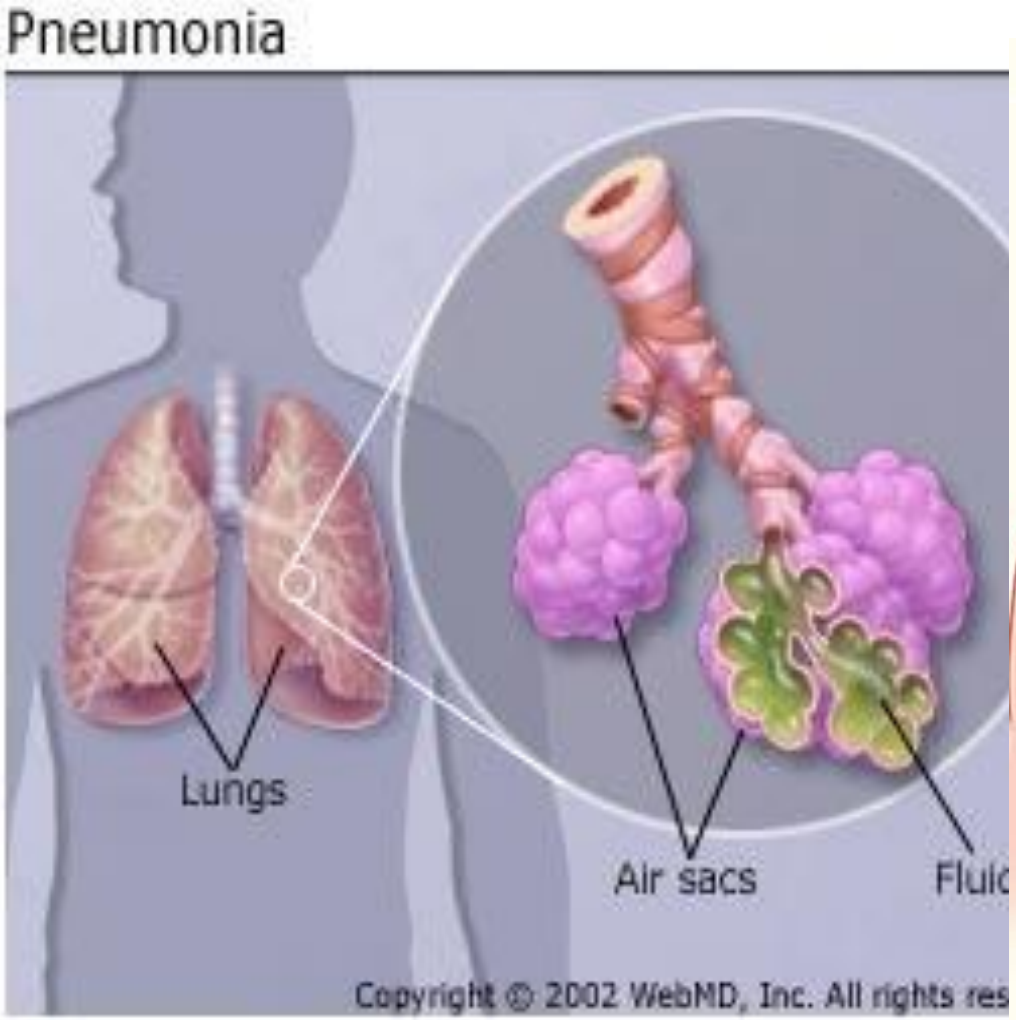
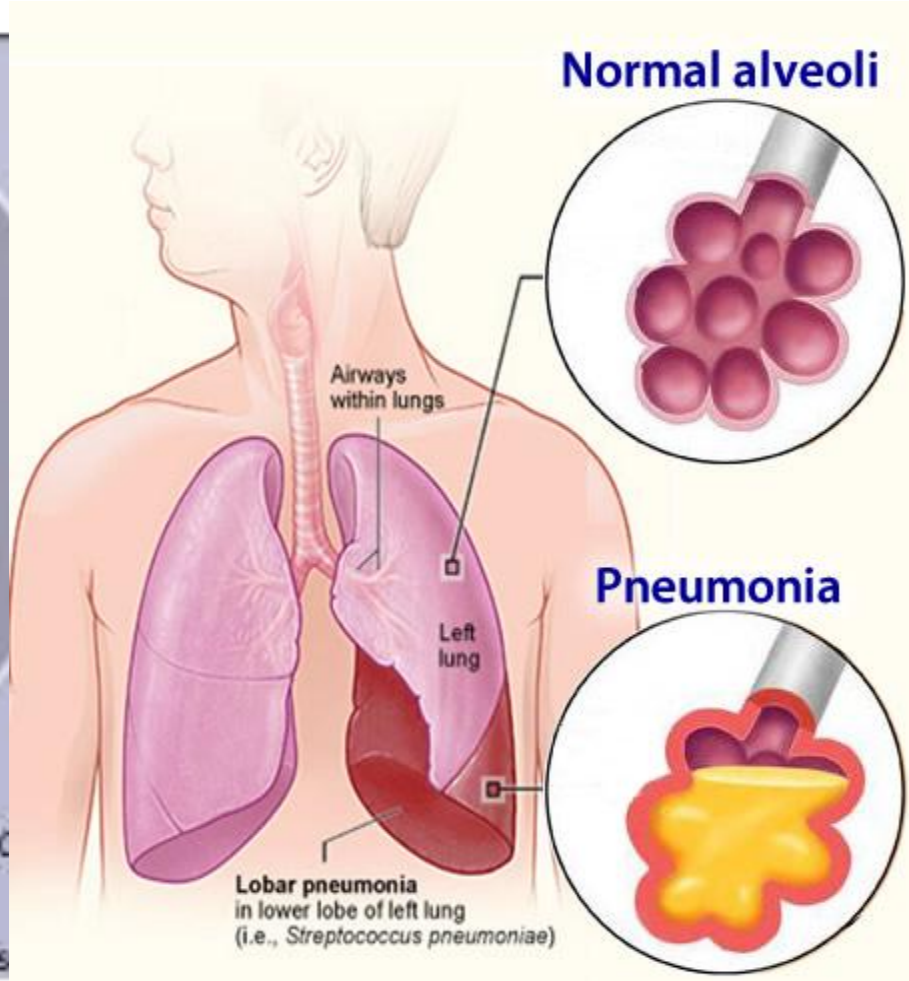
Pneumonia

- Definitions
- Ethiology (general), risk factors
- Diagnosis criteria and evaluation
- Peculiarities of the disease in different causative agents
- Treatment

Pneumonia: infection of the lung parenchyma, in which consolidation of the affected part and a filling of the alveolar air spaces with exudate, inflammatory cells, and fibrin is characteristic.





Ethiology (general)

- Bacterial – most common
- Viral
- Rickettsiae
- Fungi
- Yeasts
- Mycobacteria

Risk factors (general)

- Influenza (especially H1N1)
- local lung pathologies (tumors, COPD, bronchiectasis), smoking
- Chronic gingivitis and periodontitis
- Diseases leading to aspiration CNS diseases (seizures, alcohol or drug intoxication, stroke), GERD, scleroderma, dermatomyositis, congenital abnormalities
- Immune supression

CLASSIFICATION OF PNEUMONIA

	➢ Host immunity	➢ Environment
Community acquired (CAP)	Immunocompetent	Community
Hospital acquired (HAP)	Immunocompetent	Hospital
Immunosupressed	immunosuppressed	Community or hospital

- CAP: Pneumonia not acquired in a hospital or a long-term care facility
- Hospital acquired pneumonia (with/without multiple drug resistance risk factors):

- Healthcare associated pneumonia: other healthcare facilities such as nursing homes, dialysis centers, and outpatient clinics
- Hospital acquired pneumonia
- Ventilator associated pneumonia

Epidemiology

- 5.6 million cases of CAP annually in the United States
- total annual cost for CAP in the United States is $8.4 billion
  - 92% of cost with inpatient therapy
- Because CAP is the only acute respiratory tract infection in which there is increased mortality if antibiotic therapy is delayed, diagnostic and treatment decisions need to be made accurately and efficiently
- Mortality rate among hospitalized patients with CAP varies each year and can reach 35%

Ethiology

- Typical: up to 70%
  - Usually caused by *Streptococcus pneumoniae*
- Atypical: 30-40%
  - "**M**y **L**ungs **C**ontain **V**iruses"
    - ***M****ycoplasma pneumoniae*
    - ***L****egionella pneumophila*
    - ***C****hlamydia pneumoniae*
    - **V**iruses: Influenza, Adenovirus
  - May be co-pathogens in other cases

COMMON CAUSES

OUTPATIENT	INPATIENT(NOT ICU)	ICU
S pneumoniae	S pneumoniae	S pneumoniae
M pneumoniae	M pneumoniae	S aureus
H influenzae	C pneumoniae	Legionella spp
C pneumoniae	H influenzae	gram (-) bacilli
Respir. viruses	Legionella spp	H influenzae
	Resp. viruses	

The most common cause of bacterial respiratory infection

- Streptococcus pneumoniae
- At all levels, from the middle ear down to the alveolar space
- In all clinical severities of CAP

Risk factors for some etiological factors

- **Resistent S.pneumoniae**
- **>65 лет**
- **Beta-lactams during last 3 mo, chronic alcoholic abuse**
- **Immune deficiencies (incl steroid treatment)**
- **Multimorbidity**
- **Gram negative enterobacterial**
- **Health care houses**
- **Cardiovascular and pulmonary diseases**
- **Multiple comorbidities**
- **Antibiotics use**
- **Pseudomonas aeruginosa**
- **Structure lung diseases (f.ex.bronchiectases)**
- **Systemic steroids (prednizone >10 mg/daily)**
- **Wide spectrum antibiotics >7 days during last month**
- **Cahexia**

- Intoxication fever, chills, fatigue, dyspnea, headache and myalgia
- Cough may be persistent and dry, or it may produce sputum (rusty – Str.Pneum, greenish – Staph., H.Infl., Ps.aerug), currant gellee – K.Pneumoniae)
- Physical changes – consolidation syndrome: dull sound, broncnial/harsh respiration; rales
- Pleuritic pain
- Certain etiologies, such as legionella, also may produce gastrointestinal symptoms

- CXR (PA and Lateral):
  - American Thoracic Society (ATS) guidelines, “all patients with suspected CAP should have a chest radiograph to establish the diagnosis and identify complications (pleural effusions, multilobar disease)”
  - Lobar consolidation – more common in typical pneumonia
  - Bilateral, diffuse infiltrates – commonly seen in atypical pneumonia
    - However, radiologists cannot reliably differentiate bacterial from nonbacterial pneumonia on the basis of the radiographic appearance
  - If performed early in the course of the disease, may be negative
    - The sensitivity of chest radiography depends greatly on pretest probability

CAP DIAGNOSIS

Suspected CAP

- Acute cough +

1 of 4

- Dyspnea
- Tachypnea
- New focal signs in chest examination
- Fever > 4 days

THEN: CXR. If chest shadowing → definite CAP

Chest CT scan ???

