Pneumonia

- Definition: Acute inflammatory process at the level of respiratory bronchioli, alveolar structures and/or interstitium

- Epidemiology: Pneumonias are the most common among all infections

- 4th among causes of death worldwide
- Mortality: 18/100 000 per year

Classification (general)

A. Based on etiology: 1. Infectious

2. Non-infectious („*pneumonitis*“)

B. Based on the acuteness/chronicity

1. Acute
2. Recidive
3. Chronic

C. Based on the association with other disease:

1. Primary
2. Secondary (e.g., post-obstructive) (tumour, foreign body...)

Classification of *infectious* pneumonias

A. Based on pathological finding:

1. Lobar – primarily at the level of alveoli
2. Bronchopneumonia – primarily at the level of bronchioli, spreading into alveoli
3. Interstitial – primarily in interstitium,

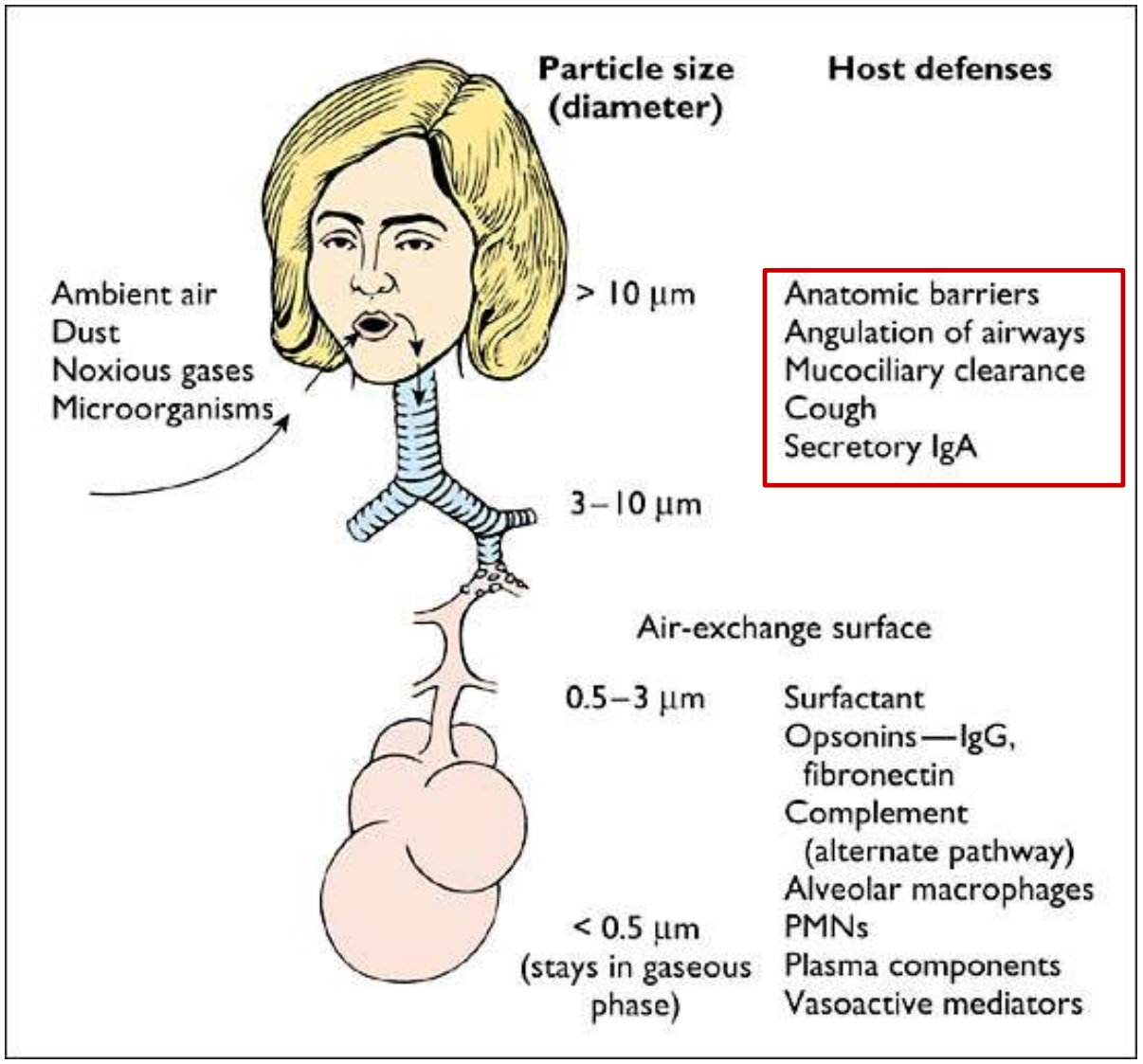
B. Based on clinical course: 1. Typical
2. Atypical

Classification of *infectious* pneumonias

C. Based on the the location of acquisition:

1. Community – acquired (CAP)
2. Hospital – ascquired (HAP)
3. Ventilator – acquired (VAP)

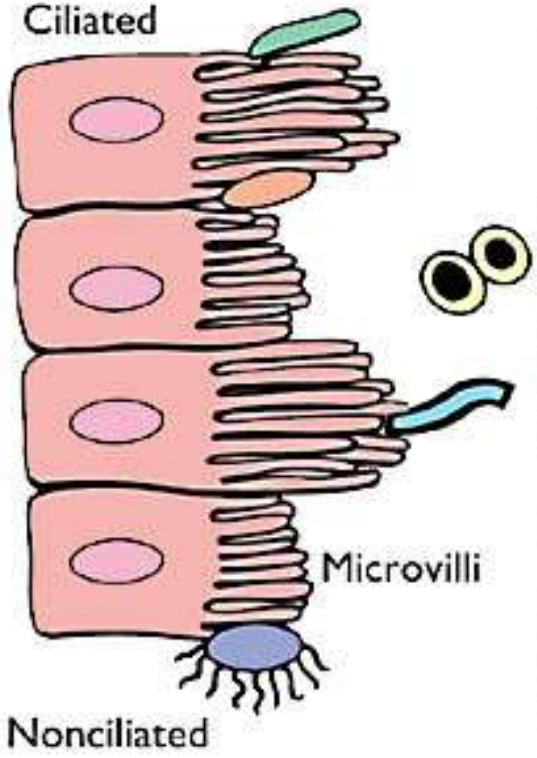
Host defenses along the airways



Cells (macrophages, PMNs)

