INTRACELLULAR ACCUMULATION

Accumulation of abnormal amount of substance in cytoplasm and nucleus thatcauses cell injury.

Causes

- Lack of enzyme.
- Ingestion of indigestible materials.
- Abnormal metabolism.

Types

1. Exogenous accumulation – Accumulation takes place outside of the cell .

Ex .Carbon deposition in lungs and Tattooing.

2. Endogenous accumulation - Accumulation takes place outside of the cell .

Ex.Lipofuschin (protein), Heamofilerin (Iron) and Melain(black pigment)

Pathological calcification

Abnormal deposition of calcium (crystalline calcium phosphate) salts with small amount of Fe, Mg and other minerals in tissues except bones and teeth enamel is called calcification.

Types of calcification

1. Dystrophic calcification

Occurs locally in dead and degenerated tissues due to repeated cycle of formation of calcium phosphate by calcium in mitochondria and phospholipids.

It occurs with normal serum levels of calcium and normal calciummetabolism.

Morphology (or) Symtoms

- Vary in size with deposition of white granules.
- Which may be gritty.
- Granular appearance in lumps.
- Concentric laminations of calcium deposition.

2. Metastatic Calcification

The deposition of calcium salts in normal tissues.

It almost always reflects some derangement in calcium metabolism andincreased levels of calcium and serum.

Disturbance in calcium metabolism like bone damage or diseases.

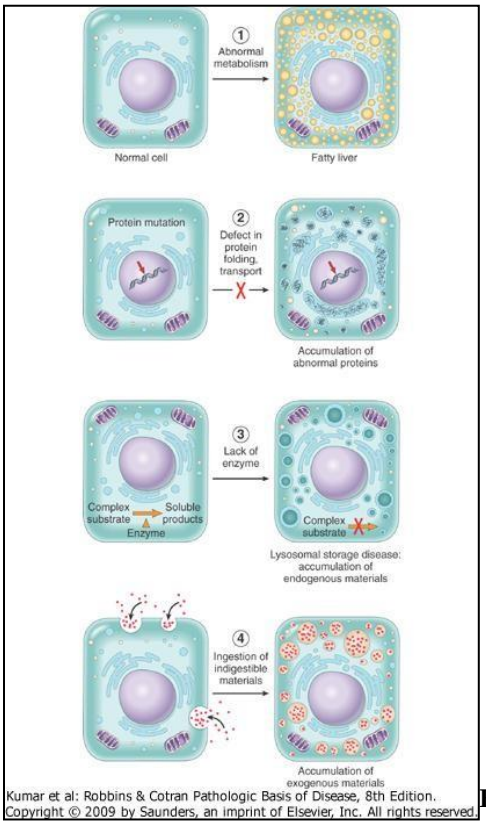
Morphology (or) Symtoms

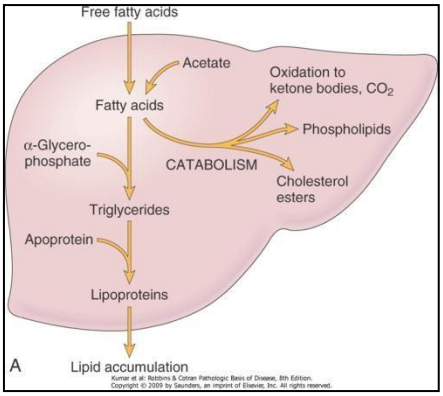
- Massive bone destruction.
- Hypoparathyroidism.

Cellular Adaptation

- Hyperplasia – increase in NUMBER (not size) of cells in an organ or tissue
  - May be seen in combination with hypertrophy
  - Physiologic hyperplasia – mechanisms include increased DNA synthesis, growth inhibitors will halthyperplasia after sufficient growth has occurred
    - Hormonal – hyperplasia of uterine muscle during pregnancy
    - Compensatory – hyperplasia in organ after partial resection
  - Pathological – not in itself neoplastic or preneoplastic, but the trigger may place patient at risk of sequelae (dysplasia, carcinoma)
    - Excess hormones – endometrial proliferation from over increased estrogen
    - Excess growth factor stimulation – warts arising from papilloma virus
- Hypertrophy – increase in cell SIZE, leading to increase in organ size
  - Usually in terminal cells which can no longer divide, so their only recourse is enlargement
  - End result is amount of increased work that each cell must perform is limited
  - Physiologic hyperplasia – hormonal stimulation (hypertrophy of uterine wall during pregnancy)
  - Pathologic – chronic cell stressors (stenotic valves, left ventricular hypertrophy from increased after load)
- Chronic hypertrophy – if stress that triggered hypertrophy is not resolves, likely result is organ failure
  - Hypertrophied tissue at increased risk for ischemia from metabolic demands outpacing blood supply