PSI

- 3 demographic characteristics
  - Age
  - Sex (male → years of age)
    (female → years of age – 10)
  - Residence in health care facility (+10)

- 5 comorbidities
  - Malignancies (+30)
  - Liver failure (+20)
  - Congestive heart failure (+10)
  - Cerebral vascular disease (+10)
  - Renal disease (+10)

- 5 clinical findings
- Disturbed level of consciousness (+20)
  - Respiratory rate > 30/min (+20)
  - SAP < 90mmHg (+20)
  - Temperature < 35°C or > 40°C (+15)
  - HR > 125/min (+10)

- 7 laboratory – radiological findings
  - Arterial pH < 7.35 (+30)
  - Urea > 30mg/dL (+20)
  - Na+< 130 mEq/L (+20)
  - Blood glucose > 250 mg/dL (+10)
  - Hematocrit < 30% (+10)
  - PO_2 < 60 mmHg (+10)
  - Pleural effusion (+10)

CURB-65 score

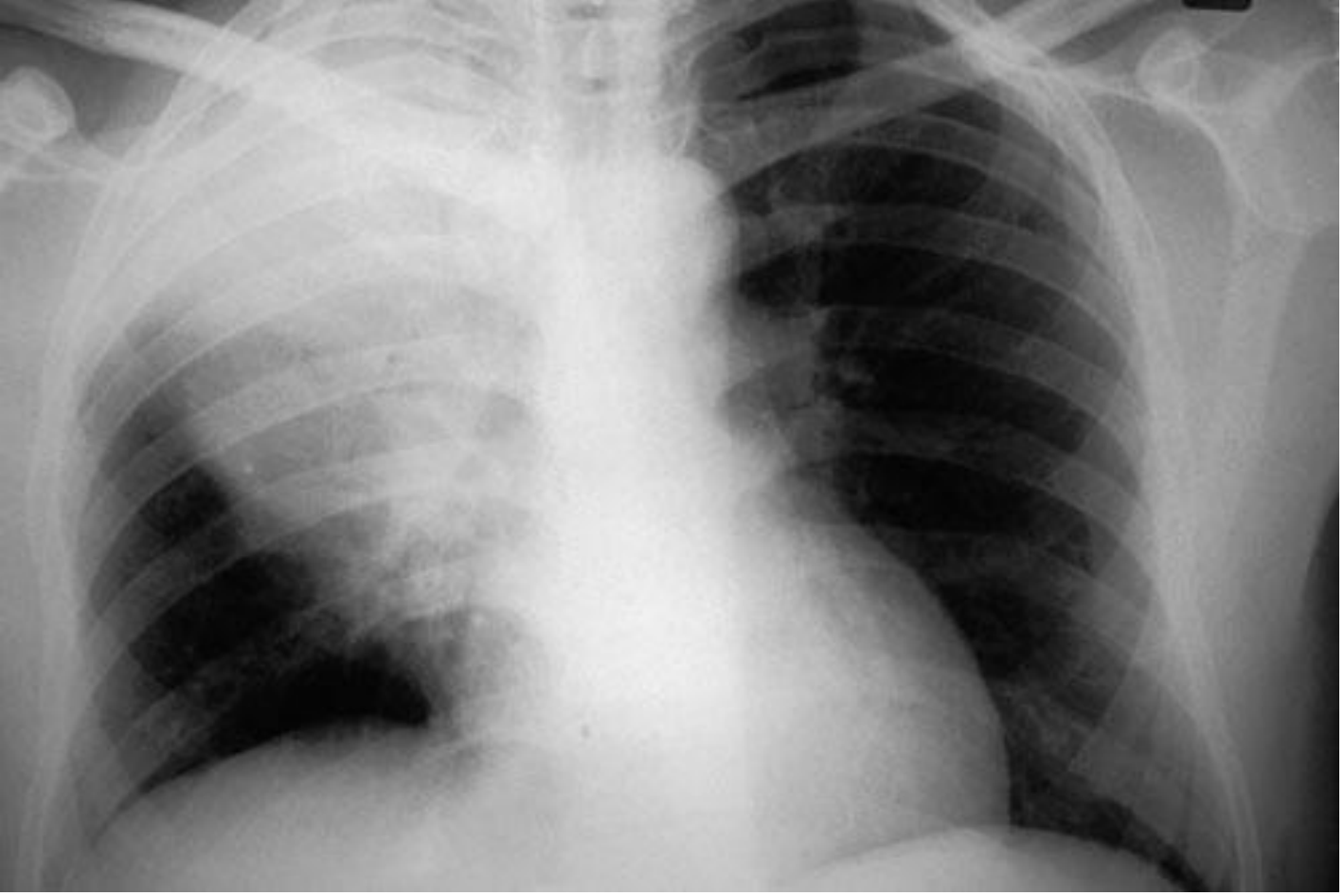
- Confusion
- Urea > 7 mmol/L
- Respiratory rate > 30/min
- Low systolic (<90mmHg) or diastolic (<=60mmHg) arterial pressure
- Age ≥ 65 y.o

Lobar pneumonia

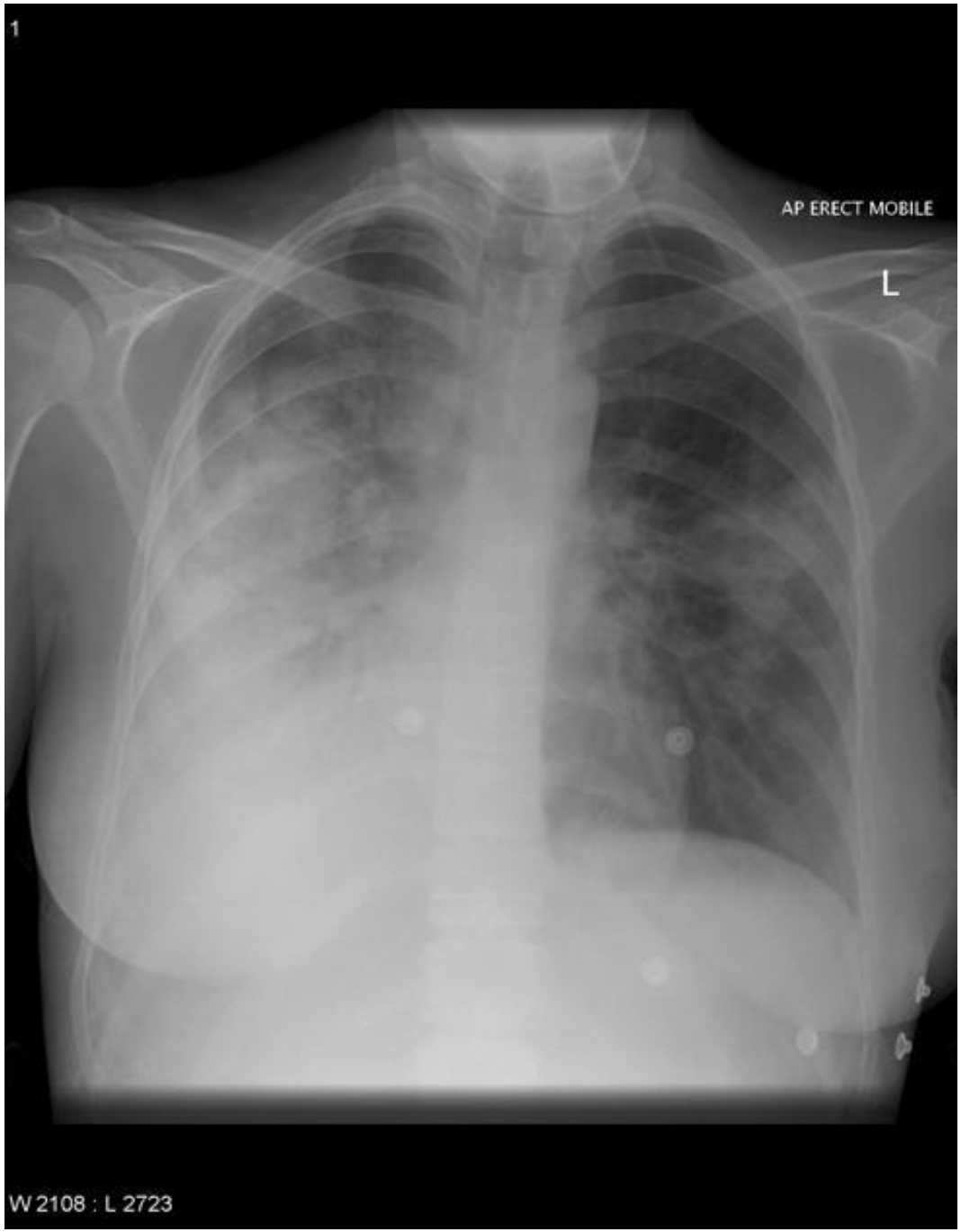
- (also known as a **non-segmental pneumonia** or **focal non-segmental pneumonia** [7]) is a radiological pattern associated with homogenous, fibrinosupparative consolidation of one or more lobes of a lung in response to a bacterial pneumonia.
- *Streptococcus pneumoniae* is the most common causative organism of lobar pneumonia.

Other causative organisms

- *Klebsiella pneumoniae*
- *Legionella pneumophila*
- *Haemophilus influenzae*
- *Mycobacterium tuberculosis*



