Inflammation – class 2

- Rheumatic endocarditis
- *Pneumocystis carinii* pneumonia
- Cytomegalic pneumonia
- Aspergillosis
- Actinomycosis

**Rheumatic fever RF**

- An acute, immunologically mediated multisystem inflammatory disease, caused by an abnormal host response to an infection with beta-hemolytic group A streptococci
- The pathogenesis of RF is not fully understood!

**Rheumatic fever - pathogenesis**

- A hypersensitivity reaction induced by group A streptococci: antibodies directed against the bacterial M proteins, cross-react with normal proteins present in the heart, joints and other tissues
- Hypersensitivity reactions - all forms of immune-mediated host tissue injury

**Hypersensitivity reactions**

- Immune activation leads to the production of antibody and T-cell responses that are generally protective, but
- these responses may damage host tissues:
  - some viral infections may require destroying tissues to eliminate the disease
  - activated macrophages and scar formation destroys adjacent parenchyma in tuberculosis
  - bacterial exotoxins (e.g. staphylococcal) may induce a polyclonal activation of T lymphocytes (*superantigens*) resulting in systemic pathology from cytokine elaboration
  - antibodies cross-react with normal host tissues

**Rheumatic fever RF**

*Rheumatic heart disease RHD* is the cardiac manifestation of RF

Inflammation involves the cardiac valves, myocardium and/or pericardium (*pancarditis*)
Rheumatic heart disease

- The attack rate of myocarditis following streptococcal pharyngitis is 1-3%
- Heart disease develops long after the infection has cleared
- Termination of the bacterial infection by antibiotic therapy prevents the development of myocarditis!

Aschoff bodies

- Central zone of fibrinoid necrosis (eosinophilic extracellular matrix, composed of fibrin, complements and protein antibodies)
- Lymphocytes (primarily T cells), plasma cells
- Activated macrophages-Anitschkow cells (abundant cytoplasm and chromatin like wavy ribbon): caterpillar cells
- Some multinucleated giant cells of Aschoff

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Chronic rheumatic valvular disease

- Diffuse fibrosis of the valves and chordae tendineae
- The functional consequence: valvular stenosis and regurgitation
- Mitral valve involvement in 70%
- Combined mitral and aortic disease in 25%
- Tricuspid valve less frequently involved

Valvular Heart Disease

- Stenosis is the failure of a valve to open completely, which impedes forward flow.
- Insufficiency, in contrast, results from failure of a valve to close completely, thereby allowing reversed flow. (Robbins)

These abnormalities can be present alone or coexist
The clinical consequences of valve dysfunction

- Generally, valvular stenosis leads to pressure overload of the heart,
- valvular insufficiency leads to volume overload of the heart.

Rheumatic fever

- The condition affects large joints, such as the knees, elbows, ankles, causing migratory polyarthritis (fever and joint pain). The arthritis is usually reversible.

Rheumatic fever „licks the joints but bites the heart”

Opportunistic infections

Some bacteria, viruses or fungi invade the tissues only because of lowering of patient’s resistance by some other disease or a side effect of treatment

(some of the fungi or viruses are seldom, if ever, responsible for illness in healthy individuals)

Pneumonia in the immunocompromised host

A pulmonary infiltrate, is one of the most common and serious complications in patients whose immune defenses are suppressed by

- disease,
- immunosuppressive therapy for organ transplants,
- chemotherapy for tumors, or irradiation

Mortality from these opportunistic infections is high.

Pneumocystosis

- Pneumocystis carinii – fungus discovered 1912
- Form cysts (3-6µm) with intracystic bodies
- When the cyst ruptures, trophozoites are released
- Both forms are vulnerable to chemotherapy
- The trophozoits attach to type I alveolar epithelial cells
- The trophozoits may disseminate widely with blood

Pneumocystis pneumonia PcP

- The commonest opportunistic infection in AIDS

- Pneumocystis pneumonia (PcP) is the second leading cause of morbidity and mortality in human immunodeficiency virus (HIV)-infected patients in the United States. Clin in Infect Dis 2013; 56(1)
- Recent clinical studies, performed in sub-Saharan Africa, using sensitive methods to detect P. jiroveci have reported high rates of PcP cases in adults and children, with mortality rates of about 50%

Pneumocystic pneumonia
Diagnosis requires demonstration of the organisms in sputum
- Giemsa stain, silver stain
- Immunofluorescence
- Detection of pneumocystis DNA by the polymerase chain reaction
- Monoclonal antibodies

