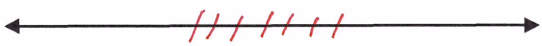
REVERSIBLE CELL INJURY, INTRACELLULAR ACCUMULATION

Degeneration: Reversible cellular dysfunction with morphological alteration
Point of no return: - Inability to preserve mitochondrial integrity
- Disturbance of membrane function and integrity
- Ca^{2+} influx – activation of autolytic enzymes

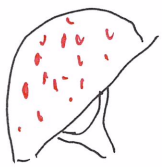


Necrosis Degeneration Living cell

1. **Cellular swelling, hydropic change, vacuolar degenaration**
   - Failure of energy-dependent ion pumps in plasma membrane
   - Inability to maintain ionic fluid homeostasis
   - First manifestation of injured cells
   - Morphology: - pallor of organ
     - increase in weight
     - increase in turgor
   - Microscopy: - small, clear vacuoles in the cytoplasm
     - distended parts of ER and mitochondria

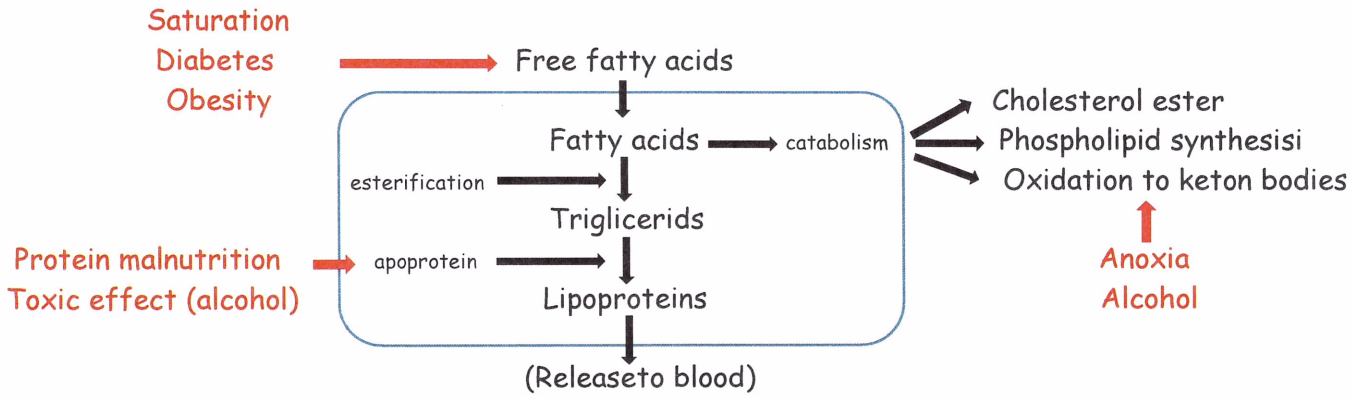
2. **Parenchymal degeneration**
   - Old terminology, morphological description
   - Morphology: - Prototype is the sepsis
     - Similar to boiled meet, gray, fragile organs
   - Microscopy: - Dilated mitochondria

3. **Fatty change / fatty degeneration**
   - Appearance of lipid vacuoles in the cytoplasm
   - Involved cell participating in fatt metabolism – hepatocytes, myocardium, kidney
   - Caused by: - Toxins (alcohol)
     - Anoxia
     - Protein malnutrition
     - Diabetes
     - Obesity



   - Morphology: - diffuse – toxic effect
     - mottled – hypoxic effect
   - Microscopy: - clear cytoplasm within parenchymal cells
     - detection – Oil-red, Sudan BB
     - vacuoles dysplaces nucleus to cell membrane
     - severe forms – disrupt cell membrane – fat globules

Pathogenesis:



4. **<u>Steatosis hepatis, degeneratio adiposa diffusa hepatis</u>**

A/ Alcoholic liver disease
- Chronic 50-60 mg/day (5-6 bottle beer) – borderline risk
- Women more vulnerable than men
- Beer more risk than wine
- Mechanism – block fat catabolism and lipoprotein synthesis – lipid accumulation
- Steatosis – (hepatitis) – chirrosis

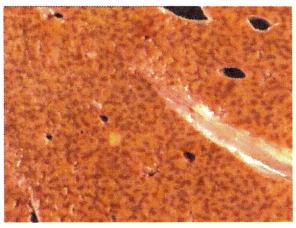
B/ Non alcoholic fatty liver disease (NAFLD)
- Type 2 diabetes mellitus
- Obesity
- Main cause – insuline resistance
- Mechanism – impaired oxidation of fatty acids
  - increase uptake of fatty acids
  - decreased synthesis of VLDL

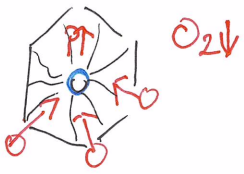
C/ Reye syndrome
- Fatty liver + encephalopathy
- Mitochondrial hepatopathy
- Children younger than 4 ys.

