PNEUMONIA

Refers to the infection and/or inflammation of the lung parenchyma.

Defn

- Pneumonia is defined as inflammation and consolidation of the lung tissue due to an infectious agent.
- Pneumonia that develops outside the hospital setting is considered community-acquired pneumonia (CAP).
- Pneumonia developing 72 hours or more after admission to the hospital is termed hospital-acquired pneumonia (HAP).

Community-acquired pneumonia (CAP)

- Caused most commonly by bacteria that traditionally have been divided into 2 groups, typical and atypical.
  - Typical organisms include *S pneumoniae* (pneumococcus) and *Haemophilus* and *Staphylococcus* species.
  - Atypical refers to pneumonia caused by *Legionella, Mycoplasma,* and *Chlamydia* species (C *pneumoniae, psittaci,* and *trachomatis)*

Epidemiology

Factors

- Age
- Seasonal variations
- Immunity
- Health status/ co-morbidity

- Is the commonest major infection of children and major killer of children<5 year.
- accounts for up to 1.5m deaths annually in Africa.
- Incidence of 5 per 100 children per year
- Responsible for 4m deaths per year worldwide

Classification

- Aetiological or anatomical
- **Anatomical**: brochopneumonia, lobar and interstitial.
- **Aetiological:** based on offending organism or agent e.g bacterial, viral, fungal , aspiration etc.

…Anatomical classification

Bronchopneumonia

- Inflammation occurs primarily in the terminal and respiratory bronchioles.
- The walls are damaged so that infection and exudate extend into the acinus supplied by the affected terminal bronchiole.
- The result is numerous discrete foci of consolidation centred around inflamed terminal bronchiole.

Anatomical classification

Lobar pneumonia

- may affect an entire lobe
- infection results in production of watery inflammatory exudate in the alveoli, which spreads together with bacteria through the lumens rather than the walls of the terminal airways.
- The lobe is diffusely affected and the consolidation is confined to the lobe.

Interstitial pneumonia

- interstitial tissue

Aetiology

country	Comm'est	2nd comm	3rd comm
USA 1987	*S. pneumo*	*H. influenza*	*Other strep*
Kenya 1985	*S. pneumo*	*H. influenza*	
Kenya 1987	*S. aureus*	*E. coli*	*Klebsiella*
Kenya 1998	*S. pneumo*	*H. influenna*	*s. aureus*
Gambia 1984	*S. pneumo*	*H. influenza*	--
Gambia 1984	*S. pneumo*	*M. Tuberculosis*	*h. influenzae*
Colombia 1976	*S. pneumo*	*S. pneumoniae*	--
Zimbabwe 1998	*S. pneumo*	*S. aureus*	*Other strep*
Kenya 1998	*S. pneumo*	*S. pnemoniae*	*=H influenza*
Kenya 2000	*Klebsiella*	*E coli*	*S. Pneumoniae*

…Aetiology

- Majority are bacterial, predominantly gram positive in normal children and gram negative in malnourished ones.
- Combined bacterial and viral occurs
- Viral- **Influenza, Parainfluenza virus**
- Fungal- pjp

- Some hospitalized patients develop pneumonia in <5 days, a condition called early HAP, which is better known as incubating CAP.
- Since nosocomial pneumonia (NP) is defined as occurring a week or more after hospitalization, the early cases should not be regarded as NP but as CAP
- Aspiration plays a central role in the pathogenesis of NP

- Both early HAP and CAP have the same etiology in that the main pathogens are *Strep pneumoniae, Haemophilus influenzae, Moraxella catarrhalis,*
- NP is caused by different pathogens, the aerobic gram-negative bacilli (ie, excluding *H influenzae*).
- *Pseudomonas aeruginosa* is not the most common cause of NP but is the most important organism in terms of mortality and morbidity.
- *S. aureus* (ie, methicillin-susceptible *S aureus* [MSSA], methicillin-resistant *S aureus* [MRSA]) and anaerobic organisms are not significant contributors to NP.

