Inflammation, healing and cellular adaptations

Dentistry

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Inflammation

„Stereotypical, defensive reaction of organism that follows the tissue injury with the aim to eliminate the pathogenic insult and remove the injured tissue components“
Inflammation

The aim

• To prevent the dissemination and spreading of pathogenic factor – containing the locus
• To dilute and eliminate the pathogenic factor
• To prepare the tissue for reparation
Historical morphological characteristics

- **Calor (warmth)** – local increase of temperature
- **Dolor (pain)**
- **Rubor (redness)** – result of vasodilatation
- **Tumor (edema)** – increased permeability of vessels
- **Functio laesa (impaired physiological function)**
Stages of inflammation

1. Vascular changes
   1. Hemodynamic changes (initial vasoconstriction → prolonged vasodilatation) → fluid exudation
   2. Increased vascular permeability (due to contraction and/or damage to endothelial cells) → fluid exudation

2. Cellular changes
   1. Leukocytic exudation (slower blood flow allows blood cells to marginate to a close vicinity of endothelial cells, eventually they pass through them and the basal layer into interstitial space)
   2. Phagocytosis (activated leukocytes ingest bacteria, fungi, cellular debris, ...)


Classification of inflammation

- according to:
  - duration (fulminant, acute, subacute, chronic)
  - reaction of organism to ethiological agent (norm-, hypo-, hyperergic)
  - ethiology (phys., chem., biol.)
  - localisation (superficial / deep)
  - morphologic changes in tissue
Classification of inflammation according to the main components

1. **Alterative inflammation** – predominant tissue damage (regressive changes or necrosis)

2. **Exsudative inflammation** – changes of extracellular matrix caused by liquid and cellular components from blood vessels
   - serous
   - catarrhal (mucous)
   - fibrinous
   - purulent
   - gangrenous
   - haemorrhagic

3. **Proliferative inflammation** – with increase of fibrous connective tissue
   - reparation of acute inflammation
   - chronic inflammation
Serous inflammation

- effusion of clear, protein poor, serous fluid
- healing (resorption)
  - serous membrane – viruses, autoimmune diseases, tumors
  - mucous membr. (catarrhal inflam.) + mucus
  - skin (blisters)
  - deep tissue – allergic
Catarrhal bronchitis (162) with purulent superinfection

- catarrhal (mucinuous) inflammation - serous inflammation on mucous membranes
  - production of serous fluid $\rightarrow$ mucus in bronchus with desquamated epithelial cells and granulocytes
  - submucosal hyperemia
  - fibrin is not present
  - mucosa is swollen and mucous cells are activated
  - 90% viruses, 10% bacteria
Catarrhal bronchitis

Mucosa of the bronchi is reddened, with edema
Mucosa of the bronchi is reddened, edematous, with mucus and pus in the lumen.
Bronchial lumen is filled with fluid with numerous neutrophils
Catarrhal bronchitis, HE
Hyperemia of adjacent vessels
Mucus overproduction
Bronchial lumen is filled with fluid with numerous neutrophils
Catarrhal bronchitis, HE
Fibrinous inflammation

- fibrinous exudate (↑ vascular permeability)
- healing (organisation with granulation tissue / fibrinolysis and resorption)

- serous membranes – microorganisms, uremia
- mucous membranes, skin (pseudomembranous) + pseudomembranes
- deep tissue – crupous (lobar) pneumonia
Fibrinous pericarditis (11)

- Exudative fibrinous inflammation in the pericardial sack

- “hairy pericardium” – pericardium covered in fibres formed from exsudated fibrin – weak adhesions

- Infections, uremia, infarction
The surface of the heart and pericardial sack is connected through pink-red fibers, pericardium is red and opaque.
The surface of the heart is covered in thick layer of opaque pink-red fibrinous matter.
Fibrinous pericarditis, HE

- Thick layer of bright eosinophilic fibrin material on the surface of pericardium
- Focal edema of deeper tissues with acute inflammatory infiltrate (neutrophils)
- Hyperemia
Hyperemia

Fibrinous pericarditis, HE
Pseudomembranous inflammation (88)

- exsudative fibrinous inflammation with necrosis
- certain types of bacteria that produce strong exotoxins – cause necrosis of surface layer of mucosa
- **pseudomembranes** – fibrin, necrotic tissue and inflammatory cells

- Diphteria, bacillar dysenteria, staphylococcal pseudomembranous enteritis
Psedomembranous colitis

- antibiotic – associated colitis (broad spectrum ATB)
- Clostridium difficile

- diarrhea with mucus and blood, fever, intense abdominal pain after a period of antibiotic treatment
Thick layer of greenish pseudomembrane firmly attached to subepithelial tissue
Pseudomembrane in trachea, HE
Pseudomembrane in trachea, HE

Dense acute inflammatory infiltrate in subepithelial tissues

Hyperemia

Pseudomembrane
Purulent (suppurative) inflammation

- Leu produce enzymes that liquify affected tissues
- PUS - consists of neutrophils, dead cells and fluid

