

# Pneumonia

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# Definition

- **Pathological anatomy:**  
Acute inflammatory disease affecting the lung alveoli, respiratory bronchioles and adjacent lung interstitium
- **Clinical:**  
Disease with new infiltrate on chest X-ray with presence of at least two typical signs\* of lower respiratory tract infection

(\* dyspnoea, cough, chest pain, elevated temperature, new finding on lung auscultation, leukocytosis with left shift)

# Epidemiology

- WHO: the third most common cause of death (annually 3-5 million)
- More common in childhood and in old age
- Risk groups: smokers, alcoholics, drug addicts and people in social care facilities and with comorbidities
- USA: 1.4 million hospitalizations and 91,000 deaths per year
- The Czech Republic:
  - 100,000 pneumonias per year
  - 20,000 hospitalizations per year
  - 3,000 deaths annually from pneumonias

# Epidemiological classification /1

- **Community-acquired pneumonia (CAP):**  
Outside the hospital environment; usually caused by pathogens sensitive to common antibiotics
- **Hospital-acquired pneumonia (HAP):**  
2 days after admission to hospital (up to 2 weeks after discharge); also resistant pathogens
- **Pneumonia in immunocompromised host (PIH):**  
HIV+, anti-cancer and immunosuppressive therapy; also opportunistic pathogens

# Epidemiological classification /2

- „End-of-life pneumonia“:
  - Pneumonia in end-stage of underlying disease and in dying people
  - Typically in end-stage of Alzheimer's disease
  - Also in terminal phase of cardiovascular, neurological, oncological and rheumatological diseases
  - High mortality, low benefit of antibiotics
  - Symptomatic treatment (dyspnea, anxiety)

# Causative pathogens in CAP

## • Typical pathogens:

- *Streptococcus pneumoniae*
- *Staphylococcus aureus*
- *Haemophilus influenzae*
- *Moraxella catarrhalis*
- *Klebsiella pneumoniae*
- *Escherichia coli*
- Anaerobic bacteria

## • Atypical pathogens:

- *Mycoplasma pneumoniae*
- *Chlamydophila pneumoniae*
- *Chlamydophila psittaci*
- *Legionella pneumophila*
- *Influenza virus*
- Other respiratory viruses (*PIV, adenovirus, RSV, MPV, SARS and MERS CoV*)

# Pathogens in HAP and PIH

- Resistant pathogens:
  - *Pseudomonas sp.*
  - *Proteus sp.*
  - *Acinetobacter sp.*
  - *Burkholderia sp.*
  - *ESBL+ gram-negatives*
  - *Enterococcus sp.*
  - Coagulase-neg. staphs
  - *Corynebacterium sp.*
  - *Candida sp.*
- Opportunist. pathogens:
  - CMV, VZV
  - *Nocardia sp.*
  - *Mycobacterium sp.*
  - *Pneumocystis jiroveci*
  - *Aspergillus sp.*
  - *Mucor sp.*
  - *Fusarium sp.*
  - *Cryptococcus sp.*
  - *Toxoplasma sp.*

# Predisposition to pathogens

Predisposition	Pathogens
Alcoholism	Pneumococcus, anaerobes, gram-negatives
Smoking / COPD	Pneumococcus, <i>Haemophilus</i> , <i>Moraxella</i>
I.v. drug addicts	<i>Staphylococcus</i> , anaerobes, <i>M. tuberculosis</i>
Poor oral hygiene / aspiration	Anaerobes, gram-negatives
Epidemics	Influenza, <i>Legionella</i> , <i>Mycoplasma</i>
Bronchiectasis / CF	<i>Staphylococcus</i> , <i>Pseudomonas</i> , <i>Burkholderia</i>
Social care facilities	Pneumococcus, <i>Staphylococcus</i> , <i>Chlamydia</i> , <i>Haemophilus</i> , anaerobes, gram-negatives
Bird breeders	<i>Chlamydophila psittaci</i>



