CELL PATHOLOGY AND AGEING

CELLULAR RESPONSE

Stimuli

1. Altered Physiologic Stimuli OR Non-Lethal Stimuli → CELLUR ADAPTATION
   Eg : i) Atrophy
   ii) Hypertrophy
   iii) Hyperplasia
   iv) Metaplasia
2. Lethal Stimuli - Transient : Reversible cell injury
   Lethal Stimuli - Persistent : Irreversible injury
   ↓
   Cell death
   ↓
   MORPHOLOGICAL CHANGES → NECROSIS, APOPTOSIS, NECROPTOSIS, PYROPTOSIS
3. Chronic Injury Stimuli : Intracellular accumulation
   Eg : Fats, Glycogen, Proteins
   ⇨ Calcification
4. Sublethal Stimuli Persistent : Induce cellular ageing

CELLULAR ADAPTATIONS

- Stimuli → Cell → Change in their Number, Size, Phenotype, functions
  ↓
- Removal → Comeback to (N) State
  : CELLULAR ADAPTATIONS ARE REVERSIBLE
- These are both Physiologic & Pathologic
  ⇩ ⇩
  Pregnant Uterus Barrett's Esophagus

HYPER TROPHY

- Definition : Size of cell ⇧ but Number of cell Same
- Mechanism : ⇧ In synthesis of cellular protein
- Is also both : Physiological & Pathological
  ⇩ ⇩
  Eg : Pregnant uterus Eg : Cardiac Enlargement d/t Valvular defect
  (both hypertrophy & hyperplasia)

HYPERPLASIA

- def : No of cell Increased But size of cell remains same
- Mechanism : i) ⇧ Growth Factor : Most important mechanism
  ↓
  (N) Cell
  ⇧ Nu Transcription Factor
  ⇧ Cell proliferation
  ii) ⇧ Tissue stem cells
  ⇩
  ⇧ no of cells

Both Physiologic & Pathological
⇩ ⇩
- Pregnant uterus
- Pregnant Breast
- Compensatory Hyperplasia → Liver Regeneration After Liver Resection

⇧ Estrogen on the endometrium
⇩
Endometrial Hyperplasia

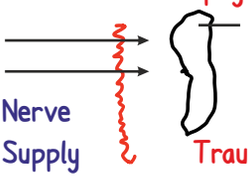
ATROPHY

- def : Size & no. of cell are decreased
- Mechanisms : i) ⇩ Protein synthesis
  ii) Ubiquitin Proteasome Degradation pathway ⟷ iii) Autophagy ⇩ Self ⇩ Eating

INTRACELLULAR PROTEIN DEGRADATION PATHWAY
Ubiquitin - Ligase Activation
⇩
Ubiquitin
+
Target Protein
⇩
These are taken into

⊕	
Activate proteasome (organelle)	Double membrane bound Autophagosome
⇩	(Contain Ubi + Tar. Pro)
degradation of Ubiquitin + Tar. protein	⇩
⇩	Combine with Lysosome
ATROPHY	⇩
	Degradation of Protein

- Both Physiologic & Pathological
  - Physiologic ⇩ during fetal development ⇩ loss of notochord & Thyroglossal duct
  - Pathological ⇩ Denervation atrophy

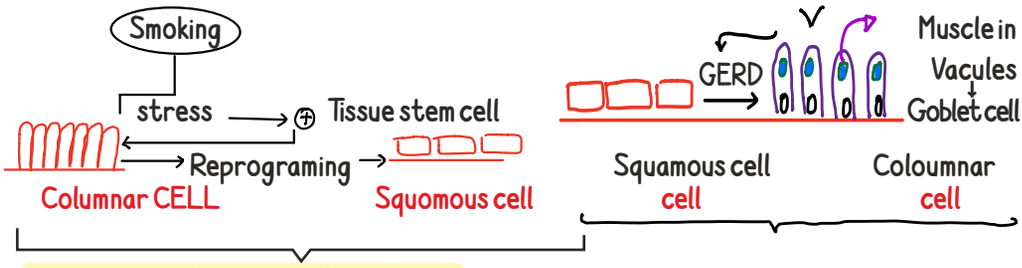


- Endometrial Adenocarcinoma a/w BOTH HYPER PLASIA & ATROPHY
  - BOTH HYPER PLASIA ⇩ a/w Type 1 Endometrial Adenocarcinoma ⇩ Good Prognosis
  - ATROPHY ⇩ a/w Type-2 Endo Adenocarcinoma ⇩ Poor prognosis