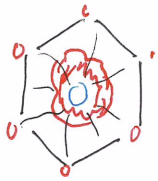
6. **<u>Degenetatio adiposa insularis hepatis - nutmeg liver – passive congestion – hepar moschatum</u>**

- Right sided cardiac decompensation – passive congestion of liver
- Hepar moschatum simplex – centrolobular congestion
- Hepar moschatum adiposum – centrolobular steatosis
- Hepar moschatum atrophicum – centrolobular atrophy + fibrosis
- Centrolobular necrosis – right sided decompensation + left sided heart failure
  - centrolobular necrosis and haemorrhage

Pathogenesis:

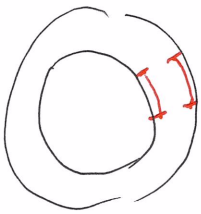


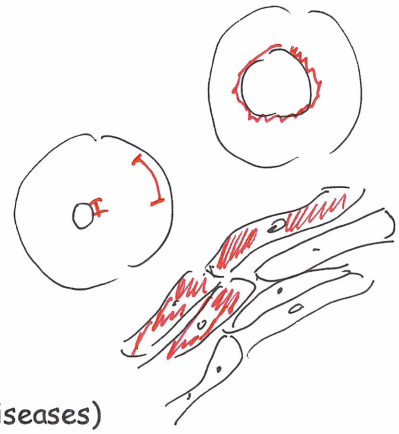




5. **<u>Degenaratio adiposa diffusa myocardii</u>**
   - Caused by toxic effests
   - Diphteria, chemotherapy (adriomycin)

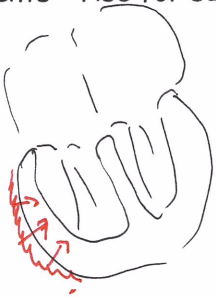
6. **<u>Degeneratio adiposa insularis myocardii (tiger haeart)</u>**

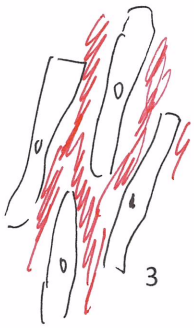




   - Caused by prolonged (subacute) moderate hypoxia (anaemia, pulmonary diseases)
   - Predispose AS, left sided hypertrophy of the heart
   - Fat accumulation in the myocytes at subendocardial localization
   - Reversible

7. **<u>Infiltratio adiposa myocardii</u>**
   - Not a degeneration (no fat in the cells)
   - Infiltration of fat tissue between muscle fibers (intersticial) of right ventricule
   - In obes patients – risc for sudden cardiac death (SCD)





APOPTOSIS

- Apoptosis is a cell death regulated by suiside program
- Activated enzymes degrade DNA, nuclear and cytoplasmic proteins
- Cell membranes are intact but altered to be a target for phagocytosis
- Cells are eliminated before enzymes leak out
- Apoptosis and necrosis may coexist, apoptosis may progress to necrosis
- Apoptosis differs from necrosis: - by loss of membrane integrity
  - by enzymatic digestion of cells
  - by leak of cellular content

A/Phisiological apoptosis

- Embriogenesis – organogenesis, developmental involution
- Hormon deprivation – endometrial cell breakdown in menstrual cycle
- Cell loss in proliferating cell population – intestinal epithelia
- Elimination of self-reactive lymphocytes

B/ Pathological apoptosis

1. DNA damage
   - Radiation, chemotherapy, high temperature may damage DNA
   - If repair mechanism cannot cope – elemination by apoptosis
   - Apoptosis is a better alternative for the cell than mutation and malignant transformation