Risk factors

- Lung diseases
- Anatomical abnormalities
- GERD with aspiration
- Neurological disorders
- Immunodeficiency or immunosuppressive conditions

Pathogenesis

- Innate and acquired defense mechanisms usually keep the LRT sterile preventing infection.
- Some of the factors/mediators include
  - Muco-ciliary escalator
  - Soluble factors
  - Secretory IgAs
  - Cough reflex
  - Alveolar macrophages
  - Reflexes-cough and sneeze, epiglottis

Pathogenesis contn

- Abnormality of one or more of the above factors results in invasion of the upper respiratory epithelium by the bacterial agents that normally colonise the nasal and oro-pharynx.
- Some organisms have the ability to escape these mechanisms upon exposure e.g Legionella, mycobacteria.

…**pathogenesis**

- Disruption of above mechanisms may occur following viral infections or injury induced by agents.
- Organisms gain entry into the lower respiratory tract via infectious aerosol or aspiration of commensals.
- Hematogenous spread from extra pulmonary sites e,g S aureus (i.v drugs)
- Direct inoculation in stab wounds and contigious spread

…**pathogenesis**

- Spread to the susceptible anatomical site-bronchial tree then follows.
- Reproduction and breach of epithelial surface and endothelial surface occurs.
- Entry via pores of Kohn (Pneumococcal)
- Establishment in the lung parenchyma
- Subsequent pathologic process varies depending on the causative organism

…**pathogenesis**

- The process of infxn induces both **cellular** and **humoral** immune responses following ag presentation by alveolar macrophages, that mediate the inflammatory responses.

- Alveolar macrophages process and present microbial Ag to lymphocytes and also secrete cytokines (IL 1, TNF) that modulate the immune process in B and T lymphocytes

…patho

- Cytokines facilitate generation of an inflammatory response, activate alveolar macrophages and recruit additional phagocytes and other immunological factors from plasma.
- The exudate is responsible for the local signs and systemic manifestations

…patho

- ***Strep pneumonia*** causes local edema that aids in proliferation and spread to adjacent lung portions resulting in local lobar involvement.
- ***Group A strep*** cause diffuse infection and interstitial pneumonia with high likelihood of pleural involvement

…patho

- ***Staph*** cause confluent bronchopneumonia often unilateral xtised by extensive areas of haemorrhagic necrosis and irregular cavitation of lung parenchyma resulting in empyema or at times broncho-pleural fistula.
- ***Mycoplasma*** inhibit ciliary action and leads to destruction and an inflammatory response in the sub-mucosa…

…pathophysiology

- The above pathologic changes result in small airway obstruction, interstitial oedema eventually resulting in V/Q mismatch, increased work of breathing and hypoxemia.

Immuno-compromised hosts and HIV

- Aetiological agents same as others in general but are also predisposed to uncommon agents e.g pneumocystis jirovesi, Aspergillus spp, cryptococcus, candida, Gram negative enteric bacteria and anaerobic bacteria and viruses- CMV, HSV, influenza,
- May have multiple infection

Clinical Presentation

- Typical or atypical
- Initial presentation often an URTI with cough and rhinitis
- Sputum +ve/-ve
- Dyspnoea
- Fever- more with bacterial than viral
- chills
- Chest pain
- GI disturbances especially in children- anorexia, vomiting, abdominal distension and constipation or diarrhoea
- Myalgia, malaise

On examination

- Usually ill, febrile
- Respiratory distress and use of accessory muscles of respiration
- May be cyanosis
- Tachypnoea
- Abnormal percusion findings- dullness, stony dullness in effusion
- Crepitations, bronchial breathing and other abnormal air entry patterns
- Wheeze/rhonchi
- Tachycardia

….presentation

Other findings related to complications and/or underlying conditions

Diagnosis and Investigations

- Diagnosis usually clinical
- Laboratory studies and radiography help in confirmation or supporting of clinical diagnosis.

Investigations

- Isolation of organism from respiratory secretions, blood or pleural aspirates
- Fibre-optic bronchoscopy
- Trans thoracic needle aspirate
- Blood culture
  - Yield is less than 30%

…..investigations

- **Chest radiographs**
  - Findings depend on the aetiology
  - Can demonstrate complications and the anatomical classification
  - Confluent lobar consolidation or patchy opacification
  - Hyperinflation and patchy infiltrates in viral pneumonia
  - Effusion

….**investigations**

- **Full blood count**
  - Can help differentiate bacterial from viral pneumonia
  - In bacterial, the total WBC is markedly increased 15000 to 40000/mm^3 mainly neutrophils
  - In viral total WBC count may b normal or elevated with relative lymphocytosis
  - ESR modestly increased but non-specific

…investigations

- **Trans-thoracic needle aspirates**
  - Not routinely done.
  - For progressive or pneumonia of questionable aetiology

…investgn

- **Serology- Ag or Ab tests**
  - Latex agglutination may useful
  - ASOT- for group A
  - Requires weeks for antibodies to develop, not useful in the early stages.