Pneumonia
- Any infection in the lung
- May present as: acute (clinically fulminant) or chronic (protracted) disease
- Histologically:
  - Fibrinopurulent alveolar exudate (bacterial infections)
  - Mononuclear interstitial infiltrate virtually localized within the walls of the alveoli - viral or atypical pneumonias,
  - Granulomatous or cavitating inflammation (tuberculosis)

Pneumocystic pneumonia histological appearances
Classic one
- Alveoli filled by a foamy, pale eosinophylic exudate „cotton candy”
Interstitial
- Lymphoid infiltrate
- Plasma cells (in children: „interstitial plasma cell pneumonia”)
Atypical
- Fibrosis
- Absence of exudate
- Macrophages
- Hyaline membranes
- Cavities
- ARDS
- Calcification
- Necrotising granulomatous infection

Cytomegalovirus
- The largest of the herpes viruses
- Is transmitted in saliva and blood, by sexual contact and organ transplantation
- Widespread – the prevalence of seropositivity in adults is over 50%
  (carriage of the virus is not equate with disease)
Opportunistic infections are often multiple.

Pneumocystis carinii and cytomegalovirus coexist particularly frequent.

P. carinii – intermediate host for virus?

Cytomegalovirus pneumonia pathological features

- May be unilateral or bilateral, involves lower lobes
- Chronic interstitial pneumonia
- Enlargement of the alveolar epithelial cells
- Intranuclear inclusions – "bird’s eye"
  - inclusion – clumped chromatin
  - clear zone – viruses
- Necrosis
- Diffuse alveolar damage

CMV: pneumocytes with viral intranuclear inclusions

Diffuse alveolar damage

- The pathological basis of the adult respiratory distress syndrome (ARDS)
- Non-specific pattern of acute alveolar injury
- High mortality rate (over 50%)

Diffuse alveolar damage the cycle of events

Viruses, irradiation, shock, high O₂ concentration

↓

Surfactant deficiency

↓

Epithelial and endothelial damage

Diffuse alveolar damage

Aspergillosis

Aspergilli – common saprophytes in decaying organic mater

Aspergillus fumigatus, flavus, niger

Visible as branching uniformly in haematoxylin-eosin or silver stain preparations ("molds" that grow by branching)
Aspergillosis

Pulmonary aspergillosis

Exposure to spores is common, but fungus is not a frequent pathogen.

Predisposing causes:
- Atopic individual (allergic)
- Previous damage of the lungs
- Lowered general resistance (invasive)

Aspergillosis

Pulmonary aspergillosis

- Invasive aspergillosis principally involves the sinopulmonary tract, a reflection of inhalation being the most common route of entry of Aspergillus spores

Pulmonary aspergillosis

Acute invasive aspergillosis is a devastating opportunistic infection in the severely immunocompromised

Patients at risk for invasive aspergillosis include those with:
- Prolonged neutropenia (e.g., following cytotoxic regimes for acute leukemia),
- Hematopoietic stem cell transplant (HSCT) recipients,
- Solid organ transplant recipients (particularly lung transplant recipients), advanced AIDS

Mortality from invasive aspergillosis has increased by several-fold in the 1980s and 1990s in the U.S. and Europe.

Aspergillosis

- Allergic bronchopulmonary aspergillosis – in patients with asthma; IgE antibodies and eosinophilia
- Invasive aspergillosis – with possible vascular invasion and central nervous system involvement
- Aspergilloma ("fungus ball") – colonization of preexisting pulmonary cavity

Aspergilloma
Invasive aspergillosis

**histological features**

The fungus preferentially localizes to the lungs

- Fibrinous exudate in the alveoli
- Many neutrophils
- Thrombosis of the capillaries
- Necrosis extending widely into the tissues
- A propensity to invade blood vessels – systemic dissemination (fatal brain involvement)

Aspergillosis – brain involvement

multiple foci of necrosis

Actinomycosis

- Caused by anaerobic bacteria *Actinomyces* that live in the human body as saprophytes and are branching, gram-positive rods
- To cause disease, *A.* must be inoculated into an anaerobic environment (dental debris – oral *A.*; traumatic or surgical disruption of the bowel – abdominal form of *A.*; aspiration of contaminated material – pulmonary location)

Actinomycosis

- Colonies grow large enough to be visible as yellow grains known as „sulfur granules“
- The disease is characterized by abscesses or sinus tracts (*fistulae*) that burrow across normal tissues into adjacent regions of the body