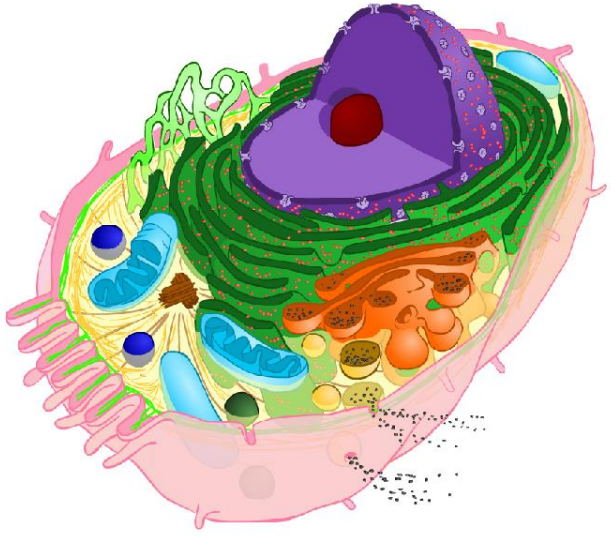
Cell injury



MUDr. Jan Balko, Ph.D.

Department of Pathology and Molecular Medicine,
2nd Faculty of Medicine, Charles University in Prague and
Motol University Hospital

Cell injury

- different behavior of the cell damaged by **pathologic influence**
- there are several responses according to the severity of the cause

dystrophy → atrophy → necrosis → death

Dystrophy

- *dystrophia*, "degeneration"
- the **mildest** level of cell injury
- **hereditary / acquired metabolism disorder**
- results in **improper nutrition** of the affected cell (*dys-* + *-trophia*), followed by a**ccumulation** of metabolites (intra- or extracellular)

dystrophy → **atrophy** → **necrosis** → **death**

Dystrophy

- metabolic disorders are classified according to **biochemistry**

1) metabolism of proteins
2) metabolism of sugars (saccharides)
3) metabolism of lipides
4) metabolism of water
5) metabolism of minerals