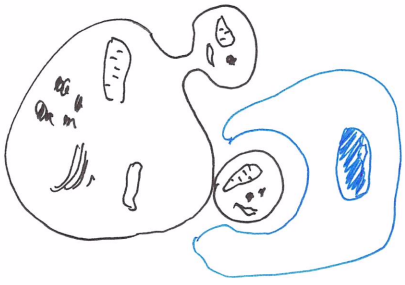
2. Accumulation of misfolded proteins

3. Cell injury in infection
   - virus infected cells are lossed by apoptosis

4. Pathologic atrophy
   - duct obstruction of pancreas, cysticus ect.

Morphology:

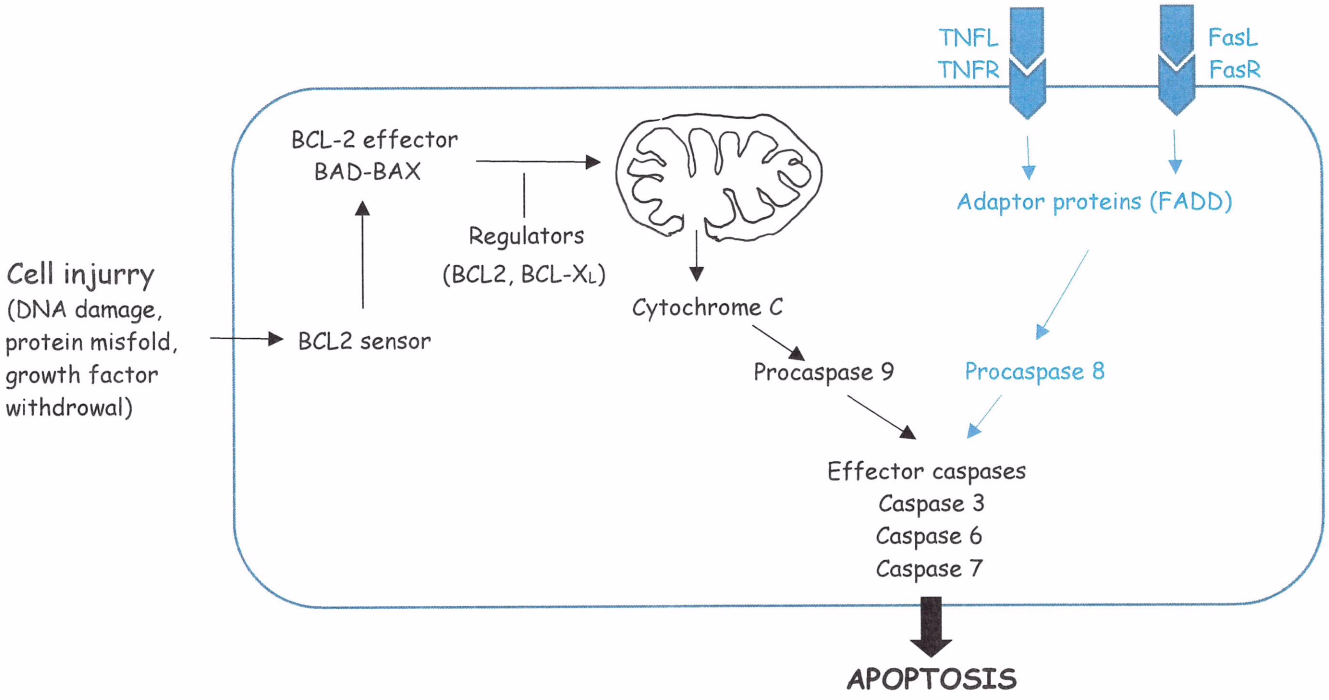
- Round or oval masses with eosinophilic cytoplasm
- Chromatin condensation and aggregation, karyorrhexis – DNA fragmantation
- Apoptotic bodies – membrane bound vesicules – cytoplasmic organella packed
- Apoptotic cells removed by phagocytosis



Mechanism:
- Activation of caspases – cystein proteases cleave after asparagic acid
- Caspases – activate enzymes by clavage – DNA degradation
  - nucleoprotein degradation
  - cytosceletal degradation

A/ Mitochondrial pathway (intrinsic)
- Mitochondrial proteins inducing apoptosis
- Main protein is the release of cytochrome C
- Controlled by BCL-2 family members (~ 20 members)

B/ Death receptor pathway (extrinsic)
- Death receptors TNF, Fas
- Fas ligand (FasL) expressd on activated T-lymphocytes



AUTOPHAGIA

- Autodigestion of cell components – survival mechanism of starving cells
- Autophag vacuolum: ER + lysosome – autophagolysosoma
- Autophagia may remove missforded proteins
- Autophagia may ended up to apoptosis