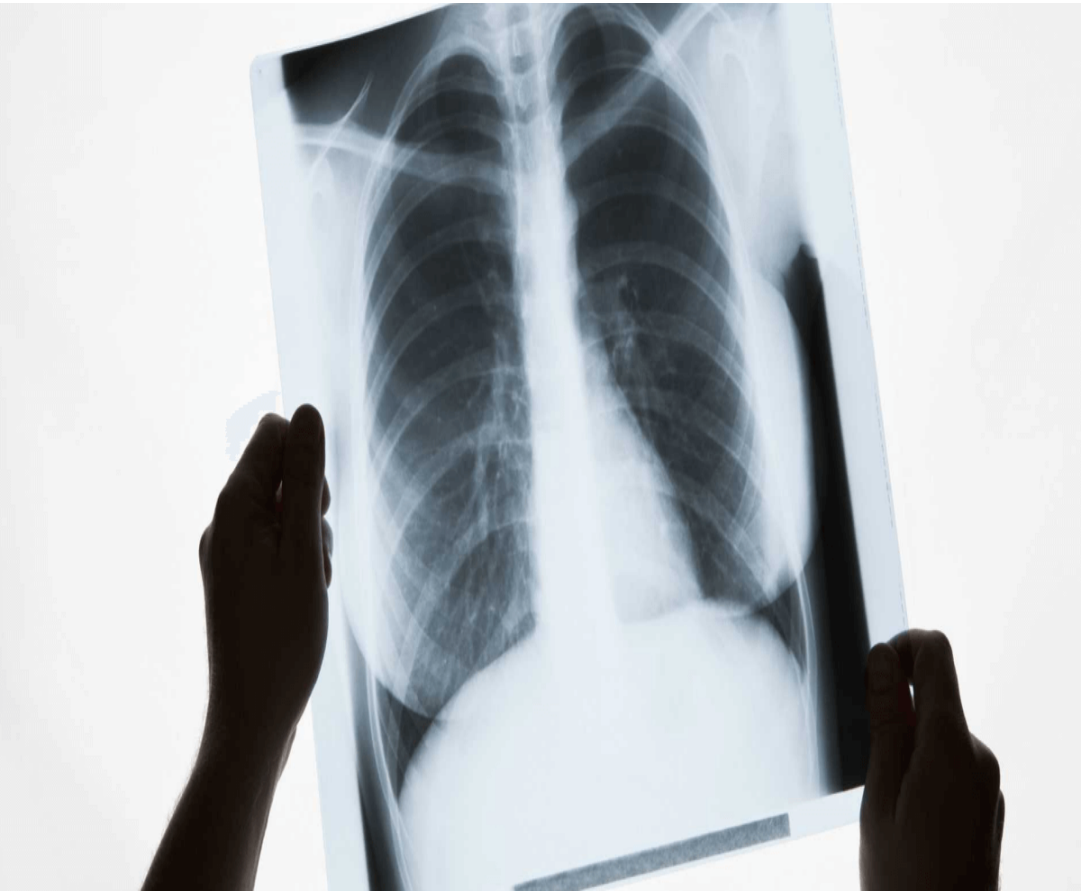
Pneumonia



Poltava State Medical University

The Internal Medicine №1 Department

Poltava - 2022

Plan of the lecture

I. **Introduction**
II. **Definition**
III. **Etiology and Pathogenesis**
IV. **Risk factors**
V. **Classification.**
VI. **Community-acquired pneumonia.**
VII. **Hospital-acquired pneumonia**

INTRODUCTION

Pneumonia is inflammation of the lungs with consolidation or interstitial lung infiltrates, most often categorised according to the causative organism. Typical symptoms might include fever, cough, dyspnoea, and chest pain. Because each specific type of pneumonia may result from a different aetiology and pathogenic mechanism, each subtype also has its characteristic risk factors, signs, and symptoms.

WHO IS AT RISK FOR PNEUMONIA?

Anyone can get pneumonia.

However, the following groups are at the highest risk:

-adults ages 65 and older

-children younger than age 2

-people with certain medical conditions

-people that smoke

What causes pneumonia?

- There are more than 30 different causes of pneumonia, and they're grouped by the cause.
- The main types of pneumonia are:

Etiology

- **Bacterial pneumonia.** This type is caused by various bacteria. The most common is *Streptococcus pneumoniae*. It usually occurs when the body is weakened in some way, such as by illness, poor nutrition, old age, or impaired immunity, and the bacteria are able to work their way into the lungs. Bacterial pneumonia can affect all ages, but you are at greater risk if you abuse alcohol, smoke cigarettes, are debilitated, have recently had surgery, have a respiratory disease or viral infection, or have a weakened immune system.

Viral pneumonia.

- This type is caused by various viruses, including the flu (influenza), and is responsible for about one-third of all pneumonia cases. You may be more likely to get bacterial pneumonia if you have viral pneumonia.

Mycoplasma pneumonia.

- This type has somewhat different symptoms and physical signs and is referred to as atypical pneumonia. It is caused by the bacterium *Mycoplasma pneumoniae*. It generally causes a mild, widespread pneumonia that affects all age groups.
- There are other less common pneumonias that may be caused by other infections including fungi.

Pathophysiology

- Common defense mechanisms that are compromised in the pathogenesis of pneumonia include:
- Systemic defense mechanisms like humoral and complement-mediated immunity that is compromised in diseases like common variable immunodeficiency (CVID), X-linked agammaglobulinemia (inherited), and functional asplenia (acquired). Impaired cell-mediated immunity predisposes individuals to infection by intracellular organisms like viruses and organisms of low virulence like *Pneumocystis* pneumonia (PJP), fungal causes, among others
- The mucociliary clearance that is often impaired in cigarette smokers, post-viral state, Kartergerner syndrome, and other related conditions
- Impaired cough reflex seen in comatose patients, certain substances of abuse
- Accumulation of secretions as seen in cystic fibrosis or bronchial obstruction

Classification.

