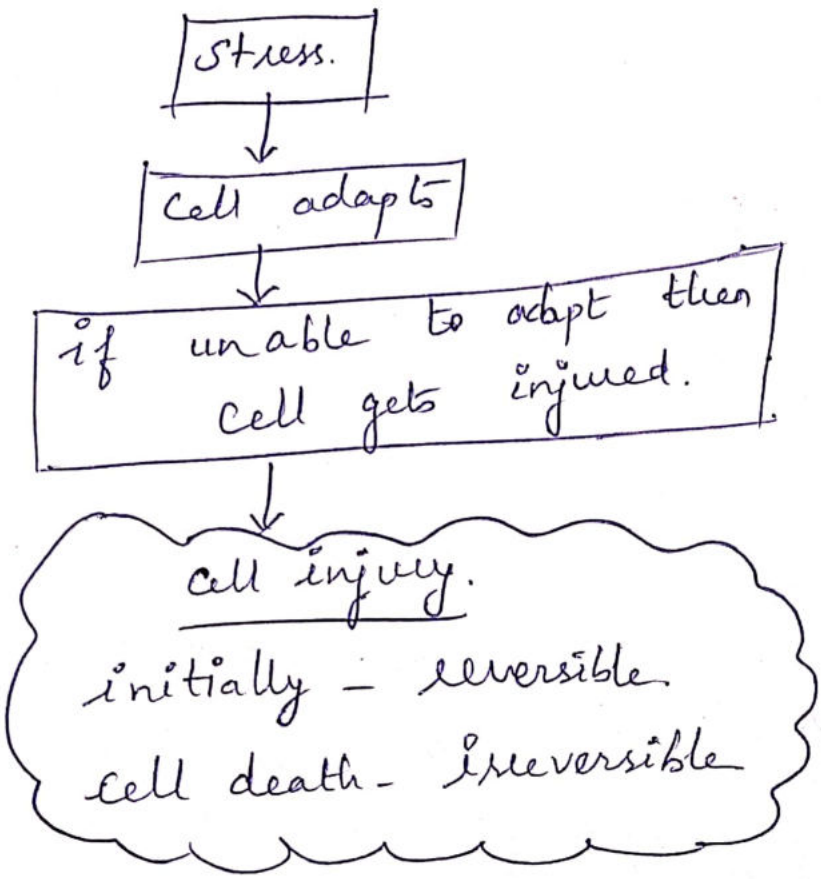
1.3 Cell death (irreversible cell injury).



(i) pyknosis. (ink dot). ⇒ Nucleus shrinks to an ink dot.

(ii) Karyorrhexis. ⇒ Nucleus breaks into fragments

(iii) Karyotysis. ⇒ Fragments broken down into basic building blocks.

② ways / mechanisms by which cells die.

- NECROSIS ⇓ murder.
- APOPTOSIS. ⇓ suicide

NECROSIS:

* Death of large grp. of cells followed by acute inflamm". (A.I).

② causes of A.I

- m/c infection.
- Necrosis.

eg: M.I. ↓ Neutrophils enter the cardiac tissue.

Entry of Neutrophils

↓

Blood level of Neutrop. ↑

↓

A.I

---

* Necrosis is ALWAYS pathologic. it indicates some disease in ur body.

Types of Necrosis

Based on Gross features:

(i) Coagulative Necrosis.

* Coagulative – Thick

* After death, cells become dry & thick.

↓

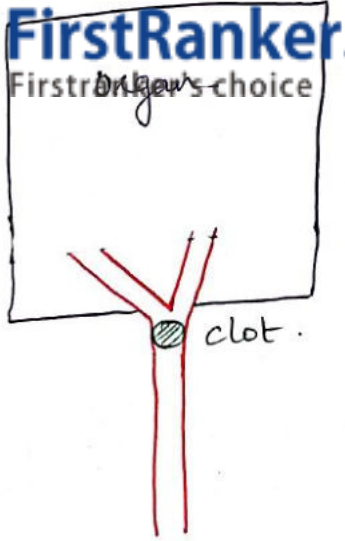
Thus the organ shape is maintained as it is

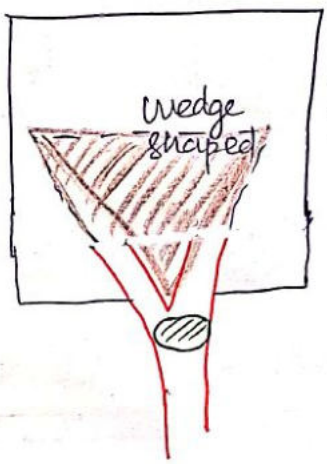
* Architecture of the cell is intact but Nucleus disappeared.

* Necrotic Tissue – remains firm.

Why? Cellular proteins coagulate and so the cells retain their shape & Organ structure is preserved. (But cells have No Nuclei).

eg: Ischaemic Infarction of any organ except Brain





↓ wedge points to the occlusion

⇓

Bcoz it points the area of Dichotomous branching.