Antibodies

Mediators



Viruses (cytotoxic)

Mycoplasma (shear off cilia)

Bordetella pertussis
(proximal part of cilium)

Streptococcus pneumoniae
(do not attach to cilia; produce IgA protease and substances that slow or paralyze cilia)

Pseudomonas aeruginosa

Neisseria meningitidis
(attach to microvilli, then phagocytized by cell; also have pili and IgA protease)

Community – acquired Pneumonia (CAP)

General Characteristics (both lobar and lobular)

1. At least one respiratory symptom:

- Cough
- Shortness of breath
- Pleuritic chest pain
- Hemoptysis
- Sputum production

2. At least one general symptom: fever, chills, myalgia, headache, arthralgia

(exogenous and endogenous pyrogens: interleukins, TNFalpha)

3. A new opacity on chest radiograph

Bronchopneumonia
Diagnostic procedures

- Assess vital functions!
- Physical examination
- Laboratory findings
- Chest X-Ray

} immediately

- Arterial blood gases (immediately in case of distress)
- Microbiology
- Bronchoscopy (for differential diagnosis, i.e., tumor, etc. – not all)
- CT (for differential diagnosis, i.e., tumor, etc. – not all patients)
- Immunological investigation (to rule out immune deficit – not all)

Bronchopneumonia

Vital functions – assessment of severity

Vital functions

1. State of conciousness
2. Heart rate
3. Blood pressure
4. Respiratory rate (>30 = severe pneumonia)

Scores of severity: - vital functions (CURB score)
- comorbidities

Determine where the patients will be treated !!

- at home
- hospital – general ward
- hospital – ICU

CURB score

A clinical prediction rule that has been validated for predicting mortality in CAP (and infection of any site).

- **C**onfusion of new onset

- Blood **U**rea nitrogen greater than 7 mmol/l (19 mg/dL)

- **R**espiratory rate of 30 breaths per minute or greater

- **B**lood pressure less than 90 mmHg systolic or diastolic blood pressure 60 mmHg or less

- Age **65** or older

1 point each. Score 0-1 low risk, 2 or more high risk of mortality

Physical Findings

Any of the findings of *consolidation of lung tissue* :

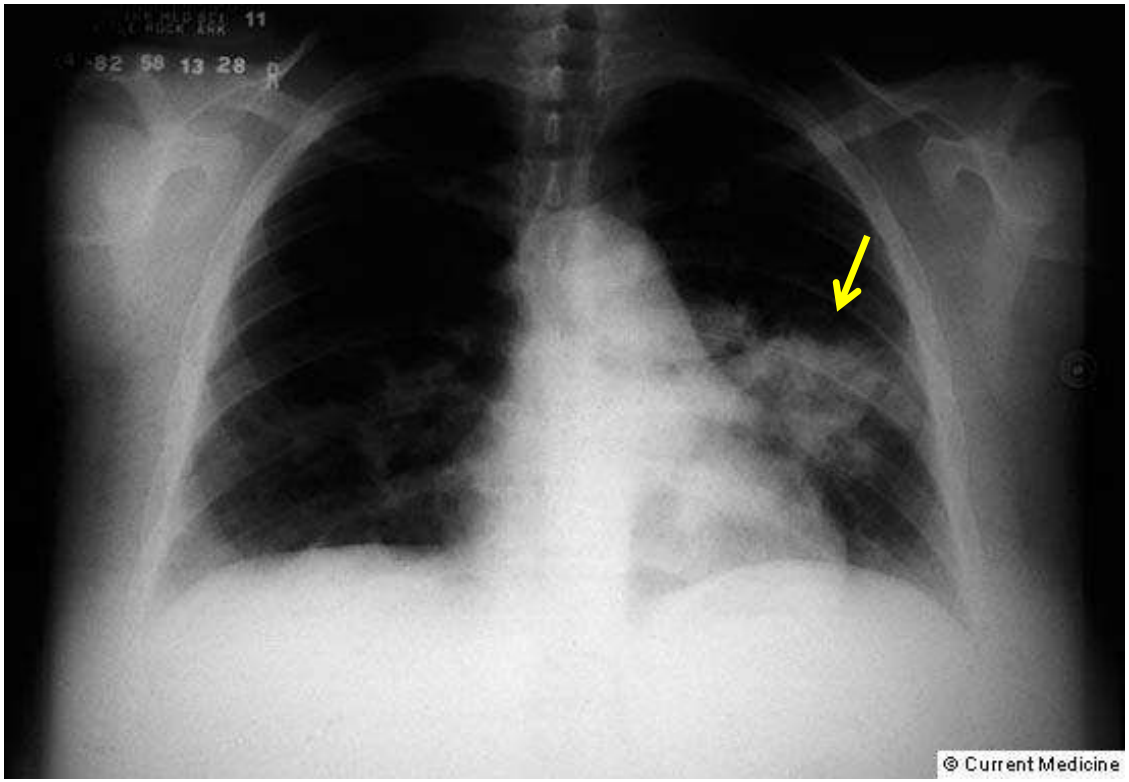
- dullness on percussion, increased tactile and vocal fremitus
- bronchial breathing
- adventitious sounds – crackles, rales

If pleura is affected by inflammation:

- pleural friction rub

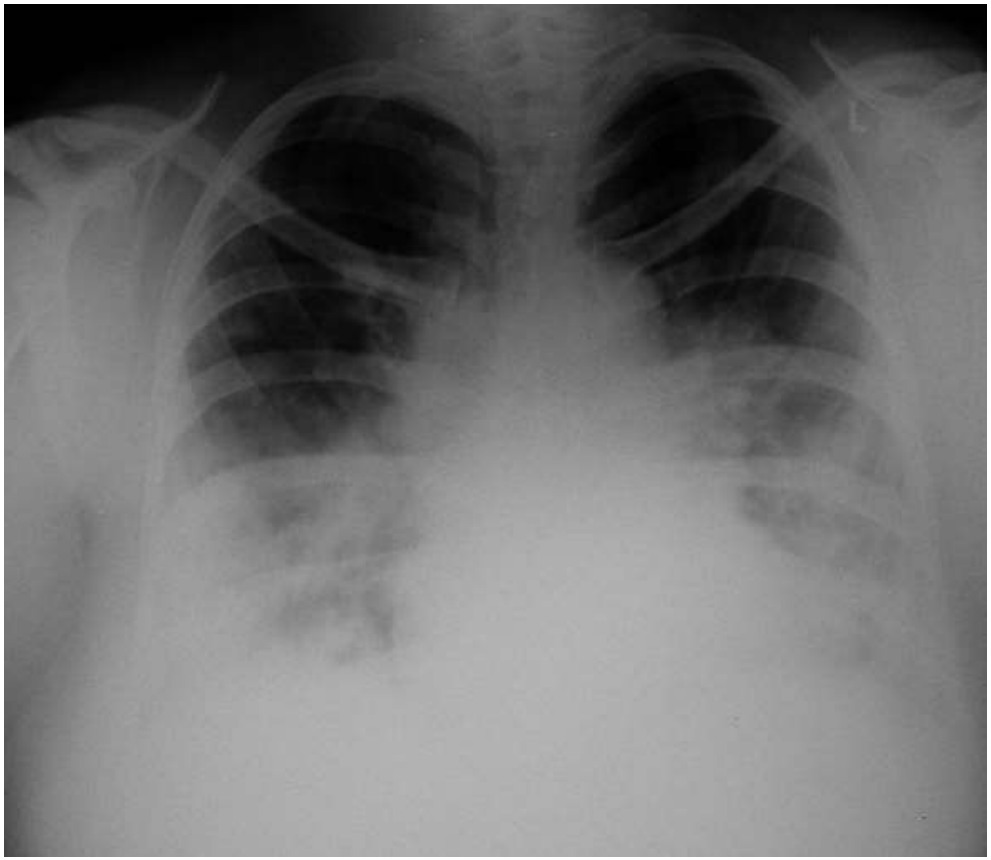
Chest X-Ray

Chest radiographs- postero-anterior and lateral views



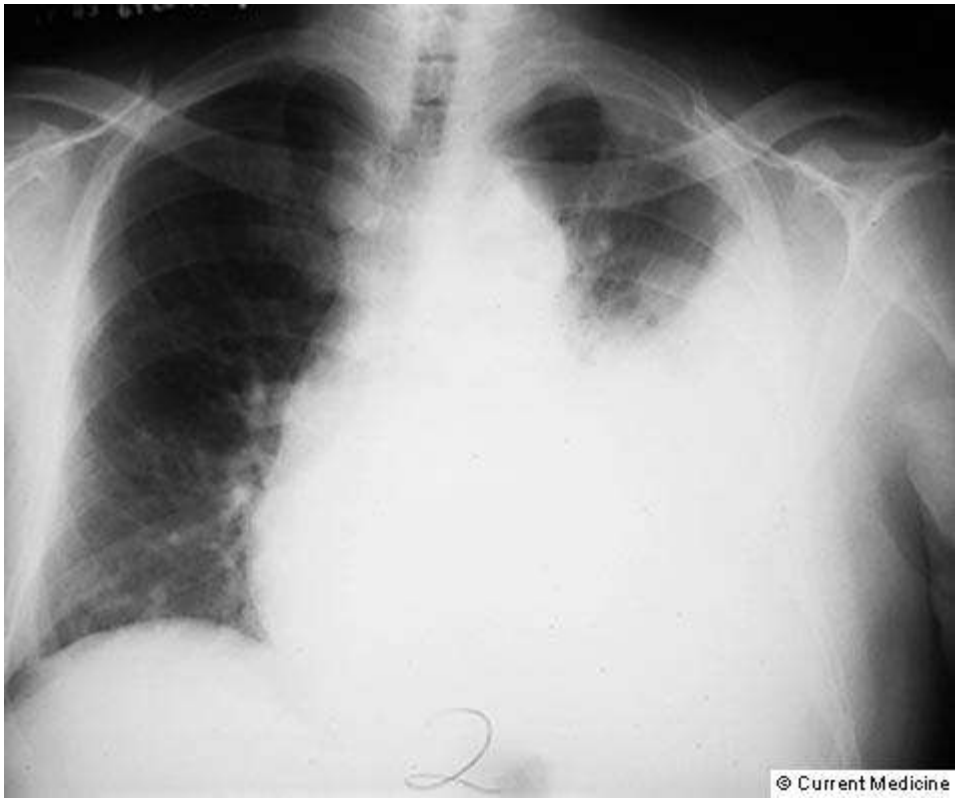
INFILTRATE !