Management

- Admit severe cases
- Supportive
  - Oxygen: cyanosis, significant hypoxemia, severe dyspnea, circulatory disturbance
  - Control of fever
  - analgesics for pleuritic pain.
  - Bronchodilators if indicated
  - Rehydration
  - Electrolyte correction
  - Bed rest,
  - **Follow-up x-rays** ; Respiratory isolation if TB is a possibility

…management

- Specific treatment- depends on the :
  - presumptive cause
  - local sensitivity patterns
  - degree of severity
- Oral antibiotics for mild infections e.g
  - amoxicillin,
  - cefuroxime axetil,
  - amoxicillin/clavulinate.
- Broad spectrum i.v antibiotics for severe hospitalised cases-
  - penicillin and amynoglycosides
  - cephalosporins.
- Vancomycin or clindamycin for staph aureus
- Resistance to commonly used first line drugs reported in various series.

Therapy for specific organisms

- *S. pneumoniae*: penicillin G or oral amoxicillin.
  - If high incidence of penicillin resistant *S. pneumoniae* in the area, consider pneumococcal-active fluoroquinolone
- *H. influenzae*: trimethoprim-sulfamethoxazole.
  - For severe infections - cefotaxime, ceftriaxone, or carbapenems
- *S. aureus*: nafcillin or vancomycin (if high incidence of methicillin resistant *S. aureus*)
- Klebsiella species: carbapenems or 3rd generation cephalosporin
- Pseudomonas: aminoglycoside plus antipseudomonal penicillin or ceftazidime

- *Moraxella catarrhalis*: 2nd generation cephalosporin (cefuroxime axetil) or b-lactam/b-lactamase inhibitors
- *Chlamydia pneumoniae*: doxycycline, fluoroquinolone
- *Mycoplasma pneumoniae*: doxycycline
- *Legionella pneumophila*: fluoroquinolone or azithromycin
- Anaerobes: clindamycin or b-lactam/b-lactamase inhibitors

PNEUMOCOCCAL PNEUMONIA Treatment

- ***Pneumonia*** *caused by Streptococcus pneumoniae*.
- For penicillin-sensitive strains of *S. pneumoniae*, penicillin G is the preferred agent; patients who are not severely ill may be treated with penicillin G or V 250 to 500 mg po q 6 h.
- The regimen recommended for parenteral treatment of uncomplicated pneumococcal **pneumonia** is aqueous penicillin G 500,000 to 2 million U IV q 4 to 6 h.
- About 25% of strains of *S. pneumoniae* are resistant to penicillin.

- Most resistant strains respond to high doses of penicillin, cefotaxime, or ceftriaxone.
- The newer quinolones (levofloxacin, sparfoxacin, grepafloxacin, and trovafloxacin) are preferred therapy for penicillin-resistant strains and as an alternative to penicillin for penicillin-sensitive strains.
- Vancomycin is the only drug with consistent activity, is active against all strains of *Strep. pneumoniae* and may be preferred for severely ill patients in areas with high rates of resistance.

Alternative drugs

- with demonstrable efficacy include cephalosporins, erythromycin, and clindamycin.
- Because tetracyclines are less predictably active against *S. pneumoniae,* they should not be used for seriously ill patients.
- Oral regimens include erythromycin or clindamycin 300 mg q 6 h.
- Parenteral regimens include cefotaxime 1 to 2 g IV q 6 h, ceftriaxone 1 to 2 g IV q 12 h, cefazolin 500 mg IV q 8 h, erythromycin 500 mg to 1 g IV q 6 h, or clindamycin 300 to 600 mg IV q 6 to 8 h.
- Most 3rd-generation cephalosporins, other than cefotaxime and ceftizoxime, are relatively inactive against *S. pneumoniae.*

- When meningitis is suspected, the patient should receive cefotaxime 2 g IV q 4 to 6 h or ceftriaxone 1 to 2 g IV q 12 h, plus vancomycin 1 g IV q 12 h with or without rifampin 600 mg/day po until sensitivity test results are known.
- For patients with empyema, treatment should include appropriate drainage as well as parenteral antibiotics.