# Severity of CAP

- **Mild CAP: outpatient treatment**  
Mild symptoms, without comorbidities or high age
- **Moderate CAP: hospital treatment**  
Marked symptoms, comorbidities, old age
- **Severe CAP: ICU treatment**  
Life-threatening symptoms, mechanical ventilation, vasopressors, progressive lung involvement, P/F ratio  $<250$  mm Hg, RR  $>30$ /min., BP  $<90/60$  mm Hg

# CURB-65 score

- C: confusion (AMT score  $\leq 8$  points)
- U: dehydration (urea  $\geq 7$  mmol/l)
- R: tachypnea (RR  $\geq 30$ /min.)
- B: hypotension (BP  $< 90$  /  $< 60$  mm Hg)
- 65: old age ( $\geq 65$  years)

# AMT = abbreviated mental test

QUESTION		Score 0 or 1
1.	How old are you?	
2.	What is the time (nearest hour)?	
3.	Address for recall at the end of test – this should be repeated by the patient, eg. 42 West Terrace	
4.	What year is it?	
5.	What is the name of this place?	
6.	Can the patient recognise two relevant persons (eg. nurse/doctor)	
7.	What was the date of your birth?	
8.	When was the second World War?	
9.	Who is the present Prime Minister?	
10.	Count down from 20 to 1 (no errors, no cues)	
<b>TOTAL CORRECT</b>		

# CURB-65: mortality & treatment

Score	Mortality	Treatment
0	0,6 %	Outpatien
1	3,2 %	Outpatient / hospital
2	13,0 %	Hospital
3	17,0 %	Hospital
4	41,5 %	ICU
5	57,0 %	ICU

# Pneumonia severity index (PSI)

Class	Score	Mortality	Treatment
I	(age <50*)	0,1%	Outpatient
II	≤70	0,6%	Outpatient
III	71-90	2,8%	Outpatient / hospital
IV	91-130	8,2%	Hospital
V	>130	29,2%	ICU

\* Without comorbidities or abnormalities on physical examination

# PSI calculation (class II-V)

<b>Demography:</b>		<b>Physical examination:</b>	
Males	+ age	Confusion	+ 20
Females	+ (age-10)	HR $\geq$ 125/min.	+ 20
Social care facility	+ (age+10)	RR $>$ 30/min.	+ 20
<b>Laboratory examination:</b>		SBP $<$ 90 mm Hg	+ 15
pH $<$ 7,35	+ 30	BT $<$ 35 / $\geq$ 40°C	+ 10
Urea $\geq$ 11 mmol/l	+ 20	<b>Comorbidities:</b>	
Na <sup>+</sup> $<$ 130 mmol/l	+ 10	Malignancy	+ 30
Glycaemia $\geq$ 14 mmol/l	+ 10	Liver disease	+ 20
Hct $<$ 0,30	+ 10	Heart failure	+ 10
p <sub>a</sub> O <sub>2</sub> $<$ 8,0 kPa	+ 10	Cerebral sclerosis	+ 10
Fluidothorax	+ 10	Nephropathy	+ 10

# CAP: examination

- Clinical examination (history, physical exam.)
- Chest X-ray (front and lateral view)
- Chest CT (pleural effusion, cavitation, tumors)
- Oxygen saturation, arterial BG & ABB
- Biochemistry (CRP, PCT, lactate)
- Hematology (blood count, coagulation)
- Bronchoscopy (sampling of respiratory secretions, mucus plugging, tumors, haemoptysis)

# Mikrobiology

- Materials:

- URT secretions
- sputum
- LRT secretions
- lung biopsy
- pleural effusion
- blood, urine

- Methods:

- microscopy
- culture
- detection of antigens
- genetic methods (PCR)
- detection of antibodies
- electron microscopy



# Lung infiltrates

Infection & inflammation	Other causes
Pneumonia incl. TB	Pulmonary oedema
Allergy, eosinophilic sy	Pulmonary infarction
Connective tissue diseases	Lung cancer, carcinomatosis
Vasculitis	Pulmonary contusion
Drug toxicity	Alveolar haemorrhage
Radiation induced lung injury	Aspiration, inhalation injury

