THE CONCEPT OF DEATH

Seneca: Death is a law, not a punishment

- The concept of death depends on the current scientific conception of medicine and the perception of a given society.

- Antiquity - Death comes after the last breath
- Middle Ages - Death comes with the last heartbeat
- Descartes (1596-1650) – „The soul is somewhere in the brain"

Legal interpretation of death

Death is a biological event, the moment when the coherent functioning of a living organism ceases, when the irreversible disintegration of the organism begins due to the complete cessation of respiration, circulation, and brain function.

Clinical death

In the state of clinical death, life phenomena (circulation, respiration, brain function) are temporarily paused.

Brain death

Brain death is a damage to the brain to such an extent that it is no longer able to consciously control the body.

Biological death

In the state of biological death, the body is irreversible and severely damaged, not viable.

POSTMORTEM CHANGES

I. Early postmortem changes

1. Algor mortis:
   - Chilling of the body
   - Depends on the temperature of the enviroment
   - Complete by 8-17 h
2. Palor mortis:
   - Do to sedimentation of blood from the upper part of the body to lower parts
3. Rigor mortis:
   - Rigidity of the muscles
   - Appears after 2-4 h of death
   - Nysten law: head- face – neck – thorax – abdomen ect.
   - Completes by 6-8 h
   - Disappears by 20-48 h
   - Due to post mortem fermentation of ATP
4. Livor mortis:
   A/ Hypostatic
   - Accumulation of blood in the lower parts of the body
   - Disappears in exposure of pressure
   - Alters in turning of the cadaver

   B/ Imbibition
   - Post mortem intravascular hemolysis
   - Hb infiltrates surrounding tissues
5. Crusta mortis:
   - Post mortem coagulation of blood
   - Appears after 4h of death
   - Devided into two layers: upper plasma, lower sedimented blood
   - In pathologic conditions: jaundice – yellow
     inflammation – greyish
     sepsis – brownish
   - Differential diagnosis of crusta mortis - thrombus

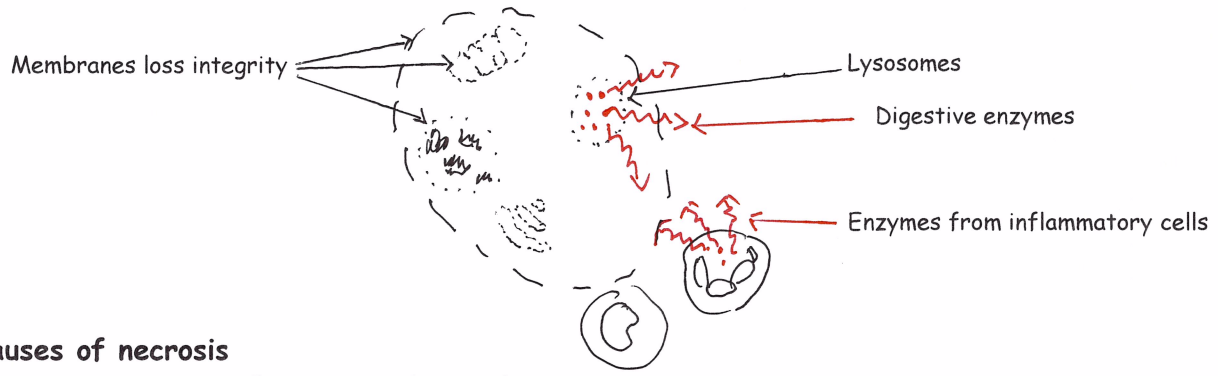
	Crusta mortis	Thrombus
Surface	shiny, slipery	opaque
Consistence	elastic	fragile
Connection to vascular vall	no adhesion	adhesion to vascular wall

II. Late postmortal changes

1. Exsiccatio postmortalis – Drying of the cadaver
2. Maceratio – Desquamation of the surface layers of cells in fluid content cavities
3. Gastromalatia – Autodigestion
4. Pseudomelanosis – SH_2 reaction with Hb – sulphur HB – blueish pigmentation
5. Adipocera – Waxy change (K^+, Na^+ reakts with fatty acids)
6. Mummification – High temperature, low humidity blocks bacterial fermentation

NECROSIS

- Necrosis is a circumscribed death of cells, tissues or organs in a living body.
- Cellular membranes fall apart and cellular enzymes leak out
- Necrosis iniciate local inflammation – eliminate cell denris



Causes of necrosis

1. O_2 deprivation (hypoxia, ischaemia)
2. Chemical agents
3. Infective agents
4. Nutritional imbalance (vit. insuff., obesity)
5. Physical agents