- topics of the **Metabolic disorders** lectures

Atrophy

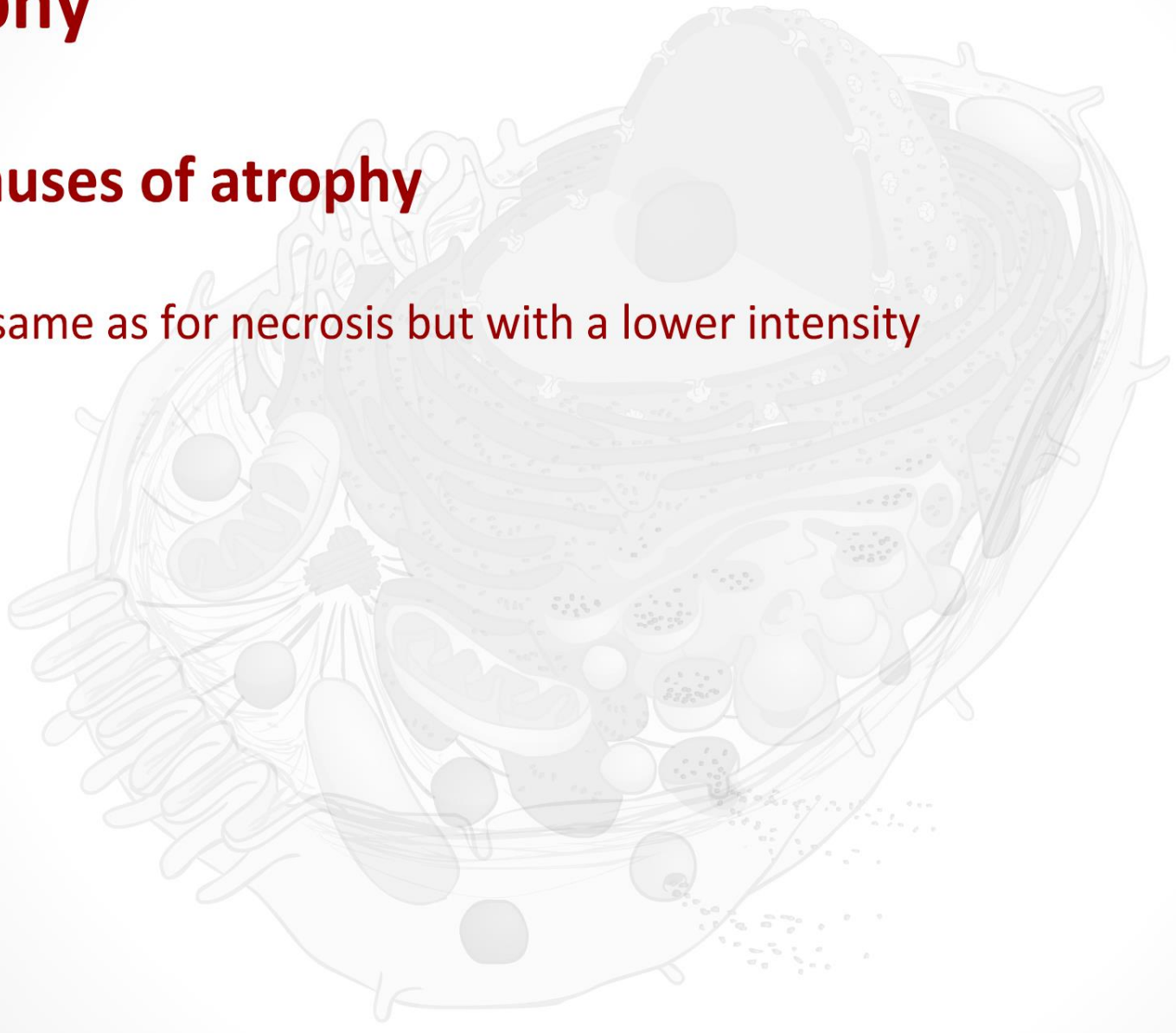
- *atrophia*
- **medium** level of cell injury (between dystrophy and necrosis)
  - closer to dystrophy
- reabsorption and breakdown of cells (size of organs is **reduced**)
  - mainly parenchymatous organs

dystrophy → **atrophy** → necrosis → death

Atrophy

Causes of atrophy

- same as for necrosis but with a lower intensity



Atrophy

1) senile
- "physiologic" decrease of muscle and bone volume during aging

2) involutional
- involution of thymus, uterus and breast after pregnancy, embryonal

3) alimentary
- malnutrition, tumour cachexy because of inappetence

4) pressure
- benign tumours, aneurysm, hydronephrosis

5) neurogenic
- peripheral palsy

6) inactivity
- muscle atrophy

Atrophy

- the whole organism can undergo atrophy and result in **marasmus**
  - metabolism disruption consequenting in a loss of neural and hormonal coordination of the body
  - fat tissue → lymphoid tissue → muscles → CNS (preserved)

Atrophy

- **microscopic** finding is discreet
  - higher basophilia, loss of fat and glycogen; lipofuscin, pyknosis

Atrophy

Types of atrophy

1) Simple

- decrease in the **volume** of cells (opposite to hypertrophy)
  - liver, muscles, myocardium...
  - e.g. *atrophia fusca* (brown atrophy of lungs, liver, heart)

2) Numeral

- decrease in the **number** of cells (opposite to hyperplasia)
  - *atrophia lipomatosa* (pancreas, heart, muscle = pseudohypertrophia)
  - *atrophia fibrosa* (bone marrow failure)

- **hypotrophy** = congenital general atrophy (hypotrophic newborn)
- **hypoplasia** = congenital bellow-average numer of cells within organ

Necrosis

- *necrosis*
- **the most severe ireversible** cell injury
- type of cell death (partial **death** of the organism *intra vitam*)
- destruction affects singe cells, tissues or the whole organ
  - can be selective (prox. renal tubules after mercury poisoning)

dystrophy → **atrophy** → **necrosis** → **death**

Necrosis

Causes of necrosis

- whole spectrum of causes (**high intensity** of affection is necessary)
- denaturation of proteins (loss of tertial structure) and **proteolysis**