- consolidation in the right upper lobe consistent with the clinical signs
- *S. pneumoniae* was isolated from blood cultures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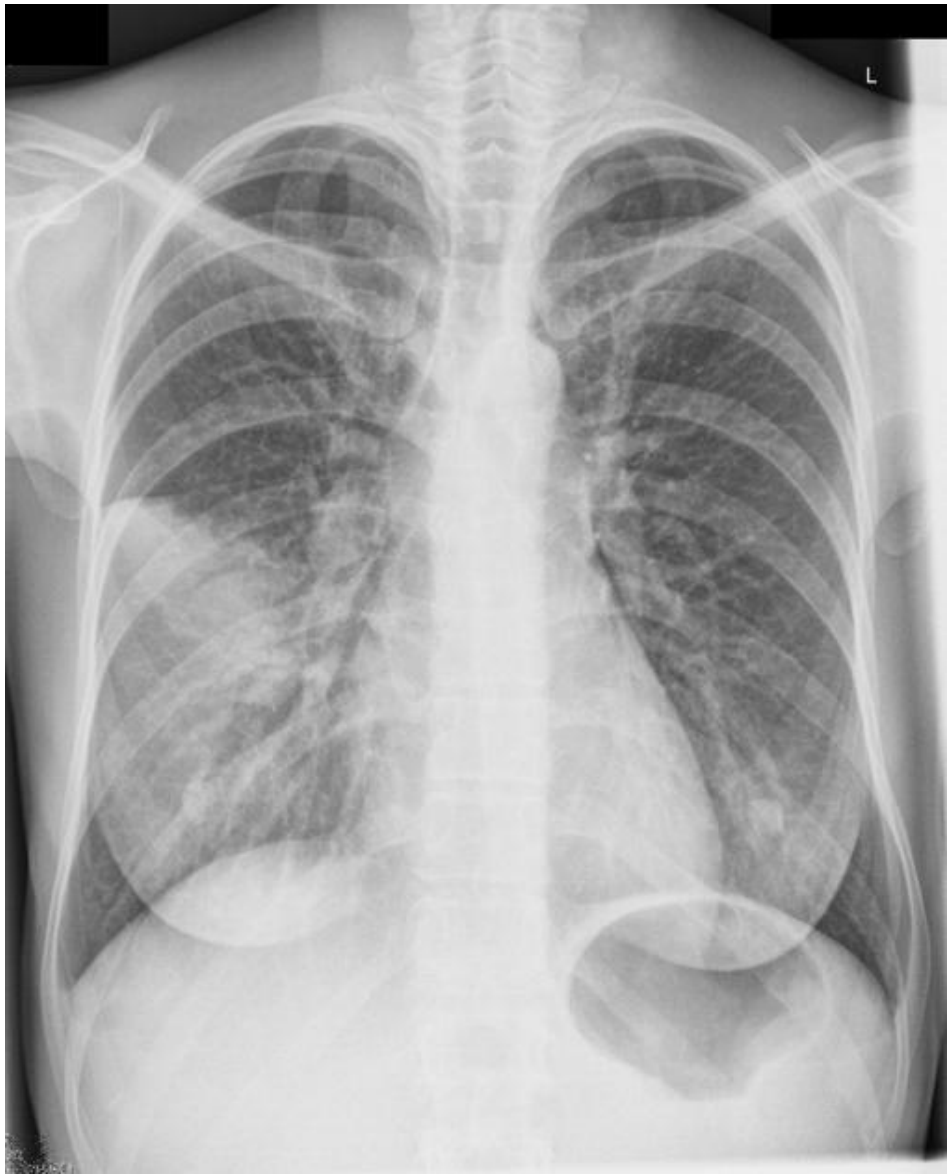
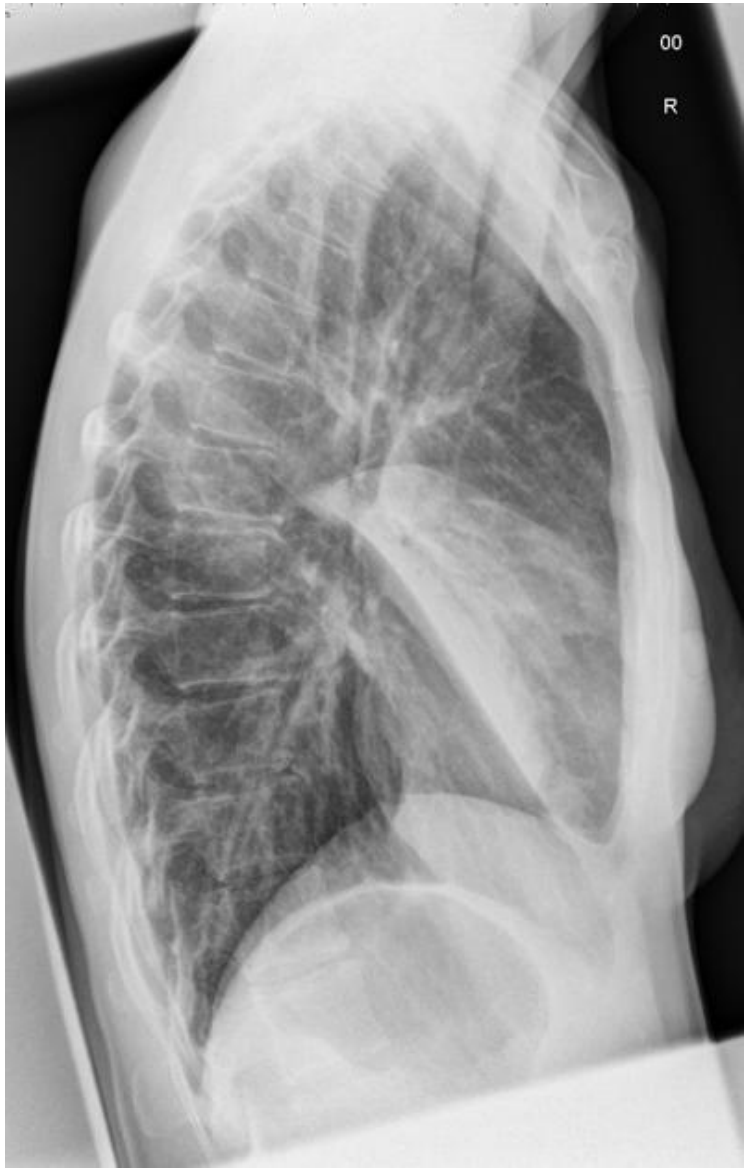
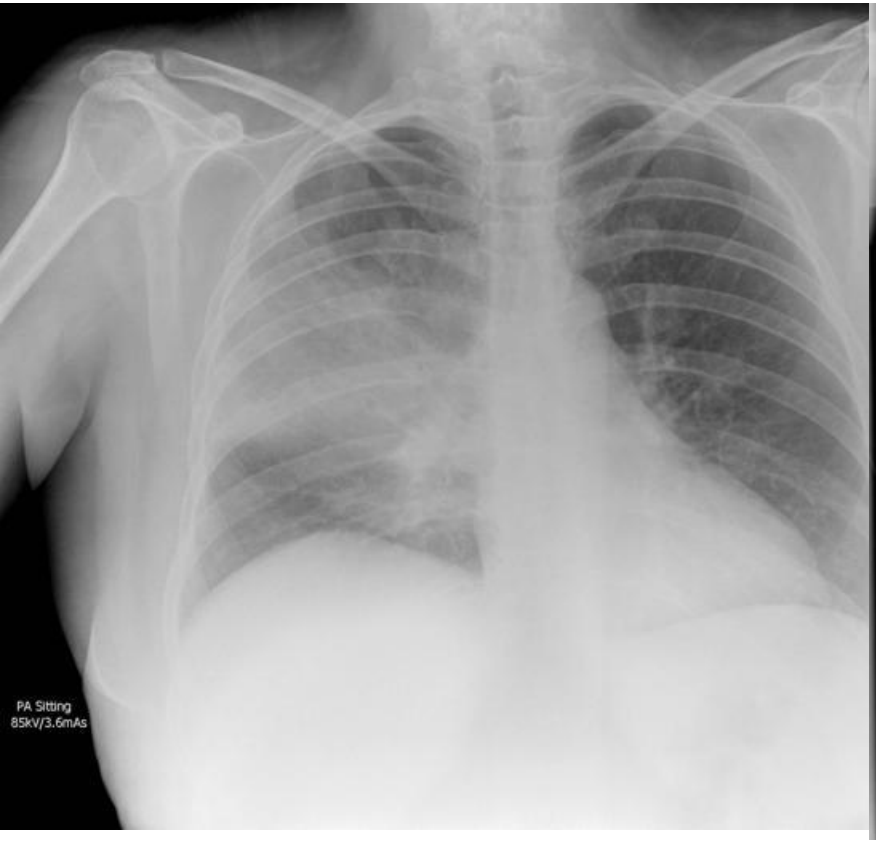
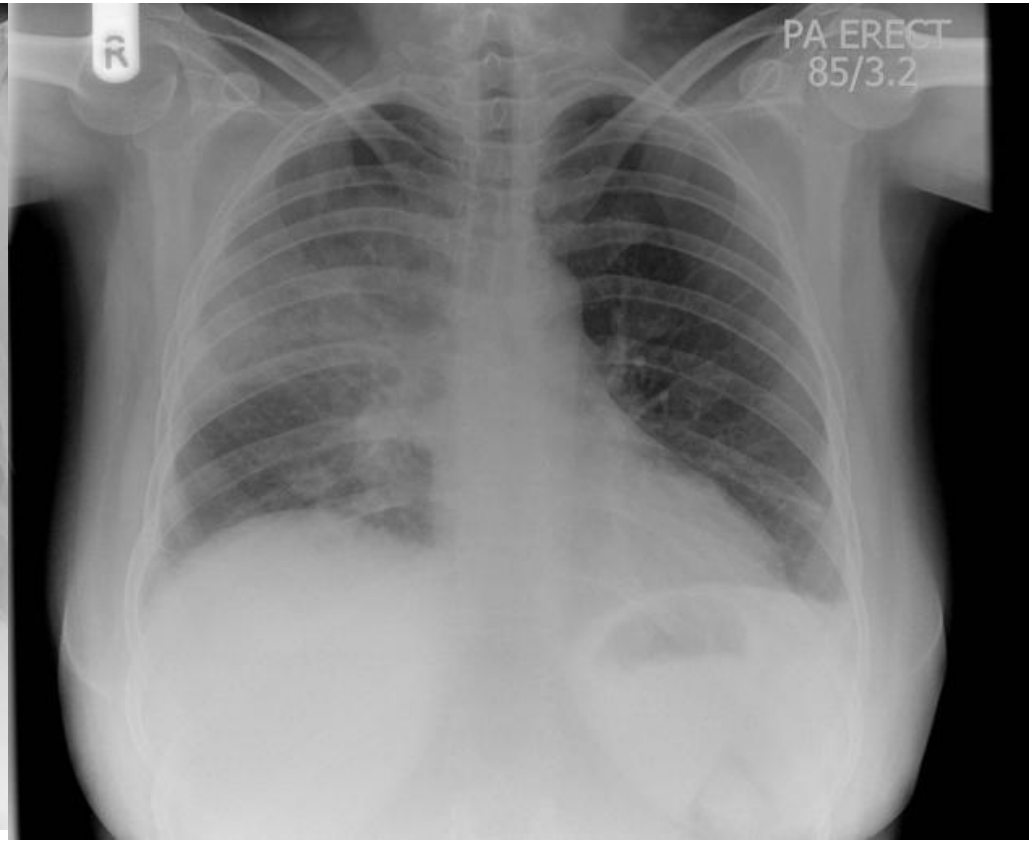
Middle lobe Str pneum

