# Non-neoplastic lung diseases

Semmelweis University – 2nd Department of Pathology

# Lung diseases

1. Developmental anomalies
2. Circulation disorders
3. Vascular lung diseases
4. **Infections, inflammatory diseases**
5. Obstructive lung diseases
6. **Diffuse parenchymal lung diseases**
7. Neoplastic lung diseases
   *(see under Respiratory system 1. (lecture) and - Pulmonary pathology II-neoplastic (practice))*

# Infectious lung diseases

**Etiology:**

- Bacterial
- Mycobacterial – TBC (specific bacterial)
- Viral
- Fungal
- Parasitic

**Manifestation:**

Bronchitis, bronchiolitis

Pneumonia

- Bronchopneumonia (typical)
- Lobar pneumonia (typical)
- Interstitial (atypical) pneumonia

Lung abscess

Granulomatous inflammation (TB, fungi)

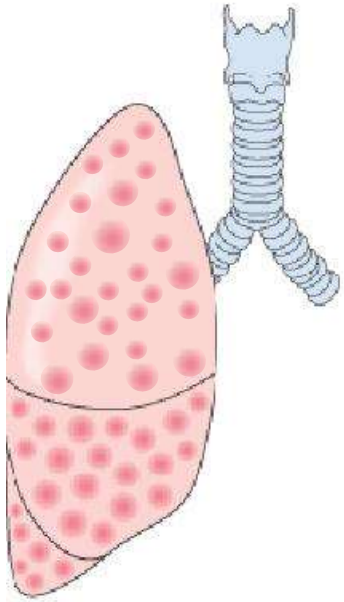
**Place of acquirement:**

community acquired pneumonia = CAP

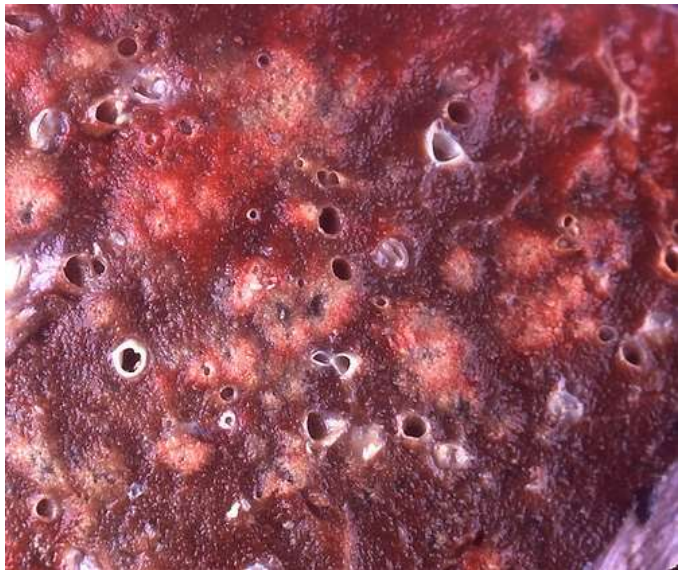
hospital acquired pneumonia = HAP

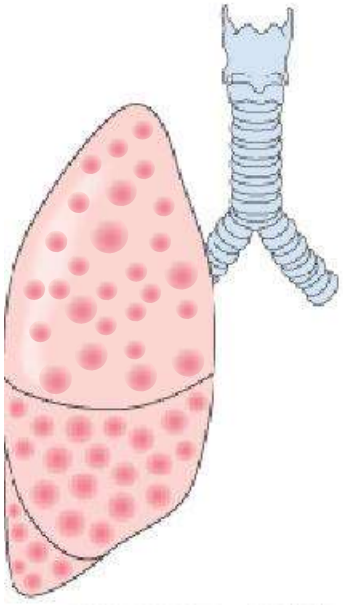
# Bronchopneumonia

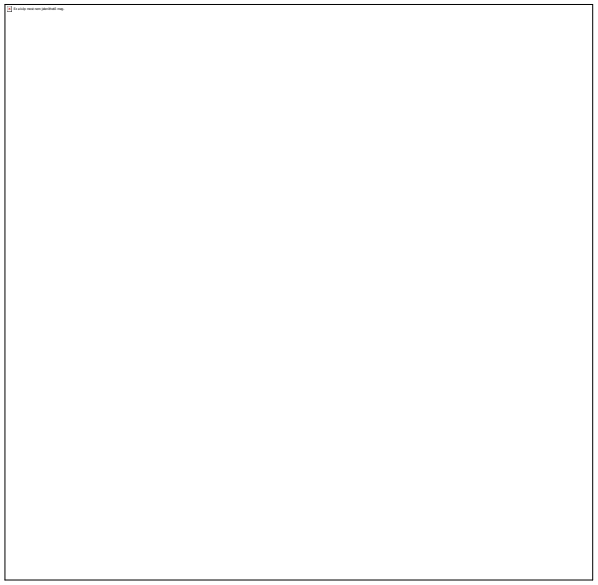
- Common microbes: *Pneumococcus* (antibiotic era), *Haemophilus influenzae*
- Less common microbes: *Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, Legionella pneumophilia, anaerobes (*aspiration pneumonia)
- **Congestion, aspiration** facilitate its development



# Bronchopneumonia







- Multiple, small foci of inflammation
- One or more lobe is affected
- Hyperemic, fragile nodules on cut surfaces

- In the lumen of bronchi, bronchioli and alveoli exudate is detectable which is rich in neutrophils

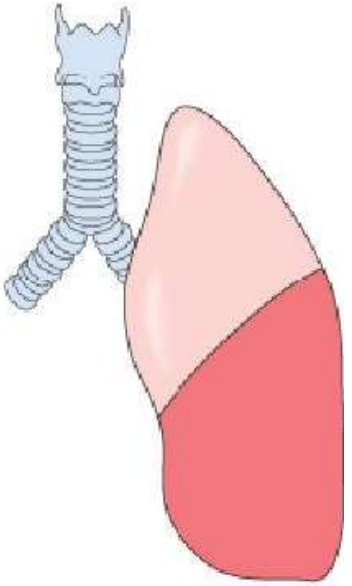
# Bronchopneumonia - Consequences

- The inflammation can lead to **pleuritis**
- By confluence of the inflammatory foci abscesses may be formed
- If the exudate do not resolve, granulation tissue fill the alveolar lumen– ***carnificating pneumonia***
- Later scar tissue appears in the lumen – ***indurative pneumonia***
- Serves as a septic focus
- **Causes sepsis**

