LOWER RESPIRATORY TRACT INFECTION

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INTRODUCTION

The normal lung is free of infective organisms – variety of innate (non-specific) defence mechanisms including:

- Size of particles
- Mucociliary action: in nose, nasopharynx, oropharynx, larynx, tracheobronchial tree: particles coughed up or swallowed. Mucus made by seromucus glands and/or Goblet cells depending on region
- Components of secretions e.g. IgA
- Alveolar macrophages: phagocytic function and travel via lymphatics that run in the bronchovascular bundles to hilar lymph nodes

Acquired (specific) immune responses are activated if the non-specific responses are unsuccessful.

Healthy persons are susceptible to disease caused by a variety of organisms, but patients with underlying disease, pulmonary or systemic, are more at risk, to certain pathogens in particular, depending on the clinical situation.

Impairment of defence mechanisms

- General immunocompromisation e.g. elderly, infants, chronically debilitated
- Specific immunocompromisation e.g.
    - Impaired humoral immunity -> certain bacterial infections
    - Impaired cell mediated immunity -> certain viral, fungal, protozoan and bacterial infections
- Pulmonary congestion and oedema
- Increased or retained mucus, which provides a medium for bacterial growth in airways e.g.
    - Impaired cough reflex e.g. coma, certain drugs, post operative pain, immobility, may also lead to aspiration
    - Bronchial obstruction e.g. tumour, cystic fibrosis
    - Impaired cilial activity e.g. viral infection, smokers
    - Chronic bronchitis in smokers

ACUTE BRONCHITIS

Causes: usually viral (rhinovirus, coronavirus, influenza, adenovirus), also *Mycoplasma pneumoniae*, bacterial (e.g. *Strep. pneumoniae*, *H. influenzae*).
Some viruses damage the epithelium leaving the lower respiratory tract (LRT) prone to secondary bacterial infection e.g. following a cold.
Acute exacerbations of chronic bronchitis: common pathogens: viruses, *Strep. pneumoniae*, *H. influenzae*, *Moraxella catarrhalis*
Causative bacteria: often normal oropharyngeal commensals
Clinically: cough productive of sputum, may be white or yellow/green, variable wheeze, fever

ACUTE BRONCHIOLITIS

Young children
Vast majority viral and most caused by respiratory syncytial virus
May spread to become interstitial pneumonia
In older children and adults, RSV may cause a common cold like illness

PNEUMONIA

- 'Old mans friend'
- Commonest cause of infection related death in developed societies
- Organisms may gain access to the lung via
    - Gross aspiration: Gross aspiration frequently leads to aspiration pneumonia, typically from anaerobic organisms and gram-negative bacilli and is most likely in postoperative patients or those with disorders of the CNS that affect swallowing e.g. seizures, strokes.

- Microaspiration: the most common route for bacterial pneumonia is microaspiration of oropharyngeal secretions containing potentially pathogenic microorganisms e.g. *Strep. pneumoniae, Haemophilus influenzae*.
- Aerosolization: *Mycobacterium tuberculosis*, fungi, *Legionella* spp., *Coxiella burnetii* and many respiratory viruses reach the lungs following inhalation of infected aerosolised droplets.
- Hematogenous spread from a distant infected site (uncommon).
- Direct spread from an adjacent infected site (uncommon).

- Classification: pathologic (pattern), aetiological, clinical (circumstances surrounding development of disease) - overlap to some extent

Knowledge of the circumstances in which a person develops pneumonia and the pathological pattern give clues to the causative organism and thus the initial therapy to use.

Causative agents

Influenced by age of patient, underlying pulmonary pathology, immunocompromisation, travel, animal, occupational contact. Clinical, epidemiologic and pathologic information help to suggest the causative organism and influence initial antimicrobial therapy, but laboratory investigations are essential to identify the specific cause and optimise antimicrobial therapy.