Morphology of necrosis

1. Cytoplasmic changes
   - increased eosinophilia
     - coagulated enzymes binds eosin
     - reduced cytoplasmic RNA – reduce basophilia
   - glassy homogenous
     - loss of glycogene particules
   - vacuolated cytoplasm
     - digested cytoplasmic organells
     - dilated mitochondria
   - mielin figures
     - degraded cellular membranes
     - dissolved lipoproteins uptake water
2. Nuclear changes
   - pycnosis
   - karyorrhexis
   - karyolysis

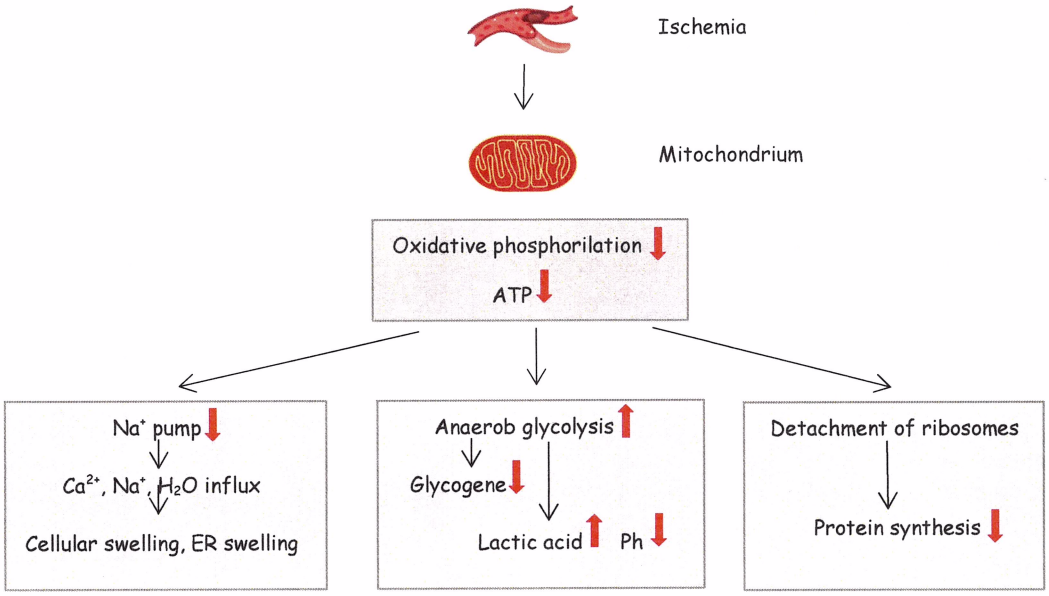
3. Fate of necrotic cells
   - persist for time
   - digested and disappear
   - replaced by myelin figure
   - calcified

Necro enzymes (toponin, alkaline phosphatase)

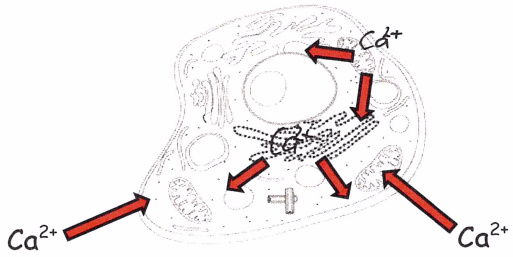
Molecular mechanism of necrosis

- The biochemical mechanism is complex and interconnected
- Difficult to point to a specific molecular alterarion
- Depending on A/ Type, duration and severity of injurry
  B/ Type of the injuried cells (adaptibility, genetic make up)
  - leg, myocardium, brain
  - citochrome P450 isoenzymes polymorphism – free radicals
  - glycogene content of hepatocytes – vulnerability