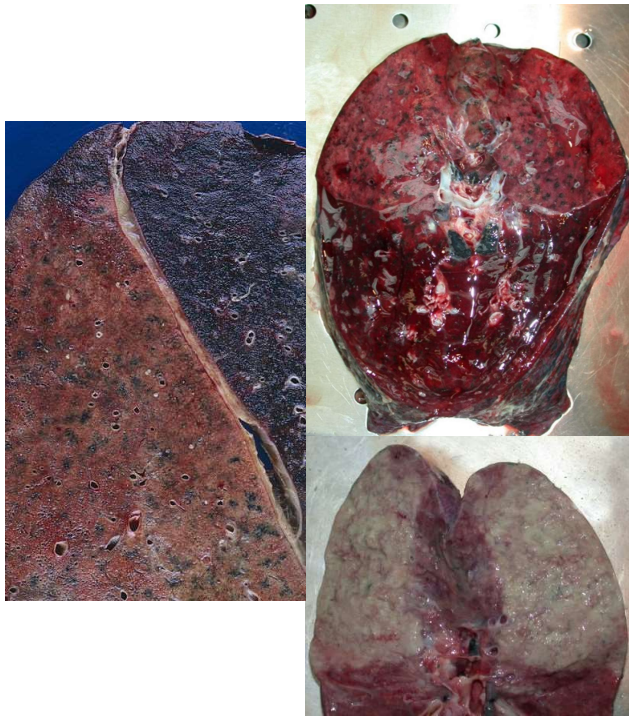
# Lobar - pneumonia

- *Pneumococcus* (before antibiotic era), less commonly *Klebsiella pneumoniae*

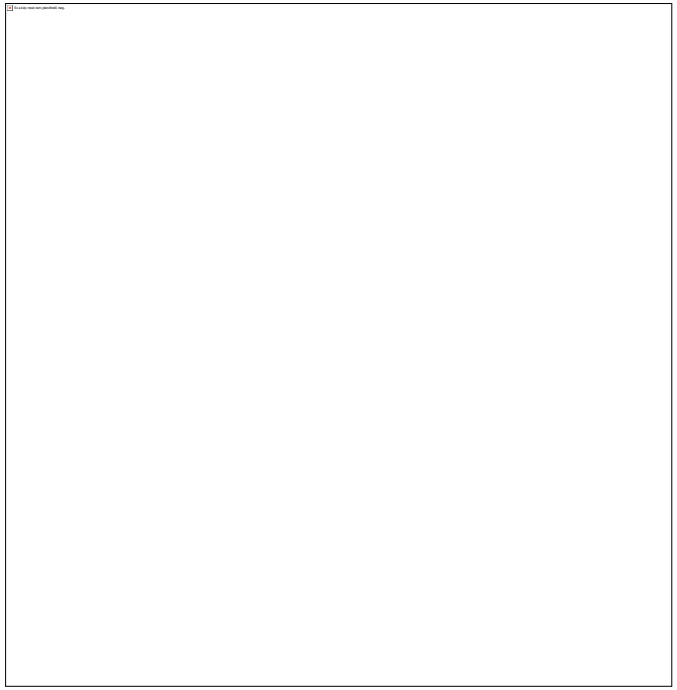
| | | | |
|---|---|---|---|
| 1st stage<br>***congestion***<br>day 1-2 | Congestion of pulmonary capillaries, intraalveolar oedema | Air and fluid in the alveoli | Crepitatio indux |
| 2nd stage<br>***red hepatisation***<br>day 3-4 | Alveolar lumen is filled with RBCs, fibrin, and fewer amount of neutrophils | Firm, liver-like, reddish cut surface | Hollow percussion sound |
| 3rd stage<br>***grey hepatisation***<br>day 5-6 | RBCs are resolved, the fibrin and the leukocytes remain | Firm, liver-like, greyish cut surface | |
| 4th stage<br>***yellow hepatisation***<br>day 7-8 | Massive infiltration of neutrophils in the alveoli filled with fibrin | Firm, liver-like, yellowish cut surface | |
| 5th stage<br>***resolution***<br>day 9-10 | Fibrinolytic enzymes originating from neutrophils dissolve the exudate | Pus (cellular debris and dissolved fibrin) and air is the lumen of the alveoli | Crepitatio redux |