- Community acquired pneumonia
  - *Strep. pneumoniae*, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae,* various viruses (respiratory syncytial, parainfluenza, influenza, adenovirus, varicella-zoster), *Haemophilus influenzae*, *Klebsiella pneumoniae*, *Staph. aureus*, *Legionella pneumophila.* The frequency of these pathogens differs with the age and co-morbidities of the patient. Young healthy adults: often *Mycoplasma pneumoniae* or *Chlamydia pneumoniae*
  - Specific occupational/animal/environmental exposure: *Legionella pneumophila, Coxiella burnetii, Brucella spp., Chlamydia psittaci*
- Hospital acquired (nosocomial): bacteria as above, however, gram negative organisms relatively more common e.g. *Escherichia coli, Klebsiella, Pseudomonas aeruginosa.* Risk factors include co-morbidities, older age, coma, intubation, general anaesthesia, post operative
- Pneumonia in severely immunocompromised, especially cell mediated e.g. AIDS, post organ transplant: causes include
  - Bacteria: *Mycobacterium* spp, *Nocardia*
  - Fungi: Aspergillus, Cryptococcus, *Pneumocystis jiroveci (carinii)*
  - Viruses: Cytomegalovirus (CMV), *Herpes simplex*

Clinically

Variable symptoms and signs. Variable severity of disease: mild – life threatening. Onset may be sudden or more insidious.

- Cough +/- sputum that may be purulent or blood stained or 'rusty'
- Rapid shallow breathing
- Tachycardia
- Malaise
- Fever, chills, rigors
- Pleuritic chest pain and pleural friction rub – typically in cases where there is more extensive pleural inflammation with exudate (e.g. lobar pneumonia) that involves parietal pleura, where somatic pain fibres become activated upon 'rubbing' of inflamed surfaces
- Dullness to percussion, bronchial breath sounds, increased vocal resonance etc, classically in lobar pneumonia, variable in bronchopneumonia
- Rhonchi, crepitations
- Reduced movement of chest wall on affected side/s
- Sometimes pleural effusion
- With some causes, systemic features e.g. headache, muscle aches and pains, malaise, may predominate over the respiratory features
- Certain organisms (e.g. *Coxiella burnetii, Mycoplasma pneumoniae*) may cause clinical manifestations from involvement of other systems also
- Course variable: acute or subacute depending on cause

Investigations

May include: Sputum microscopy, culture and antibiotic sensitivities, blood culture and antibiotic sensitivities, serology, CXR, CBE, electrolytes, urea, creatinine, glucose, arterial blood gases, other

Management

Initial empirical antibiotic therapy is commenced based on the likely causative organism/s, which is influenced by patient and clinical features and severity of illness. Guidelines/protocols on what to use in different situations are available. Therapy is later tailored to the specific causative organism based on specific culture and sensitivity or serological results.

Pathologic patterns

Main pathologic patterns: lobar pneumonia, bronchopneumonia, interstitial pneumonia. Patterns frequently overlap.

Lobar pneumonia

- Involves a large portion of or an entire lobe - organisms gain access to distal airspaces and spread through alveolar spaces until limited by anatomic barriers between segments or lobes of lung. May involve multiple lobes.
- Cause: most due to *Streptococcus pneumoniae,* also *Klebsiella*
- Often follows a viral upper respiratory tract infection, not uncommon in vagrants and alcoholics
- Usually community acquired

- Morphology
    - Acute fibrinosuppurative consolidation of large areas, consolidation maximal days 2-6, fibrinosuppurative pleuritis
    - Classically 4 stages - congestion, red hepatization, grey hepatization, resolution
- Potential outcomes and complications
    - Resolution (most): with prompt treatment, there is little necrosis and the alveolar framework is retained. Neutrophils die, macrophages phagocytose debris, fluid and macrophages drain via lymphatics to local lymph nodes and any damaged alveolar epithelial cells regenerate. Fibrinous serosal exudate frequently organises.
    - Abscess formation (uncommon, depends on causative organism): via toxins/enzymes released by organisms and neutrophils that lead to tissue death
    - Empyema: pus within the pleural cavity. Uncommon, depends on organism. From bacterial spread or rupture of abscess into pleural cavity
    - Associated septicaemia +/- bacteraemic dissemination

<u>Bronchopneumonia</u>

- Patchy distribution, generally involving several lobes, infection of bronchi and bronchioles which spreads down to alveoli
- Common at extremes of life, in patients with underlying lung pathology and in debilitated and immobile patients. Common cause of death in elderly and debilitated patients.
- Causes include: *Staph. aureus, Strep. pneumoniae, Klebsiella, Haemophilus influenzae*
- Predisposing factors:
    - Immunosuppression: e.g. infancy, old age, general debility, drug induced
    - Retention of secretions: cilial damage (e.g. in viral bronchitis, chronic bronchitis), cough suppression, immobility
    - Excess or abnormal mucus production e.g. chronic bronchitis, cystic fibrosis
- Morphology
    - Acute fibrinosuppurative inflammation of airways which spreads to alveoli -> patchy consolidation, often basal, bilateral
- Potential outcomes and complications
    - Resolution
    - Focal scarring
    - Abscess formation (more common than with lobar pneumonia)
    - Empyema: pus within the pleural cavity. More common than with lobar pneumonia From bacterial spread or rupture of abscess into pleural cavity
    - Associated septicaemia +/- bacteraemic dissemination