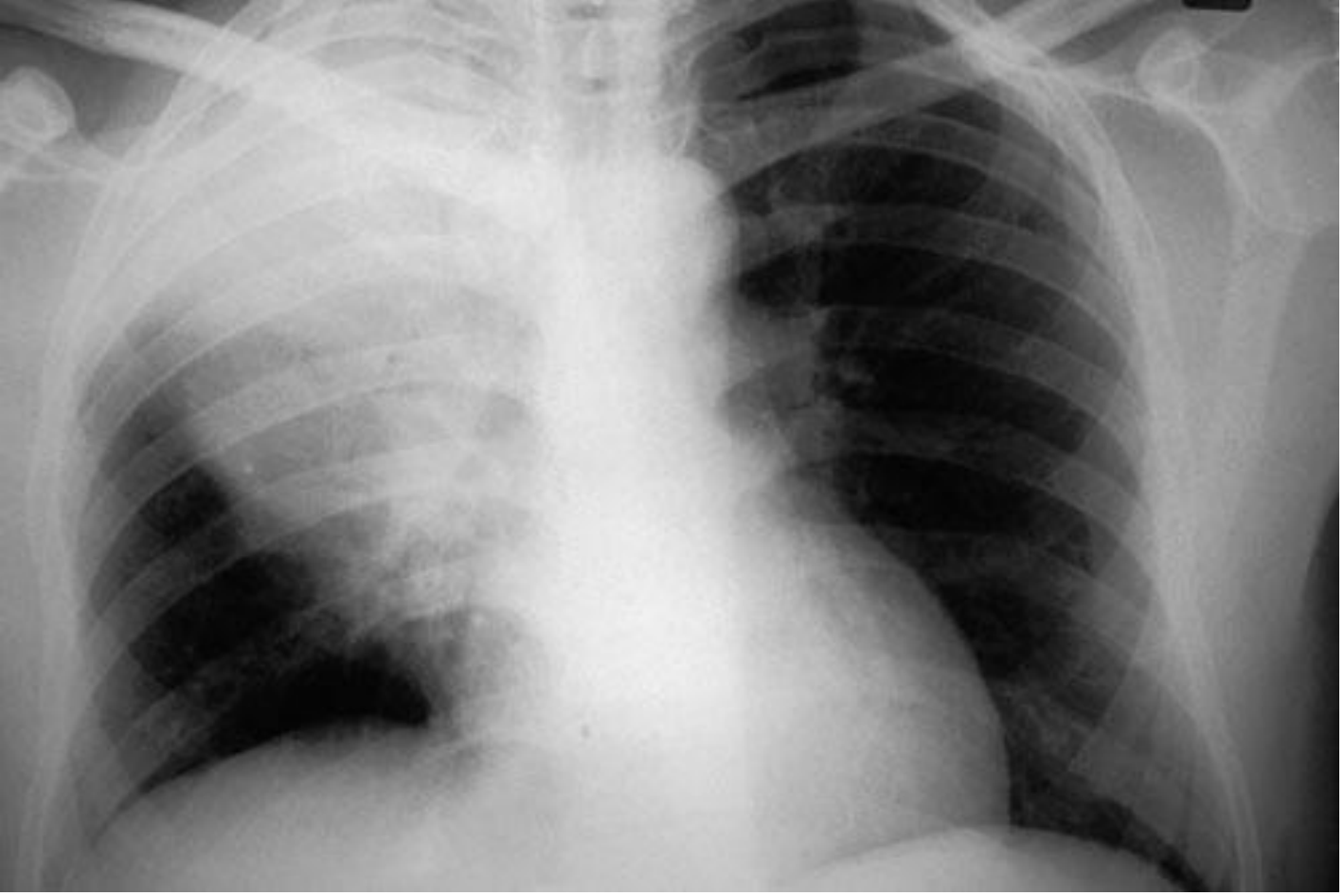




Right upper lobe







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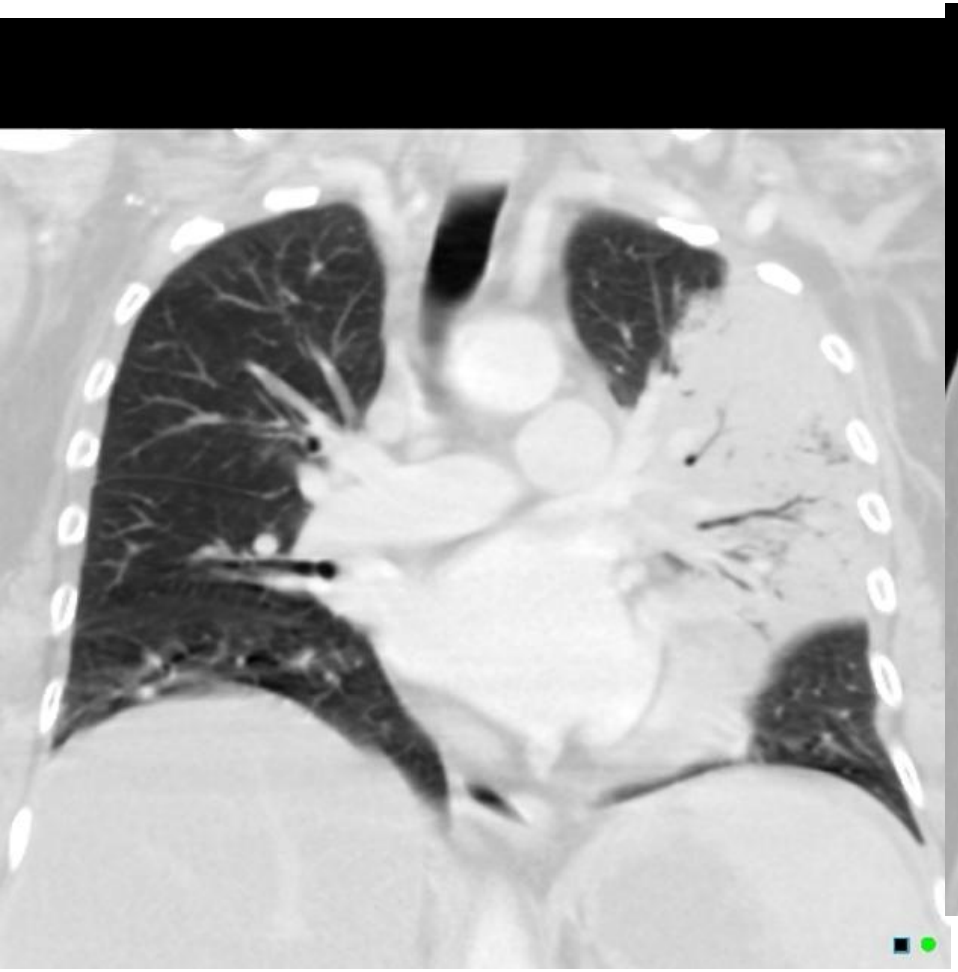
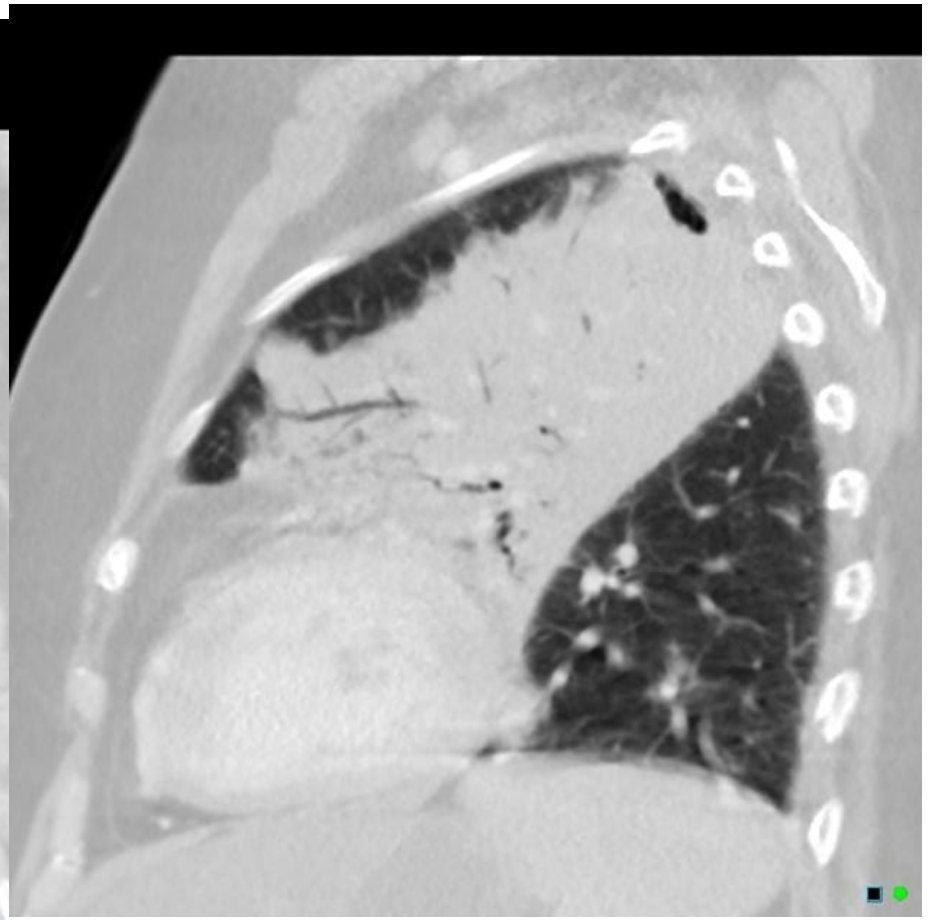
Coronal and saggital lungs windows





