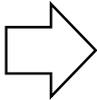


Lower airway infections

Gábor Smuk M.D.

Predisposing factors for pulmonary infections

- Suppression of **cough reflex** (chest pain, anesthesia, neuromuscular disorders, coma)
- Decreased **muciliary clearance** (smoking, viral disease, toxic gas, Kartagener sy)
- Accumulation of **mucus** (bronchiectasia, airway obstruction) Disturbed **innate immune response**: decreased phagocytic function related to tobacco smoke, anoxia, oxygen intoxication 
- **Congestion** and edema (hypostatic pneumonia - in patient confined to bed)

Types of airway infections

- **Bronchitis**: coughing up mucus
- **Bronchiolitis**: frequently obstructive
- **Pneumonia**: exsudate in alveolar spaces
- **Pneumonitis**: interstitial inflammation (inflammation in alveolar septae)

Viral infections

Normal host

Primary respiratory infection

- Respiratory syncytial virus
- Parainfluenza
- Influenza
- Adenovirus

Secondary to systemic infection

- Measles
- Varicella-Zoster virus
- Adenovirus

Immunocompromised host

- Cytomegalovirus
- Herpes simplex virus
- Varicella-zoster virus
- Adenovirus

Viral infections

Characteristic clinical conditions:

- **Rhinoviruses provoke acute exacerbations of chronic bronchitis.**
- **Respiratory Syncytial Virus** is the most common cause of obstructive bronchiolitis in children. RSV may occur in patient with chronic lung disease.
- **Parainfluenza** viruses are the most frequent **cause of viral pneumonia in children**, followed by the measles and adenoviruses
- **Influenza** virus is the most frequent cause of **viral pneumonia in adults**, followed by varicella virus.
- **Immunocompromised patients are susceptible to cytomegalovirus** and herpes simplex virus

Viral infections

May manifest in bronchitis (coughing) or bronchiolitis (stridor).

Much of the damage caused by respiratory viruses is due to a **direct cytopathic effect** on the infected cells.

Alveolar epithelial necrosis is a feature of severe viral pneumonia → **DAD**.

Secondary infections

- Depression of immunity by the virus facilitates secondary infections.
- In fatal cases **secondary bacterial infection usually plays major role**.
- **Viral cytopathic injury to the epithelium** facilitates bacterial attachment → increased incidence of bacterial pneumonia.

Viral infections

Patomechanism of tissue injury



The cytopathic effect kills the infected host cells (influenza, adenovirus, etc...)



Infection stimulates proliferation of epithelial cells (**RSV**, measles)

Pathomorphology of viral pneumonia

1. Interstitial mononuclear inflammation
2. Alveolar epithelial necrosis
3. Formation of hyaline membranes

Microbiology and epidemiology **Influenza**

epidemics occur annually in the **winter months**

originally bird viruses, crossing from birds to different species (humans, pigs). 3 types exist: A, B and C

haemagglutinin and neuraminidase – surface antigens – may undergo change (antigenic lability).

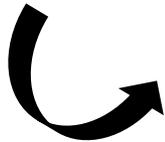
- a. Minor changes ('antigenic drift') - from season to season.
- b. Major changes ('antigenic shift') due to replacement of haemagglutinin and neuraminidase RNA through recombination.

Serotypes:

H1N1 – Spanish Flu (1918), Swine Flu (2009)

H5N1 – Bird Flu (1997 Hong Kong)

antigenic shift results in **new subtypes (a subtype of infl. A)**



populations have little immunity to new subtypes



epidemics or pandemics

Influenza - morphology

- characteristic degenerative changes in the epithelial cells of the bronchial and bronchiolar mucosa.
- In deeper tissues: oedema, hyperaemia and accumulation of lymphocytes.
- destroyed bronchial epithelium **predisposes to bacterial superinfection**

Severe Acute Respiratory Syndrome (SARS)

- SARS first appeared in southern China in 2002
- Caused by **coronavirus** (Chinese horseshoe bats serve as a reservoir)
- **air-borne** infection (requires close contact)
- Symptoms: fever, cough and dyspnoea
- laboratory findings: **lymphopenia** involving both CD4 and CD8 lymphocytes, thrombocytopenia, prolonged thromboplastin time
- **diffuse alveolar damage (DAD)**
- Pathomorphology: **cytomegaly** with granular amphophilic cytoplasm

Cytomegalovirus

- widespread and persisting for life
- infection is symptomatic **in adults** who have undergone **organ transplantation** or **infected with HIV**

Cytomegalovirus Mononucleosis

- Immunocompetent host
- infectious mononucleosis-like illness, with fever, atypical lymphocytosis, lymphadenopathy, and hepatitis
- the virus is never cleared, persisting in latently infected leukocytes

Cytomegalovirus in immunosuppressed individuals

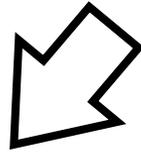
- **primary infections or reactivation of latent CMV**
- CMV was the most common opportunistic viral pathogen in AIDS
- Recipients of solid-organ transplants (heart, liver, kidney) may **contract CMV from the donor organ**
- Disease primarily affect the lungs (pneumonitis) and gastrointestinal tract (colitis)