- There are some general forms of pneumonia according to the conditions of the development, lung tissue infection's peculiarity, so as the state of patient's immune reactivity.
- Pneumonia that develops outside the hospital setting is considered community-acquired pneumonia (CAP).
- Pneumonia developing 48 hours or more after admission is termed nosocomial or hospitalacquired pneumonia (HAP).
- Pneumonia that develops more than 48 to72 hours after endotracheal intubation is ventilator-associated pneumonia (VAP).
- Widespread uncontrolled use of potent oral antibiotics formed multidrug-resistant (MDR) pathogens, general aging of population, extensive immunomodulatory therapies has led to health-care-associated pneumonia (HCAP) such as transition form between classic CAP and HAP.

Clinical examination of patients

- the symptoms of bacterial pneumonia include:
- bluish color to lips and fingernails
- confused mental state or delirium, especially in older people
- cough that produces green, yellow, or bloody mucus
- fever
- heavy sweating
- loss of appetite
- low energy and extreme tiredness
- rapid breathing
- rapid pulse
- shaking chills
- sharp or stabbing chest pain that’s worse with deep breathing or coughing
- shortness of breath that gets worse with activity

Early symptoms of viral pneumonia are the same as those of bacterial pneumonia, which may be followed by:

- headache
- increasing shortness of breath
- muscle pain
- weakness
- worsening of the cough

Mycoplasma pneumonia

- has somewhat different symptoms, which include a severe cough that may produce mucus.

Community-acquired pneumonia (CAP).

- is a leading cause of morbidity and mortality worldwide. The clinical presentation of CAP varies, ranging from mild pneumonia characterized by fever and productive cough to severe pneumonia characterized by respiratory distress and sepsis.

Julio A Ramirez, Sep 07, 2021.

Incidence

- — CAP is one of the most common and morbid conditions encountered in clinical practice. In the United States, CAP accounts for over 4.5 million outpatient and emergency room visits annually, corresponding to approximately 0.4 percent of all encounters

Risk factors

- Older age
- Chronic comorbidities
- Viral respiratory tract infection
- Impaired airway protection
- Smoking and alcohol overuse

Common causes

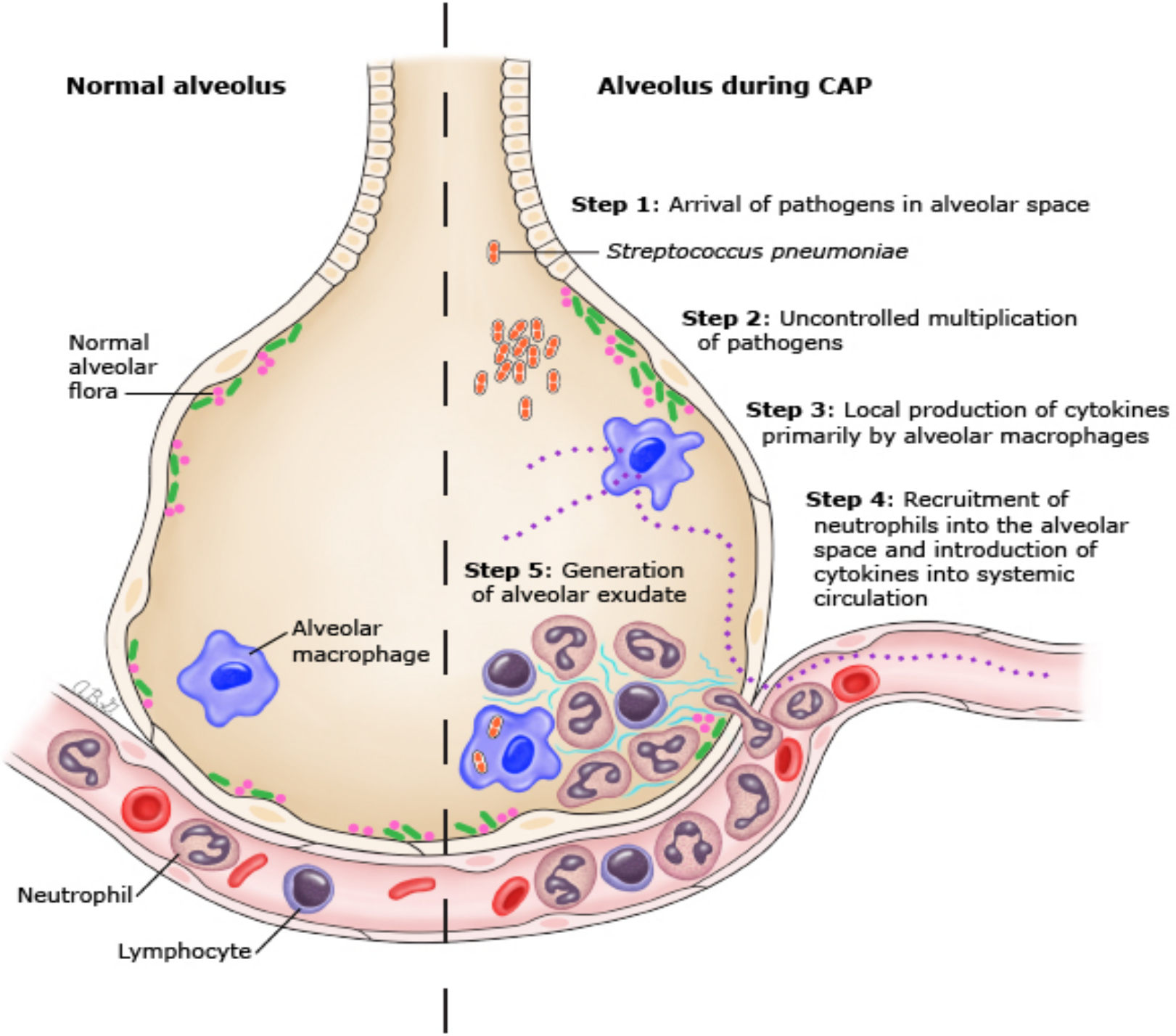
- The most commonly identified causes of CAP can be grouped into three categories:
- **Typical bacteria**
- •*S. pneumoniae* (most common bacterial cause)
- •*Haemophilus influenzae*
- •*Moraxella catarrhalis*
- •*Staphylococcus aureus*
- •Group A streptococci
- •Aerobic gram-negative bacteria (eg, Enterobacteriaceae such as *Klebsiella* spp or *Escherichia coli*)
- •Microaerophilic bacteria and anaerobes (associated with aspiration)