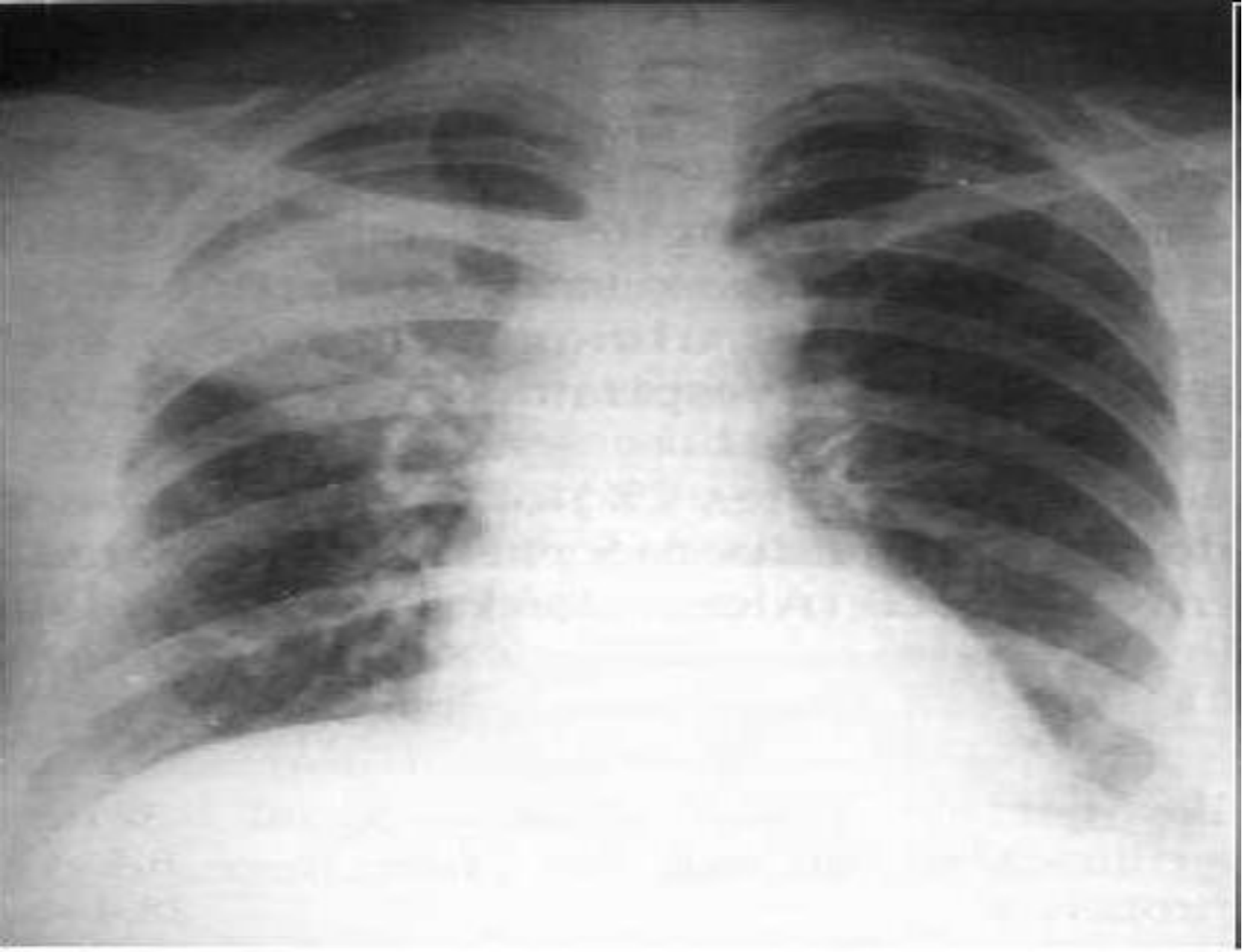
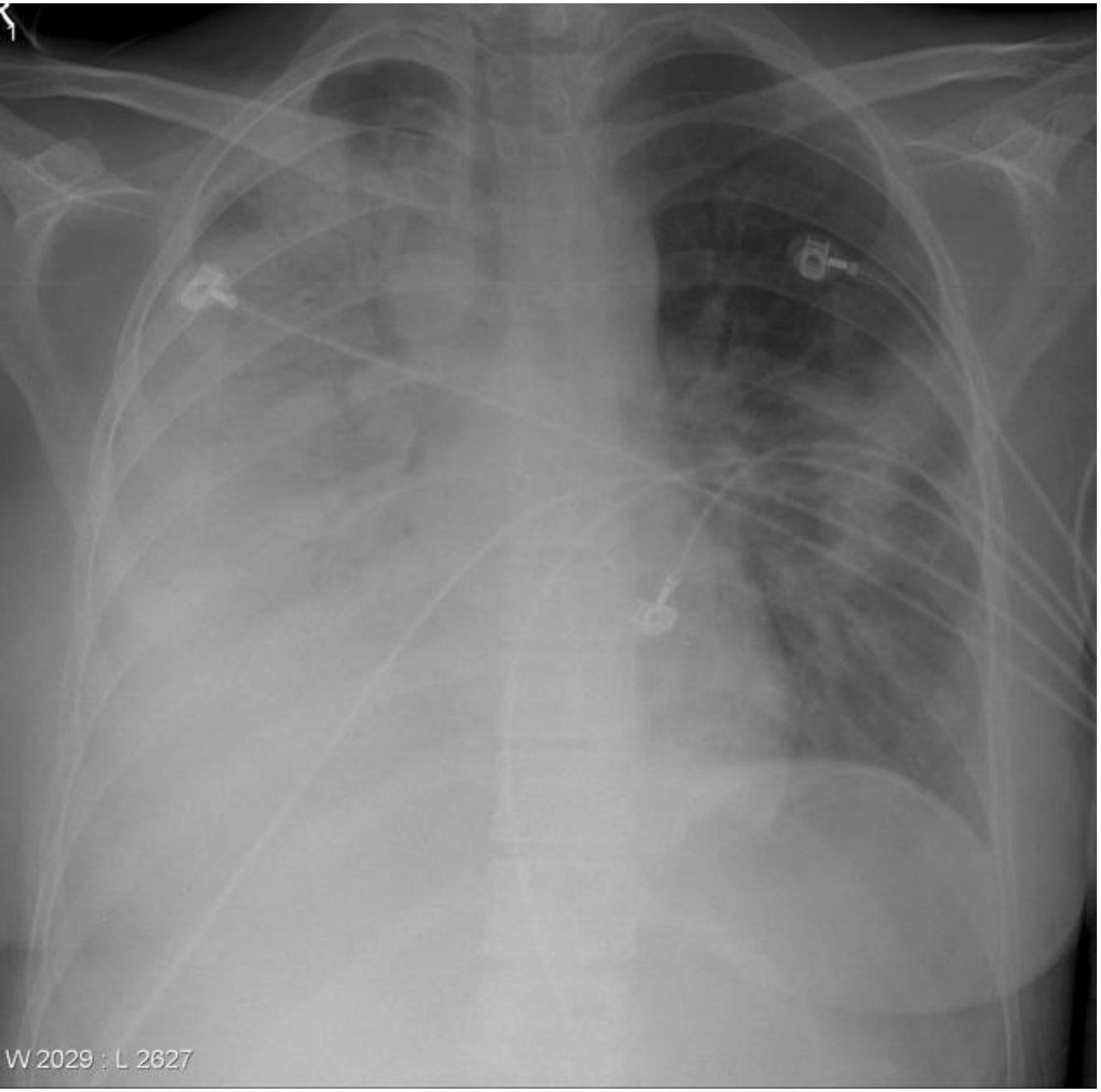


Fig. 4 : Lobar pneumonia showing dense consolidation mostly confined to one lobe, cavitation is rare- air bronchogram is seen in this right upper lobe consolidation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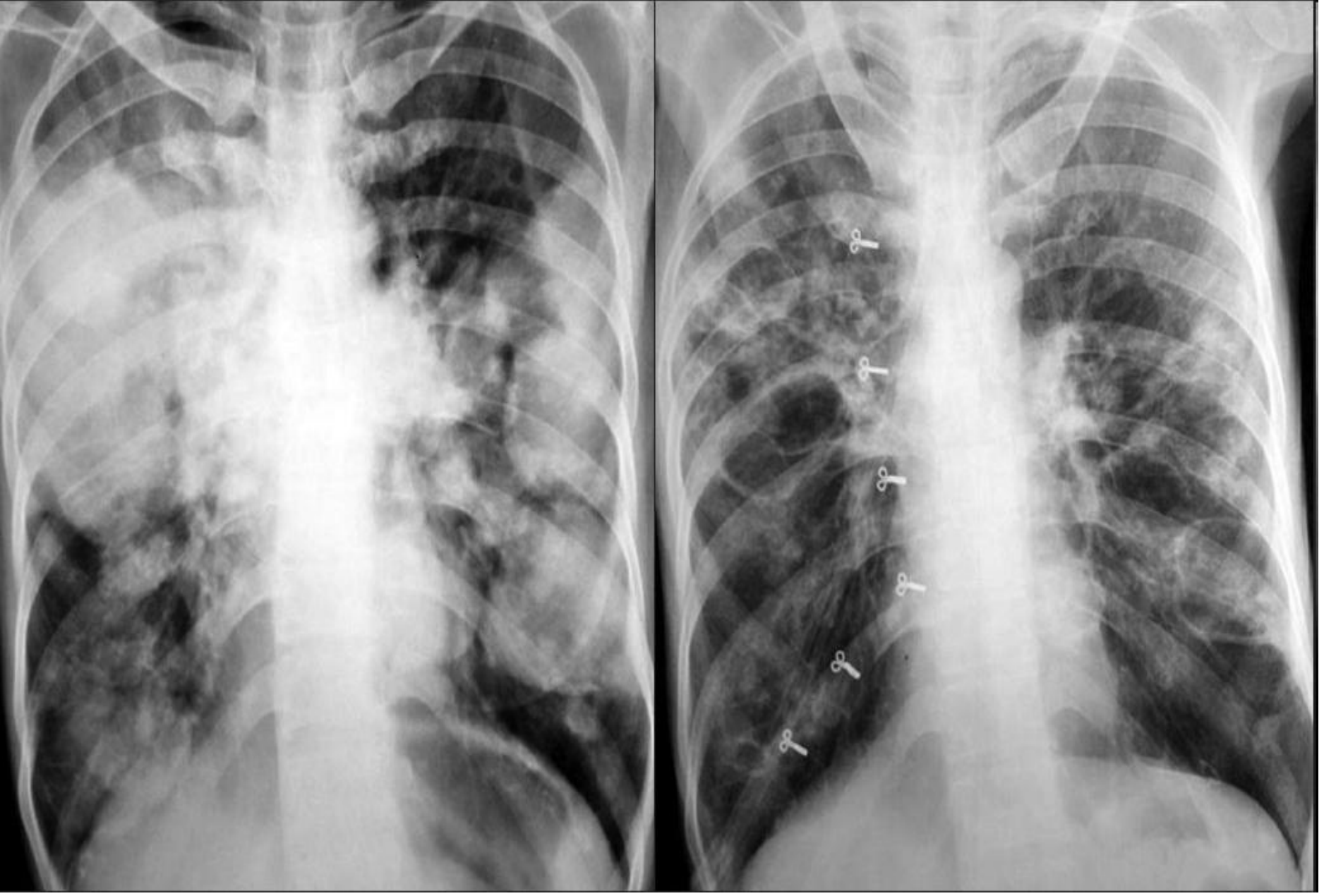
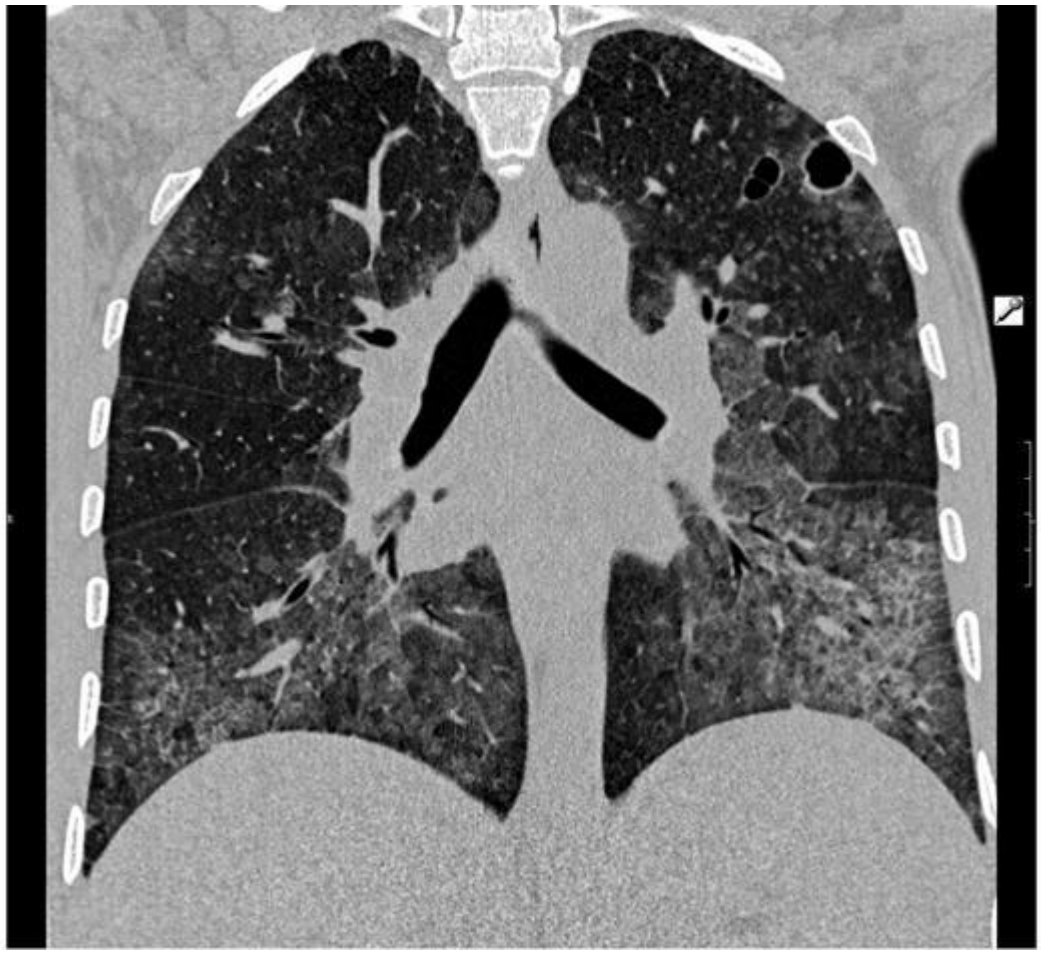
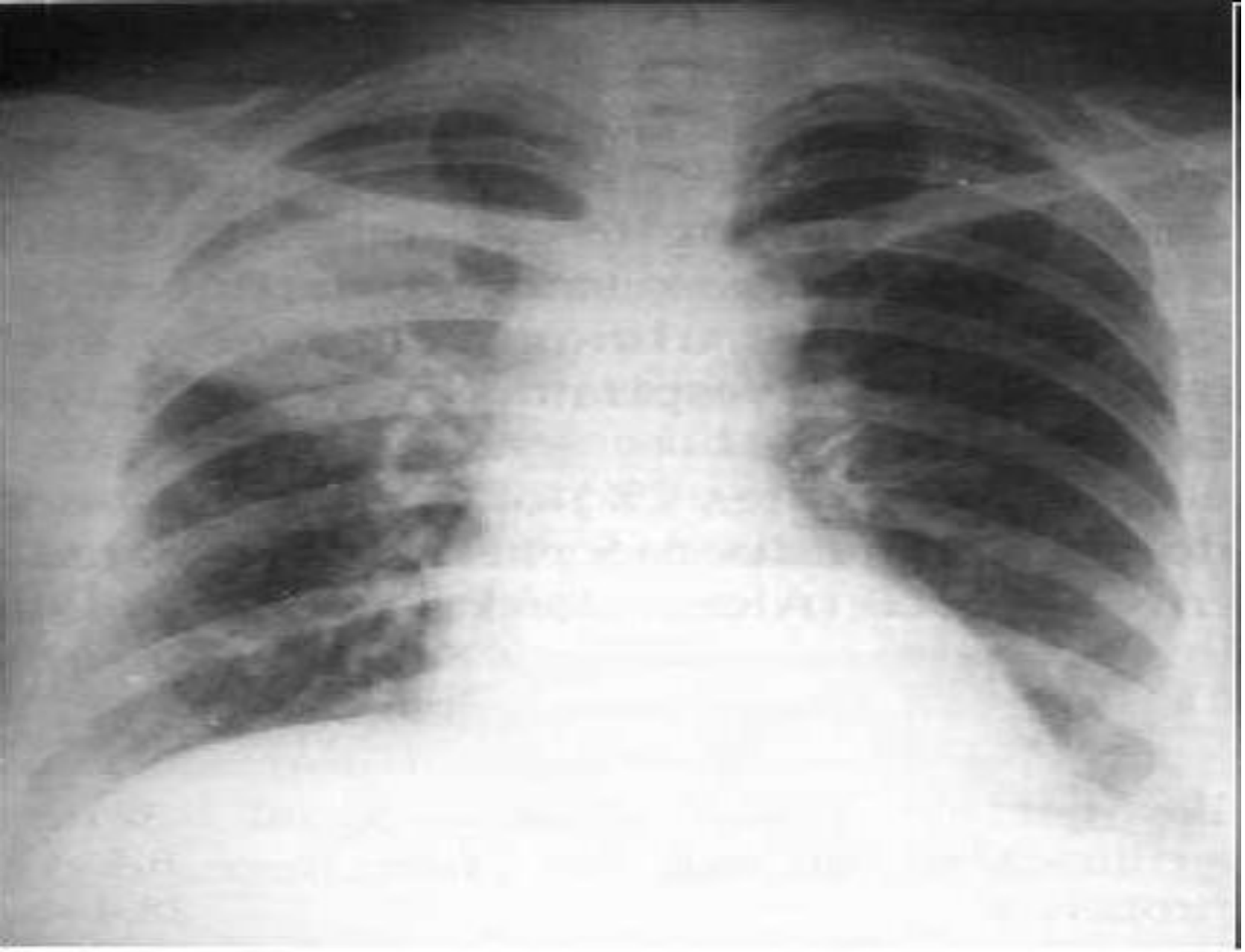