Characteristic inclusions: owl's eyes

- Intranuclear incl up to 10 μm in diameter, surrounded by a clear zone inside the nuclear membrane
- Cytoplasmic inclusions up to 2 μm in diameter

- **typical enlarged cells with inclusions**
- **interstitial mononuclear infiltrate** with foci of necrosis
- diffuse alveolar damage (DAD)
- Detection: viral culture, rising antiviral antibody titer, CMV antigens and PCR-based detection of CMV DNA

Bacterial pneumonia



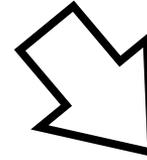
Community acquired

Lobar pneumonia

- Haemophilus influenzae
- Staphylococcus aureus
- Streptococcus pneumoniae

Atypical pneumonia

- Mycoplasma pneumoniae
- Legionella
- Chlamidia pneumoniae



Nosocomial pneumonia/hospital- acquired infection

Lobular/Bronchopneumonia

- Gram-negative enteric bacilli
- Pseudomonas aeruginosa
- Enterobacteriaceae family
(Escherichia coli,
Proteus and Klebsiella species)

Bronchopneumonia

Intraalveolar exsudate with patchy distribution

Lobar pneumonia

Intraalveolar exsudate involving the entire lobe

Interstitial pneumonia - pneumonitis

Inflammatory infiltrate localized to alveolar septae

Bronchopneumonia

Occurs in conditions with weakened local or general defence mechanisms:

- local predisposing conditions: acute viral infections
- chronic airway diseases predispose, such as chronic bronchitis and cystic fibrosis.
- Bronchopneumonia may also follow inhalation of irritant gases, **aspiration of food or vomit**, and **obstruction of a bronchus by a foreign body or tumour**.
- bronchopneumonia is a very common terminal event in patients debilitated by cancer
- generalised metabolic disorders (DM) predisposes
- Postoperative bronchopneumonia: the pain may reduce the normal ventilation of the lower parts of the lungs

Pneumococcal pneumonia - community acquired lobar type

Usually an **endogenous infection** - from the nasopharynx to the lungs (Streptococcus pneumoniae may also cause bacteraemia and meningitis).

In temperate climates much commoner in winter than in summer.

Predisposing factors

alcoholic binge-drinking, non-functioning spleen, respiratory-depressant drugs, diabetes mellitus, nephrotic syndrome, cirrhosis

Symptoms

The onset is typically abrupt.

Sharp pain in the side of the chest that is made worse by deep breathing,

Patient coughs up 'rusty' sputum, and quickly develops a fever of about 40°C.

Leukocytosis of $15-20 \times 10^9/l$

Rapid recovery follows the appearance of specific antibodies against the pneumococcus.

Lobar pneumonia

Red hepatisation

- fluid exudate
- clotted abundant fibrinogen

Grey hepatisation

large numbers of inflammatory cells are present

- first **neutrophils appear**
- later macrophages will be activated

Yellow hepatisation/Resolution

- air spaces reopen due to **fibrinolysis**
- apoptotic neutrophils are ingested by **macrophages**

Complications of lobar pneumonia

- Pneumonia is the commonest cause of **septic shock**
- Acute endocarditis, pneumococcal meningitis, peritonitis
- incomplete digestion of the fibrin leads to organisation:
fibrosis/Carnification

Community acquired pneumonia

Haemophilus pneumonia

- Gram-negative bacillus frequently present in upper resp. tract infection
- It was first isolated in the 1889–90 influenza pandemic: Pfeiffer thought it was responsible for influenza (it was proven wrong)
- Predisposing factor: old age, alcoholism, chronic bronchitis

Staphylococcus aureus

- Gram-positive coccus
- frequent after influenza
- frequently abscesses, pleuritis

Nosocomial pneumonia

Klebsiella pneumonia

- Klebsiella pneumoniae is inhabitant of the oral cavity
- Alcoholics, elderly and diabetics are particularly susceptible, the role of poor dental hygiene
- **predilection for the upper lobes**, only part of the lobe is involved: demarcated edge along the interlobular septa
- Klebsiella pneumonia is particularly prone to form lung abscesses (possibility to progress into gangrene). High mortality rate: 21% (64% in alcoholics)

Pseudomonas pneumonia

- Inhalational or blood-borne infection.
- Infection can be related to antibiotic treatment that destroy the normal flora of the upper respiratory tract
- **tracheostomy and mechanical ventilation**
- P. aeruginosa adheres to normal epithelial cells
- Gross morphology is characterised by well-demarcated pale areas of necrosis.

Legionella pneumonia - Legionnaire's disease

Legionella pneumophila (acid fast aerobic Gram-negative bacilli)

Spread is usually due to atmospheric contamination (air conditioner, inhalation of aerosolized organisms)

Hospital-acquired infection is particularly likely to affect immunocompromised patients, such as transplant recipients.