- Infiltrate „may not be visible“:
  - not sufficiently created (emphysema, neutropenia)
  - overlapped with underlying disease (lung fibrosis)

# Complications of pneumonias

- Local:
  - Lung abscess
  - Haemoptysis
  - Pleural effusion, empyema
  - Pneumothorax
  - Bronchiectasis
  - Lung fibrosis
- Systemic:
  - Respiratory failure
  - Sepsis, MOFS
  - Metastatic infections (joints, kidneys,...)
  - Anemia
  - Malnutrition
  - Amyloidosis

# Choice of antibiotics in CAP

- Typical pathogens:
  - $\beta$ -lactams: ampicillin-sulbactam, amoxicillin-clavulanate, cefotaxime
  - Lincosamides: clindamycine
  - Aminoglycosides: gentamicin
  - Respiratory fluoroquinolones: moxifloxacin
- Atypical pathogens:
  - Macrolides: clarithromycin, azithromycin
  - Tetracyclines: doxycycline
  - Fluoroquinolones: ofloxacin, moxifloxacin

# Outpatient therapy for CAP

- Patients without comorbidities or old age:
  - Choose one from: amoxicillin (1 g TID), clarithromycin (500 mg BID), doxycykline (200 mg OD), moxifloxacin (400 mg OD)
- Patients with comorbidities or in old age:
  - Combination of  $\beta$ -lactam and macrolide, alternatively moxifloxacin
- Duration of treatment: 10-14 days (7-20 days)

# Inpatient therapy for CAP /1

- Moderate CAP (without comorbidities or old age):
  - I.v. combination of  $\beta$ -lactam (ampicillin, cefuroxime) and macrolide (clarithromycin); alternatively moxifloxacin
- Severe CAP, comorbidities or old age:
  - I.v. combination of  $\beta$ -lactam (ampicillin-sulbactam, amoxicillin-clavulanate, cefotaxime) and macrolide (clarithromycin); alternatively moxifloxacin; in aspiration pneumonia plus lincosamide (clindamycine)

# Inpatient therapy for CAP /2

- CAP with risk of *P. aeruginosa* infection :
  - I.v. antipseudomonal  $\beta$ -lactam (piperacillin-tazobactam, cefoperazone-sulbactam, ceftazidime) and/or fluoroquinolone (ciprofloxacin), event. in combination with aminoglycoside (amikacin); in reserve carbapenems (meropenem)
- Risk of *P. aeruginosa* infection:
  - Bronchiectasis, long-term systemic corticosteroids therapy, previous broad-spectrum antibiotic therapy, previous *P. aeruginosa*+ culture, persons in social care facilities

# Further treatment of CAP

- ICU, monitoring
- Oxygen therapy, mechanical ventilation
- Infusions, minerals, analgesics, antipyretics
- LMWH, vasopressors
- Systemic corticosteroids, insulin
- Antitussives, mucolytics, bronchodilators
- Blood derivatives, nutritional support
- Lung abscess/pleural effusion drainage, surgery

# Treatment failure

- Incorrect diagnosis (it is not pneumonia)
- Incorrect therapy (e.g. low dose  $\beta$ -lactam)
- Non-compliance of patient
- Uncommon or resistant pathogen (legionella)
- Local immunity disorder (BCA, BE)
- Systemic immunity disorder (HIV)
- Untreatable pneumonia (end-of-life)



# Pneumococcal pneumonia

- Severe CAP: 20-60 % pneumococcus
- Pneumococcal antigen in urine
- Blood culture
- Typically high PCT
- High doses of  $\beta$ -lactam needed
- Quinolones (except moxifloxacin) ineffective

