25/9

INTRACELLULAR ACCUMULATIONS

→ under some circumstances, cells may accumulate abnormal amounts of various substances.

Effects:
Mild. → No damage/injury.
Severe

May be found
→ in cytoplasm
→ organelles (typically lysosomes)
→ nucleus

come to cell through
→
→

Accumulations of
① → Normal constituents of cell metabolism.
↓
May be due to defects in packaging / transport
↓
fats, protein, carbo.

② Accumulations of metabolites due to enzyme deficiency.
↓
storage diseases
of inborn errors of metabolism.

③ Acc. of abnormal substances resulting due to acquired or genetic defects.
eg: α1 antitrypsin deficiency

④ Accumulations of pigments
↓
No enzymatic mechanism to degrade
↓
Endogenous pigments
Exogenous pigments.

PATHWAYS
① Abnormal metabolism
Normal / ↑ rate of prodn of a normal substance, but metabolic rate is inadequate to remove it
eg: fatty liver.

② Defect in protein folding, transport, secretion.

~~A no~~

③ Lack of enzyme.
eg: lysosome storage disease.
failure to degrade a metabolite

④ Ingestion of indigestible metabolism.
cell has no means to degrade the substance.

Accumulation of Lipids

→ Acc. of neutral fat (fatty change)
→ cholesterol and cholesteryl esters.

Fatty Change

→ Steatosis
→ Fatty metamorphosis.
→ Intracellular acc. of neutral fat (TAG) within the parenchymal cells.
→ liver. (most common).
→ heart, skeletal muscle and kidneys can also have fatty change

causes of fatty liver.

→ Alcohol abuse.
→ diabetes mellitus. (NASH)
→ Obesity
→ Protein Malnutrition (starvation)
→ Drugs / toxins.
→ Anoxia / Hypoxia
→ Pregnancy.

Gross.

organ enlarges, becomes progressively yellow, soft and greasy.

Microscopy.

Initially → microvesicular.
later → macrovesicular.
then → fatty cysts. (vesicle fuse together & ruptures to form fatty cysts)

Other lipid Accumulations:

cholesterol & cholesterol Esters

→ Atherosclerosis, cholesterol accumulates in smooth muscle cells & macrophages in the intima of arteries
→ In hereditary hyperlipemia, cholesterol accumulates in macrophages, usually under the skin, forming tumor like structures known as xanthomas.

Foam cells. → fatty macrophages

Fat stains (1 mark)

→ demonstrated in fresh unfixed tissue by frozen section.

Special stains for fat	colour taken by fat.
Sudan III	Yellow.
Sudan IV	Orange.
Oil red O	Red.
Osmic acid.	Black.
Sudan Black B	Black.

Protein Accumulations

→ morphologically visible proteins are are less common.

- Hyaline droplets
  small, eosinophilic, homogenous deposits

→ In proximal tubular epithelial cells.

causes: diseases associated with increased protein folkation.
Nephrotic Syndrome.

Mech: increased reabsorption

② Russell Bodies.
→ Acc. of newly synthesized immunoglobulins in RER of plasma cells.

③ Mallory body or alcoholic hyalin
→ Eosinophilic cytoplasmic in liver cells
→ alcoholic liver disease
→ composed predominantly of aggregated intermediate

④ Neurofibrillary tangles.
→ cond: Alzheimer's disease
abnormal folding & acc. of protein called tau in nerve cell body & dendrite.

Accumulation of Carbohydrates

→ associated with abnormalities in metabolism of glucose or glycogen

→ diabetes mellitus.
glycogen storage disorders.

DM → glycogen accumulates in renal tubular epi, cardiac myocytes and β cells of islets of langerhans.

Glycogen accumulates within cells in a group of closely related genetic disorders
← vacuolar degeneration of vacuoles
↓
glycogen Storage Disorders.

Pigments (VIVA)

→ coloured substances normal constituents (eg: melanin)

Exogenous Pigments

① carbon / coal dust
→ Anthracosis
→ coal workers pneumoconiosis

② Tattooing
→ India ink, carbon.

③ Ingested
→ Argyria: silver.
→ lead, carotenemia.

1. Lipofuschin
2. Melanin ※
3. Hemosiderin

Exogenous pigments

Carbon (anthracosis)
coal dust (pneumoconiosis)
lungs pick up by alveolar macrophage
↓
Blackening the tissue of the lungs.
↓
Regional lymph nodes.

→ Black streaks seen b/w lobules of lung beneath the pleural serosa due to accumulation of anthracotic pigment.

Lipofuschin

→ Insoluble.
known as lipochrome or wear and tear pigment / aging pigment.
→ composed of polymers of lipids & phospholipids in complex with protein.
→ Brown lipid.
→ Not injurious to the cell or its function.
→ Telltale sign of free radical injury and lipid peroxidation.

→ In sulphur → yellow brown, finely granular cytoplasmic often perinuclear pigment
→ liver & heart of aging patients "Brown atrophy".
→ pigment appears as perinuclear electron dense granules by electron microscopy.

Melanin (Greek. Melas - Black)

→ non-hb derived, ~~but~~ brown-black pigment.
→ only endogenous brown-black pigment.
→ formed when the enzyme tyrosinase catalyses the oxidation of tyrosine to dihydroxy phenyl alanine in melanocytes and dendritic cells.

※ Masson Fontana stain for melanin

disorders of melanin pigmentation
↓ hypo ↓ hyper.

hypo pigmentation

Generalised
1. Addisons disease (ACTH)
2. chloasma (pregnancy, oral contraceptives)

Localised.

1. Cafe au lait spots
2. Peutz Jeghers syndrome (lips)
3. Melanosis coli (colon)
4. Nevi and tumors.

Hypo pigmentation

Generalised.
→ Albinism

localised
→ Vitiligo.

Hemosiderin.

→ Hb derived, golden yellow to brown, granular / crystalline pigment
→ major storage form of iron
→ represents aggregates of ferritin micelle.
→ Hemosiderin is ferric iron.
→ Small amounts of hemosiderin seen in.

Prussian blue / Perls
for iron demonstration

Causes of iron (Hemosiderosis).

- local → common bruise.
- Systemic
  1. Acquired Hemosiderosis
     → hemolytic disorder
     → blood transfusion
     → leukemia
  2. Hereditary hemochromatosis
     → ↑ absorption.