Necrosis

1) anoxia
- loss of oxygen supply (follows hypoxy)

2) ischemia
- loss of blood supply (follows oligemia) → **infarct** (infarction)

3) physical
- trauma, thermal damage, electrical, RTG and gamma radiation

4) chemical
- hyperkalemia, parathormon, pancreatic enzymes, poisoning

5) biological
- bacterias, viruses, mycotic infection, parasites

Necrosis

Microscopic findings

- **cytoplasm** looses basophilia and becomes deeply eosinophilic
- **nucleus** degenerates (*pyknosis*, parietal hyperchromasia) and undergoes decay (*karyorhexis*, *karyolysis*)
- tissue is replaced with eosinophilic amorphous material

- **demarcation** from the surrounding tissue and **inflammaion**
- in time the necrosis **sequestrates** (separation), or undergoes **resorption**, followed by **reparation**

+ sometimes other changes can occur (e.g. calcification)

Necrosis

Types of necrosis

- types of necrosis designated according to it's **macroscopy**
- **response** of the surrounding tissue determines the image
  - it depends which organ is affected + what is the cause of necrosis

Necrosis

1) Simple necrosis

- only **1 tissue type** is affected
- **macroscopy** is discreet, usually consistency and colour is changed (e.g. fragile brownish muscles)
- muscle ischemy, mild burn of epidermis, mercury poisoning

Necrosis

2) Coagulative necrosis

- affects **protein-rich** organs
- **macroscopy** = gelatinous dry yellowish edematous deposits
  (its shape depends on blood supply = spheric / lamellar in heart)
- reparation results in a formation of **scar** (grey, from periphery)

Zenker's necrosis

- glassy or waxy appearence of the muscles (flu, typhus, tetanus)

Caseous necrosis

- special subtype caused by 4th type of hypersensitivity (TBC)
- **macroscopy** = clumped cheese-like deposites (white, friable)
- **microscopy** = basophilic debris, granulomatous inflammation

Necrosis

3) Colliquative (liquefactive) necrosis

- affects **water-rich** organs (brain, pancreas, or abscess anywhere)
- **macroscopy** = necrotic tissue forms viscous liquid mass
  - **CAVE** liquefactification in brain is secondary due to liquor
- reparation results in formation of **pseudocyst**

Necrosis

4) Hemorrhagic necrosis

- secondary **bleeding** into necrotis mass due to reflux of the blood
  - **collaterals** (lungs)
  - **infarsation** (blockage of venous drainage, e.g. intestines)
  - **reperfusion** (revascularisation of MI)

- **macroscopy** = necrotic tissue is soaked with bloood
  - lung embolism, infarsation of intestine, HSV encephalitis, Waterhouse-Fridrichsen syndrome...