E.Coli

Pneumocystis pneumonia





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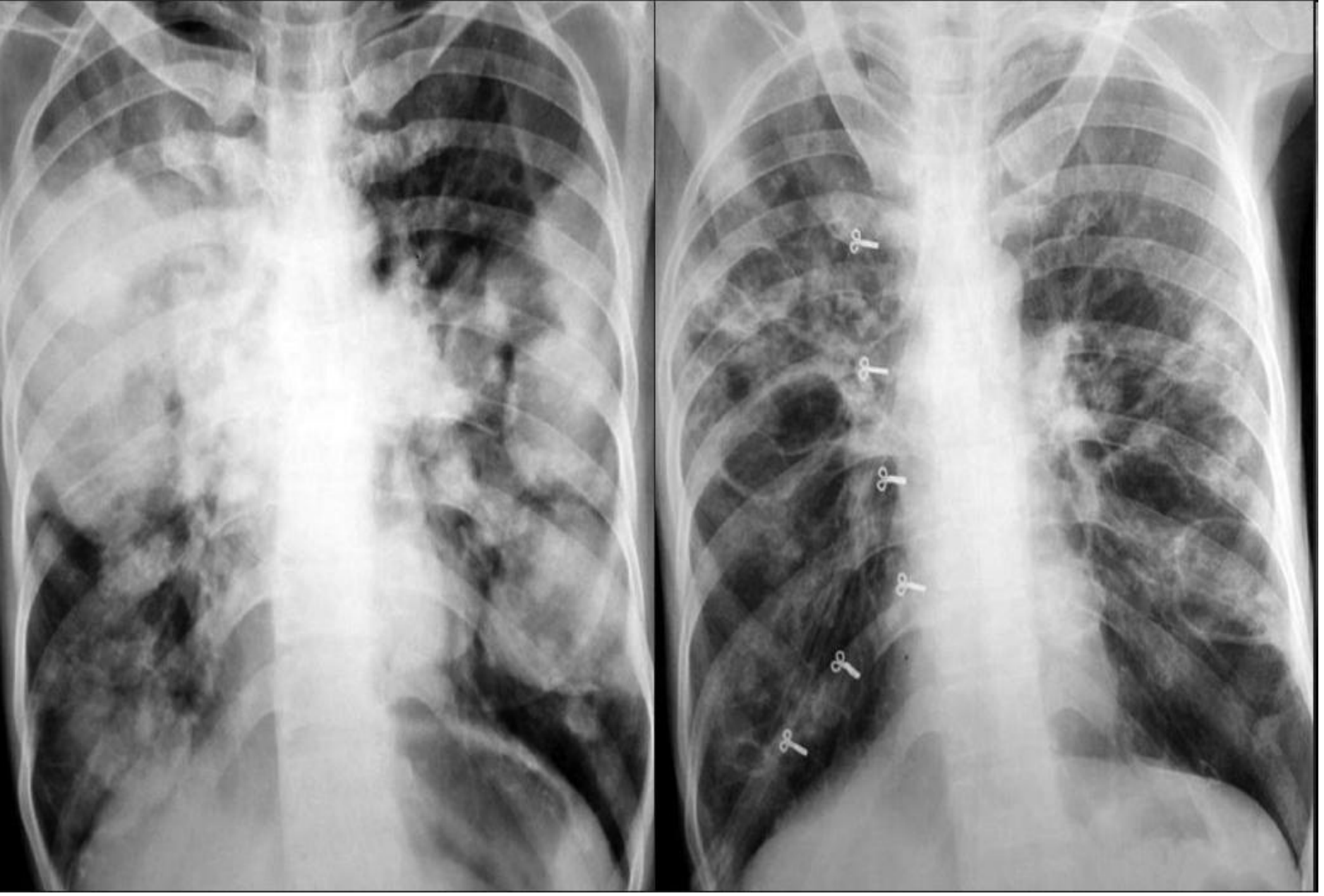


E.Coli

DECISION FOR HOSPITALIZATION

- PSI class IV, V

  Mortality, age, complicated
- CURB ≥ 2

  Pneumonia severity, easy
- Social reasons
- The treatment may be given p.o in mild pneumonia from the beginning if the patient is hospitalized due to social reasons

CAP and ICU

Major

- Requirement for invasive mechanical ventilation
- Septic shock requiring vasopressors

1 of 2

Minor

- Hypotension requiring aggressive fluid resuscitation
- PaO_2/FiO_2 < 250
- Involvement of > 2 lobes on CXR
- Respiratory rate >30/min
- Confusion/disorientation
- Uremia (BUN > 20m/dl)
- Leukopenia (WBC < 4000 cells/mm^3)
- Thrombocytopenia (PLT < 100000 cells/mm^3)
- Hypothermia(<36^oC)

3 out of 9

FACTORS THAT DETERMINE THE GUIDANCE OF EMPIRICAL INITIAL TREATMENT

- General patterns of expected pathogens
- Regional and local patterns of microbial resistance
- Considerations of tolerability and toxicity of antimicrobial agents in the individual patient

Acute respiratory failure severity – necessity of non-invasive ventilation

Strept.pneumoniae: Susceptibility breakpoints to penicillin

MIC (µg/ml)

Susceptibility	**≤0.06**
Intermediate susceptibility	**0.12-1**
Resistance **High level resistance**	**>1** **≥4(≥8)**

RISK FACTORS FOR PRSP

- Age < 2years and > 65 y.o
- β-lactam treatment within the last 3 months
- Alcoholism
- Comorbidities
- Immunosuppresive disease or treatment
- Exposure to a child in a day-care centre

β-lactams and strept.pneumoniae

- MIC > 2-4 μg/ml. There is no documented clinical treatment failure with adequate doses of β-lactams in pts with bacteremic pneumonia
- Amoxicillin: at an adequate dose it is the most active oral β-lactam
- Strains of strept. pneumoniae with an MIC of 4-8 μg/ml have responded to an oral formulation of 2000mg/125mg amoxycillin/clavulanate twice daily

Time-dependent killing

- β-lactams
- Macrolides
- Clindamycin
- Oxazolidinones

- Time above the MIC (maximum killing at concentrations X4-5 times the MIC)
- 40-50% of the dosing interval

Macrolides

- Resistance to erythromycin = resistance to clarithromycin, azithromycin, roxithromycin
- Different resistance rates from country to country

Respiratory quinolones

- High activity against streptococcus pneumoniae
- Concentration-dependent activity
- Cmax / MIC
- AUC_{24} / MIC
- Aminoglycosides, Quinolones
- Dosage once / daily
- Resistance to levofloxacin in strains of strept.pneumoniae with an MIC > 4 up to > 32 mg/L

Identifying the Patient at Risk for a Pneumococcal Infection Due to a Resistant Strain to Fluoroquinolone

- Residents of long-term care facilities
- Chronic obstructive pulmonary disease (COPD)
- Nosocomial origin of the bacteria
- Residence in a nursing home
- Previous exposure to fluoroquinolones

CAP TREATMENT

- The first antibiotic dose should be administered while still in the ED
- In patients with CAP and septic shock, delay must not be more than 1 h after diagnosis

CAP – outpatient treatment

- Previously healthy and no risk factors for PRSP

  Macrolide (Level I)

  Doxycycline (Level III)
- Presence of comorbidities (CHF, renal-respiratory or hepatic disease, diabetes melitus, alcoholism, asplenia, malignancies, immunosuppressing conditions or medication, use of antimicrobials within the previous 3 months)

  Respiratory fluoroquinolone (Level I)

  B-lactam + macrolide (Level I) - high dose amoxicillin or amoxicillin-clavulanate

CAP – inpatient treatment

- Respiratory fluoroquinolone (Level I)
- B-lactam (cefotaxime, ceftriaxone, ampicillin, ertapenem) + macrolide or doxycyclin (Level I)
- For penicillin-allergic patients a respiratory fluoroquinolone

CAP – inpatient ICU treatment

- B-lactam (cefotaxime, ceftriaxone, ampicillin-sulbactam) + azithromycin or a fluoroquinolone (Level I)
- For penicillin- allergic patients

  respiratory fluoroquinolone + aztreonam
- With risk for P. aeruinosa

  antipseudomonal β-lactam (pip-taz, cefepime, imipenem, meropenem) + cipro- or levofloxacin OR

  antipseudomonal β-lactam + aminoglycoside + azithromycin

  OR

  antipseudomonal β-lactam + aminoglycoside + respiratory fluoroquinolone
- For MRSA in the community vancomycin or linezolid

THE CURRENT POSITION OF MACROLIDES IN CAP TREATMENT

- In the medical literature of the past 10 years, the addition of a macrolide to a β-lactam

1. Reduces the 1-month mortality
2. Reduces the length of hospital stay

EMPIRIC COMBINATION TREATMENT

- B-lactam + macrolide
- The benefit of combination therapy that includes a macrolide applies not only to CAP in general but also to CAP specifically associated with strept.pneumoniae bacteremia
- Coexistence of atypical pathogens ?
- Immunomodulating effect of macrolides ?