Atypical bacteria

- ("atypical" refers to the intrinsic resistance of these organisms to beta-lactams and their inability to be visualized on Gram stain or cultured using traditional techniques)
- •*Legionella* spp
- •*Mycoplasma pneumoniae*
- •*Chlamydia pneumoniae*
- •*Chlamydia psittaci*
- •*Coxiella burnetii*

Respiratory viruses

- Influenza A and B viruses
- Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)
- Other coronaviruses (eg, Middle East respiratory syndrome CoV, severe acute respiratory syndrome CoV, CoV-229E, CoV-NL63, CoV-OC43, CoV-HKU1)
- Rhinoviruses
- Parainfluenza viruses
- Adenoviruses
- Respiratory syncytial virus
- Human metapneumovirus
- Human bocaviruses


Normal alveolus
Alveolus during CAP
Step 1: Arrival of pathogens in alveolar space
Streptococcus pneumoniae
Step 2: Uncontrolled multiplication of pathogens
Normal alveolar flora
Step 3: Local production of cytokines primarily by alveolar macrophages
Step 4: Recruitment of neutrophils into the alveolar space and introduction of cytokines into systemic circulation
Step 5: Generation of alveolar exudate
Alveolar macrophage
Neutrophil
Lymphocyte

Pathogenesis

- Traditionally, CAP has been viewed as an infection of the lung parenchyma, primarily caused by bacterial or viral respiratory pathogens. In this model, respiratory pathogens are transmitted from person to person via droplets or, less commonly, via aerosol inhalation (eg, as with *Legionella* or *Coxiella* species). Following inhalation, the pathogen colonizes the nasopharynx and then reaches the lung alveoli via microaspiration. When the inoculum size is sufficient and/or host immune defenses are impaired, infection results. Replication of the pathogen, the production of virulence factors, and the host immune response lead to inflammation and damage of the lung parenchyma, resulting in pneumonia

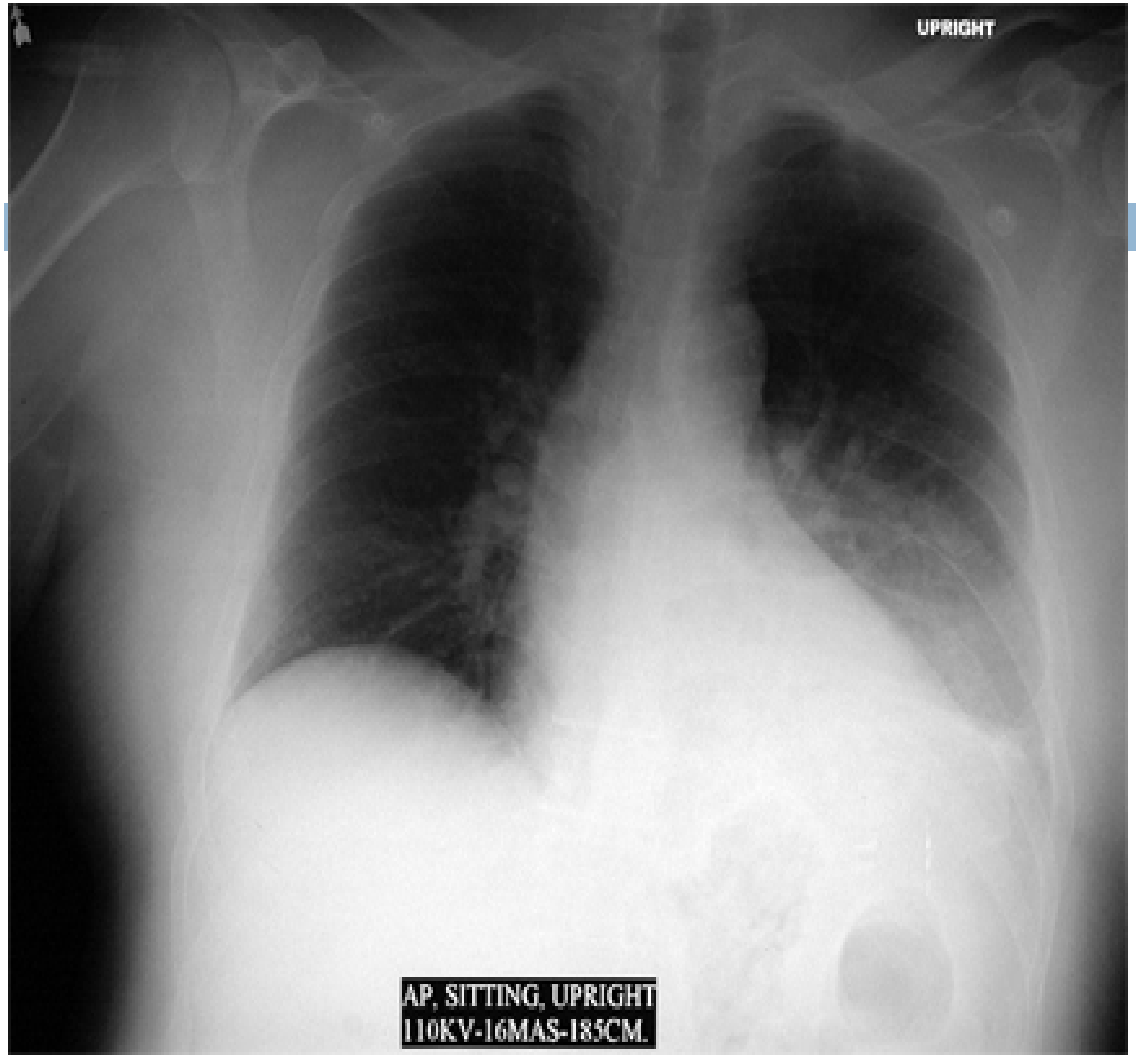
CLINICAL PRESENTATION

- **Pulmonary signs and symptoms** –

  Cough, dyspnea, and pleuritic chest pain are among the most common symptoms associated with CAP. Signs of pneumonia on physical examination include tachypnea, increased work of breathing, and adventitious breath sounds, including rales/crackles and rhonchi. Tactile fremitus, egophony, and dullness to percussion also suggest pneumonia. These signs and symptoms result from the accumulation of white blood cells (WBCs), fluid, and proteins in the alveolar space. Hypoxemia can result from the subsequent impairment of alveolar gas exchange.