1. Hypoxia and ischaemia – Damage of mitochondria



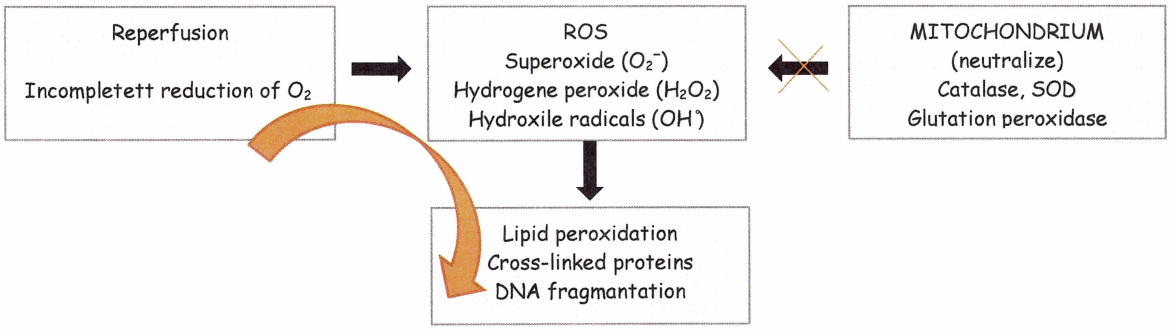
2. Ca^{2+} influx – point of no return
   - Cytosolic Ca^{2+} 10.000 times lower than extracellular
   - Maintained by ATP dependent Ca transporter
   - Intracellular Ca^{2+} sequestred in mitochondria and ER
   - Ischaemia, toxins – influx of extracellular Ca^{2+}
     – release intracellular Ca^{2+}



- Cytosolic Ca^{2+} acticates enzymes - phospholipase – membrane damage
  - proteases – cytosceleton digestion
  - endonucleases – DNA degradation
  - ATPases – ATP depletion

3. <u>Ischaemia – reperfusion injury</u>
   - oxidative stress
   - in case of restoration of blood flow to ischaemic but viabile tissues

   A/ Increase ROS



   B/ Increase influx of leukocytes – generate ROS

   C/ Reperfusion of plasma proteins – C' activation generate cell lysis

4. <u>Cell injurry by toxins</u>

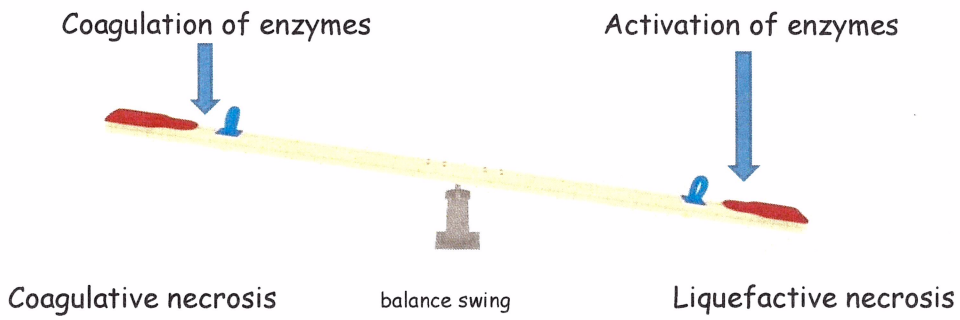
   A/ Direct-acting toxins
   - Act directly with molecules and organells
   - Mercuric chloride – blocks ATP dependent transporters
   - Most chemopherapeutic drugs

   B/ Latent toxins
   - First must be converted to reactive metabolites
   - The convertion mosly made by citochrome P450
   - Analgetic acetaminophen – phenacetin

<u>Pathological typeas of necrosis</u>

1. Coagulative necrosis
   - Basic tissue architectures (cell outlines) are preserved for several days
   - The affected tissue takes a firm texture
   - The proteins and enzymes are denaturated – no autolysis
   - Microscopically eosinophilic cells (cellular acidosis)
   - Necrotic cells removed by heterolysis and phagocytosis of inflammatory cells

2. Liquefactive necrosis
   - Can be the result of autolysis or heterolysis of inflammatory cells
   - Cells do not preserve outlines
   - Cells go through liquefaction – complete digestion of cells
   - Primary autolysis – brain infarct
   - Secondary heterolysis – all necrotic (coagulative) cells



3. Gangrenous necrosis
   - Not a distinct type – coagulative necrosis
   - Clinically applied for extremities
   - Dry gangrena – mumification of necrotis tissue
   - Wet gangrena – necrotic tissue superinposed by bacterial infection

4. Caseous necrosis
   - Cells do not preserve outlines
   - Cells go through coagulation (no cellular outlines are preserved)
   - Inflammatory border (Langhans-type giant cells, epitheloid cells, lymphocytes)

5. Fat necrosis
   - Result of pancreatitis
   - Release of activated pancreatic enzymes
   - Enzymatic digestion of membranes – triglicerids + fatty acids
   - Fatty acids combine Ca^{2+} - fat saponification

6. Fibrinoid necrosis
   - Not a separate necrosis type
   - Associated with immunreaction – usually in vessels
   - Immuncomplexes (Ag, Ab, C') + fibrin likage
   - Fibrinoid = fibrin like