- healing (resorption/chron.inflam. – pyogennic membrane)
  - serous membranes – plaques of pus ... empyema
  - mucous membranes (purulent catarrhal inflammation)
  - skin - folliculitis
  - deep tissue - diffuse (phlegmona)
    - localised (abscess)
Appendicitis (81)

- most common abdominal surgical emergency (peak incidence 10-30y)

- obstruction of appendical orifice (feaces, parasites, Tu, foreign bodies, ...)
- secretion → distension → venostasis → ischaemia → ulceration of mucosa → invasion of bacteria

- exsudation of granulocytes into the lumen, interstitium and into the peritoneum
- lymphatic tissue activation

- perforation → diffuse acute peritonitis
Numerous neutrophils inside lumen and through the entire wall

Lymphatic follicle

Appendicitis, HE
Neutrophils

Appendicitis, HE
Neutrophils in muscular layer

Appendicitis, HE
Transmural inflammatory response reaching the peritoneal surface

Appendicitis, HE
Cerebral abscess (14)

- Exsudative purulent inflammation
- Intensive tissue injury by pathological agent without significant propagation and spreading (e.g. Staphylococcus)

- ways of spreading:
  1. local extension from adjacent foci
  2. hematogenous spread
  3. direct implantation
Cerebral abscess (14)

- Leu lyse the tissue (proteolytical enzymes) → liquefactive necrosis
- Abscess cavity is formed

- in other organs and tissues the abscess is bordered by granulation tissue and a pyogenous membrane is formed
Focus of well defined collection of acute inflammatory infiltrate
Clump of bacteria among neutrophils

Cerebral abscess, HE
Influenza – trachea, lungs (213)

• Nonspecific, nonpurulent viral inflammation

• **Trachea and bronchi**
  
  – necrosis of *epithelium* (*dry cough at first*)
  – hyperaemia
  – *endoteliulm* function impairment
  – exudation of plasma and Ery
  – infiltration with Ly, Ma and plasma cells
  – squamous epithelial *metaplasia* in bronchi
  – *mucin* production (*productive cough later*)
  – necrotic tissue is good soil for bacterial growth – *bacterial superinfection* → infiltrate becomes mixed (*Neu*)
Influenza – trachea, lungs

- **Lungs**
  - interstitial pneumonia
  - lymphocytic infiltration
  - edema and hyperemia of interstitium
  - alveolar oedema
  - alveolar bleeding
  - hyaline membranes
Mucosal hyperemia

Influenza - trachea
Influenza – trachea, HE

Necrosis of epithelium

Hyperemia

Mucus overproduction
Hyperemia

Mucus overproduction

Neutrophils

Influenza – trachea, HE
Influenza – lungs, HE

Severe lung edema
Influenza – lungs, HE

Formation of hyaline membranes

Lymphocytes in alveolar septs
Parasitic inflammation

Oxyuriasis (144)

Enterobius vermicularis (pinworm)

- ingestion of pinworm eggs (hands, food, water)
- hatches in duodenum, larvae migrate towards colon
- adults mate in ileum
- females settle in i, c, a, ca and attach to the mucosa, their body becomes filled with eggs
- migrate through colon, emerge from the anus and lays eggs
- these are transmitted to other surfaces
Oxyuriasis, HE

Feces

Pinworms
Oxyuriasis, HE

- Intestine
- Eggs
- Alae
Granulomatous inflammation

- chronic specific inflammation
- **ethiology**: mycobacteria, foreign bodies, rheumatoid nodules...

**formation of granulomas:**
- macrophages
  - epitheloid cells
  - multinucleated giant cells
    (Langhans type, foreign body giant cells)
- lymphocytes
- fibrosis at the periphery of granuloma
causative agent: *M. tuberculosis hominis / bovis / avium*... (acid fast mo, strict aerobe – thrives best in tissues with high oxygen concentration)

specific inflammation: A/E/P

**miliary TBC** = chronic granulomatous i. (P)

formation of specific **granulomas** = **TUBERCULES**

epitheloid cells, Langhans cells (Ly, plasma cells, fibrobl.) (HARD)

caseous necrosis (SOFT)

lungs are most commonly affected by TBC

2 types:
1. **PRIMARY TBC** – in patients not previously infected / immunised
2. **SECONDARY TBC** – in patients previously infected / immunised
PRIMARY TBC

- microorganisms enter the organism (aeroin., inn.)
- form **PRIMARY COMPLEX:**
  1. pulmonary component (tbc pneu)
  2. lymphatic vessel component (Ma with bacilli)
  3. affected mediastinal lymph node

- lesion **heals** by fibrosis (calcification) or
- lesion **progresses** into PPT – spread by bronchi or
- bacilli enter vessels and **spread** to organs = PMT
SECONDARY TBC

- occurs in reinfection / reactivation of PC (in lowered resistance...)
- dormant bacilli are activated
- spread hematogenously to apex of the lungs
- form lesions with caseous n.
- mo can be spread also to other organs = SMT
Multiple granulomas affecting several lobes