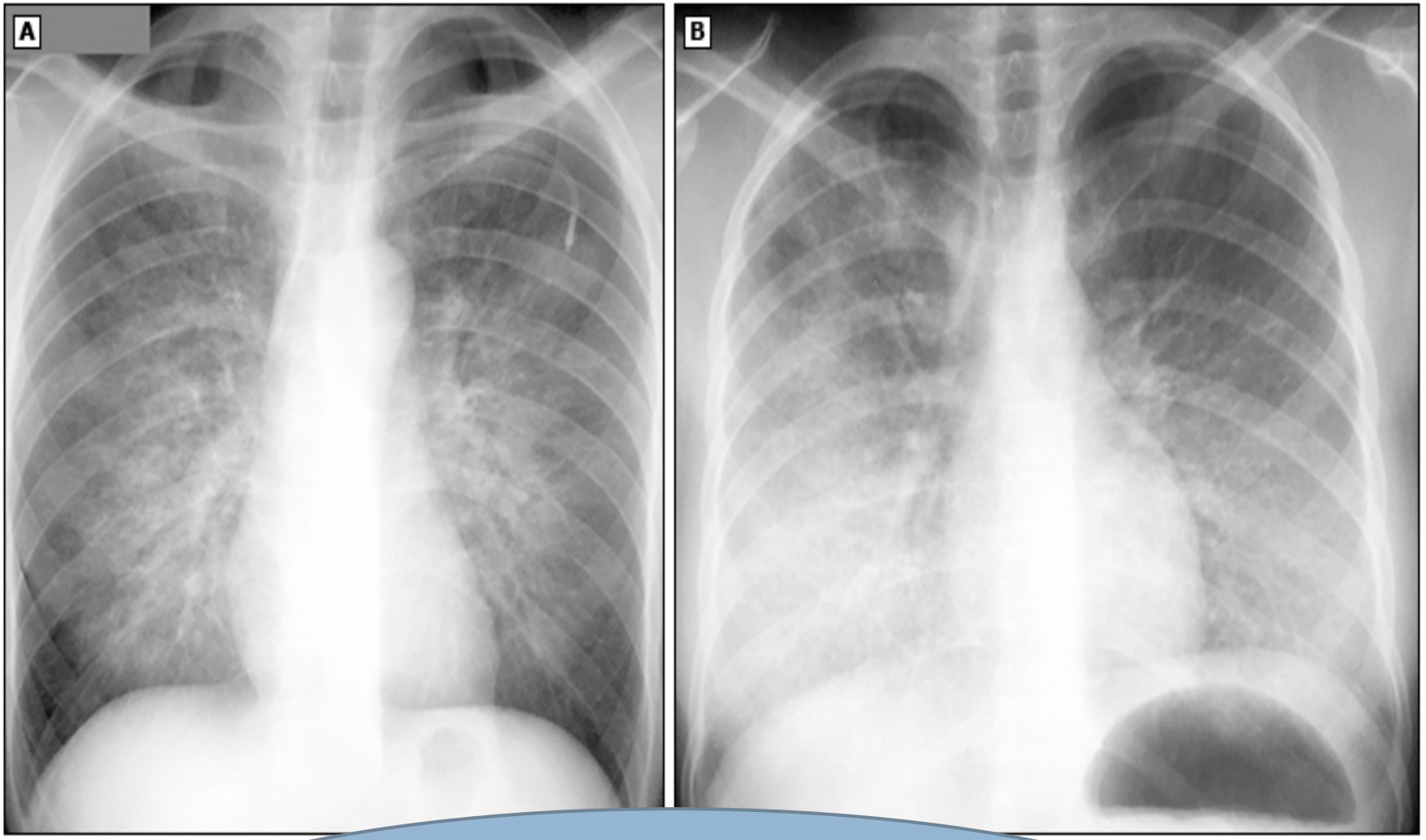
Diagnosis.

- Clinical, radiographic methods, laboratory techniques may help the physician in correct diagnosis. Specificity of clinical findings on physical examination is not so high.
- Radiography may show the localization and spread of lung consolidation, possible complications, someone differential diagnostic signs. Computed tomography (CT) may be more informative in patients with suspected postobstructive by tumor or foreign body pneumonia.



- On chest radiograph, accumulation of WBCs and fluid within the alveoli appears as pulmonary opacities

Note the left lower lobe opacity.



Chest radiograph in patients with *Pneumocystis jirovecii* pneumonia, one that shows perihilar ground-glass opacification with early consolidation (A) and the other that shows left-sided ground-glass opacification and right-sided early consolidation (B).

Diagnosis.

- Staining and culturing respiratory secretions. Gram's staining may identify some pathogens in expectorated sputum sample with determination of sensitivity to antibacterial medicines. Blood tests – neutrophylic with left shift leukocytosis, increasing of ESR, in biochemical blood analysis – increasing of acute-phase reactants (C-reactive protein, procalcitonin) Blood cultures may be positive in the patients with sepsis, septicemia. Polymerase chain reaction (PCR) can help to detect the respiratory viral infection, some bacterial ones and associated with increased risk of complications, unfavorable prognosis.

Treatment.