Chest X-Ray in bronchopneumonia



INFILTRATE – bilateral in atypical CAP (Mycoplasma, viruses)

Pleural effusion (exsudate, empyema)



Typical *versus* atypical pneumonia

Typical: Clinical status + physical finding (bronchial breathing + rales)
corresponds with chest X-Ray

Atypical: Clinical status + physical finding (no major pathology on auscultation !!)
do NOT correspond with the extent of chest X-Ray finding
atypical – different pathogens

Oxygenation status

Transcutanous oxygen saturation ($SatO_2$)
should be measured in all patients presenting to an emergency room

An arterial blood gas – in everyone with $SatO_2 < 92\%$,
and those with COPD or another underlying lung disease

Respiratory failure

- **Hypoxemic** – reduction of $PaO_2 < 8$ kPa
- **Hypercapnic** – increase of $PaCO_2 > 6.3$ kPa
- **Acidosis** – reduction of $pH < 7.36$

Laboratory findings

- WBC count: leucocytosis – neutrophilia
  (also leucopenia and lymphopenia possible !)
- C-reactive protein (CRP) 40 – 500 mg/l
- Procalcitonine

} Markers of inflammation

- Blood cultures (if suspected sepsis)
- Serology (antibodies against pathogens: IgM, IgG, IgA) (mycoplasma, chlamydia species)
- Routine blood chemistry: glucose, urea (BUN), sodium

Pneumonia-specific Severity of Illness Score

- a predictive tool for mortality including also laboratory and CXR findings

Patient characteristic	**Points assigned**
Males	age (years)
Females	age (years)mínus 10
Nursing home residence	+30
Comorbid illness	
Neoplastic disease	+30
Liver disease	+10
Congestive heart failure	+10
Cerebrovascular disease	+10
Renal disease	+10

Physical examination findings	
Altered mental status	+20
Respiratory rate >30/min	+20
Systolic BP< 90 mm Hg	+20
Temperature<30ºC or>40ºC	+15

Laboratory findings	
Pulse>125/min.	+10
pH<7,35	+30
BUN>10,7 mmol/L	+20
Sodium<130mmol/L	+20
Glucose>13,9 mmol/L	+10
Hematocrit<30%	+10
pO2<60mm Hg	+10
Pleural effusion	+10

Microbiological examination

- Aim: Identification of the infectious agens

- Material: pharyngeal swab (beware: contamination, colonisation)
  sputum
  bronchoalveolar lavage fluid
  bronchial secretion gained by suction (in an intubated patient on ventilator)

- Methods: Microscopy – staining: Ziehl-Neelsen, Gomori, etc.....
  Aerobic and anaerobic cultivation
  Special methods: PCR

Most common pathogens in CAP

A. Treated on the outpatient basis (*i.e.*, mild)

Mycoplasma pneumoniae	24%
Streptococcus pneumoniase	5%
Chlamydia pneumoniae	5%
Haemophilus influenzae	2%
Unknown	48%

B. Requiring hospital admission (mild or severe)

Streptococcus pneumoniae	17-50%
Haemophilus influenzae	7%

Staphylococcus, Legionella, Mycoplasma, Chlamydia, Pneumocystis, Fungi, anaerobes

Pathogens involved in atypical CAP

Mycoplasma pneumoniae	24%
Chlamydia pneumoniae	5%
Legionella pneumoniae	
Rickettsie	
Viruses	

Intracellular pathogens!!

They require antibiotics with intracellular mode of action !!

Beware: Up to 10% of patients have more than one pathogen identified.

Mycoplasma – frequent in young adults , co-pathogen

Pathogens involved in hospital-acquired pneumonia

Staphylococcus aureus

Escherichia coli

Klebsiella

Enterobacter

Pseudomonas aeruginosa

Proteus and other gramnegatives

Legionella

Pathogens involved in immune deficiency

Viruses – cytomegalovirus, herpes virus

Fungi – aspergillus, cryptococcus, candida, mucor

Protozoa – pneumocystis carinii, toxoplasma gondii

Mycobacteria (TB, non-TB)

Points to remember in CAP

- Many microbial agents can cause pneumonia but the clinical presentation in general does not allow an etiological diagnosis.

  However, **Streptococcus pneumoniae accounts for about 50%** of all cases of CAP that require hospital admisssion.

  Atypical microbes – co-pathogens

- Each microbe can results in an illness that spans the spectrum from mild to life threatening.

CAP – Goals of Therapy

1. To assess the severity of the pneumonia as a guide to decision on the appropriate location of treatment (*i.e.*, home, hospital ward or intensive care unit)

2. To relieve symptoms (fever, cough, pleuritic chest pain, sputum production, dyspnea)

3. **To treat the infection**

4. To promptly recognize and minimize complications: metastatic infection (meningitis, purulent pericarditis, endocarditis, osteomyelitis)

Antibiotics

- Patients pressenting to an emergency room with pneumonia should receive antimicrobial therapy **as soon as possible!**

INITIAL EMPIRIC THERAPY !

- **Macrolides:** erythromycin, clarithromycin, azithromycin...
- **Cephalosporins:** cefotaxime, ceftriaxone, ceftazidime...
- **Beta lactams/lactamase inhibitors:** amoxycillin-clavulanat...
- **Fluoroquinolones:** levofloxacin, ciprofloxacin ...

- Antipseudomonade: imipenem, meropenem...
- Antistaphylococci: oxacillin...

Initial Management of CAP
ATS, BTS, ERS ...guidelines

Severity of illnes score

90 points

Treat as an outpatient

Macrolide
or
Chinolone

91 points

Treat in hospital

ICU	**Ward**
shock; assisted vent.	Levofloxacin or
IV levofloxacin plus	2nd or 3rd
beta lactams	generation
or	cephalosporin
IV beta lactam plus	plus
macrolide plus aminoglycoside	macrolide