# Mycoplasma pneumoniae

- Prototyp of atypical pathogen
- Teenagers and young adults
- Epidemics in 3-4 year cycles
- Occurrence in late summer and in autumn
- Dg. PCR, serology; risk of haemolytic anemia
- Th. macrolides (doxycycline, quinolones)
- $\beta$ -lactams ineffective

# Legionella pneumonia

- Severe CAP and HAP
- Water systems
- Old age, smokers
- Commonly also diarrhea and CNS disorders
- Biochemistry: hyponatraemia and high LD
- Dg. PCR, serology and urinary antigen
- Th. macrolides, quinolones, doxycycline, rifampicin
- $\beta$ -lactams ineffective

# H1N1 influenza pneumonia

- Letality of H1N1 infection <0,3 %
- Affinity of virus to small airways
- In 3-5 days from first symptoms
- Progression to ARDS in 24 hours
- Risk groups: young age, asthma, diabetes, obesity, pregnancy, heart diseases, immunodeficiency and children with neuromuscular diseases
- Superinfection: pneumococcus, staphylococcus, haemophilus

# HAP: sources of infection

- Endogenous infection (dental caries)
- Other patients
- Health care personnel
- Health care material and instruments
- Environment (air, water)
- VAP: ventilator-associated pneumonia

# HAP: treatment

- Epidemiological situation in ward!
- Antipseudomonal  $\beta$ -lactams (penicillins or cephalosporins in combination with aminoglykoside; carbapenem monotherapy)
- In case of treatment failure: antibiotics effective against resistant gram-positives (vancomycin, linezolid) and candida (fluconazole)
- Regular change of antibiotics: prevention of resistance

# Immunocompromised patients

- HIV/AIDS
- Solid organ transplantation
- Hematopoietic stem cells transplantation
- Antitumor therapy (chemotherapy, radiotherapy)
- Immunosuppressants and corticosteroids
- Biological therapy
- Hyposplenism and asplenia
- Congenital immunodeficiency disorders

# Immunodeficiencies

- Phagocytosis (neutrophils)
  - acute leukemia, chemotherapy, CGD

↑

- Humoral immunity (B cells, antibodies)
  - myeloma, splenectomy, CVID

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- Cellular immunity (T cells)
  - AIDS, immunosuppressants, SCID



# Immunosuppressants

## „Classical“:

- Cyclophosphamide (Endoxan)
- Methotrexate (Trexan)
- Azathioprin (Imuran)
- Leflunomide (Arava)

## „New“:

- Cyclosporine (Sandimmune)
- Tacrolimus (Prograf)
- Sirolimus (Rapamune)
- Mycophenolate (CellCept)

# Biological therapy

- Anti TNF  $\alpha$ :
  - etanercept (Enbrel)
  - infliximab (Remicade)
  - adalimumab (Humira)
- Anti CD20:
  - rituximab (MabThera): B lymphocytes
- Anti CD56:
  - alemtuzumab (MabCampath): T and B lymphocytes

# Important pathogens

- *Aspergillus sp.* and other moulds
- *Pneumocystis jiroveci*
- *Cytomegalovirus* and other herpesviridae
- Non-tuberculous mycobacteria (*M. avium*)

# Pneumonia in pulmonary department...

- Moderate and severe pneumonia without significant comorbidities (heart, liver, kidney, diabetes, CNS)
- Complications of pneumonia: lung abscess, haemoptysis, pleural effusion, pneumothorax
- Significant pulmonary comorbidities: lung cancer, COPD, bronchiectasis, lung fibrosis
- Chest tubes, non-invasive mechanical ventilation
- Need for bronchoscopies

# Pneumonia in other departments...

- Pneumonia as complication of significant comorbidity in old age (incl. end-of-life pneumonia)
- Questionable pneumonia („right paracardiac infiltrate“: prominent bronchovascular markings in right lower lung field on chest X-ray are normal!)
- No pneumonia (e.g. elevated temperature and dyspnea in old age: urinary tract infection and left heart failure – „pneumonia“ „miraculously disappeared“ after diuretics in 24 hours 😊)