- The most commonly used severity scores are the Pneumonia Severity Index (PSI) and CURB-65.
- According to severityof-illness score CURB-65 which includes some criteria – confusion (C); urea >7mmol/L (U); respiratory rate (R); blood pressure (B) systolic 65 years(Tabl.1)

Table 1. CURB-65 Scoring[46]

Symptom	Points
Confusion	1
Urea: BUN >19 mg/dL (>7 mmol/L)	1
Respiratory rate ≥30 breaths/min	1
Systolic BP <90 mm Hg or diastolic BP ≤60 mm Hg	1
Age ≥65 years	1
Total	_____

Score	Risk	Disposition
0 or 1	1.5% mortality	Outpatient care
2	9.2% mortality	Inpatient versus observation admission
≥3	22% mortality	Inpatient admission; consider ICU admission with score of 4 or 5

Abbreviations: BP, blood pressure; BUN, blood urea nitrogen; ICU, intensive care unit.

- The three levels of severity (mild, moderate, and severe) generally correspond to three levels of care:
- **Ambulatory care**
- **Hospital admission**
- **Intensive care unit (ICU) admission**

The patients with CAP can be divided into four groups:

- I – patients without comorbidities and without antibiotics using history at previous 3 months;
- II - patients with comorbidity states and with antibiotics using history at previous 3 months;
- III – patients with not dangerous course but with presence of unfavorable factors;
- IV – severely ill patients with possible grave complications.

The presence of three of these criteria warrants ICU admission:

- •Altered mental status
- •Hypotension requiring fluid support
- •Temperature <36°C (96.8°F)
- •Respiratory rate ≥30 breaths/minute
- •Arterial oxygen tension to fraction of inspired oxygen (PaO_2/FiO_2) ratio ≤250
- •Blood urea nitrogen (BUN) ≥20 mg/dL (7 mmol/L)
- •Leukocyte count <4000 cells/microL
- •Platelet count <100,000/mL
- •Multilobar infiltrates

DIFFERENTIAL DIAGNOSIS

- Noninfectious illnesses that mimic CAP or co-occur with CAP and present with pulmonary infiltrate and cough include:
- •Congestive heart failure with pulmonary edema
- •Pulmonary embolism
- •Pulmonary hemorrhage
- •Atelectasis
- •Aspiration or chemical pneumonitis
- •Drug reactions
- •Lung cancer
- •Collagen vascular diseases
- •Vasculitis
- •Acute exacerbation of bronchiectasis
- •Interstitial lung diseases (eg, sarcoidosis, asbestosis, hypersensitivity pneumonitis, cryptogenic organizing pneumonia)

Outpatient antibiotic therapy

- For the I group outpatient site of treatment should be recommended by macrolide (clarithromycin 0,500 PO every 12 hours or azithromycin 0,500 first dose, then 0,250 every 6 hours) or doxycycline 0,100 PO every12 hours;
- For most patients aged <65 years who are otherwise healthy and have not recently used antibiotics, we typically use oral amoxicillin (1 g three times daily) plus a macrolide (eg, azithromycin or clarithromycin) or doxycycline. Generally, we prefer to use a macrolide over doxycycline.

Microbiologic testing

- For most patients with mild CAP being treated in the ambulatory setting, microbiologic testing is not needed (apart from testing for severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2] during the pandemic). Empiric antibiotic therapy is generally successful, and knowledge of the infecting pathogen does not usually improve outcomes.
- For most patients with moderate CAP admitted to the general medical ward, we obtain the following:
  - Blood cultures
  - Sputum Gram stain and culture
  - Urinary antigen testing for *S. pneumoniae*
  - Testing for *Legionella* spp (polymerase chain reaction [PCR] when available, urinary antigen test as an alternate)
  - SARS-CoV-2 testing

For the II group

- - outpatient site of treatment should be recommended by fluoroquinolone (moxifloxacine 0,400 PO every 6 hours, gemifloxacine 0,320 PO every 6 hours, levofloxacine
- 0,750 PO every 6 hours) or Beta-lactam (amoxicillin 1,0 every 8 hours, or amoxicillin/clavulanate 2,0 every 12 hours;) or cefalosporines (cefuroxime 0,500 PO every 12 hours, ceftriaxone 1,0-2,0 IV every 6 hours)+ macrolide (clarithromycin 0,500 PO every 12 hours or azithromycin 0,500 first dose, then 0,250 every 6 hours) or doxycycline 0,100 PO every12 hours.

For the III group

- - inpatient non-ICU(inpatient intensive care unit (ICU) of treatment should be recommended by fluoroquinolone (moxifloxacine 0,400 PO or IV every 6 hours, levofloxacine 0,750 PO or IV every 6 hours)
- Beta-lactam (ampicillin 1,0-2,0 IV every 4-6 hours), cefotaxime 1,0-2,0 IV every 8 hours,
- ertapenem 1,0 IVevery 6 hours)+ macrolide (clarithromycin 0,500 PO every 12 hours or
- azithromycin 0,500 PO first dose, then 0,250 PO every 6 hours; or azithromycin IV 1,0 first dose, then 0,500 every 6 hours). An alternative to the macrolides is doxycycline 0,100 IV every 12 hours.

For the IV group

- - inpatient intensive care unit (ICU) of treatment should be recommended by beta-lactames (ampicillin/sulbactam 2,0 IV every 8 hours), cefalosporines (cefotaxime 1,0-2,0 IV every 8 hours, ceftriaxone 2,0 IV every 6 hours)+macrolide (azithromycin IV 1,0 first dose, then 0,500 every 6 hours) or fluoroquinolone (moxifloxacine 0,400 PO or IV every 6 hours, levofloxacine 0,750 PO or IV every 6 hours).

Adjunctive glucocorticoids

We suggest giving adjunctive glucocorticoids to patients with CAP who have evidence of an exaggerated or dysregulated host inflammatory response, defined as septic shock that is refractory to fluid resuscitation and vasopressor administration or respiratory failure with a fraction of inspired oxygen requirement of >50 percent plus one or more of the following criteria: metabolic acidosis with an arterial pH of <7.3, lactate >4 mmol/L, or a C-reactive protein >150 mg/L.

- When using adjunctive glucocorticoids, we treat for five days. For patients who are unable to take oral medications, we use methylprednisolone 0.5 mg/kg IV every 12 hours. For patients who can take oral medications, we use prednisone 50 mg orally daily. We do not use adjunctive glucocorticoids in patients with influenza or other forms of viral pneumonia or in patients at risk of aspergillosis.

Duration of therapy.