⇩
∴ Both are precancerous lesion

METAPLASIA

- def : 1 mature cell replaced by another type of mature cell
- Mechanism : CYTOKINE/GF
  ⇩
- Alteration of tissue-stem cell Reprogramming
- Both Physiologic & Pathologic
  - Physiologic ⇩ In cervix (during / menustruation) Squamous metaplasia at squamo colournhar junction
  - Pathologic → EPITHELIAL / CONNECTIVE TISSUE MESENCHYMAL METAPLASIA
    - Eg : Myositis ossificans
      Trauma → Muscle Injury ↓ Bone within Muscle
    - ♦ MC Type :
    - ♦ BARRETT'S EOSOPHAGUS
      - MCC : Gastro esophageal Reflux ⇩ Disease (GERD)

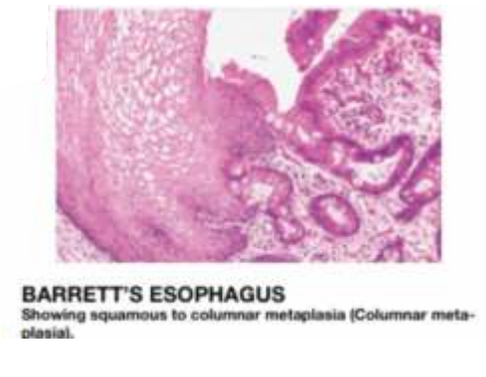


Squamous Metaplasia of Resp. Tract
(MC Type of Metaplasia)
d/t Vitamin A Deficiency
Vitamin A excess

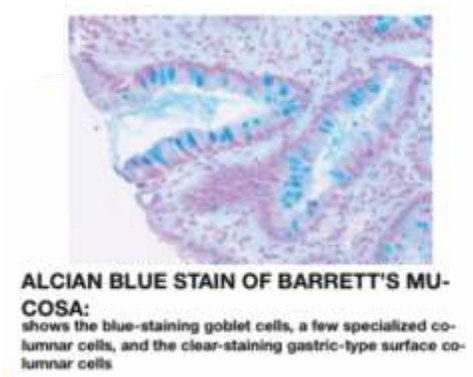
Colourmnar Metaplasia
d/t to the presence of Goblet Cell
aka INTESTINAL METAPLASIA
(Hall mark of barret's Esophage.)
Stain for GOBLET CELL :
Alcial Blue Stain : pH-2.5
for intestinal Goblet : pH - alkaline

Risk of Barret's Esophages : Adenocorcinoma of Esophagus
Metaplasia → Dysplasia → Carcinoma

Exception : Apocrine metaplasia of breast tissue have no risk of malignancy



BARRETT'S ESOPHAGUS
Showing squamous to columnar metaplasia (Columnar metaplasial.



ALCIAN BLUE STAIN OF BARRETT'S MUCOSA:
shows the blue-staining goblet cells, a few specialized columnar cells, and the clear-staining gastric-type surface columnar cells

CELL INJURY

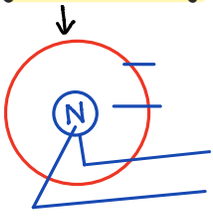
- MCC of cell injury : ISCHAEMIA
  ⇩
  HYPOXIA

OXIDATIVE STRESS
on mitochondria
⇩
Free radicals production

FREE RADICALS aka = Oxidants

= Reactive oxygen species (ROS)

- FR are normally produced d/t incomplete oxidation within mitochondria
- Def : Any chemical species with unpaired e- outer orbit
- Mechanism of action : by oxidative damage



Damage of
i) Cell membrane
ii) Cytoplasmic Proteins organelle
iii) Nu. membrane
iv) Nu. chromatin
DNA damage

FREE RADICAL (Oxidant)

i) OH : MOST REACTIVE
ii) H_2O_2
iii) 02
iv) ONOO

Anti Oxidant

i) Vitamins A/C/E
ii) Proteins : Transferrin Ceruloplasmin
iii) Enzymes : Catalase Glutathione
SOD (Superoxide dismutase)

1. Catalase
2. Glutathione : MOST POTENT ANTIOXIDANT
3. SOD

} PEROXISOMAL ENXYMES

→ Responsible for Brain protection from FR damage
→ Multation in SOD gene : Amyotrophic Lateral Sclerosis (Motor neuron disease)

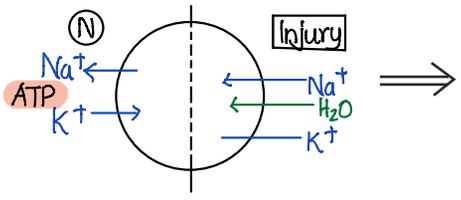
*** HYPOXIA

Most - Susceptible
- NEURONS : Survival time 3-4 Min
- CARDIAC : 20-40Min (~ 30Min)
- FIBROBLAST : Hrs to days