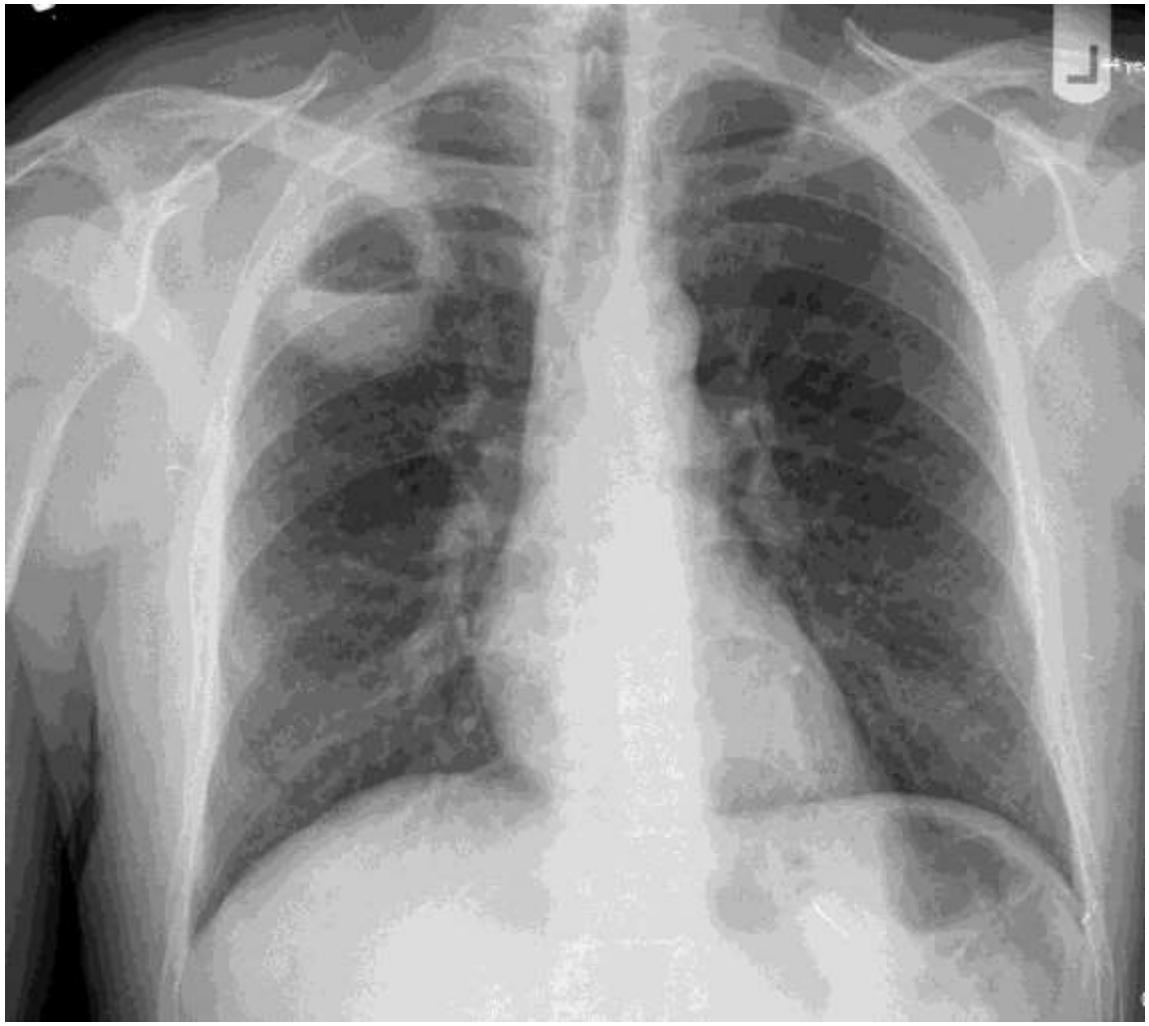
Combination of antibiotics

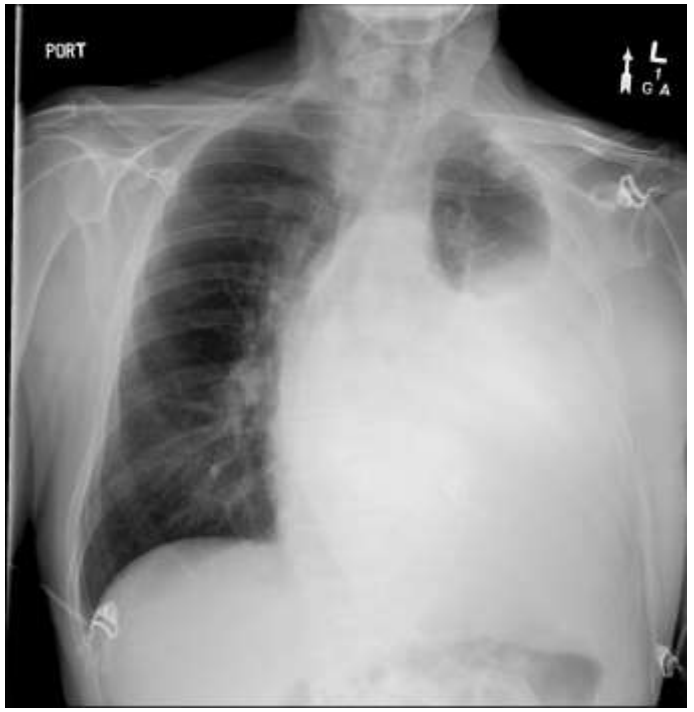
To cover intracellular pathogens: macrolides or quinolones !!!

Complications

- empyema
- cavitation
- pneumothorax
- septic shock
- respiratory failure
- worsening of comorbid conditions (e.g., ischemic heart disease,diabetes mellitus)

- adverse drug reactions (common: allergies, impairment of renal or liver function ...)