- Autotrophy – shrinkage in cell size (may or may not include shrinkage of organ size)
  - Cells are smaller than normal, but are still viable. They do not normally undergo apoptosis or necrosis
  - Physiologic autotrophy – tissues/structures present in embryo or childhood may undergo autotrophy as growth and development process progresses
  - Pathologic – decreased workload, loss of innervation, decreased supply, inadequate nutrition, decreased hormonal stimulation, pain, physical pressure
- Metaplasia – REVERSIBLE change in which one type of adult cell (epithelial or mesenchymal) is replaced by another type – if stress/injury abates, metaplastic tissue may revert to original cell type
  - This is a protective mechanism, not a premalignant change
  - Reprogramming of epithelial stem cells (reserve cells) from one type of epithelium to another
  - Reprogramming of mesenchymal (pluripotent) stem cells to differentiate along different mesenchymal path
  - Bronchial (pseudostratifie, ciliated columnar) to squamous epithelium – smokers
  - Endocervical (columnar) to squamous – chronic cervicitis
  - Esophageal (squamous) to gastric or intestinal – barret esophagous (acid reflux)





- Intracellular accumulations – transient or permanent, may acquire substances that arise either from cell itself or from nearby cells
  - Normal cellular constituents accumulated in excess from increased production, decreased metabolism, etc (lipid accumulation in hepatocytes)
  - Abnormal substances via decreased metabolism or excretion (storage disease)
  - Pigments via decreased metabolism or transport (carbon, silica)

- Lipid accumulation
  - Steatosis (fatty changes) – accumulation of lipids in hepatocytes
    - From ^OH, drugs, toxins
    - Can occur at any step in the pathway
- Cholesterol
  - Seen as needle-like clefts in tissue, washes out with processing so looks cleared out
  - Atherosclerotic plaque in arteries
  - Accumulation in macrophages (called "foamy" macrophages) – seen in xanthomas, areas of fat necrosis, cholesterolosis in gall bladder
- Proteins
  - May be due to cell inability to maintain proper metabolic rate
    - Increased reabsorption of proteins in renal tubules eosinophilic, glassy droplets in cytoplasm
  - Defective protein folding
    - α-1-AT deficiency intracellular accumulation of partially folded intermediates
    - may cause toxicity – some neurodegenerative diseases
- Glycogen
  - Intracellular accumulation can be physiologic (hepatocytes) or pathologic (glycogen storage disease)
  - Easiest seen with a PAS strain – deep pink to magenta color
- Pigments
  - Exogenous pigments – anthracotic (carbon) pigments in lungs, tattoos
  - Endogenous pigments
    - Lipofuscin ("wear and tear" pigments)
      - Results from free-radical peroxidation of membrane lipids
      - Finely granular yellow/brown pigment
      - Often seen in myocardial cells and hepatocytes
    - Melanin
      - Only endogenous brown-black pigment

- Often (not always) seen in melanomas
- Hemosiderin
- Hemoglobin derived and represents aggregates of ferritin micelles
- Granular or crystalline yellow/brown pigment
- Often seen in macrophages in bone marrow, spleen, liver (lots of RBC and RBC breakdown); also in macrophages in areas of recent hemorrhage
- Best seen with iron stains (Prussian blue) – makes granular pigment more visible

- Calcification
  - Dystrophic – occurs in areas of nonviable or dying tissue in the setting of NORMAL serum calcium
    - Also occurs in aging/damaged heart valves, atherosclerotic plaque
    - Tissue, not serum, is calcified
    - Gross – hard, gritty, tan-white, lumpy
    - Micro – deeply basophilic H&E stain, glassy, amorphous, may be either crystalline or non-crystalline
  - Metastatic – may occur in normal, viable tissues in the setting of hypercalcemia due to any number of causes
    - Most often seen in kidneys, cardiac muscle, soft tissue
    - Serum, not tissue, is calcified (unlike dystrophic)