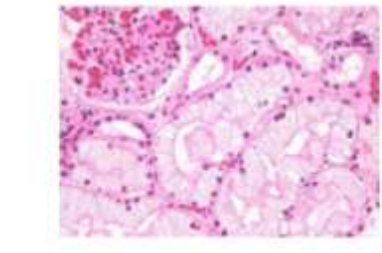
Types of cell injury
- Transient Stimuli → Reversible injury
- Persistent Stimuli → Irreversible Injury

REVERSIBLE INJURY

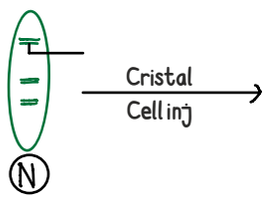
Ischaemia (↓O_2)
↓
↓ Oxidative phosphorylation in mitochondria
↓
ATP production (↓ 5 lot of Normal)



1. First sign : Cell Swelling
   Except for Apoptosis
   → First sign : Cell Shrinkage
2. Vacuolar Degeneration / HydropicDegeneration
   d/t intracellular water accumulation
   Aka Cloudy Swelling
   Eg : Acute Tubular necrosis of kidney
3. Organelle changes : EM Examination
   i) Ribosomes → Er Swelling (H_2O)
   ii) Ribosomal Detachment
   iii) Mitochondria



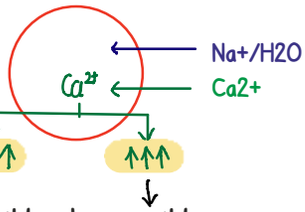
HYDROPIC CHANGE OR CLOUDY SWELLING
Sign of reversible injury due to cytoplasmic distension by excessive water entry.



REVERSIBLE INJURY :
Electron microscopy (Ultrastructurally) showing markedly swollen mitochondria containing small amorphous densities made up of electron dense deposits consisting of calcium and proteins.

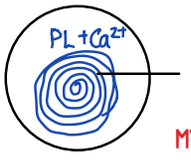
M. Important Factor for cell injury : Ca^{2+} (Cytosolic Ca^{2+})

iv)

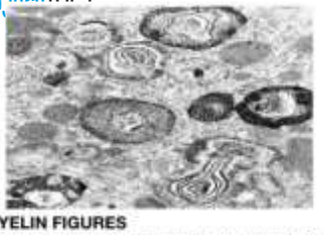


Reversible → cytosolic Ca2+ (Mild ⇧) → ⇩ ⊕ → Phospholipase → ⇩ → PL (on cell membrane)

Irreversible

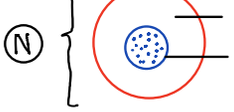


WHORL LIKE
↓
MYELIN-FIGURES
Made up of PL+Ca2+
seen in both reversble & irreversible injury (MC)



MYELIN FIGURES
Electron microscopy (Ultrastructurally) showing myelin figures derived from damage of the cell membrane (whorls of lamellated phospholipid and calcium).

Nucleus - Damage



Eosino philic (Pink/red)
Bascophilic
of granulomy / fibrillany chromatin

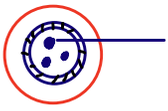
In Reversible injury

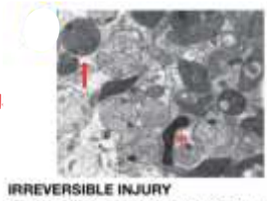
1. Dis aggregation of granular/fibrillary Nu. chromatin

REVERSIBLE INJURY

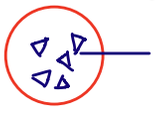
- Because of Persistent lethal stimuli
  ⇩
  ⇧ Cytosolic Ca^{2+}
  ⇩ ⊕ / Activates

Phospholipase	Proteases	Endo nuclease
⇩	⇩	⇩
Cell membrane damage	damage of cytoskeleton protein	Nu - damage
⇩	⇩	⇩
i) Myelin figures (max)	Loss of cell architecture	DNA chromatin)
ii) EM: Large, flocculent, amorphous densities in mitochondria		I) Pyknosis ii) Karyo-rrherix iii) Karyo - lysis } SEQUENTIAL DAMAGE

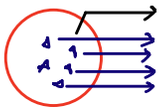
I) PYKNOSIS :  Clumping / Condensation of chromotin + Shrinkage of Nucleu


IRREVERSIBLE INJURY
Electron microscopy (ultrastructurally) showing markedly swollen mitochondria containing large flocculent amorphous densities made up of electron-dense deposits consisting of calcium and proteins.