CLINICAL FOLLOW UP

- The first 48-72 hours are of critical importance
- Fever
- Respiratory rate
- Oxygenation
- Hemodynamic instability
- Consciousness
- NO CXR alone (unless there is clinical deterioration)

CRITERIA FOR CLINICAL STABILITY

- Temperature < 37,8°C
- HR < 100/min
- Respiratory rate < 24/min
- SAP > 90mmHg
- $SatO_2$ > 90% or PO_2 > 60mmHg (FiO_2 0.21)
- Ability to maintain oral intake
- Normal mental status

DURATION OF TREATMENT

- 5-10 days (ATS/IDSA) – not exceed 8 days (ERS)
- 14 days in Legionella
- Should be afebrile for 48-72 hours more
- NOT > 1 criterion of clinical instability before discontinuation of therapy
- Switch from i.v to p.o when the patient has clinically improved, is hemodynamically stable, is able to ingest medications and has a normally functioning gastrointestinal tract.

Criterion to stop antibiotic treatment is the clinical improvement of the patient

- Radiological improvement delays
- Pneumococcal pneumonia: 4 weeks
- Pneumonia due to *Legionella*: 12 weeks

TREATMENT FAILURE

- 6-15% of hospitalized 40% in the ICU
- Progressive pneumonia (ARF±septic shock within the first 72 hours)
- If > 72 hours after initial treatment → complications, deterioration of underlying disease, nosocomial superinfection
- Persistent (non responding) pneumonia (lack or delay in achieving clinical stability)
- Nonresolving or slowly-resolving pneumonia (persistence of pulmonary infiltrates > 30 days after initial pneumonia-like syndrome)

- Full re-evaluation (chest CT scan, bronchoscopy, blood cultures) and in unstable patients a second empiric antibiotic course. Transfer to a higher level of care
- No studies to compare invasive vs. non-invasive techniques in non-responding CAP (in contrast to VAP)

TREATMENT FAILURE

- FAILURE TO IMPROVE

Early (<72 hours of treatment)

Normal response

Delayed

Resistant microorganism

Uncovered pathogen

Parapneumonic effusion/empyema

Nosocomial superinfection(pneumonia/extrapulmonary)

Non-infectious (complication:BOOP, misdiagnosis:PE, CHF, vasculitis, drug fever)

TREATMENT FAILURE

- DETERIORATION OR PROGRESSION

Early (<72 hours of treatment)

Disease severity at presentation
Resistant microorganism
Uncovered pathogen
Metastatic infection (empyema/parapneumonic effusion, endocarditis, meningitis, arthritis)
Inaccurate diagnosis (PE, ARDS, vasculitis)

Delayed

Nosocomial superinfection (pneumonia, extrapulmonary)
Exacerbation of comorbid illness
Other non-infectious disease (PE, myocardial infarction, renal failure)

PREVENTION OF CAP

- Influenzae vaccination

  > 50 y.o, chronic cardiovascular or pulmonary disease, diabetes melitus, renal dysfunction, hemoglobinopathies, pregnancy, immunocompromising conditions/medications, residence in a long-term care facility, health care providers

- Antipneumococcal vaccination

  > 65 y.o, chronic cardiovascular, pulmonary renal or liver disease, diabetes melitus, cerebrospinal fluid leaks, alcoholism, asplenia, immunocompromising conditions/medications, residence in a long-term care facility, current smoking habit

  PPV (23-valent, polysacharide)

  Pneumococcal conjugate 7-valent or 14-valent

SMOKING HABIT

- S.O.S
- Cigarette smoking is the strongest independent risk factor for CAP in healthy adults

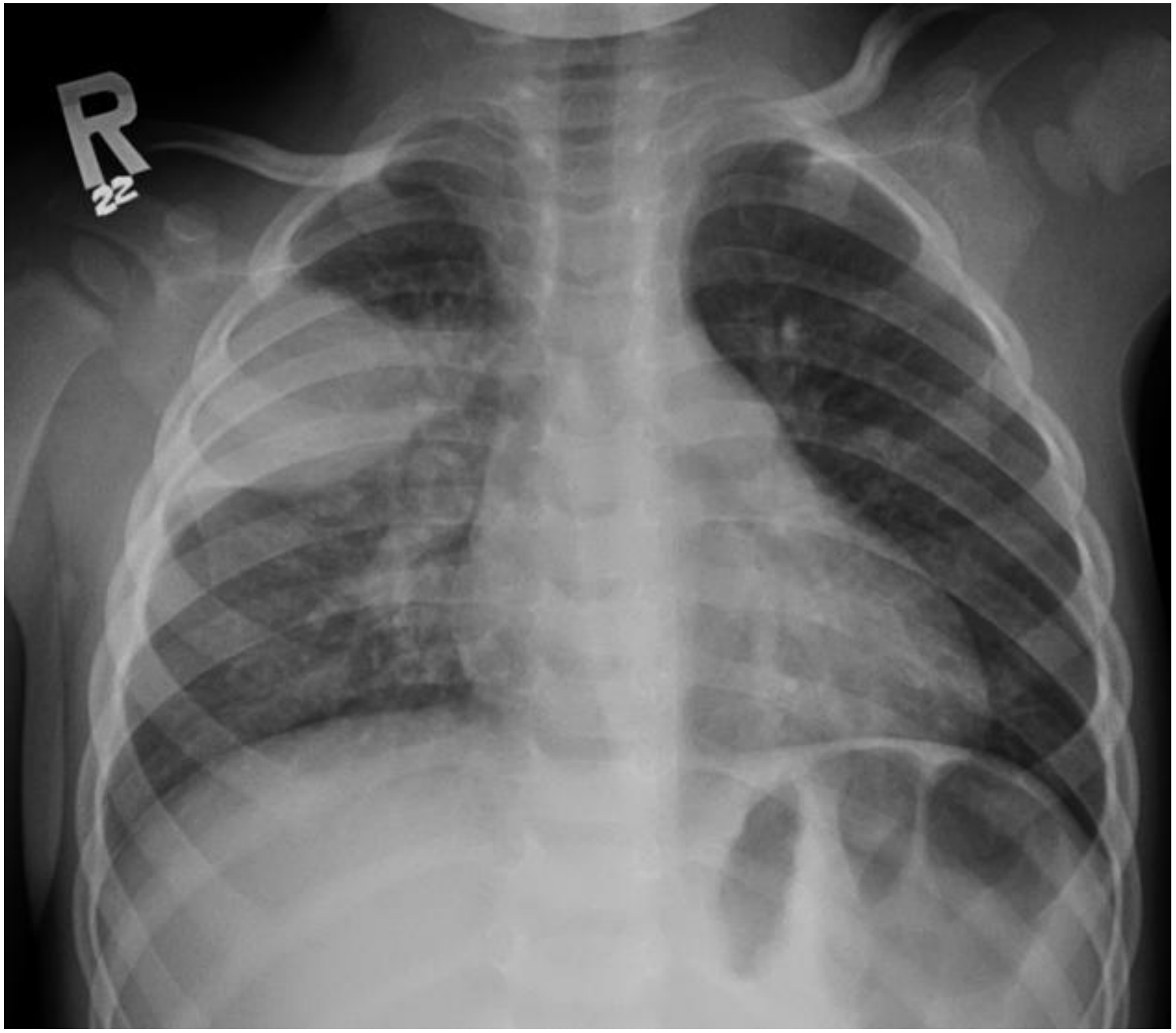
CAP due to *Staphylococcus aureus*

- 3% of CAP requiring hospitalization
- 25% in influenza outbreaks
- Predisposing factors: Diabetes melitus, chronic renal failure, influenza
- Infection through the respiratory tract or blood-borne (from a distant focus of infection)
- Severe illness
- 20-30% abscess
- 60% bacteremia
- 20-30% mortality

CAP due to *Staphylococcus aureus*

- Severe necrotizing pneumonia with complications and fast progression to respiratory failure in otherwise healthy subjects with no risk factors
- **Panton-Valentine leucocidin (PVL)**
- **Blood-stained sputum, hemoptysis and leukopenia**
- Sensitivity to many antibiotics
  (quinolones, erythromycin-clindamycin, minocyclin, cotrimoxazole)
- Treatment: Linezolid, clindamycin