Lung tuberculosis (15)
Granuloma with central caseous necrosis

Lung tuberculosis, HE
Lung tuberculosis, HE

Granuloma with central caseous necrosis

Giant multinucleated cell
Lung tuberculosis, HE

- Epitheloid cells
- Giant multinucleated cell of Langhans type
- Lymphocytes
Giant multinucleated cell of Langhans type

Lung tuberculosis, HE
Lung tuberculosis, Ziehl-Neelsen
Healing

• Body response to injury – to restore normal structure and function

• Regeneration
  – Replacement of damaged tissue by equivalent tissue, proliferation of parenchymal cells

• Repair
  – Replacement of damaged tissue by second rate tissue, proliferation of connective tissue elements → fibrosis, scar formation

- mostly combination of both
Regeneration

– replacement of damaged tissue by equivalent tissue
Regeneration

• According to regeneration capacity the cells are classified:
  – **Unstable** – regularly replaced: hematopoiesis, epithelia (GIT, resp.), axon
  – **Stable** – renewed only if tissue is damaged: glandular epithelium, proximal canaliculi, vascular smooth muscle
  – **Permanent** – ganglion cells, crosst striated muscle, cmc
Repair

- replacement of damaged tissue by second rate tissue (fibrous)
Repair

1. **Granulation tissue formation**
2. **Contraction of wounds**

- **Wound healing**
  - primary (per primam intentionem)
  - secondary (per secundam intentionem)
- **Organisation of hematoma and thrombus**
- **Healing of bone fracture**
- **Healing of foreign bodies**
- **Organisation of fibrinous exudates**
1. GRANULATION TISSUE FORMATION

3 phases:
• **PHASE OF INFLAMMATION** – exsudation of plasma and Leu
• **PHASE OF CLEARANCE** – cell debris, Ery and necrotic tissue is cleared by Ma
• **PHASE OF GRANULATION TISSUE INGROWTH**
  • **ANGIOGENESIS** – formation of new blood vessels from margins of injured ones
  • **FIBROGENESIS** – production of fibrous tissue by fibroblasts that migrate to previously injured area

2. WOUND CONTRACTION
- size of the wound is reduced by 80% of it’s original size
- results in rapid healing
Wound healing

• combination of regeneration and repair
• primary / secondary union

• Primary (wound clean, without infection, surgically closed, without much loss of tissue)
• Secondary (wound opened, infected, large tissue defect → slow healing, larger scars)
Healing of fractured bone

- fractured bone
Healing of fractured bone

- bleeding from injured vessels -> hematoma
- local *inflammatory* response (exs. of fibrin, Leu)
- clearance (osteoclasts) -> organisation of hematoma (from periost) -> fr. *connected*
Healing of fractured bone

- formation of woven bone and cartilage = PROCALLUS / FIBROUS CALLUS
Healing of fractured bone

- procallus is a framework for ossification
- **OSSEUS CALLUS** (from lamellar bone) is formed
Healing of fractured bone

- osseus callus is remodeled by osteoblasts and osteoclasts = **DEFINITIVE CALLUS** is formed
Granulation tissue after myocardial infarction, HE

Capillaries in fibrous tissue with numerous fibroblasts
Recanalised thrombus, HE

Formation of new lumen inside the thrombus, lined by endothelium

Vascular lumen completely obstructed with thrombus
Foreign body granuloma (19)
Granuloma around foreign body, HE

Foreign body type giant cells

Suture filaments
Cellular adaptations

- **Physiologic adaptation** – to modified physiological stimuli
- **Pathologic adaptation** – to non-lethal pathologic injury

**Adaptations:**
1. **atrophy** – reduction of the number and/or size of cells
2. **hypertrophy** – increase in size of cells
3. **hyperplasia** – increase in number of cells
4. **metaplasia** – reversible change of one type of mature, differentiated cells to another type of mature, differentiated cells
5. **dysplasia** – disordered cellular development
Hypertrophy

- enlargement of cell volume
Hypertrophy

- **Physiologic** (enlarged size of the uterus in pregnancy, also hyperplasia)

- **Pathologic:**
  1. hypertrophy of cardiac muscle
  2. hypertrophy of smooth muscle
  3. hypertrophy of skeletal muscle
  4. compensatory hypertrophy
Left ventricle hypertrophy
Myocardial hypertrophy

• Hypertension in PC
  - **acute** — RV dilatation (cor pulmonale acutum)
  - **chronic** — RV hypertrophy (cor pulm.chron.)

• Hypertension in SC
  • essential / secondary hypertension
  • LV hypertrophy (cor hypertensivum)
    → cor bovinum
  • Hypertrophy
    – **concentric** — pressure overload
    – **eccentric** — volume overload
Hyperplasia

- increase of cell number
Metaplasia (174)

replacement of one type of differentiated tissue by another type of differentiated tissue
Metaplasia – bronchus, HE

Replacement of respiratory cylindric epithelium by stratified squamous epithelium.
Questions

1. Which cells are involved in inflammatory response? Can you distinguish which type of causative agent may predominantly involve each type of cell?

2. What is the difference between granulation tissue and a granuloma?

3. Is tuberculosis only found in lungs? Can you name other organs which may be affected by tuberculosis?

4. What happens in a bone fracture if the healing bone is not immobilised properly?