Prophylaxis

- Vaccine containing the 23 specific polysaccharide antigens of the pneumococcus types that account for 85 to 90% of serious pneumococcal infections is available.
- Most children > 2 yr old and adults have an antigenic response within 2 to 3 wk after vaccination

Staph. aureus

- Most strains produce penicillinase, and methicillin resistance is increasing.
- The recommended therapy is a penicillinase-resistant penicillin (eg, oxacillin or nafcillin 2 g IV q 4 to 6 h).
- The major alternative is a cephalosporin, preferably cephalothin or cefamandole 2 g IV q 4 to 6 h, cefazolin 0.5 to 1 g IV q 8 h, or cefuroxime 750 mg IV q 6 to 8 h.
- 3rd -generation cephalosporins are somewhat less active than 1st - or 2nd -generation cephalosporins.
- Clindamycin 600 mg IV q 6 to 8 h is active against 90 to 95% of strains.

- Methicillin-resistant strains are considered resistant to all b-lactam antibiotics.
- These strains may account for up to 30 to 40% of nosocomially acquired staphylococcal isolates in many hospitals but < 5% of community-acquired infections.
- Vancomycin is preferred when methicillin resistance is suspected or established with in vitro sensitivity tests.
- The usual dosage is 1 g IV q 12 h, with modifications when renal failure is present.

H. influenzae

- **Prophylaxis and Treatment**
- Prophylaxis with *H. influenzae* type b (Hib) conjugate vaccine is advocated for all children to be given in three doses at 2, 4, and 6 mo of age.
- About 30% of *H. influenzae* strains produce b-lactamase and are resistant to ampicillin.
- Thus, preferred treatment is trimethoprim-sulfamethoxazole (TMP-SMX) 8/40 mg/kg/day po or IV for children or 1 or 2 tablets of 160/800 mg bid for adults;

- cefuroxime 0.25 to 1 g IV q 6 h; cefaclor 40 mg/kg/day po in 3 divided doses for children or 500 mg po q 6 h for adults; or
- doxycycline 100 mg po bid (contraindicated in children <= 8 yr).
- Ampicillin 100 mg/kg/day IV in 4 divided doses (maximum, 2 to 3 g/day) for children < 20 kg or 250 mg to 1 g q 6 h for children > 20 kg and adults can be used to treat nonresistant strains.
- Alternative regimens are amoxicillin 20 to 40 mg/kg po tid for children < 20 kg or 250 to 500 mg po tid for children > 20 kg and adults. Fluoroquinolones and azithromycin r also active.

Mycoplasma pneumoniae

- **Prognosis and Treatment**
- Nearly all patients recover with or without treatment. Because mycoplasmas do not have a cell wall, they do not respond to antibiotics that interfere with cell wall structure, including b-lactam antibiotics.
- The preferred drugs are tetracycline or erythromycin 500 mg po q 6 h for adults or erythromycin 30 to 50 mg/kg/day for children < 8 yr.
- Clarithromycin and azithromycin are also effective.
- Antibiotic treatment reduces the period of fever and pulmonary infiltrates and hastens symptomatic recovery.
- However, antibiotics do not cause a microbial cure; treated patients continue to carry the organism for several weeks.

CHLAMYDIAL PNEUMONIA

- The drug of choice is tetracycline or erythromycin, given for 10 to 21 days in doses as for mycoplasmal **pneumonia**. b-Lactam drugs are inactive.

nosocomial pneumonia

- :either ceftazidime or an antipseudomonal penicillin (piperacillin, mezlocillin, or ticarcillin) plus an aminoglycoside.
- Vancomycin should be considered if strong suspicion of *Staphylococcus aureus*.

Complications of Meningitis

- Can b due to direct or hematogenous spread, include:
  - Pleural effusion
  - Empyema thoracis
  - Meningitis
  - Osteomyelitis
  - Arthritis
  - Respiratory failure