# Lobar pneumonia



Liver-like appearance of the lung parenchyma

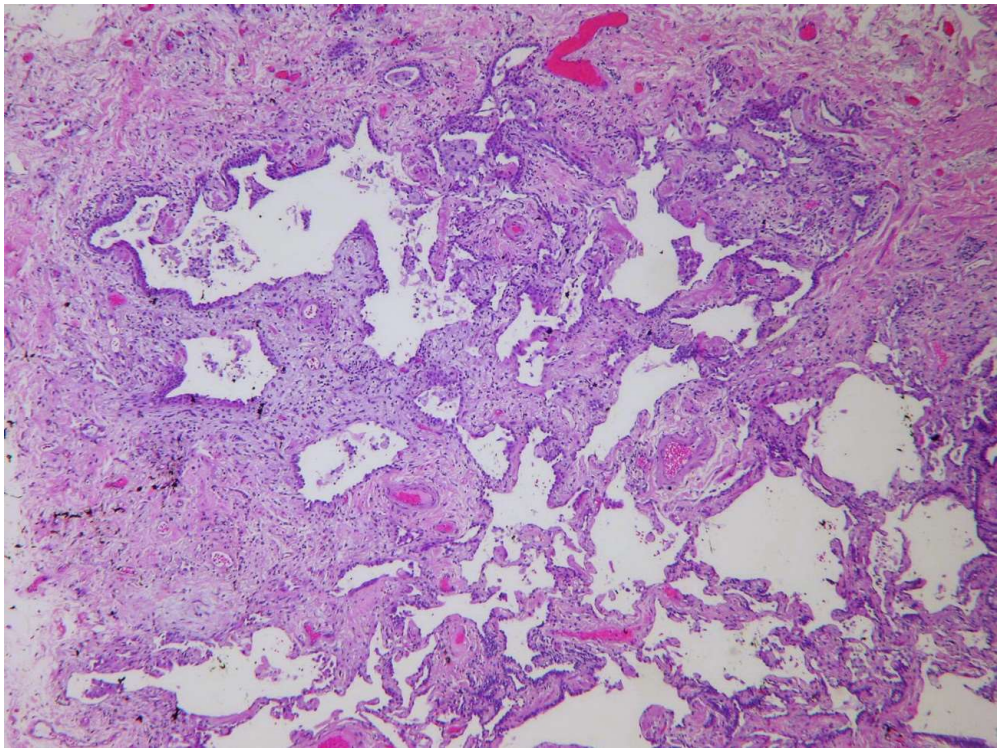


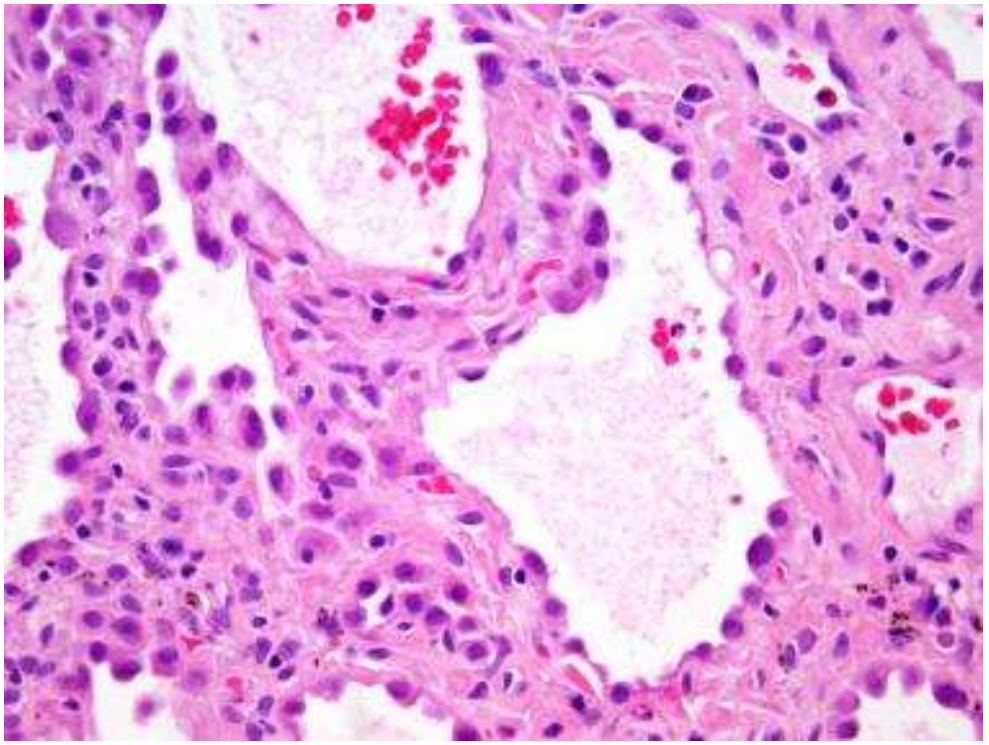
Alveoli are filled with RBCs, neutrophils and fibrin

# Interstitial (atypical) pneumonia

- *Mycoplasma pneumoniae, Chlamydia pneumoniae, Chlamydia psittacci*
- Young adults
- Lymphoplasmocytic infiltration of alveolar septa
- Moderate, prolonged course of disease – mild fever, unproductive coughing
- Difficult diagnosis (compared to the modest symptoms X-ray changes are prominent)
- Ophthalmologic symptoms

# Interstitial pneumonia





Thickening of alveolar septa by lymphoplasmocytic infiltration

# Pneumonitis

- Non-infectious inflammatory lung disease
- Mostly occupation disease
- Hypersensitive reaction (hypersensitive pneumonitis) to the inhaled antigens
- The disease develops at alveolar level → decreased diffusion capacity, decreased compliance, decreased lung volume (restrictive lung disease)
- Immunocomplex-mediated (type III) and „delayed” (type IV) immunoreactions take part in pathophysiology
- Infiltration of mononuclear cell in the interstitium and along the bronchi, in acute form neutrophils are also present
- non-caseating granulomas within the interstitium
- In chronic forms interstitial fibrosis
- Examples:
  - Farmer’s lung
  - Malt worker's lung
  - Bird fancier’s lung
  - Cheese-washer's lung

# Granulomatous inflammations

- Infectious and non-infectious origin
- Type IV hypersensitivity reaction
- Epithelioid histiocytes, multinucleated giant cells

| **Infectious** | **Non-infectious** |
|---|---|
| Mycobacterium tuberculosis | Boeck sarcoidosis |
| Fungi | Granulomatosis with polyangiitis (Wegener-granulomatosis) |
| Actinomyces | Eosinophil Granulomatosis with Polyangiitis (Churg-Strauss syndrome) |
| Nocardia | |

# Tuberculosis

- A disease that most commonly affects the lungs and caused by *Mycobacterium tuberculosis* (**Koch's bacillus**)
- The microbe is detectable by direct staining, culturing and PRC in the tissues, exudates, sputum and bronchoalveolar lavage
- Clinically the immunoreactivity can be detected by **Mantoux test and** by so called Quantiferon-test from blood sample (special interferon, non-specific)
- The prevalence of the disease has decreased, but nowadays it started to increase again (patients in poor conditions, immunodeficient patients, AIDS, drug resistant microbes)

# Pulmonary tuberculosis

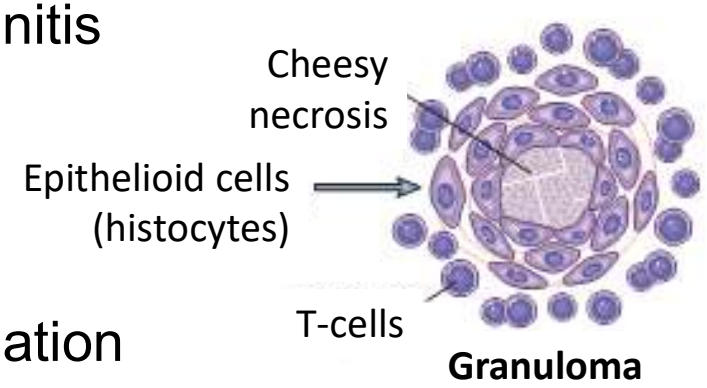
- Many people get over tuberculosis infection during his life, medics have increased risk
- Most of the cases are asymptomatic (screening test — X-Ray)
- The severity of the disease and the appearance of symptoms depend on the general condition of the patient
- Those patient are contagious who expectorates the microbe – open tuberculosis
- However it is rare - never forget extra-pulmonary tuberculosis!