ii) Karyo rrhexis : Nuclear fragmentation

 Fragmented Nuclei

iii) Karyo lysis : Chromatin Lysis dissolution

 Decreased basophilia, Thrown out

Irreversible Injury - Cell death
⇩
Morphological Changes

Necrosis | Apoptosis | Necroptosis | Pyroptosis

NECROSIS

- 2 Patterns of Necrosis

i. COAGULATIVE NECROSIS

⇨ Mc pattern of necrosis
⇨ Denaturation of Protein
⇩
Tissue architecture: Preserved
Eg: Ischaemic infarction of solid to organs Eg: Heart (Mc)
Kidney
Liver

EXCEPT IN BRAIN :
Ischaemic infarction

ii. LIQUEFACTIVE NECROSIS

⇨ d/t ⇧ Lysosomal permeability
⇩
Enzymes leak out
⇩
Enzymes leak out
⇩
Enzymatic damage of cell (HYDROLYTIC DAMAGE)
⇨ Tissue architecture Lost
Eg: i) Ischaemic infarction of Brain
Brain
: there is no stromal support of absence of collagen also brain is rich in Liquefactive enzymes
ii) Infections

SPECIAL TYPES

1. GANGRENE

- MC site I : LOWER LIMB

ⓐ Dry gangrene ⓑ Wetgangrene

* Tissue architecture is presevered
  : Eg of Coagulative necrosis

* Bacterial Contamination
  Toxin Enzyme release
* Type of Lique factive necrosis

2 CASEOUS NECROSIS

- It's called like this : of cheesy appearance Gross
  → Yellowish-White debris
- Seen in TB : Cheesy d/t presence of MYCOLIC ACID
- On microscopic examination : Coagulative Liquefactive Necrosis
  &
  → Amorphous Granular Pink structure

Considered as Variant of coagulative Necrosis

3 FAT NECROSIS

It may be due to

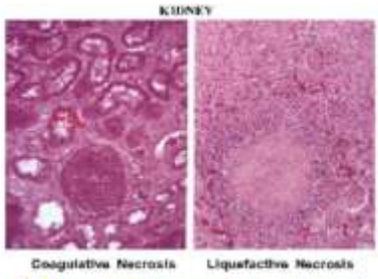
a) Enzymes
Acute pancreatitis
⇩
Lipase released
⇩
Act on Lipids
⇩
Release FA
Combine with Ca^{2+}
Called Saponification

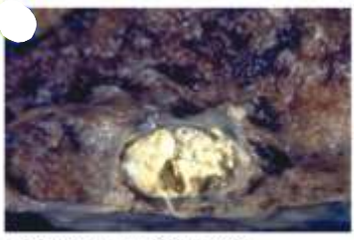
b) Trauma
Eg Breast inj

: GROSS : ∴ Chalky white appearance

M/E :
Normal Fat cell
Eccentric Nu
Anucleated
Fat cell (GHOST CELL)
Pink Cytop
Amorphous Basophilic deposits

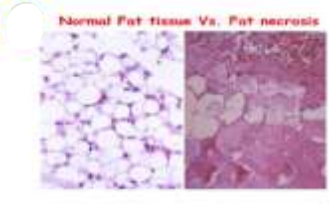
S/O Calcium deposits



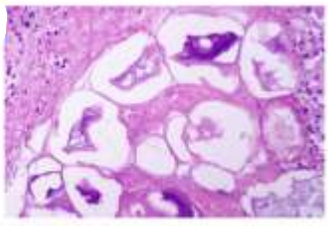


CASEOUS NECROSIS (GROSS).
Lung Tuberculosis with caseous necrosis consisting of yellow-white and cheesy debris.

CASEOUS NECROSIS (MICROSCOPY)
Lung Tuberculosis with eosinophilic caseous necrosis and epithelioid cells.



FAT NECROSIS
Normal fat cells with eccentric nuclei is seen in image (a). Image (b) shows fat necrosis where anucleated ghost cells are seen

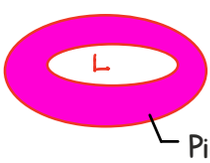


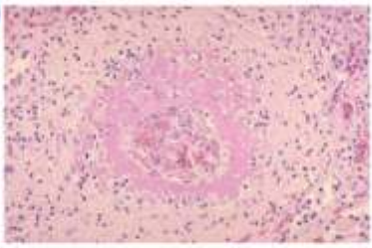
FAT NECROSIS
Showing Amorphous basophilic calcium deposits within cells having fat necrosis.

FAT NECROSIS
showing Chalky white necrosis.