- reparation results in a formation of **scar** tissue

Necrosis

5) Fibrinoid necrosis

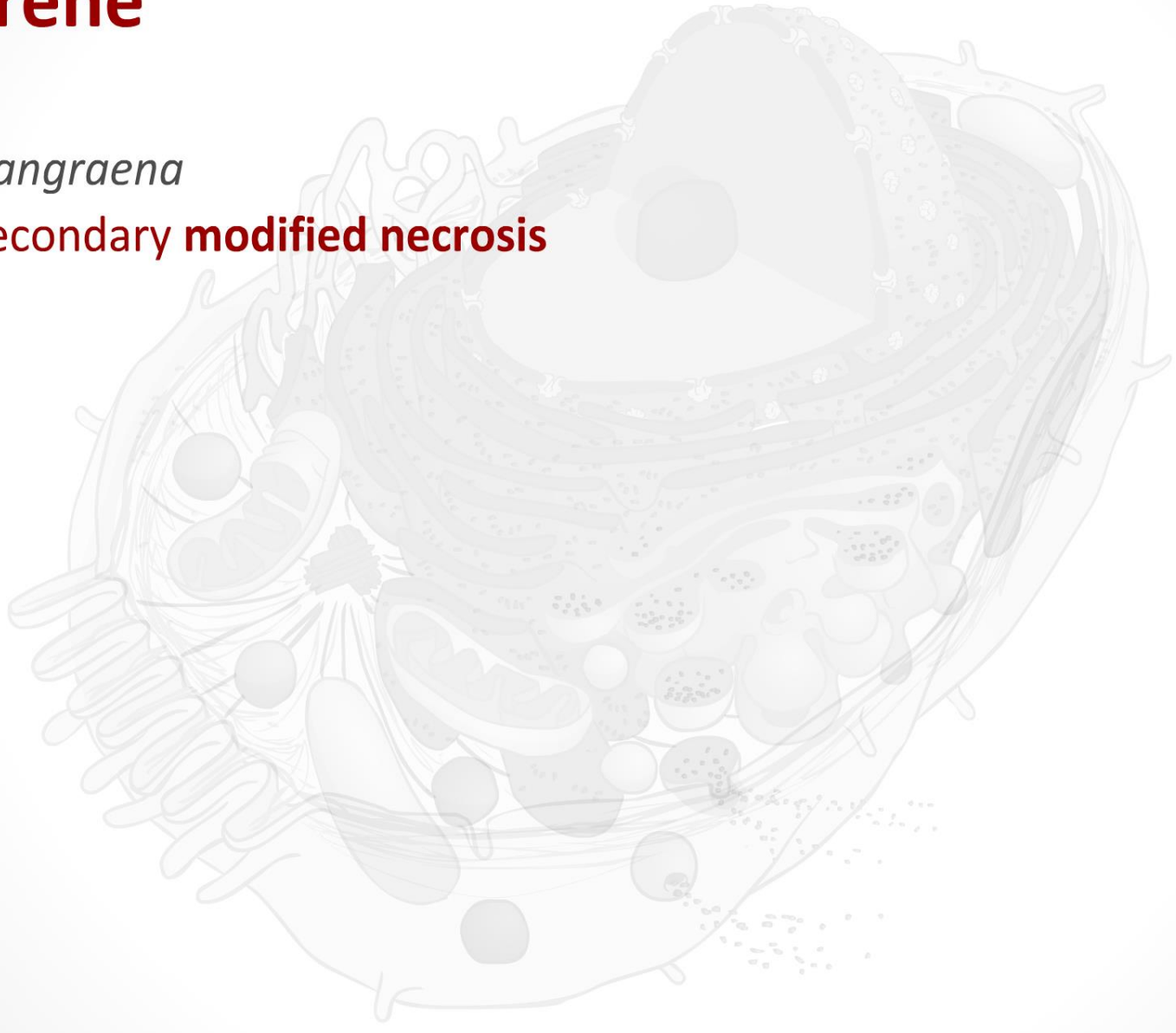
- caused by **immune complex-mediated vascular damage**
  - SLE, scleriodermia, vasculitis, RA, malignant nephrosclerosis...

- **macroscopy** = invisible (just complication can be noticeable)
  - aneurysms, endocardial or joint nodules...

- **microscopy** true fibrin deposits within the vessel wall
  - "fibrinoid" (= fibrin) is eosinophilic amorphous material (H&E), stained red in trichrome staining

Gangrene

- *gangraena*
- secondary **modified necrosis**



Gangrene

1) Dry gangrene

- mummification
- necrosis is modified by **drying out** (ischemy is usually causative)
  - limited oxygen limits putrefication (bacteria fail to survive)

- **macroscopy** = dry dark reddish-black shrunked part of the body
  - sharp demarcation with a possibility of auto-amputation
  - Hb oxygenation leads to the development od hematin (black)

- e.g. peripheral artery disease of the limb, umbilical cord

Gangrene

2) Wet gangrene

- *gangraena humida, sphacelus*
- necrosis modified by **bacteria**

- **macrocopy** = swollen putrified green-greyish mass emiting bad smell
  - thriving bacteria produce hydrogen sulfide

- noma (Fusospirilosis), Vincent-Plaut's angina, stercoral peritonitis, Fournier's gangrene, acute appendicitis, sacral decubitus, lung gangrene, "diabetic foot"...