<u>Interstitial pneumonia</u>

- Inflammatory process largely confined to the interstitial tissue (of alveolar walls and bronchovascular tree) rather than the alveolar spaces. The alveoli, however, may contain variable amounts of cellular and/or proteinaceous exudate
- The inflammatory cells are predominantly mononuclear i.e. lymphocytes, macrophages and plasma cells, with fewer neutrophils
- There may also be bronchiolitis histologically, depending on the cause
- Patchy or lobar involvement
- Occurs with viral pneumonias and those caused by *Chlamydia* and *M. pneumoniae, Coxiella burnetti*
- Tends to cause a different clinical pattern than the usual bacterial pneumonias e.g. dry or even no cough and few or no signs localising infection to the chest, though sometimes there may be consolidation, thus sometimes referred to as primary atypical pneumonia
- Disease generally mild with complications rare, although certain viral infections in the lungs can cause a more severe necrotising pneumonia and/or a pattern of diffuse alveolar damage

LUNG ABSCESS

Caused by a variety of organisms including *Staph. aureus*, various *Streptococci*, Gram negatives and anaerobes e.g. *Bacteroides*

Risk factors

- Aspiration i.e. of gastric contents and/or oropharyngeal organisms. Generally in patients with impaired consciousness or neuromuscular or obstructive diseases that interfere with gag or cough reflexes and swallowing (e.g. alcohol intoxication, coma, tumours)
- A complication of a primary bacterial infection i.e. associated with pneumonia, especially infection with certain organisms such as *Staph. aureus*, *Klebsiella pneumoniae*, type 3 pneumococcus
- Immunosuppression
- Septic embolism or seeding in septicaemia
- Impaired mucociliary clearance e.g with bronchial obstruction or bronchiectasis
- Direct extension from infection in adjacent organs
- Penetrating trauma

Clinically: patients have fever and cough productive of purulent sputum. Weight loss if chronic.

Morphology

- Cavitating necrotic mass surrounded by suppurative inflammation +/- surrounding pneumonic consolidation
- May be single or multiple
- If becomes chronic, becomes surrounded by granulation tissue and a fibrous capsule

Complications

- Empyema

- Bronchopleural fistula
- Pulmonary haemorrhage
- Bacteraemic dissemination e.g. -> cerebral abscess
- Amyloidosis if chronic

ASPIRATION PNEUMONIA

- Aspiration of acidic gastric contents (causing chemical pneumonitis) and/or oropharyngeal organisms into lung, generally in patients with impaired consciousness or neuromuscular or obstructive diseases that interfere with gag or cough reflexes and swallowing
- Oropharyngeal aspiration often leads to anaerobic infection that may be complicated by abscess formation
- Often severe pneumonia with high mortality

BRONCHIECTASIS

- Bronchiectasis refers to the irreversible dilatation of bronchi and bronchioles as a consequence of the destruction of the muscular and elastic elements of their walls resulting from or associated with chronic necrotizing infections.
- May be focal or more generalised
- Pathogenesis: the two main factors that lead to bronchiectasis are obstruction and infection. Bronchial obstruction may be caused by tumours, foreign bodies or mucus plugs e.g. in cystic fibrosis. Impaired cilial activity e.g. in Kartagener's syndrome, may also predispose. Chronic bronchial obstruction and/or mucus retention predisposes to recurrent or persistent infections causing necrosis, ongoing acute and chronic inflammation and fibrosis. Damage to bronchial smooth muscle and elastic tissue leads to weakening of their walls with dilatation. Bronchiectasis may also develop in the setting of recurrent necrotizing pneumonias leading to non-obstructive bronchiectasis (now uncommon), particularly in children.
- Clinically: episodic (with infective exacerbations) cough, foul purulent sputum, fever, dyspnoea
- Complications
  - Potentially life threatening haemoptysis
  - Obstructive ventilatory problems and destruction of lung tissue lead to chronic respiratory failure and cor pulmonale
  - Bacteraemic seeding -> e.g. brain abscesses
  - Amyloidosis (rare)