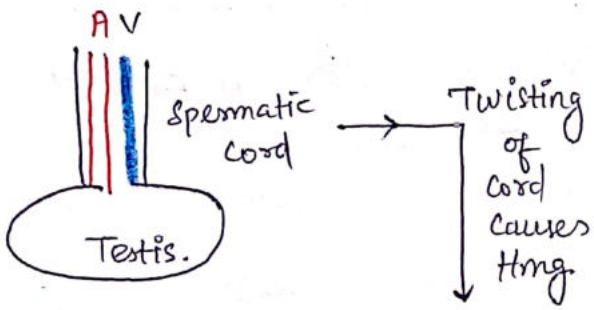
Why ~~dead~~ infarcted tissues are pale?

⇓

No blood supply.

(Expections possible)

pale ~~tissue~~ but if ~~a tissue~~. blood re-enters a loosely organized tissue then Red infarch. arises.



* Since artery is thick walled it is patent but vein gets occuled.

⇓

So as we seen earlier in ~~Hypoxemia~~. Ischemia. (Pg 7).

Hypoxia occurs even if vein is occluded.

Enzymatic lysis of
Cells & proteins.

↓

Liquefaction

occurs in ③ situation

↓

BRAIN INFARCTION. → microglia → Hydrolytic enzymes

Abscess. → Neutrophils

PANCREATITIS → self enzymes. ⇓ Auto digestion.

Why Brain is an exception?

* Brain Contains microglia (derivatives of macrophages)

↓

After infarction, destructive enzymes are released from microglia.

III^{ly} in

Abscess.	Pancreatitis.
* Neutrophils release. Hydrolytic enzymes.	Enzymes are activated within pancreatic parenchyma.

pancreas itself undergoes liquefactive Necrosis.

fat surrounding it undergoes FAT NECROSIS

(iii) Gangrenous Necrosis.

* Actually a Coagulative Necrosis but the necrosed tissue looks mummified (Dry gangrene).

eg: Ischaemia of lower limb & GIT.

Wet gangrene. Necrosed tissue is ~~infected~~ superimposed with infection, then liquefactive Necrosis ensues.

Cottage cheese like appearance

eg: Granul. infl. of Fungi/TB.

Combination of Coagulative & liquefactive - Necrosis.

⇓ ANALOGY

Imagine a gravy at 1st its liquid but after putting the vegetables it becomes Semi-solid

⇓

IIIly Caseous Necrosis is liquefactive Necrosis with some vegetables added.

- * wall of Fungi
- * Mycobacterium

↓

which leads to a semi-solid like appearance

eg: Granulomatous inflamm. of Fungi (or) TB.

Fatty acids are released.

+(Ca++).

Saponification Rxn

chalky white appearance of Necrotic Adipose Tissue.

Eg:

(i) Trauma to fat (eg: Breast).

(ii) Pancreatitis - mediated damage of peripancreatic fat.

Fat necrosis due to Trauma of Breast can present as

- A mass.
  - ⇓
  - B_{CO_2} during Fat necrosis, there occurs a GIANT CELL RXN. (Inflammatory response).
- Findings of Mammography
  - ↓
  - Calcification.

Dystrophic Calcificatn

* Normally Catt doesn't deposit on tissues of Human Body.

But can deposit under (2) circumstances

Dystrophic

Catt gets
* deposited on dying tissues.

* Catt & PO_4^{3-} levels Normal.

eg: Saponification.
Sumomo bodies.
(papillary Ca of Thyroid, meningioma, papillary serous Ca. of ovary).

Ca grows, Blood Supply increases, Cells dies & on top of that Catt deposits

&

Metastatic Calcificatn.

* Either Catt (or) PO_4^{3-} levels High which forces Catt to ppt. on Tissues..

* Metastatic doesn't necessarily mean, the pt. has metastatic cancer.

* But metastatic cancer of the bone can lead to metastatic Calcificatn due to High serum levels.

Leaking of proteins into V/S wall.

Bright pink staining on H/E

eg:

* MALIGNANT H.T.
* VASCULITIS.

Benign vs Malignant H.T

Low grade H.T → long term progressive chronic damage to organs.

V. High BP. presenting with

Headache.
papilledema
Renal failure

Medical Emergency (CODE BLUE).

In what Circumst., a 30yr old woman present with Fibrinoid Necrosis.

* PRE-ECCLAMPSIA. [elev. BP with proteinuria]

↓

Fib. necrosis of placental blood V/S.

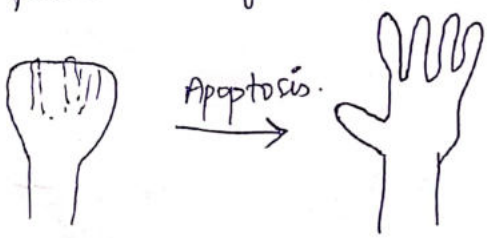
genetically programmed

↳ CELL death.

* Involves one / small gp. of cells. (but in Necrosis ----).