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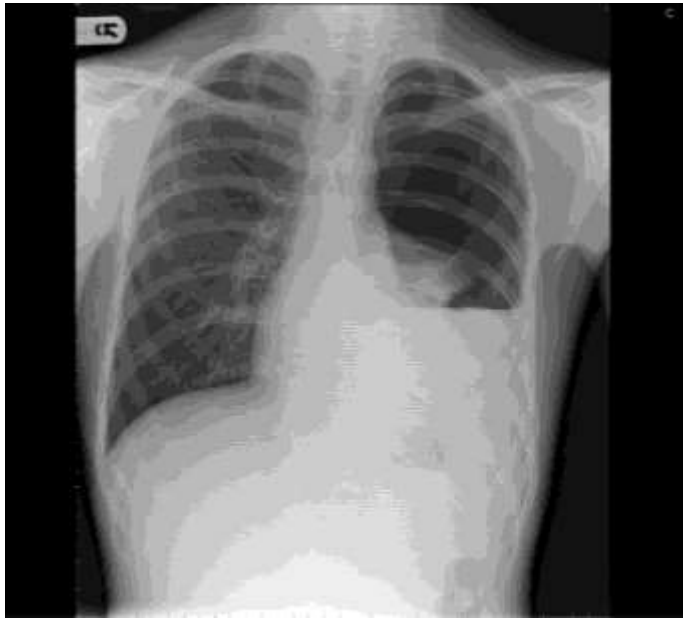
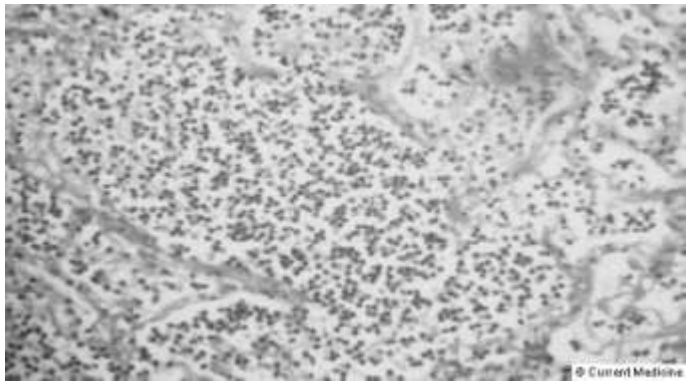


Lobar pneumonia *versus* bronchopneumonia

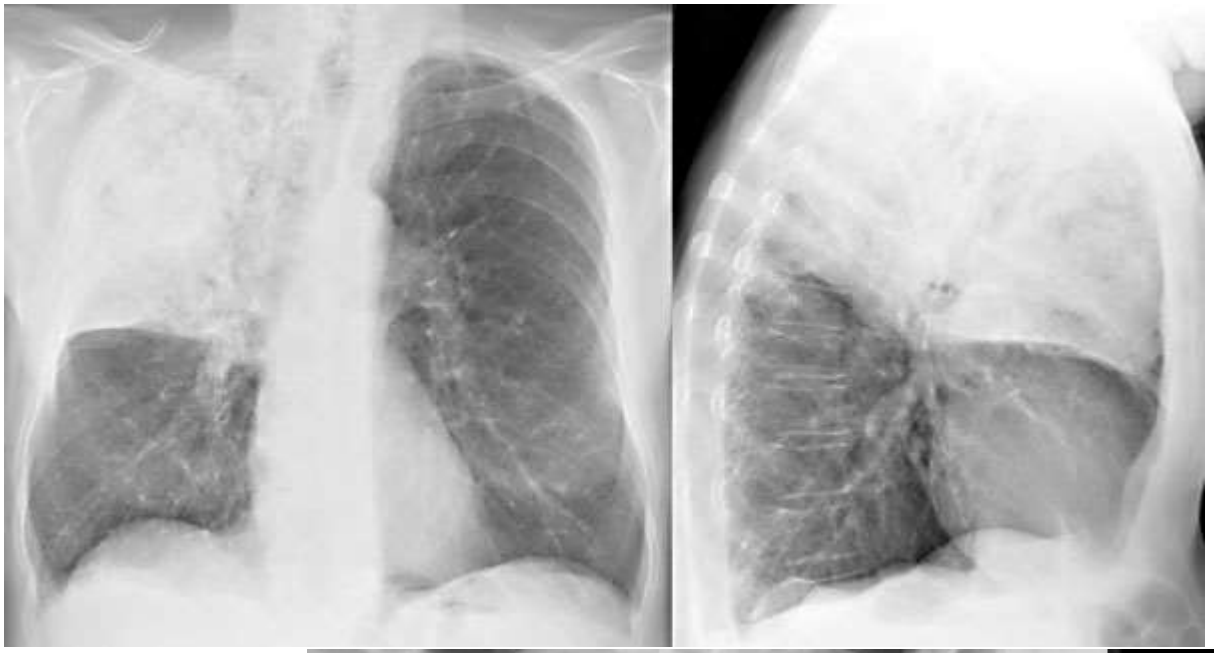
- Lobar pneumonia - rare nowadays
- Associated with very severe condition
- Intraalveolar inflammation