5 FIBRINOLD NECROSIS

- Presence of Fibrin + Immune Complex [Ag + Ab]
- Pathology : Vessel Wall Damage
  ⇩
  Coagulation Pathway ⟶ Fibrin Formation

- Seen in i. Vasculitis : Polyarteritis Nodosa
  ii. Malignant HTN
- M/E
- 
  Blood vessel
  Pink, amorphous homogenous
  ⇩
  FIBRINOID NECROSIS

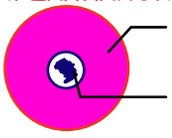
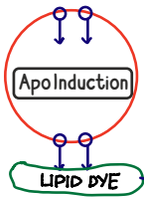


FIBRINOID NECROSIS
Showing deposition of fibrin (pink material) on the wall of arteriole as a consequence of malignant hypertension.

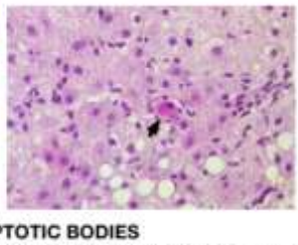
NECROSIS	APOPTOSIS
* ⇧ Lysosomal permeability ⇩ Enzymes ⇩ Cell Membrane damage ⇩ IC Content leak outside & Acts as chemoattractant ⇩ INFLAMMATION	* d/t ⇧ Mitochondrial Permeability ⇩ Intact Cell membrane intact ∴ No Leacking ⇩ ∴ NO INFLAMMATION
* Alwaysp Pthological	* Apoptosis Both physiological & Pathological

APOPTOSIS

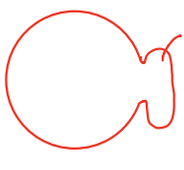
- Falling - off the cells from the tissue (literal meaning)
- Programmed cell death Is seen in
  I. Apoptosis
  II. Necroptosis
  III. Pyroptosis
  IV. Neutrophilic Extra Cellular Trap (NET)
- Energy depend. process >> Programmed Cell Death (active process)
- Apoptosis is PHYSIOLOGICAL (MC) ⇩
  Eg: 1. Organogenesis /Embryogenesis
  2. Neo Vascularisation
  3. Killing of inflammatory cells after completing their function
  4. Elimination of auto-reactive cell (To prevent Auto immunity
- PATHOLOGICAL ⇩
  Eg 1. Chemotherapy or Radio therapy (Apoptosis + Necrosis)
  2 Glucorticoid induce apoptosis (∴ Prevent autoimmune)
  3. Graft V/s Host disease
  4 Councilman bodies in Viral Hepatitis : There are Apoptic bodies
  5. Misfolding of Protein

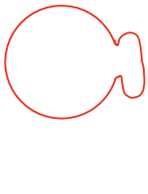
- MORPHOLOGY : a. Cell Shrinkage
  b. MOST CHARACHERISTIC FEATURE : Chromatin Condensation
  c. 2nd MOST : Cell Membrane intact
  d. NO INFLAMMATION
  e.  Hyper Eosinophilic Cytoplasm (Not Specific) By chromatin Condensation
  f. N cell → 

Phosphatidyl - Serine Receptor (Lipid Receptor) → EAT-ME SIGNAL
Flipped Receptors
ANNEXIN -V: MARKER OF APOPTOSIS


APOPTOTIC BODIES
Cell membrane bound structures with tightly arranged organelles with or without nuclear fragments. Examples are Councilman Bodies in viral hepatitis


AGAROSE GEL ELECTROPHORESIS
A) Step ladder pattern of apoptosis. It is due to endonuclease induced internucleosomal damage
B) Diffuse smearing pattern seen in necrosis.


"Bleb"
↓ Detach
Mitochondria
Apoptotic Bodies
Membrane bound structure with organelle they may & may not have nuclear remenents
→ Eg : Councilman Bodies

h. 

END OUTCOME = Phagocytosis

- BIO CHEMISTRY : Pro Caspase (Pro-C)

⇩ Activation

Caspase → Endo Nuclease Activation

↓

Chromatin Condensation

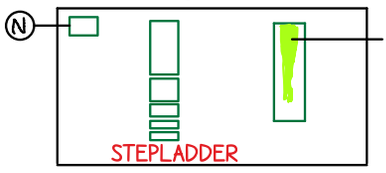
Function : Nu DNA Damage As specific Fragments

INTER NUCLEOSOMAL DNA DAMAGE

Size of fragments : 180-200 Base pairs

Can be Observed Agarose Gel Electrophoresis

AGAROSE GEL ELECTROPHORESIS
A) Step ladder pattern of apoptosis. It is due to endonuclease induced internucleosomal damage
B) Diffuse smearing pattern seen in necrosis.