# Pulmonary tuberculosis - primary TB

- In an organism which has not met the microbe yet
- Primary lesion (**Ranke-Ghon** lesion)
  - 1-2 cm
  - Lower region of upper lobe (less commonly upper region of lower lobe or middle lobe), in sub-pleural location
  - It spreads to lymph nodes through lymphatic vessels lymphangitis, lymphadenitis

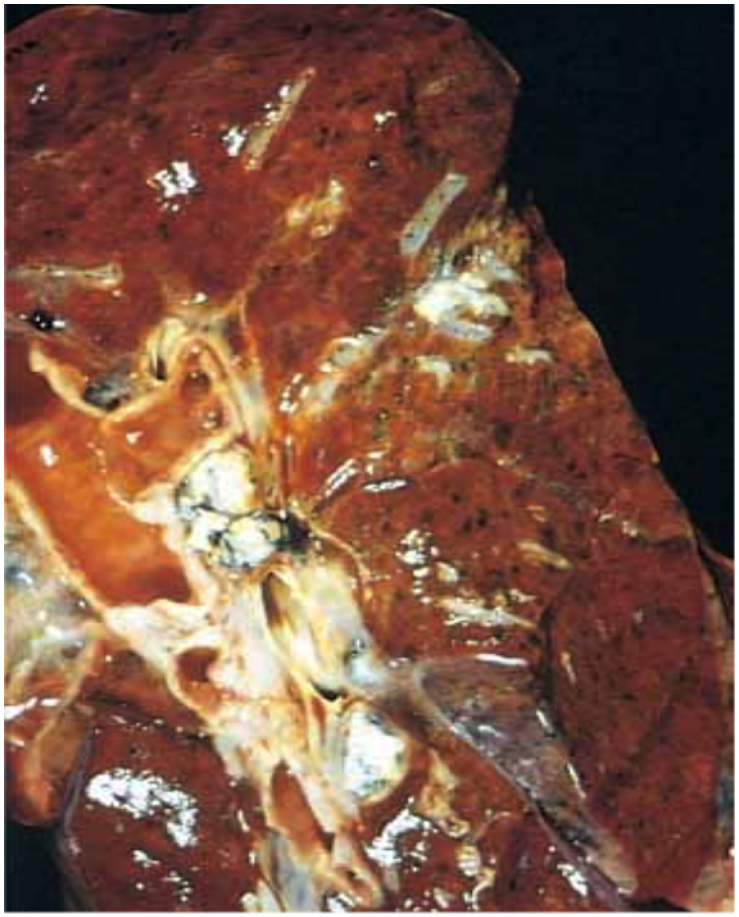
**Primary complex:**
primary lesion
+
lymphangitis
+
lymphadenitis

- 90 % is asymptomatic
- Heels with scar tissue formation

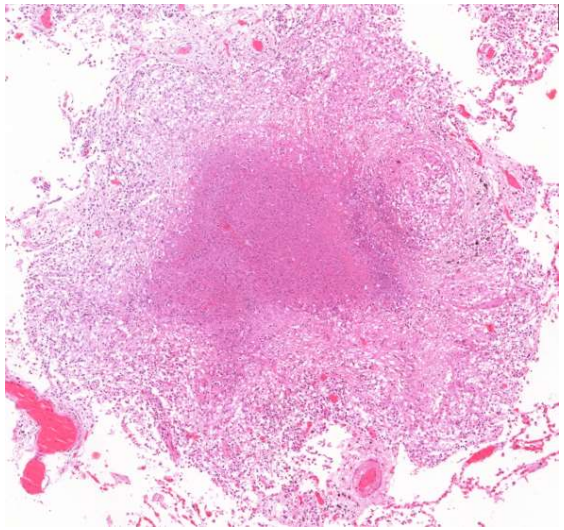


**Granuloma**

# Pulmonary tuberculosis - primary TB

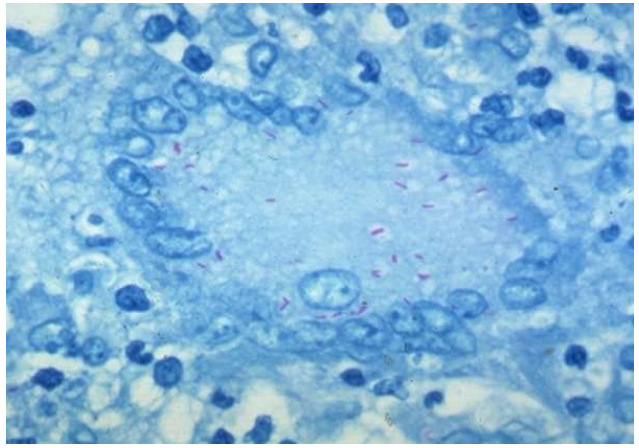


**Ranke-Ghon** lesion



Caseating granulomas

Acid-fast stain
(**Ziehl-Neelsen**)



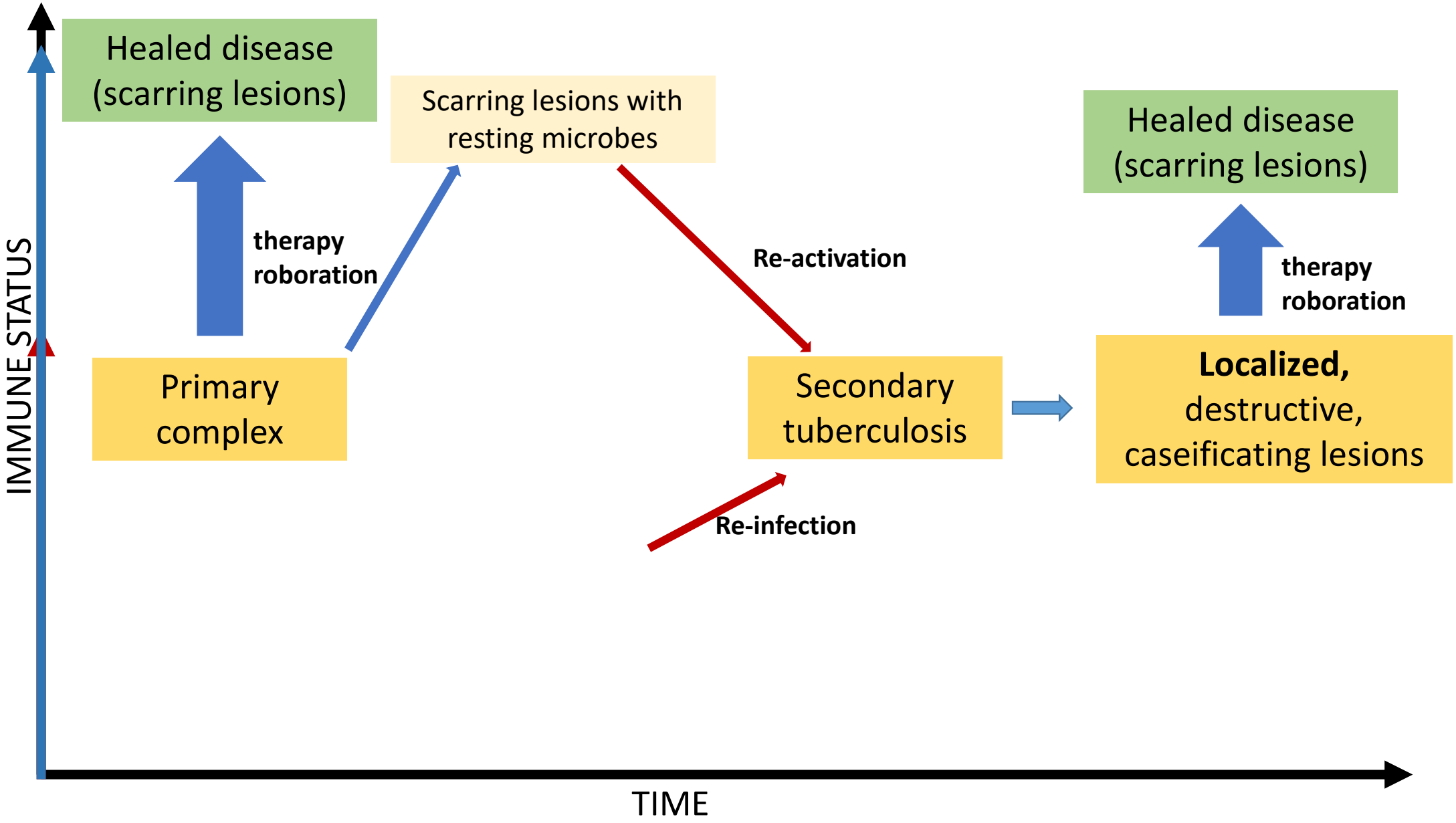
# Pulmonary tuberculosis – secondary (post-primary) TB