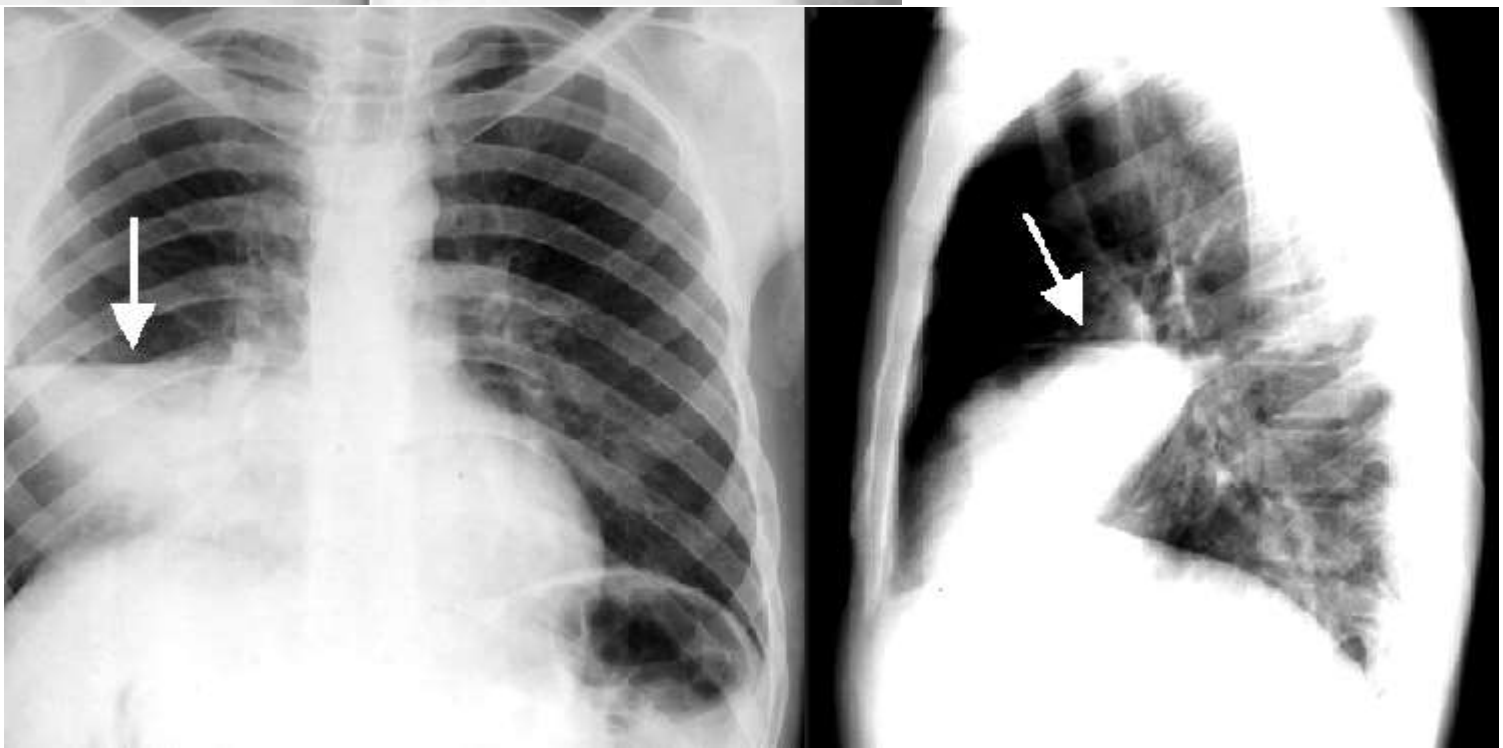
Neutrophils in alveoli



- Physical findings – typical for condensation of lung parenchyma:
  - percussion sound – shortened
  - bronchial breathing above the affected lobe/-s
  - **„crepitus indux and crepitus redux“ –** crackles and rales present initially and then re-occur before recovery

- X-Ray: **homogenous condensation/infiltration of the whole lung lobe**





Viral pneumonias

Virus infections of the respiratory tract – most common acute infection worldwide with a wide variety of affected site and severity (varies from common cold to pneumonia)

Clinically important viruses

1. Influenza virus (A, B)
2. RS virus
3. Adenovirus
4. Parainfluenza virus
5. Herpes family (varicella-zoster virus, cytomegalovirus)
6. Coronavirus

Viral pneumonias

Imaging features

CXR – markedly bilateral infiltrates with interstitial involvement and dominantly affecting lower parts of lungs

CT - alveolar affections (ground-glass opacities)

- interstitial affections (fibrosis)

DDX: - pneumonias of other aethiology

- idiopathic (non-infectious) interstitial lung diseases
- lung congestion in heart failure, uremic lung
- malignancy (lymphangoitis carcinomatosa)
- bronchiectasis

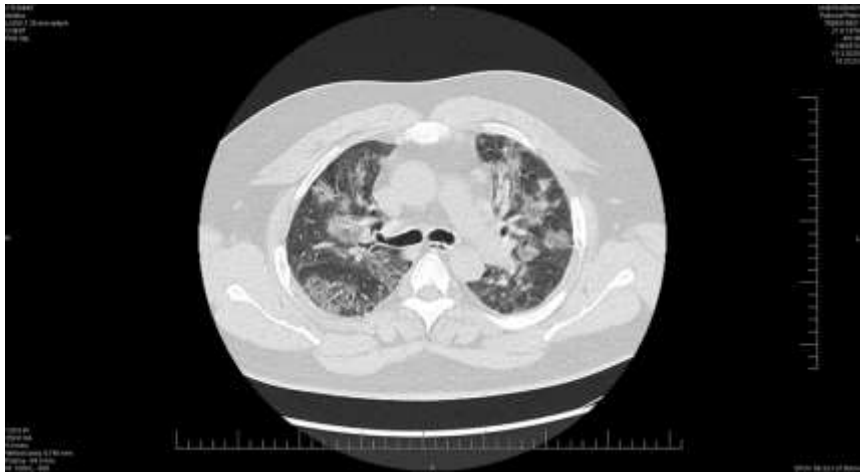
Viral pneumonias

Physical examination bilateral inspiratory non-accentual crackles and crepitations, ↑ fremitus pectoralis

Lab. diagnosis

1. Cytology (BAL fluid, secretions, lung tissue biopsy)
   DNA viruses - intranuclear inclusion bodies
   RNA viruses - cytoplasmic inclusion bodies
2. Serology - EIA
3. Cultures – protein-rich medium
4. Antigen detection: direct or indirect immunofluorescence, ELISA
5. Genetic amplification methods:
   - PCR (frequently first choice), high sensitivity and specificity

COVID-19 pneumonia



- Infection by a coronavirus SARS-CoV2
- CT scan - extensive bilateral ground glass opacities combined with dense condensates
- Microbiology – PCR tests – nasopharyngeal swab or bronchoalveolar lavage fluid
- Progression of respiratory distress, ARDS – requires mechanical ventilation applied preferably in prone position
- No specific antivirotic treatment available, experimental administration of hydroxychloroquin, antiretroviral drugs (for HIV)
- Bacterial super-infection and sepsis – broad-spectre ATB

Nosocomial Pneumonia – HAP

- Definition: infection that occurs 48 to 72 hours following admission to hospital and one that is not incubating at the time of admission

- increase in length of hospital stay
- the hospital—acqured infection that is most likely to result in a fatal outcome
- mortality 33-50%
- mortaligy higher in patients who are bacteremic or who are infected with particulary virulent pathogens (*Pseudomonas aeruginosa, Klebsiella, Acinetobacter, E. coli, Proteus ...)*

Predisposing factors

1. Prolonged hospitalization
2. Underlying comorbid disease
3. Compromised host defenses
4. Recent antibiotic therapy
5. Aspiration

Anaerobes normally found in the oropharynx are the usual cause of aspiration pneumonia.