Smering pattern ⇩ Seen in Necrosis

Step ladder seen in
i) Apoptosis : Charachteristic
ii) Necrosis

MECHANISM OF APOPTOSIS

2events

INITIATION ⊕ EXECUTIONAL

Pathways

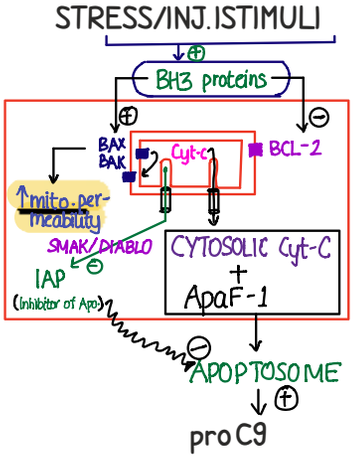
INTRINSIC PATHWAY ↓⊕ C9

EXTRINSIC PATHWAY ↓⊕ C 8 (In lower Animal) C10 (In Humans)

EXECUTIONAL → C^7, 6,3 Activation ↓⊕ Endonuclease ↓ Chromatin condensation (= Apoptosis)

INTRINSIC PATHWAY

– Aka Mitochondrial Pathway as mitochondria is the M. Important Organelle It's a Major Pathway



PROTO-ONCOGENE

a. PRO-APOPTOTIC
- BAX
- BAK
- $BCL\text{-}X_S$
- BH_3 only proteins family (on cell surface)

*STRESS-SENSORS
- Bim
- Bad
- Bid
- PUMA
- NOXA

b. ANTI-APOPTIC
- BCL-2
- $BCL\text{-}X_L$
- MCL-1

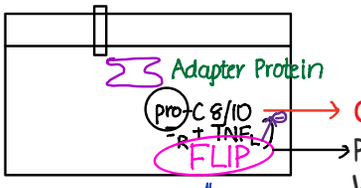
SMAK/DIABLO : Inhibits IAP
: ∴ They are pro-apoptic

EXTRINSIC PATHWAY

– Aka Death Receptor mediated pathway

i) TNF-Receptor : MOST WELL-DEFINED
ii) FAS / CDD5

Death (R) + D-Ligand (Eg : TNF_R + TNF_2)



→ C 8/10 → Press in *(N) Cell Viruses (HIV)

⇩

Anti aptotis ⊖ apoptotic in Ext. Patyway

FLIP : Anti-apoptotic protein present in : Normal cell
: Virus (HIV)

⊖ Apoptosis at extrinsic pathway by inhibiting the formation of C8/10

Hallmark of Apoptosis Activation : Caspase Activation

Hallmark of neuronal apoptosis activation : AIF (Apoptosis Inducing Factor)

→ No caspaces

Clinicopathological Co-relation

⇨ Misfolding of proteins ⟶ ⇧⇧ Mis folded protein Feature of neurological disorders

Caspase ⊗

⇩

Apoptosis

I. Alzheimer ds
II. Parkinsons ds
III. Hunligton ds

NECROPTOSIS

- Programmed Cell Death Without Caspase Activation
- Necrosis + Apoptosis

⇩

- Morphology Programmed Cell death

Mechanism :

TNF_R + TNF

⇩ Recruits

RIP-1 + RIP-3 (Receptor Interacting Protein)

⊕

without caspase

Mitochondrial Stress

⇩

FR Production

I) Cell Swelling
II) CM damage
III) Inflammation

C-8

⇩

Apoptosis (Extrinsic

MORPHOLOGY OF NECROSIS = NECROPTOSIS

Considered as variants of Necrosis

NECROPTOSIS is both Physiologic & Pathological

⇩ ⇩

Eg : Mammalian Bone growth plate formation

I) Neurological disorder
II) Pancreatitis

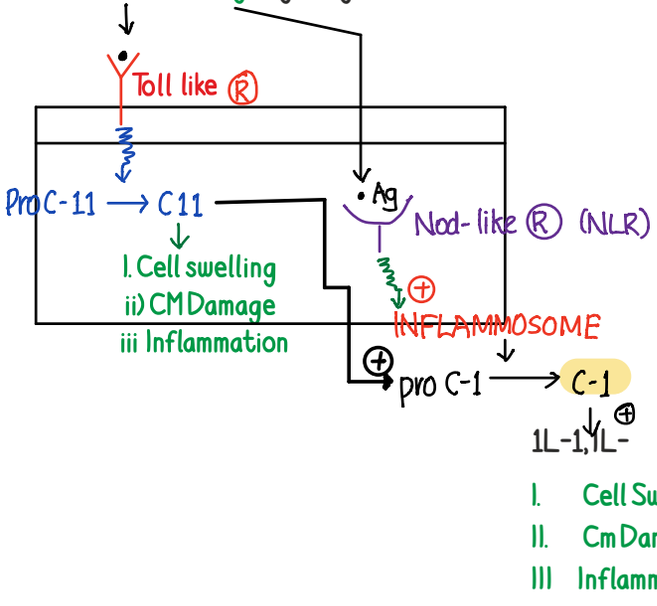
PYROPTOSIS

- Pyrogen induced Apoptosis

→ IL-1

- Variant of necrosis

Mechanism : Bacterial Ag (Eg : Flagellin)