Gangrene

3) Gas gangrene

- *gangraena emphysematosa*
- necrosis modified by **gas-producing bacteria** (*Cl. perfringens*)

- **macroscopy** = rapid spreading, massive edema, gas bubbles within the tissue (methane)

Apoptosis

- **programmed** cell death ("induced suicide of the cell")
  - 2nd type of the cell death next to the necrosis
  - there is **no reaction** of the surrounding tissue

- necessary part of **tissue homeostasis** (opposite to cell division)
  - embryonal development = separationn of fingers and toes etc.
  - disposal of dangerous cells = tumour cells, virus infected cells...
  - disposal of old cells = proliferating tissues (epithelium, hepatocytes, lymphocytes)

Apoptosis

Process of apoptosis

- highly **regulated** and controlled process

- divided into several **phases**

- key role of the tumour suppresor gene ***p53***
  - "the gurdian of the genome"
  - non-mutaded form allows natural destruction of cells with irreversibly damaged DNA

Apoptosis

Process of apoptosis

1) Initial phase
- ligand transfered to the "death receptors" + activation of caspases

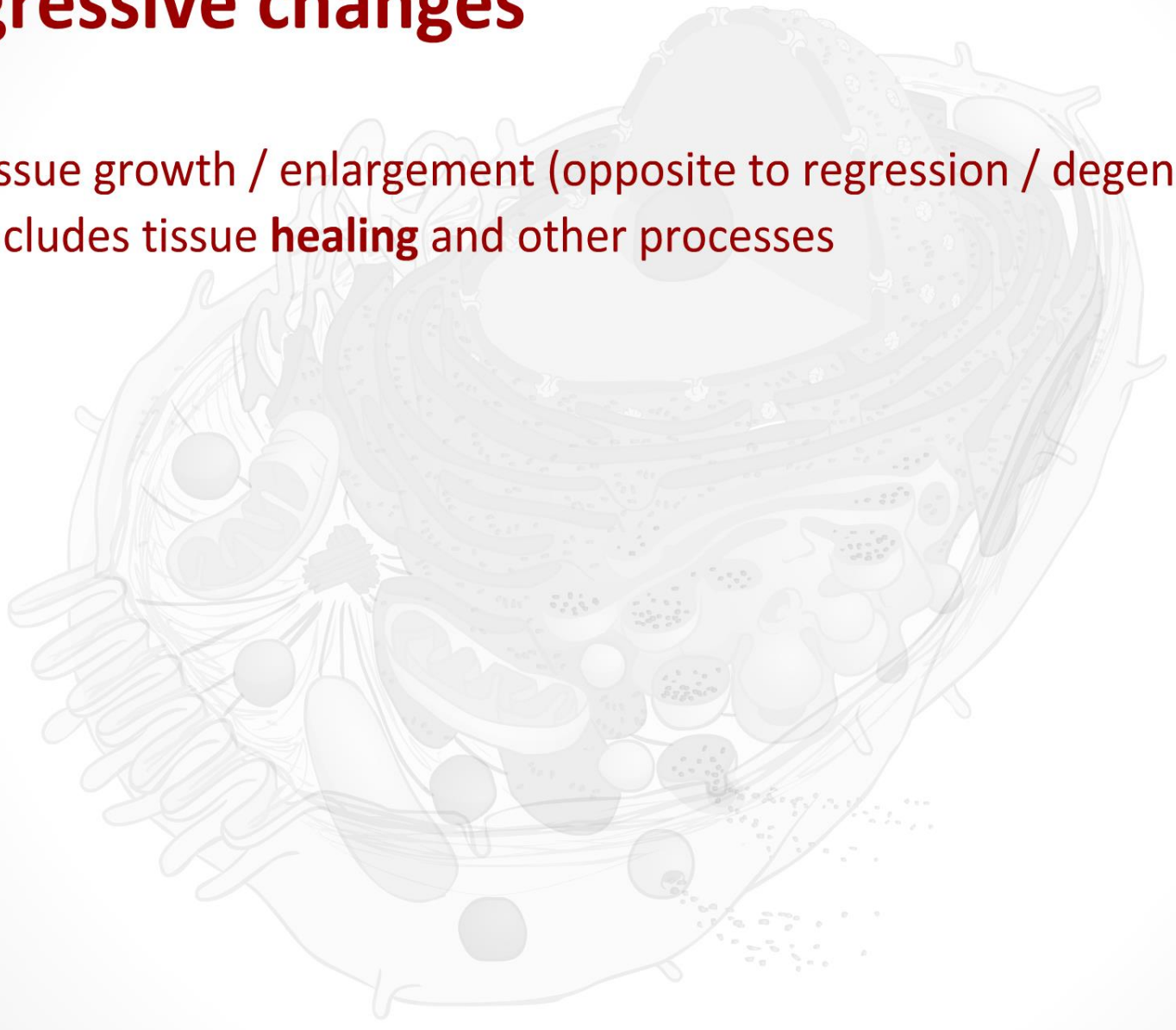
2) Executive phase
- caspases evocate cell death
- cell **shrinkage** and **chromatin condensation** (pyknosis, or parietal chromasia) → **karyorhexis** (selective DNA fragmentation) → **eosinophilia** of the cytoplasm (membranes stay intact) → blebbing with formation of **apoptotic bodies** → **phagocytosis**