- We generally determine the duration of therapy based on the patient's clinical response to therapy.
- The course of treatment for the patients without any complications may be several days, but more often it is necessary 10-14 days to favorable treatment effect. The severely ill patients with complications, bacteriemia, high virulent pathogen infection should be treated for a longer course

Hospital-acquired pneumonia

- Hospital-acquired pneumonia (HAP) is an infection of the pulmonary parenchyma caused by pathogens that are present in hospital settings, and also termed nosocomial.

- Nosocomial pneumonia develops in patients admitted to the hospital for >48 h and usually the incubation period is at least 2 days.

- HAP is the second most common nosocomial infection and the leading cause of death from nosocomial infections in critically ill patients. Its incidence ranges from 5 to more than 20 cases per 1000 hospital admissions, with the highest rates in immunocompromised, surgical and elderly patients.

- Several reports have estimated that a third to a half of all VAP-related deaths are the direct result of the infection, with a higher mortality rate in cases caused by *Pseudomonas aeruginosa* and *Acinetobacter* spp. Attributable VAP mortality is defined as the percentage of deaths that would not have occurred in the absence of the infection. Recent studies have reappraised the impact of VAP on mortality [

Pneumonia types

- 1. Actually nosocomial pneumonia:

- • *Early nosocomial pneumonia - occurs within the first 5 days (> 48-120 hours) from the time of hospitalization and due to pathogens that have been in the patient before admission to hospital - S. pneumoniae, H. influenzae, MRSA and other representatives of the oropharynx cavity normal flora. Most often, these pathogens are susceptible to antimicrobial agents, which are conventionally used, and pneumonia have a more favorable prognosis;*

- *Late nosocomial pneumonia - developed not earlier than 6 days of hospitalization (> 120 hours) and the resulting actual hospital microflora with a higher risk of having vysokoviru- valent and multi-drug resistant pathogens such as P. aeruginosa, Acinetobacter spp, representatives of the Enterobacteriaceae family, methicillin-resistant S. aureus. (MRSA). This GP is characterized by less favorable prognosis.*

2. Ventilator-associated pneumonia.

3. Nosocomial pneumonia in patients with significant impairment of immunity:

a) in recipients of donor organs;

b) in patients receiving cytotoxic therapy.

4. Hospital aspiration pneumonia.

Health-care-associated pneumonia (HCAP)

- is the transition form between classic CAP and HAP. More common etiology agents are community-acquired methicillin-resistent Staphylococcus aureus (MRSA) or multidrug-resistant (MDR) pathogens. In the case of culture-positive HCAP pneumonia the treatment is the same to that in the patients with nosocomial ventilator-associated pneumonia.

Pathophysiology

Inhalation, aspiration, and hematogenous spread are the 3 main mechanisms by which bacteria reach the lungs. The primary route by which organisms enter the lower airways is aspiration of oropharyngeal secretions into the trachea.

Primary inhalation pneumonia develops when these organisms bypass normal respiratory defense mechanisms or when the patient inhales aerobic gram-negative organisms that colonize the upper respiratory tract or respiratory support equipment.

Aspiration pneumonia results from aspiration of colonized upper respiratory tract secretions. In healthy individuals, roughly 45% of the population is estimated to aspirate during sleep, with critically ill patients likely aspirating more frequently.

The stomach appears to be an important reservoir of gram-negative bacilli that can ascend and colonize the respiratory tract. A prospective observational study found that patients who used acid-suppressive medications were more likely to develop hospital acquired pneumonia (HAP) than were patients who did not (5% vs 2%). The risk for pneumonia was significantly increased with proton pump inhibitors, but not with histamine 2-blocking agents. [

Hematogenously acquired infections originate from a distant source and reach the lungs via the bloodstream.

Etiology

- The development of hospital-acquired pneumonia (HAP) represents an imbalance between normal host defenses and the ability of microorganisms to colonize and then invade the lower respiratory tract.
- Because aerobic gram-negative bacilli (eg, *Pseudomonas aeruginosa)* are the major pathogens associated with HAP, the pathophysiology of nosocomial pneumonia relates to the destructive effect on lung tissue. Aerobic gram-negative pathogens may be divided into 2 categories. The first category includes organisms that cause necrotizing pneumonia with rapid cavitation, microabscess formation, blood-vessel invasion, and hemorrhage (eg, *P aeruginosa).* Alternatively, other non-necrotizing gram-negative bacilli (eg, *Serratia marcescens)* may be responsible for nosocomial pneumonia.

Common bacteria involved in hospital-acquired pneumonia (HAP) include the following :

- *Staphylococcus aureus,* including methicillin-susceptible S *aureus* (MSSA) and methicillin-resistant S *aureus* (MRSA)
- *Klebsiella pneumoniae*
- *Escherichia coli*
- Non-Enterobacteriaceae bacteria such as S. *marcescens, Stenotrophomonas maltophilia,* and *Acinetobacter* species are less common causes. *Acinetobacter* species commonly colonize respiratory tract secretions in patients in the ICU. HAP caused by *Acinetobacter* species or *B cepacia* may be associated with outbreaks. *Streptococcus pneumoniae* and *Haemophilus influenzae* are recovered only in early-onset HAP.