Ventilator-associated pneumonia - VAP

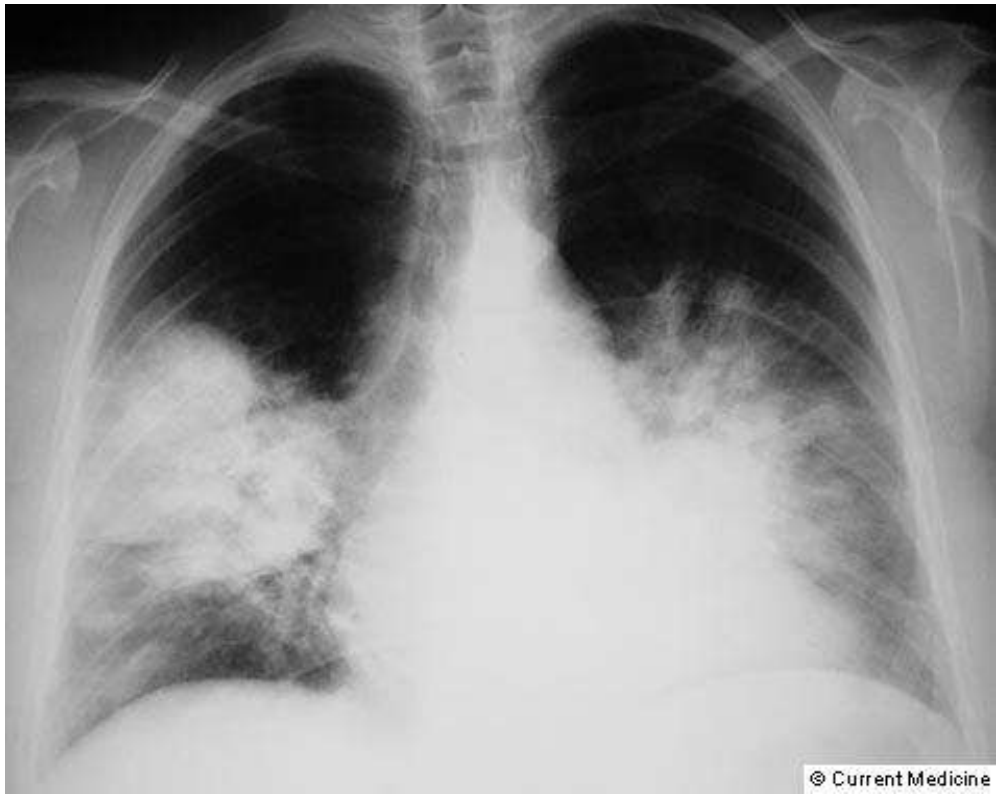
- Prospective cohort studies – incidence of VAP: 10-65%
- Patients at highest risk:
    - COPD
    - Burns
    - Neurosurgical illness
    - ARDS
    - Reintubation
    - Witnessed aspiration
    - Receiving paralytic agents, or continuous enteral nutrition

Ventilator-associated pneumonia

- **Early** – 4 - 7 days of onset of mechanical ventilation
  - easily treated organisms (Streptococcus pneumoniae, Haemophilus influenzae, Staphylococcus aureus)

- **Late** – after 7 days of ventilation
  - difficult-to-treat organisms (Pseudomonas species, Acinetobacter)

Nosocomial pneumonia - HAP
Pseudomonas aeruginosa



HAP – VAP : diagnosis

- **Clinical approach**: careful history, clinical examination, chest x-ray, sputum and blood cultures
- Invasive/quantitative methods: bronchoscopis techniques –

  protected specimen brush, bronchoalveolar lavage, deep suction

  aspirates in patients who are mechanically ventilated

- Even in tertiary level university centres using multiple approaches, an etiologic pathogen may not be found in over one half-cases
- Invasive methods do not appear to alter mortality in severe cases

Pulmonary infections in HIV (AIDS)

- Immunocompromised patients are *extremely susceptible* to the development of respiratory tract infections with a variety of organisms, some of which rarely cause disease in the immunocompetent host.

Bacteria

- Gram-positive cocci, specially Staphylococcus
- Gram-negative bacilli
  - *Mycobacterium tuberculosis*
  - Atypical mycobacteria
  - *Nocardia*

Continued....

- **Viruses**
- *Cytomegalovirus*
- Herpesvirus

- **Fungi**
- *Aspergillus* (invasive pneumonia)
- Cryptococcus
- Candida
- Mucor

- **Protozoa**
- *Pneumocystis carinii*
- Toxoplasma gondii (rare)

Pneumocystic carinii pneumonia in HIV

- In patients with AIDS, often has an indolent onset
- Diagnosis is made most commonly on samples obtained by induction of sputum or bronchoalveolar lavage
- Symptoms: dyspnea, fever, hypoxemia
- Chest radiograph: frequently *diffuse* alveolar infiltrates

- Standard therapy:
    1. Trimethoprim – sulfamethoxazole (21 days)
    2. Trimetoprim – dapsone
    3. Pentamidine (atypical presentations in patients receiving aerolized pentamidine)

Viral infections in AIDS

- The most common virus – **Cytomegalovirus** (CMV, herpesvirus family)
- The most common site – **eye** (CMV retinitis) **and gastrointerestinal** tract
- Frequently found in cultures from lung tissue or bronchoalveolar fluid, almost always with the **coexistent Pneumocystis** that is thought to be the primary pathogen

Mycobacterial infections in patients with AIDS

1. Tuberculosis may be an **early opportunistic** infection

2. In the late stage of the disease, the clinical manifestation of tuberculosis is often atypical: upper lobe cavitary less frequent, disseminated disease more frequent

3. The other species that frequently causes opportunistic infection in AIDS is **Mycobacterium avium-intracellulare**, often with disseminated disease