Apoptosis

	Necrosis	Apoptosis
Extension	large (area of the tiussue)	sparse cells
Cell volume	increases	decreases (shrinkage)
Membrane	rupture	intact
Nucleus	decay of the envolope and DNA	DNA condensation and fragmentation
Mitochondria	bulging	intact
Cell integrity	decay	apoptotic bodies
Reaction of the surrounding tissue	inflammation	phagocytosis

"Progressive changes"

- tissue growth / enlargement (opposite to regression / degeneration)
- includes tissue **healing** and other processes



"Progressive changes"

1) Hypertrophy

- *hypertrophia*
- organ **enlargement** due to the increase of the **volume** of cells
- increased synthesis of cell components (**without** cell division)
- mainly "postmitotic cells" (cardiomyocytes, skeletal muscle fibres)

"Progressive changes"

1) Hypertrophy

1) physiologic

- functional (heart, muscles), hormonal (pregnancy)

2) pathologic

- ineffective work of the cells with high metabolic demand
- Cor hypertonicum and pulmonale, valvular heart disease, morbus Hirschprung, trabeculasion of smooth muscle of the urinary bladder

"Progressive changes"

2) Hyperplasia

- organ **enlargement** due to the **proliferation** of cells
- increase of the number of the cells (cell division)
- **"labile"** (epitehelium, mucosal cells) or **"stabile"** cells (parenchyma)
- may be in combination with hypertrophy

"Progressive changes"

2) Hyperplasia

1) physiologic

- lymp nodes activation, hormonal (breast in puberty, uterus during pregnancy), liver egeneration, agenesis of the lung, kidney resection

2) pathologic

- hyperplasia of the prostate or endometrium

"Progressive changes"

3) Metaplasia

- **conversion** in cell type
- reversible **replacement** of differenciated tissue with another one
- usually occures in connection with cronic inflammation, mechanical irritation oravitaminosis A...

- ranges from bare **modulation** to **"reprogrammed"** tissue
- epithelial (leukoplakia, squamous or intestinal metaplasia), mesenchymal (ossification, extramedullar hematopoiesis)

- risk of developing **malignancy**

"Progressive changes"

4) Dysplasia

- change in cell phenotype (**precancerous** condition)
- genetic aberrations in dysplastic cells
- several levels of dysplasia to the point of **carcinoma in situ** (non-invasive ca)
- caused by radiation, viruses (HPV)...

CAVE

- **organ dysplasia** stands for pathologic development of the organ
- e.g. Tuberous sclerosis (aglomerates of ganglion cells in brain cortex without hexalaminar structure)

Literature

- POVÝŠIL, C.; ŠTEINER, I. Obecná patologie, 1. vydání. Nakladatelství galén, 2001

- STEJSKAL, J. Obecná patologie v poznámkách, 2. vydání. 2001

- BEDNÁŘ, B.; MIŘEJOVSKÝ, P., Obecná patololgie. 1994

- www.wikipedia.com