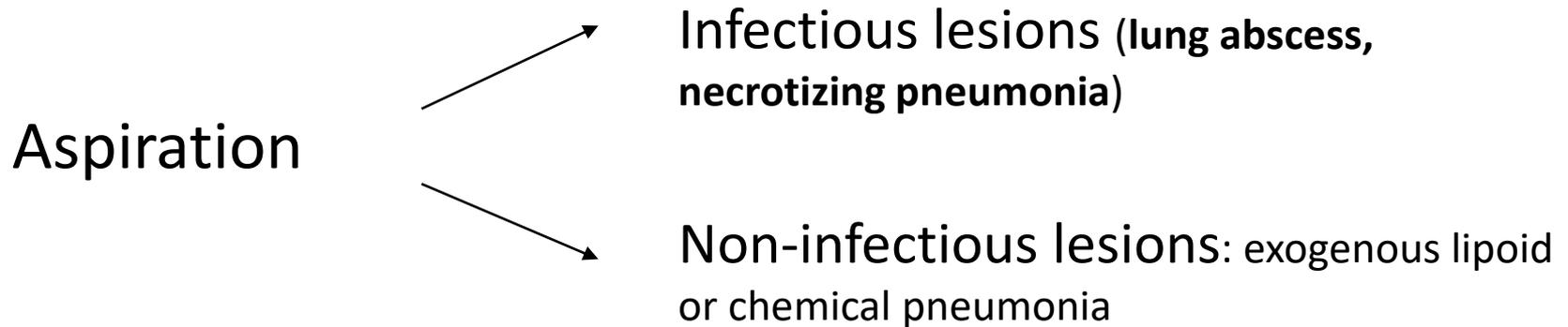
Community acquired infections are more common in elder patient, in case of alcoholism

Histomorphology: necrotizing fibrinopurulent pneumonia (without involvement of airways)

Limited effectiveness of humoral and neutrophilic response, macrophage plays the main role in immune response

Pontiac Fever (a less severe upper resp. tract disease)

Aspiration pneumonia



Aspiration is promoted by loss of consciousness and suppression of the cough reflex (absence of pharyngeal reflex)

Complication of drunkenness, general anaesthesia, cerebrovascular accidents, drug overdose or other causes of coma

Aspergillosis

- In spite of abundance of *Aspergillus* spores, the fungus is not a frequent pathogen
- ***Aspergillus fumigatus*** is most frequent of aspergillus species found in human disease
- The hyphae are septate and regular in diameter
- Typically, the hyphae branch dichotomously at relatively acute angles (35–45°)
- PAS and Grocott–Gomori methenamine silver method is useful
- Bronchopulmonary diseases can be classified as **allergic, saprophytic and invasive**

Allergic bronchopulmonary aspergillosis

Allergic response to *Aspergillus*

- confined to the airways
- raised blood eosinophil count
- Circulating antibodies to *Aspergillus* antigens
- In asthmatic patients mainly

Mucoid impaction: large mucous plugs develop, typically 1–2 cm thick and 2–5 cm long, expectoration of mucous plugs

- The dilated airway shows chronic inflammatory changes with eosinophilic cell infiltrate

Bronchiectasis may develop

Aspergilloma

Definition:

- the fungus grows **in the lumen of a cavity** in the lung (e.g.: old tuberculous cavity, bronchiectasis, abscess, necrotic center of carcinoma)
- No invasion of the lung parenchyma
- Ball like accumulation of fungus

Macroscopic appearance :

- grey or reddish brown, friable or gritty
- dense feltwork of hyphae
- surrounding zone of chronic inflammatory granulation tissue

Invasive aspergillosis

- **vascular invasion leading to thrombosis, infarction**
- generalisation of the infection through the body

Pneumocystis jirovecii

Organism:

- primitive fungus: mycelium is reduced to a unicellular state
- The fungus forms cysts (3–6 μm in diameter) with a thick wall
- In case of impaired cell mediated immunity (AIDS, transplantation recipients)

Macroscopic morphology of pneumocystis pneumonia:

- characterised by widespread bilateral consolidation
- rarely solid or cavitating pulmonary nodules

Histological appearances

- Cyst and trophozoites
- alveoli are filled by a foamy, pale, eosinophilic exudate („*cotton candy*“)
- unstained in H&E
- Grocott's methenamine silver stain: round cysts (5 μm in diameter)
- Crescent-shaped forms represent collapsed cysts (thick walled spherules)
- Interstitial inflammation

Chronic pneumonia

Granulomatous inflammations:

Mycobacterium tuberculosis (see inflammation topic)

Atypical mycobacteria (*Mycobacterium avium intracellulare*): widespread disease in HIV+ patients, absence of granuloma formation due decreased number of CD4+ T-cell. Foamy histiocytes (containing large number of mycobacterium) are observable.

Histoplasmosis (*Histoplasma capsulatum*): necrotizing epithelioid granulomas

Coccidiomycosis (*Coccidioides immitis*): epithelioid granulomas

Blastomycosis (*Blastomyces dermatitidis*): suppurative granulomas

Lung abscess

Aspiration (anaerobic bacteria)

Preceding pneumonia

Septic embolisation

Neoplasia or foreign body leading to airway obstruction (postobstructive pneumonia)

Traumatic event: penetration into lungs

Infection spreading from a neighboring organ (subphrenic abscess, esophagus, etc.)