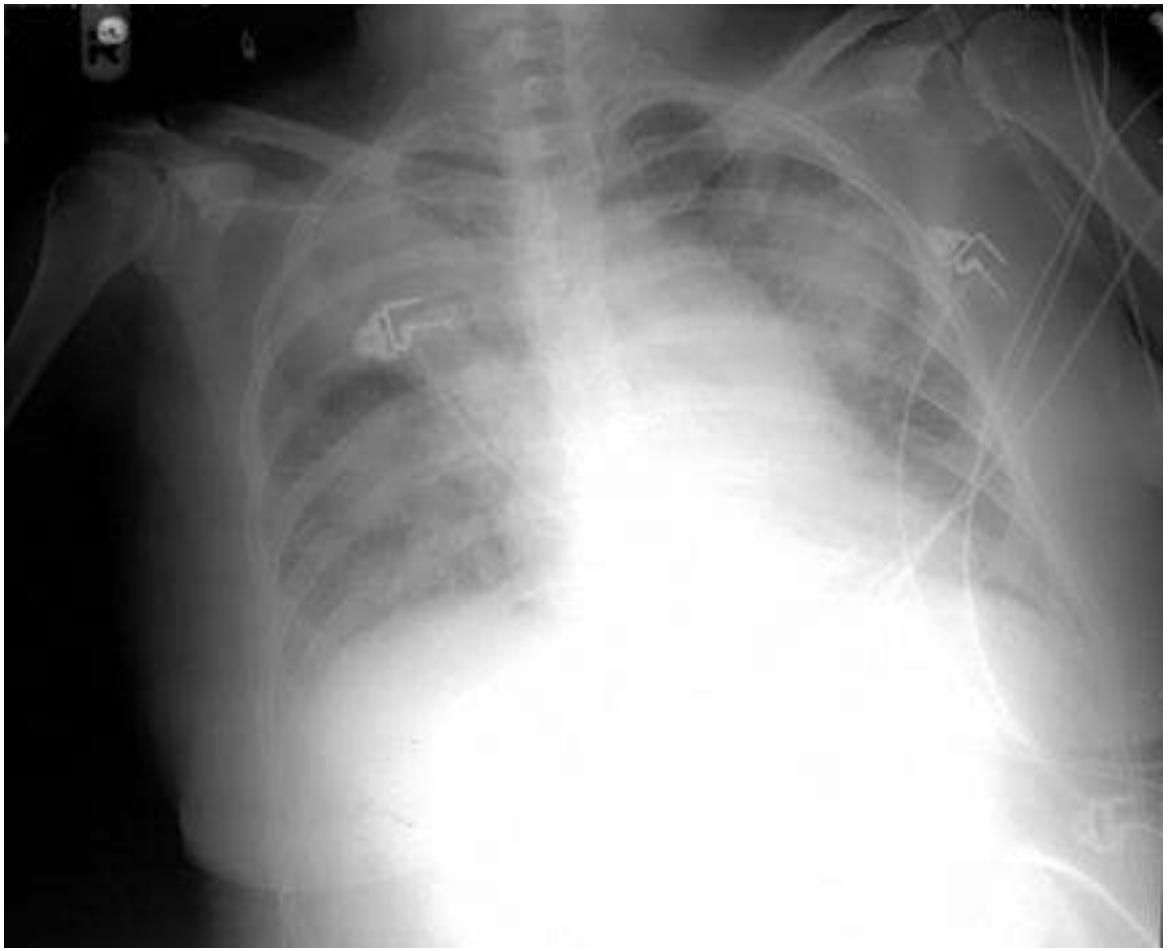
Clinical symptoms.

- Fever, breathlessness, increased bronchial secretions, the signs of lung consolidation at physical examination, neutrophylic leukocytosis, increased acute-phase reactants, radiographic pulmonary infiltration, tachypnea, tachycardia, decreased oxygenation are the main clinical criteria of VAP diagnosis.

Diagnosis.

- White Blood Cell Count and Blood Cultures
- Radiography
- Computed tomography (CT) scanning or spiral CT scanning may be useful in differentiating mimics from actual nosocomial pneumonia.
- Bronchoscopic Techniques
- Histologic Findings

Typical chest radiograph of a patient with nosocomial pneumonia



Differential diagnosis.

- Pulmonary edema, pulmonary contusion, alveolar hemorrhage, hypersensitivity pneumonitis, acute respiratory distress syndrome (ARDS), pulmonary embolism are the states with similar to VAP clinical manifestations. Presents of bacteria in gram-stained endotracheal aspirate samples makes pneumonia as a real cause of fever, pulmonary consolidation, lung infiltration.

Treatment.

- Empirical antibiotic monotherapy can be provided in the patients without high risk for MDR/MRSA pathogens (ceftriaxone 2,0 IV every 24hours or cefotaxime 2,0 IV every 6-8 hours; or moxifloxacine 0,400 IV every 24 hours or ciprofloxacin 0,400 IV every 8 hours or levofloxacine 0,750 IV every 24 hours; or ampicillin/sulbactam 3,0 IV every 6 hours; or ertapenem 1,0 IVevery 24 hours).

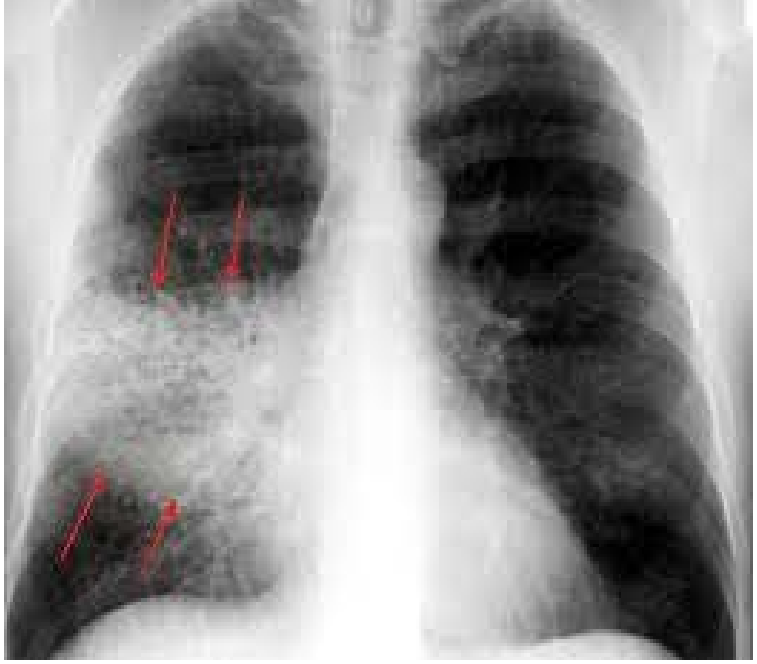
- In the patients with risk for MDR pathogens infections initial three antibiotics are recommended (two directed against P.aeruginosa and one against MRSA).
- At these schemes are proposed beta-lactames, cefalosporines, carbapenems, aminoglycosides, fluoroquinolones (ceftazidime 2,0 IV every 8 hours or cefepime 2,0 IV every 8-12 hours; or piperacillin/tazobactam 4,5 IV every 6 hours; or imipenem 0,500 IV every 6 hours or 1,0 IV every 8 hours or meropenem 1,0 IV every 8 hours)+(gentamicin or tobramicin 0,007/kg IV every 24 hours or amikacin 0.020/kg IV every 24 hours;
- or ciprofloxacin 0,400 IV every 8 hours or levofloxacine 0,750 IV every 24 hours)+(linezolid 0,600 IV every 12 hours or vancomycin 0,015/kg IV every 12 hours initially with doses correction).