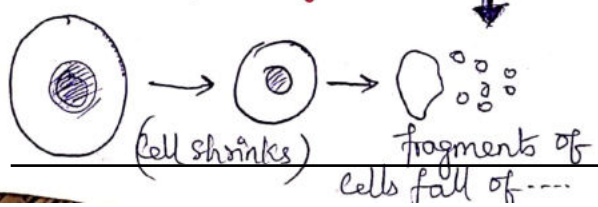
eg:
i) endometrial shedding.
ii) Formatn of digits (phalanges) during embryogenesis.
iii) CD8+ T-cell mediated killing of Virally inf. cells.

Syndactyly : fusion of ② phalanges due to failure of Apoptosis.

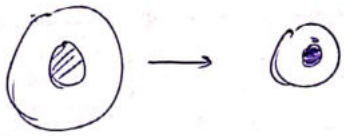


Apoptosis – in Greek.

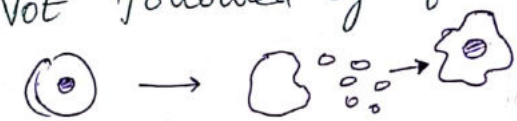
means falling of leaves.



Step ②: Nucleus condenses & fragments



Step ③: Apoptotic bodies (like to dry leaves) fall from cell & are cleared by MACROPHAGES. Not followed by inflamm

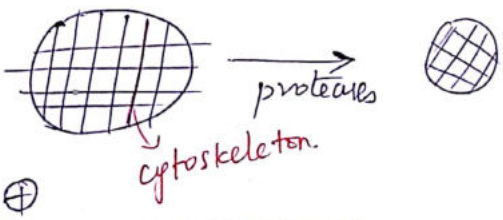


Apoptosis is mediated by **CASPASES**

⊕

proteases

breakdown cytoskeleton.



⊕

Endonucleases

Fragmentation of DNA.

* Cellular injury (membrane damage).,
* DNA damage. (mutation).
* ↓ Hormonal stimulatn (↓ progestrone in endomet cell.)

⊖

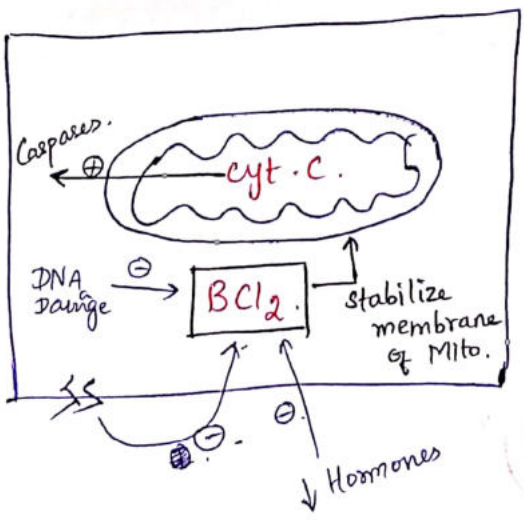
BCl_2

cyt. C. leaks out of mitochondria. into cytoplasm

⊕

Caspases

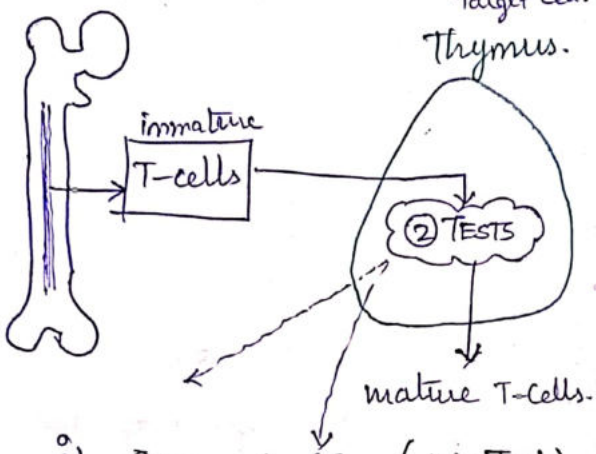
APOPTOSIS.



FAS Death Receptor (CD 95).

on Target cell. &

* TNF binds TNF-(R) on Target cell.



i) ⊕ve selection (1st Test).

⇓ (T-cell).

Do you, have the ability to bind self antigen + MHC?

↓ if T-cells says 'Yes'

ii) ⊖ve selection. (2nd Test)

⇓

Do you (T-cell). have the ability to bind to the self A.g. Too Avidly?

↓ if T-cells says. 'Yes'

T-cell will be destroyed.

Inorder to prevent "Auto Immunity"

↓

MECHANISM by which T-cells are destroyed thro' ⊖ve selection is FAS ligand - FAS death Receptor pathway. (CD95).

present
Antigen on MHC-I

CD8+ T-cells recognize Antigen on MHC-I

↓

Releases "PERFORINS"

↓

perforates the memb. of Target cell.

↓

Now an enzyme released by T-cell. called "Granzyme" enters the Target cells & Activate CASPASES

↓

APOPTOSIS