Chronic Injurious Stimuli

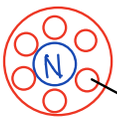
↓ Leads to

Intracellular accumulations

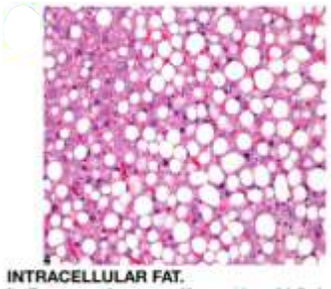
I, (N) substances — ii. Abnormal substances — iii. Calcification

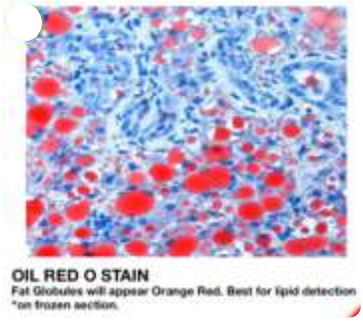
Lipid (Mc)	Pigments	Coal / Silica
Glycogen	I. Lipofuschin	
Proteins	II. Hemosiderin	
	III. Melanin	

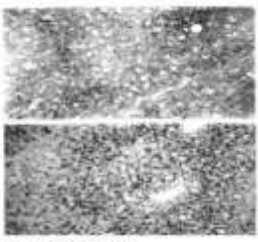
LIPID : – Mc intracellular accumulation
– Aka STEATOSIS (⇧Lipid deposit in cell)
– It can be Triglycerides (TG) : MC Lipid Accumulation
Cholesterol
C Esteraces — Alcoholic / INAFLD/Hepatitis/viral
Phospholipid



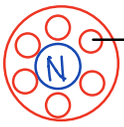
Clear Vacoules : SPECIAL STAIN (Best stain in frozen / Crosection)
i. Oil-Red-O-stain : Lipid will be Red
ii. Sudan Black-B : Lipid will be black


INTRACELLULAR FAT.
It will appear as clear space with eccentric nuclei displaced by fat within cells.


OIL RED O STAIN
Fat Globules will appear Orange Red. Best for lipid detection on frozen section.


SUDAN BLACK STAIN
showing Fat Globules as black deposit

GLYCOGEN :



SPECIAL STAIN
i. PAS +ve
ii. Best's carmine Stain
} GLYCOGEN IN RED COLOUR

PROTEINS : ⇧ Protein Synthesis
⇩
Mis folding of proteins
⇩
Response : UPR (Unfolding Pr. Response)

Stress on ER	Autoplay	Caspases
⇩	(Programmed cell death)	⇩
Synthesis of chaperons	⇧ prt. Misf ⟶ ⊕ IC	Apoptosis
(Req. for proper folding of proteins)	↓ Protein Degradation	
	Ubiquitin + Protein (Target)	
	⇩	
	Taken in to Autophagosome & combine with Lycosome	
	⇩	
	Degradation of proteins	

Failure of Unfolding Protein Response
⇩
Misfolding Protein Disorder

Autophagy / Ubiquitin Proteasome Degradation Pathway
is a/w i. Atrophy
ii. Inflamation (TB)
Atgs - 5 gene controls : N Phagocyle function of macrophage
⇩
Deletion
⇩
⇧TB
iii. Concers (Dsyregulated)

IV. Mitochondrial Inheritance

PIGMENT ACCUMULATION

N. Pigment
i. Lipo fuschin
ii. Hemosiderin
iii. Melanin

Abnormal Pigment
i. Lipofuschin
ii. Hemosiderin
iii. Melanin

PIGMENTS

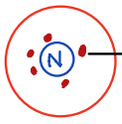
BROWN

LIPOFUSCHIN
* Oil-Red-O
* Sudan Black B
LIPO FUSCHIN : Aka Ageing Pigments
FR ⟶ Damage CM

HEMOSIDERIN
* PEARL'S PRUSSIAN Blue Stain

BLACK

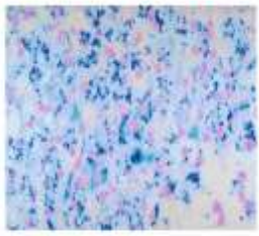
Melanin
* In : Skin (Normal : Melanoma)
* Special Stain : Fontana Masson



Brown Perinuclear pigment

Made up of Phospholipid + Proteins (Dominants)
Seen in :
* Cancer Cachexia
* Severe Malnutrition
* Ageing
It's aka TELL-TALE SIGN OF FR-INJURY aka WEAR & TEAR Pigment