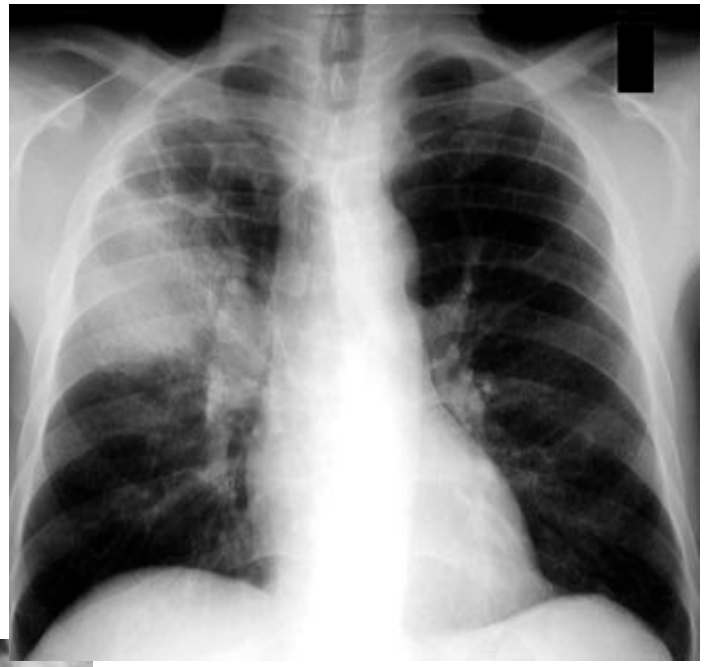
- Etiological treatment can be provided after the positive results of quantitative culture. In the case of CPIS level decreasing during 3 days, antibiotic therapy should be finished at 8 days to protect formation of antibiotic-resistant strains.

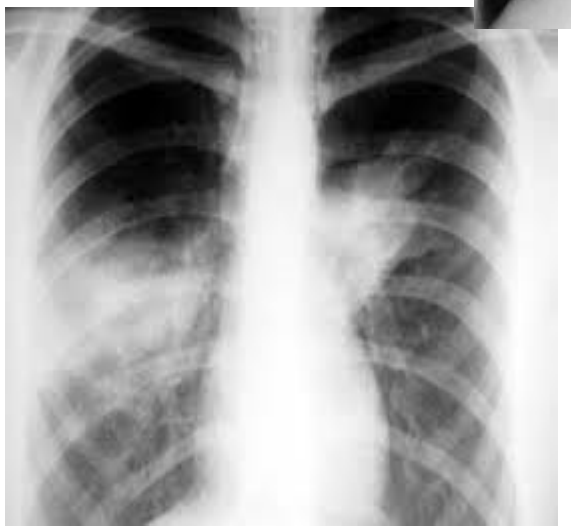
complications

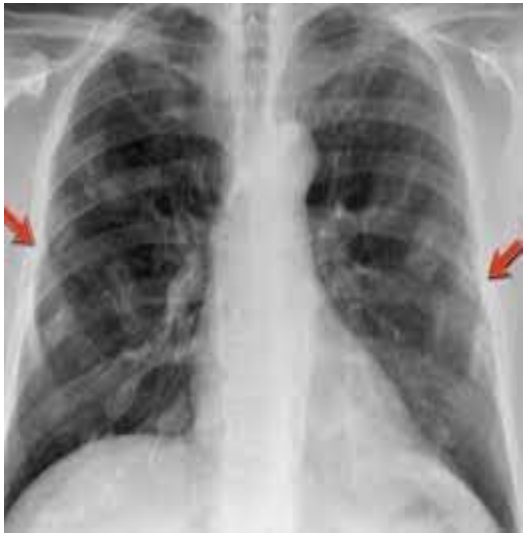
- Most complications connected with underlying disease and with necessity of mechanical ventilation prolongation (prolonged rehabilitation, inability for independent function).
- The development of purulent pleural empyema, broncho-pleural fistula formation, lung abscess, sepsis, and septic shock.

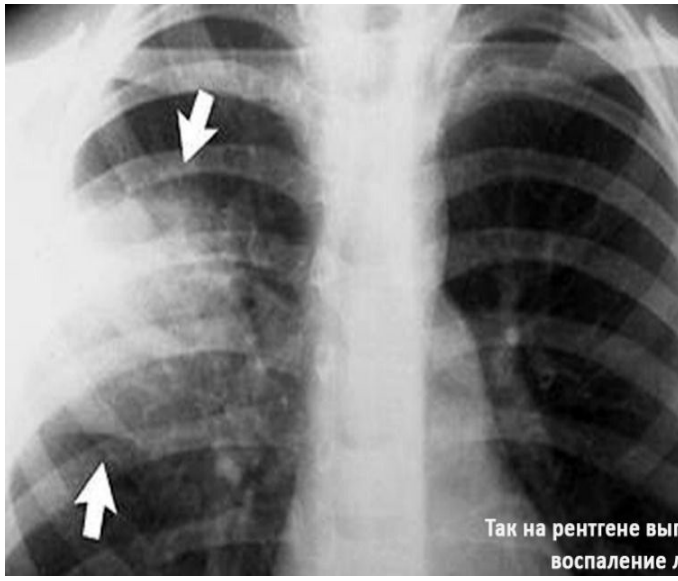
- Fatal prognosis may be inevitable in the cases of MDR associated pneumonia and in the imunocompromised or immunodeficiency patients.







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