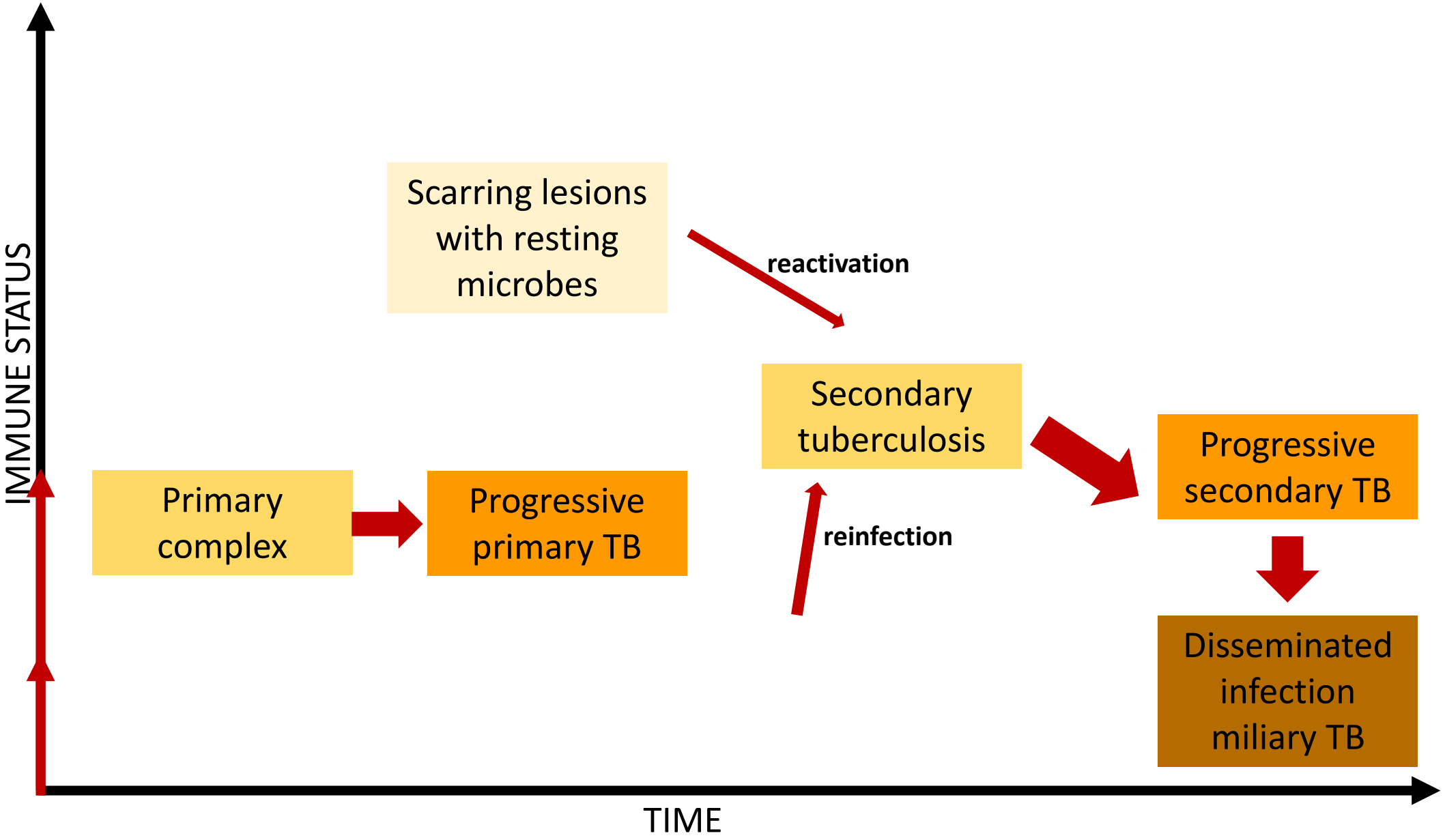
- In patients who have already got through the infection, after sensitization
- *Re-activation* of primary TB (after decades due to the weakening of the immune system) or *re-infection*
- Most commonly in the apex of the lung: **Simon's apical lesion**
- Fibrotic and necrotic foci, calcifications

# Pulmonary tuberculosis - secondary TB

**Simon’s apical lesion**

Several granulomas, extensive necrosis


Healed disease
(scarring lesions)
Scarring lesions with
resting microbes
Healed disease
(scarring lesions)
therapy
roboration
Re-activation
therapy
roboration
IMMUNE STATUS
Primary
complex
Secondary
tuberculosis
Localized,
destructive,
caseificating lesions
Re-infection
TIME


IMMUNE STATUS
Scarring lesions with resting microbes
reactivation
Secondary tuberculosis
Progressive secondary TB
Primary complex
Progressive primary TB
reinfection
Disseminated infection miliary TB
TIME

# Pulmonary tuberculosis

Local, complicated forms
(characteristically in secondary or progressive primary TB)