CALCIFICATION
- Seen in ⇧alkaline pH of tissue
- Starts in [redacted] except for Kidney
  - Starts in Basement Memb.
- Pathological Calcification

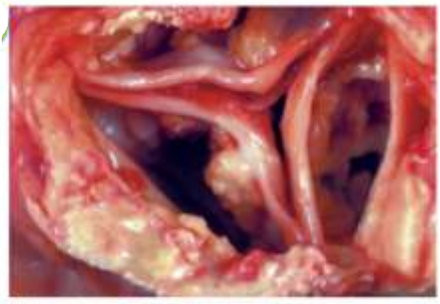

PERL'S PRUSSIAN BLUE STAINING
Showing Ferric Iron Deposits as Bright Blue.

DYSTROPHIC
* Tissue - Damage
* Ca2+ Level : Normal
Eg : I. TB Lymph Node
II. Rheumatic Heart Disease
Volve Damage
III. Mancke berg Medial Calcific Sclerosis
IV. Psammoma Bodle
Seen in : Menhgoma
Mestholioma
Repillary RCC Thyroid

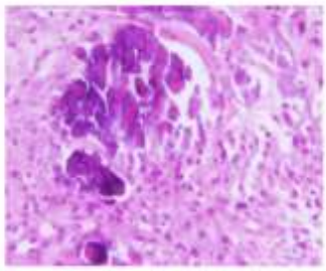
METASTATIC
* Normal tissue
* High Ca2+
* MCC
1° HYPER PARATHYROIDISN
⇩
MCC : Parathyoird Adenoma
* Other Causes
I. Rena Failure '(2 Hyper Para.
II.) Excessive Vit A&D Synthesis
* MC Site : Lung (Alveoli)
Gastric Mucosa Systemic Artery
Least common : Parathyroid

M/E : Basophilic Amorphous Material (H&E)
↓ Confirmation
MC & BEST : I) Von-Kassa Stain : Black
II) Alizanh - Red : Red Colour

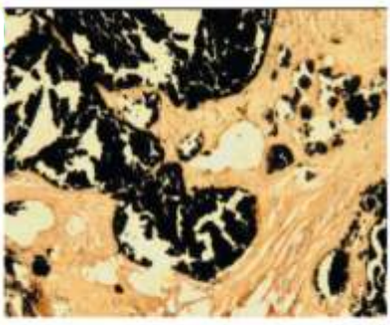
Retinoic acids
↓ ⊕
Osteoclast
(modified macrophage)
↓
Bone - eating
↓
↑↑ Ca^{2+}



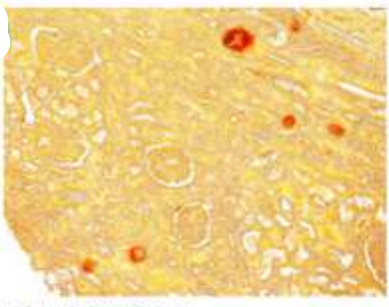
DYSTROPHIC CALCIFICATION
Dystrophic calcification of damaged valve in RHD.



CALCIUM DEPOSITS (HEMATOXYLIN AND EOSIN STAIN)
calcium will be basophilic (blue) amorphous deposits.



VON KOSSA BLACK STAIN
showing calcium as black deposit.



ALIZARIN RED STAIN
showing calcium as red deposit.

AGEING

1. Progressive accumulation of sublethal inj. stimuli
   ⇩
   FR production : Most Widely Accepted Hypothess
   ⇩
   Ageing
2. Increased collagen deposition or Increase cross-linking of collagen
   ⇩
   Ageing

Most effective method to prolong life spon : Colorie - Restriction

I.) ⇩ FR Injury
II) ⇧ Proper pr. Folding
III) ⇩ Apoptosis
IV) ⇧Insulin Sensitivity ⇨ ⇧ Glucose Metatolism
V) ⇩ Overall Metabolism

↓ ⊕/ Induction
SIRUTUIN
↓
M.O.A

⊕ Induce
Small Amount of Red- Wine

Changes in ageing :
I. Cell Damage
II. Mito Chondrial Damage
III. Glucose Metabolism
IV. DNA Damage
V. Telomere Shorting

TELOMERE : Short stretches of DNA @ the end of chromesome

Function : I. Ensure complete replication of chromosome
II. Prevent fusion & degradation of chromosome

Progressive cell division
⇩
Telomere shorteing
⇩
Fusion / degradation of Choromosome
⇩
Ageing

WERNER SYNDROME	v/s	WERMER SYNDROME
* Pre mature ageing d/t Defect in DNA Helicase		* MEN-I Endorine disorder

⇩
Required for repair & Replication Defective