**Cavern** :

- The necrotic focus is emptied to a central bronchus, a cavity is formed→ outworld, infection
- Scaring wall, calcification
- Erosion of small vessels → hemoptoe
- Rarely the damage of large arteries → **Rasmussen's aneurysm,** severe lung hemorrage

**Bronchopulmonary fistula**

- the caverna is emptied into the thoracic cavity
- tuberculotic empyema and pneumothorax

Tuberculotic **laryngitis** (expectoration), intestinal tuberculosis (swallowing of sputum)

# Pulmonary tuberculosis

Systemic, complicated forms
(characteristically in secondary or progressive primary TB)

**Extrapulmonary TB** (can be also primary)

- Tuberculosis of adrenal gland
- Tuberculotic meningitis (basal cisterns)
- Tuberculotic osteomyelitis (vertebrae) – **Pott's** disease
- Renal tuberculosis
- Lupus vulgaris (skin)
- Tuberculotic epididymitis, tuberculotic salpingitis

# Pulmonary tuberculosis

Systemic, complicated forms
(characteristically in secondary or progressive primary TB)

**Miliary TB:**

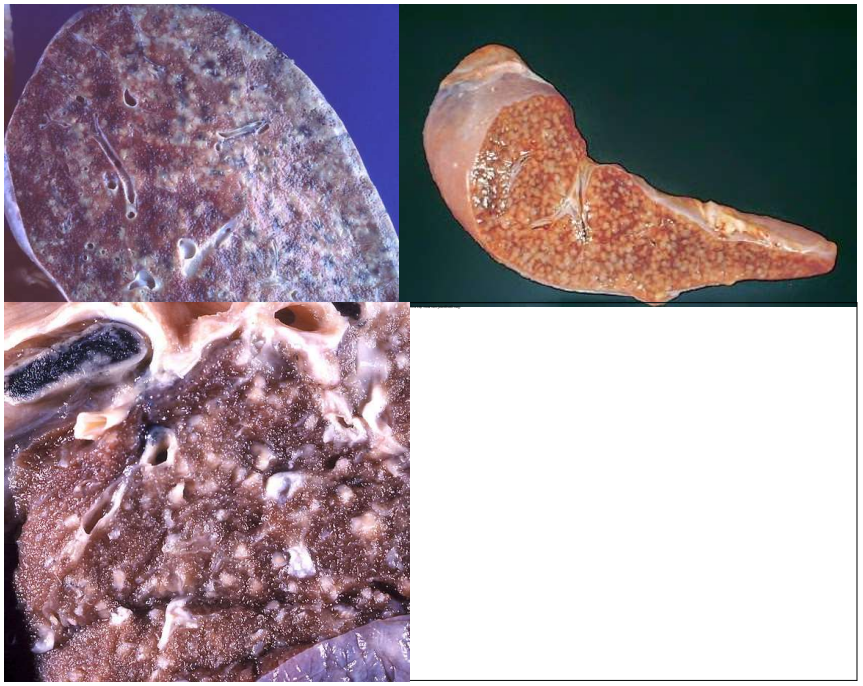
- Hematogenic spread of the microbe
- liver, spleen, bone marrow, adrenal gland
- Several tiny tuberculotic nodules
- Heals with prominent fibrosis

**Landouzy's typhobacillosis** (most severe form):

- Dispersed tuberculotic foci everywhere in the body without inflammatory response

# Pulmonary tuberculos - Complications

**Cavity** formation



**Miliary TB**

# Pulmonary tuberculosis - Prevention, therapy

- Vaccination : BCG (**Bacillus Calmette-Guérin**)
  - 0-6 days after birth
  - Basically for the prevention of childhood tuberculosis (bovine tuberculosis)

- Protection of immune system (if we are sick we do not examine patients bed-side, if so masque is obligatory!)
- Masque, hand disinfection (tuberculocidal disinfection agent)

- Medical therapy: 4-drug regimen, then 2-drug regimen (**isoniazid, rifampicin**, ethambutol, pyrazinamide) + ROBORATION (high-calorie diet, no sports and exercises)

Therapy: 6-9 months

Family members have to be screened by X-Ray

To close contacts, who are in poor general health, INH prophylaxis has to be given

# Boeck's sarcoidosis

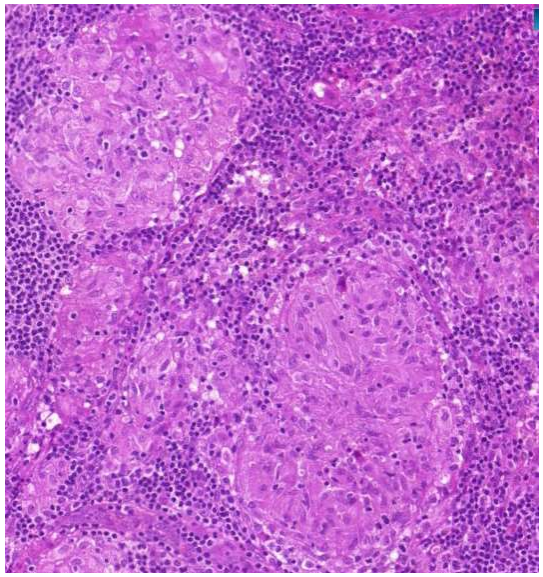
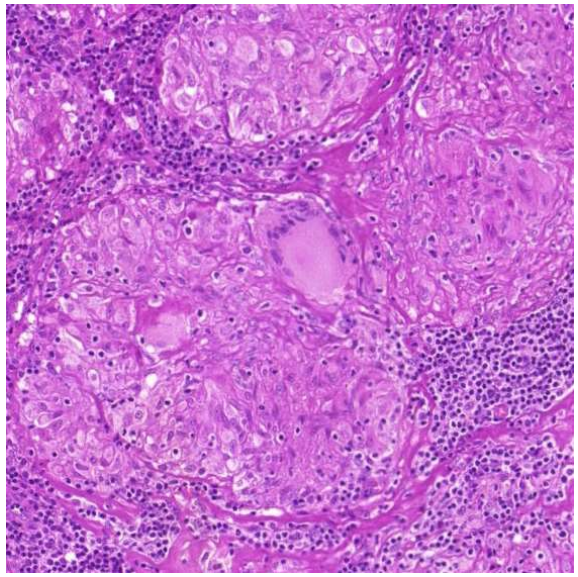
- Granulomatous disease of unknown etiology
- Characteristically in young adults
- Acute and chronic form
  - *Acute:* **Löffgren's** syndrome: fever, lethargy, severe pain in joints (ankle), erythema nodosum, BHL (bilateral hilar lymphadenopathy)
  - *Chronic:* less symptoms, difficult diagnosis, recognized by X-Ray usually indicated by another reason
- Almost every organ can be affected, but most commonly present in the lungs (lymph nodes, skin, eyes)
- Type IV hypersensitivity reaction

# Boeck's sarcoidosis

- Granulomas along the lymphatic vessels (pleura, interlobular septa, peri-bronchial regions)
  - Over time they get fibrotic – starts at the edge of the lesion, lamellar structure
  - In the giant cells characteristic, but not specific so called **asteroid bodies** (star shape) and **Schaumann bodies** (lamellar appearance)

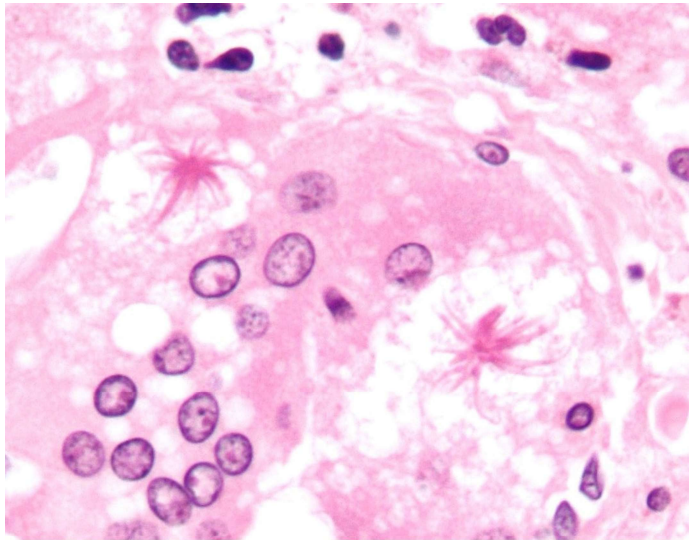
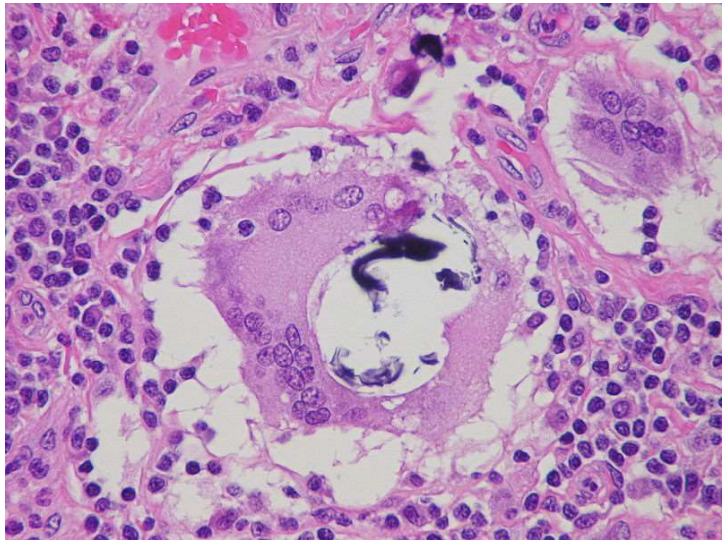
- In severe cases interstitial fibrosis can occur causing so called honey comb lungs (severe restrictive lung disease)

- Therapy: immunosuppression (corticosteroids)

Non-caseating granulomas

asteroid bodies

Schaumann’s bodies

# Diffuse parenchymal lung diseases

A)Diffuse alveolar damage

a) **ARDS** – *adult respiratory distress syndrome*

b) **IRDS** – *idiopathic/infantile respiratory distress syndrome*

B) Pneumoconiosis

- Anthracosis
- Silicosis
- Asbestosis

Etc.

# Diffuse alveolar damage- ARDS

- Diffuse alveolar injury – pathological term ←→ ARDS – clinical term
- Suddenly developing, rapidly progressing respiratory disorder which is refractory to oxygen therapy
- End-stage of several pulmonary diseases – common feature: damage of alveolar epithelia and capillary endothelium
  1. *Infections*
  2. *Inhalation of toxic chemicals (chlorine, ammonia)*
  3. *Pharmaceutics (chemotherapeutic agents, gold products)*
  4. *Shock*
  5. *Sepsis*
  6. *Acute pancreatitis*
  7. *Burn*
  8. *Uremia*
  9. *Unknown etiology (acute idiopathic interstitial pneumonia)*
- Destruction, necrosis of type I pneumocytes and capillary endothelium, production of exudate rich in proteins (fibrin) → HYALINE MEMBRANE
- Always diffuse

# Diffuse alveolar damage- ARDS

- Bilateral firmness of lung parenchyma, fluid cannot be squeezed out
- The alveolar wall is diffusely affected (epithel, endothel, interstitium)

2 stages:

1. ***Acute (exudative):***
    - Approx. one week
    - Damage of type I pneumocytes and capillary endothelium
    - Edema
    - Hyaline membrane
    - Infiltration of lymphocytes, plasmocytes and macrophages in the interstitium
    - Fibrin thrombi in the lumen of arterioles and capillaries
2. ***Regeneration (proliferative):***
    - After one week
    - Interstitial fibroblast proliferation
    - Hyperplasia of type II pneumocytes

# Diffuse alveolar damage- IRDS

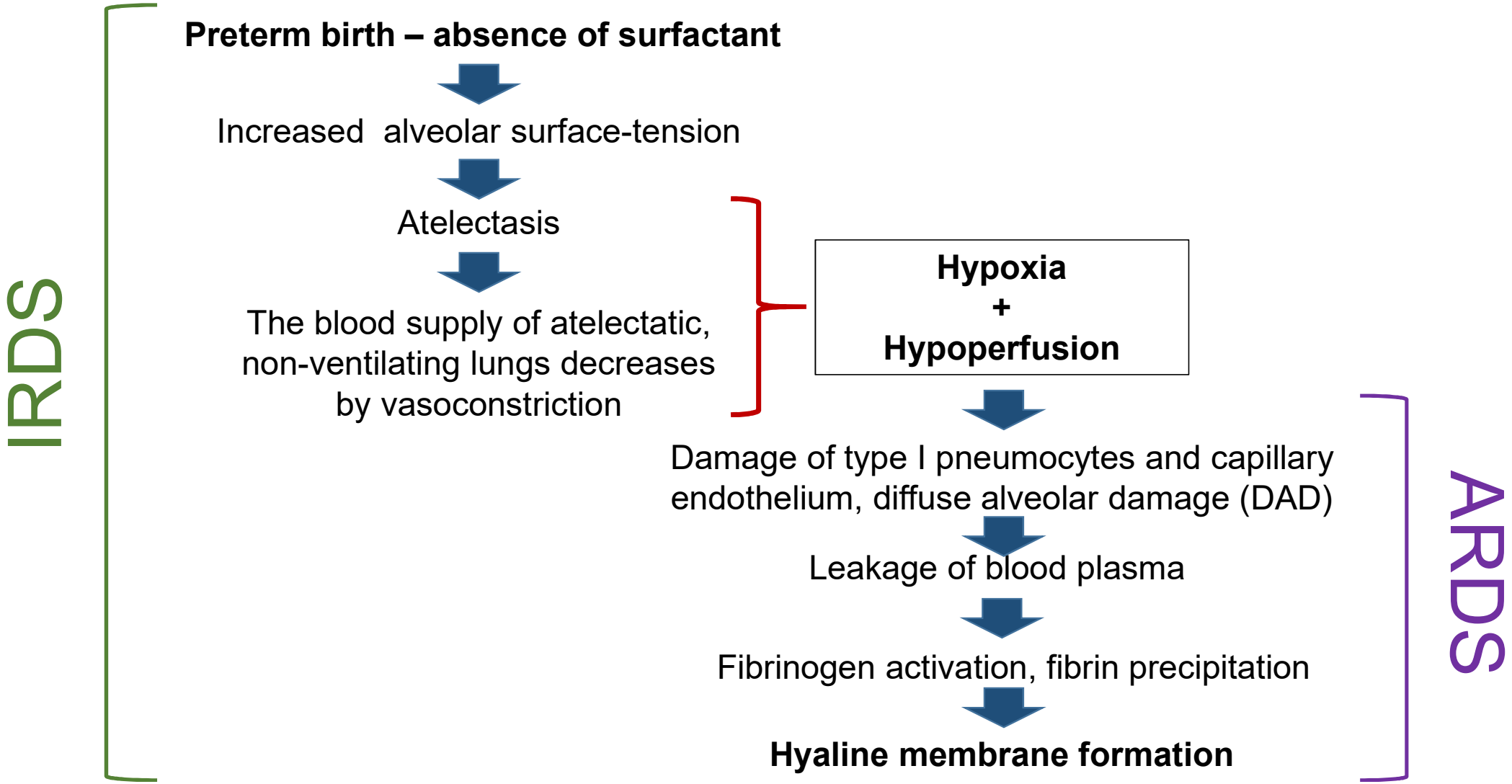
- Hyaline membrane disease
- New-born, especially premature infant
- Absence of surfactant

- At imminent preterm delivery corticosteroids should be given to the mother, which stimulates surfactant production in the fetus

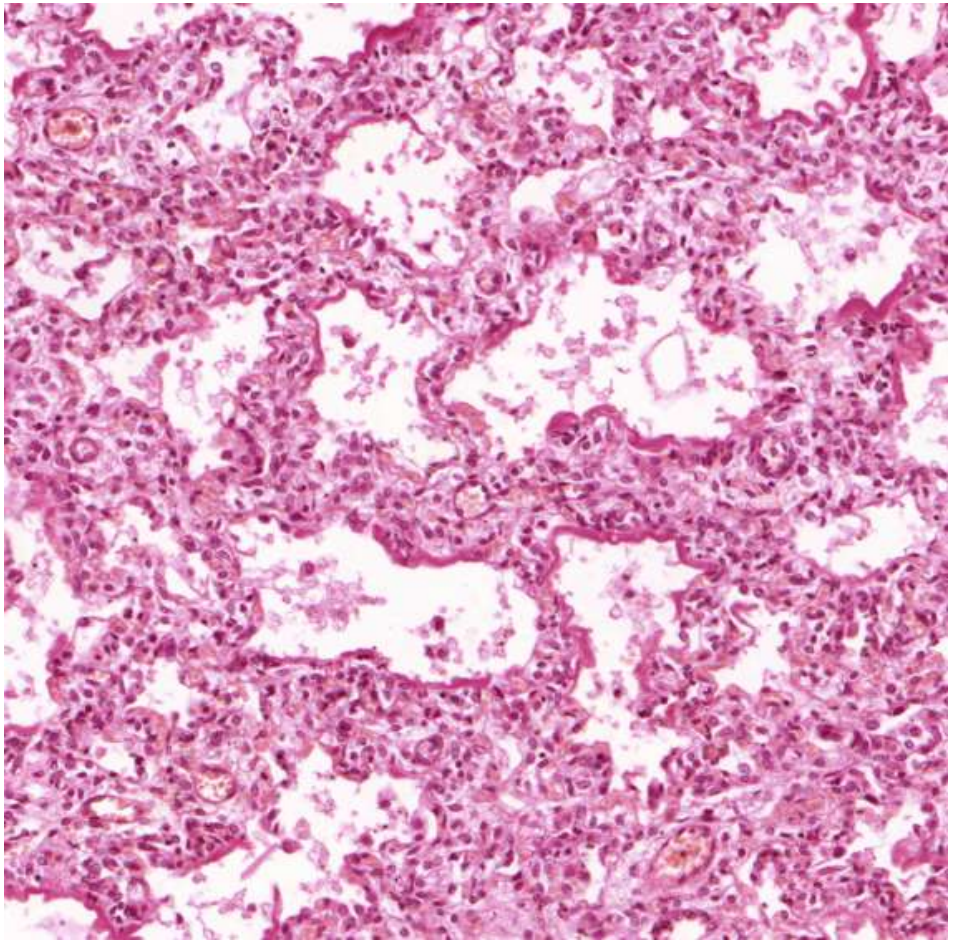
**Therapy:**

- Surfactant supplementation
- Positive pressure ventilation→ complication: bronchopulmonary dysplasia (oxygen toxicity)

# Diffuse alveolar injury



# Diffuse alveolar injury - IRDS



Collapsed alveoli
Hyaline membrane

# Links to pictures

https://commons.wikimedia.org/wiki/File:Lobar_Pneumonia_and_bronchopneumonia_illustrated.jpg
http://nanda-nursing.blogspot.hu/2011/07/nursing-care-plan-for-bronchopneumonia.html
https://emedicine.medscape.com/article/2078612-overview
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http://ertektar.rs/ertektar/ertek/A-horgosi-es-martonosi-piros-paprika/57
Robbins & Cotran Pathologic Basis of Disease, 9e (Robbins Pathology) 9th Edition
by Vinay Kumar MBBS MD FRCPath (Author), Abul K. Abbas MBBS (Author), Jon C. Aster MD PhD
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