- **Round pneumonia:** usually seen in paediatric patients. They are well defined, rounded opacities that represent regions of infected consolidation.
- **Epidemiology**
- mean age - 5 years and 90% of patients who present with round pneumonia are younger than twelve [5].
- uncommon after the age of eight because collateral airways tend to be well developed by this age [2,5]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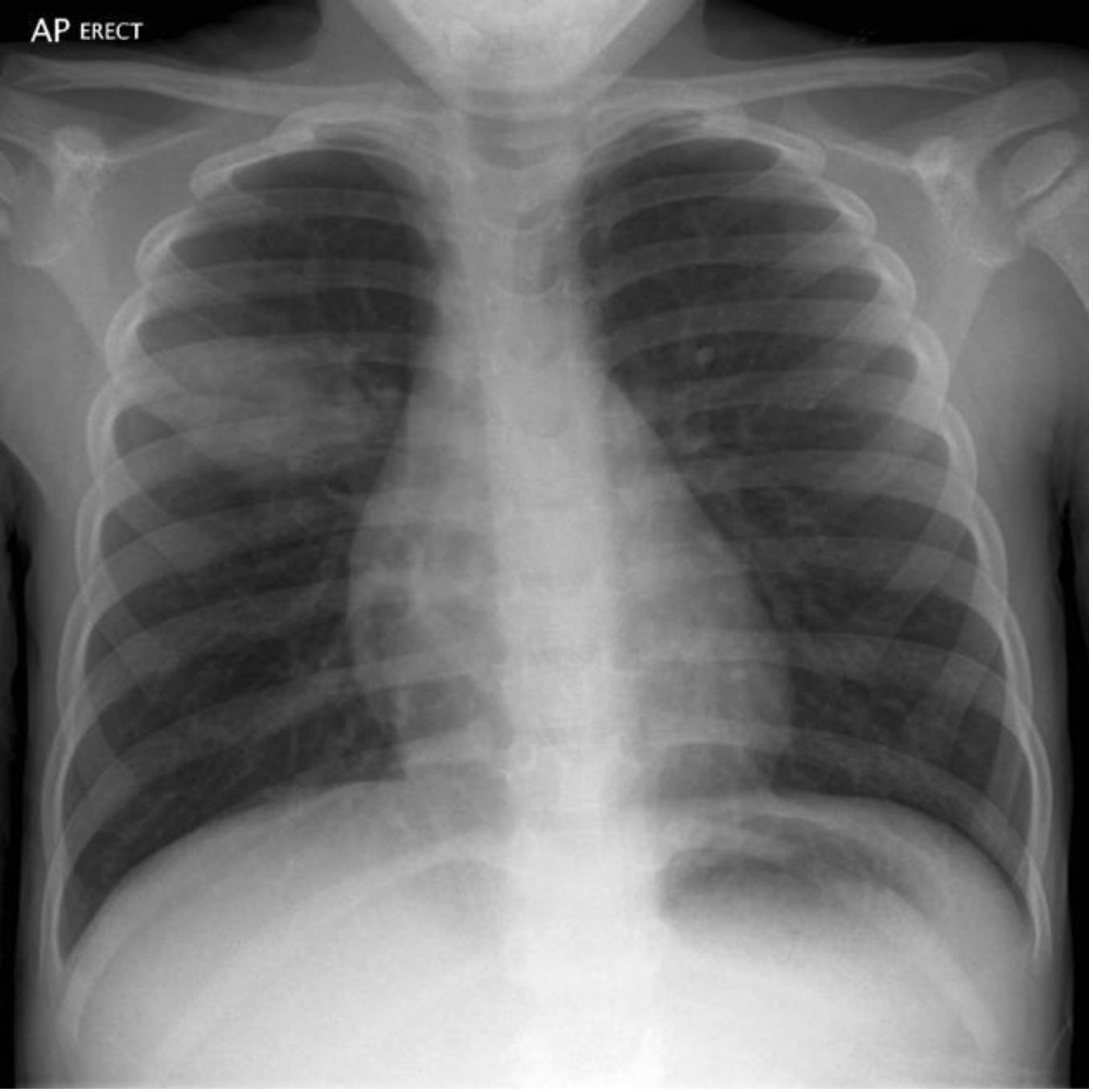
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Bronchopneumonia

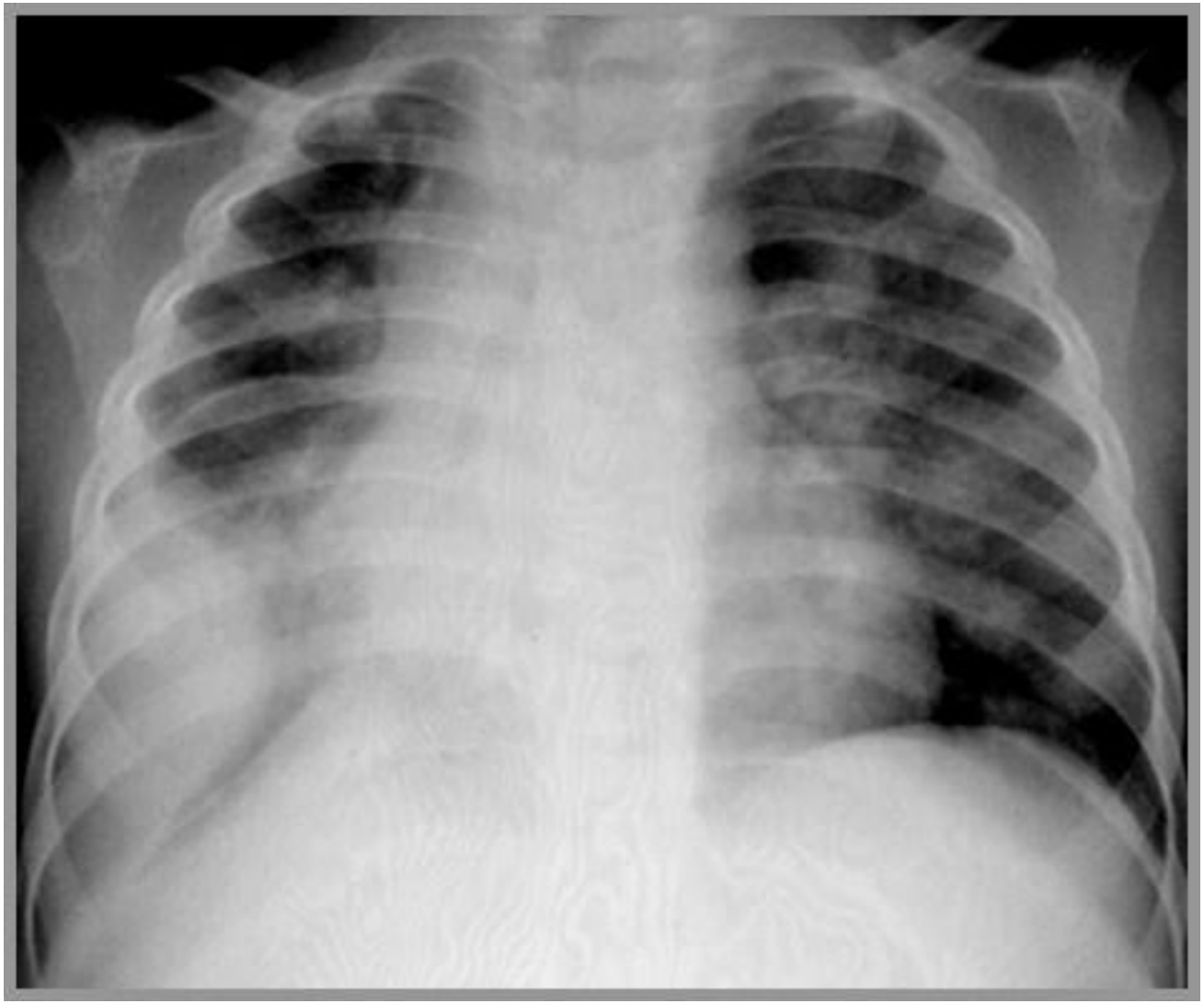
- also sometimes known as **lobular pneumonia**
- radiological pattern associated with suppurative peribronchiolar inflammation and subsequent patchy consolidation of one or more secondary lobules of a lung in response to a bacterial pneumonia.
- radiological appearance of bronchopneumonia is not specific to any single causative organism, although there are organisms which classically have a radiological presentation of bronchopneumonia and hence the identification of bronchopneumonia can provide information regarding the likely aetiological pathogens

- Causative organisms of a bronchopneumonia pattern include [3]:
- *Staphylococcus aureus*
- *Klebsiella pneumoniae*
- *Haemophilus influenzae*
- *Pseudomonas aeruginosa*
- *Escherichia coli*
- Anaerobes, such as *Proteus* species
- Histologically, multiple small foci of inflammation can be demonstrated. Extensive congestion and dilation of bloods vessels and areas of poorly circumscribed consolidation can be seen in affected areas [8]. These areas of inflammation are seperated by areas of normal lung parenchyma [3].

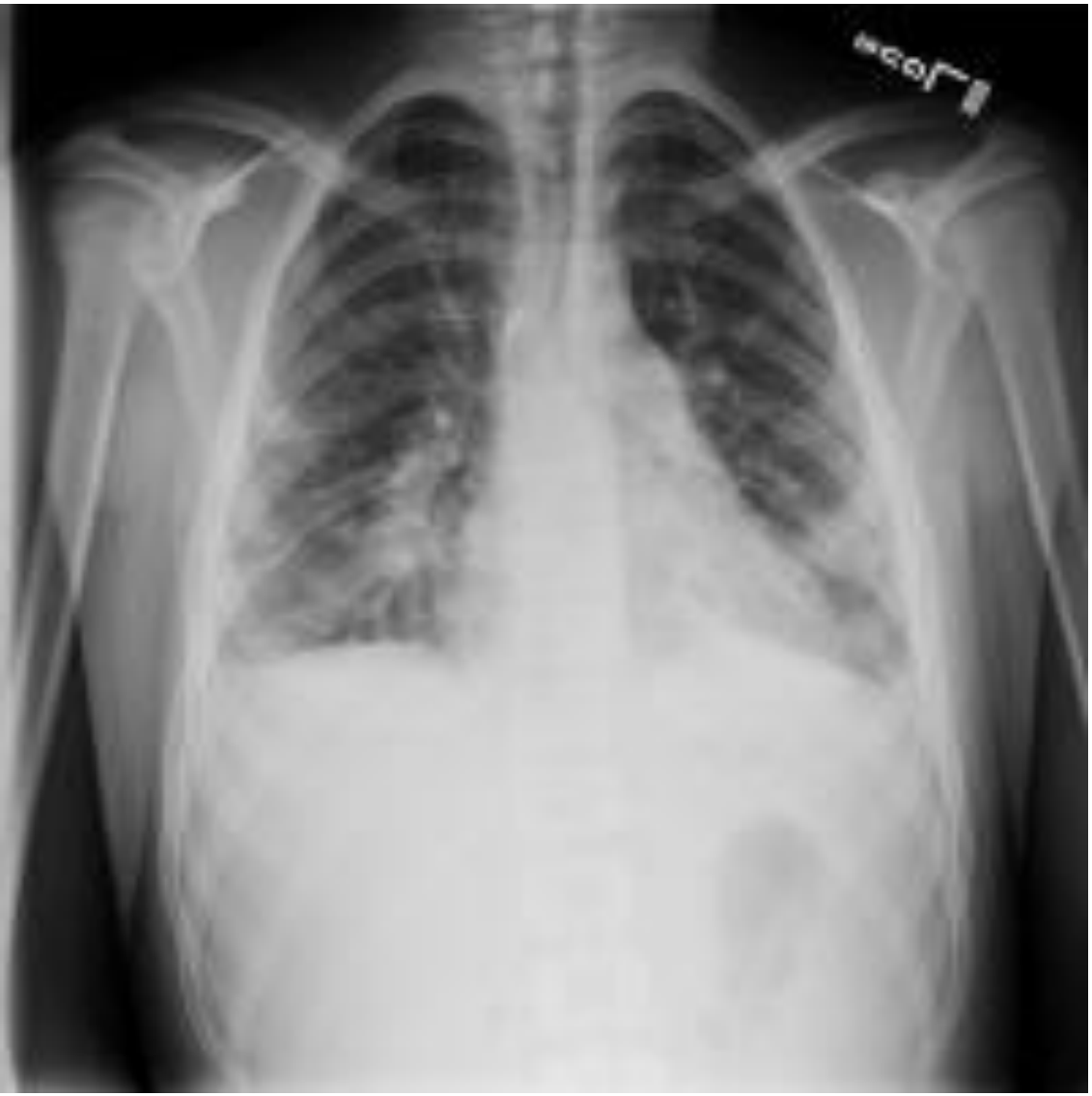
Radiology

- **Plain film**
- Bronchopneumonia is characterised by multiple small nodular or reticulonodular opacities which tend to be patchy and/or confluent. This represents areas of lung where there are patches of inflammation separated by normal lung parenchyma. [2].
- The distribution is often bilateral and asymmetric, and predominantly involves the lung bases [8].
- **CT - HRCT chest**
- Multiple foci of opacity can be seen in a lobular pattern, centred at centrilobular bronchioles. This may result in a tree-in-bud appearance. These foci of consolidation can overlap to create a larger heterogeneous confluent area of consolidation or 'patchwork quilt' appearance [6].

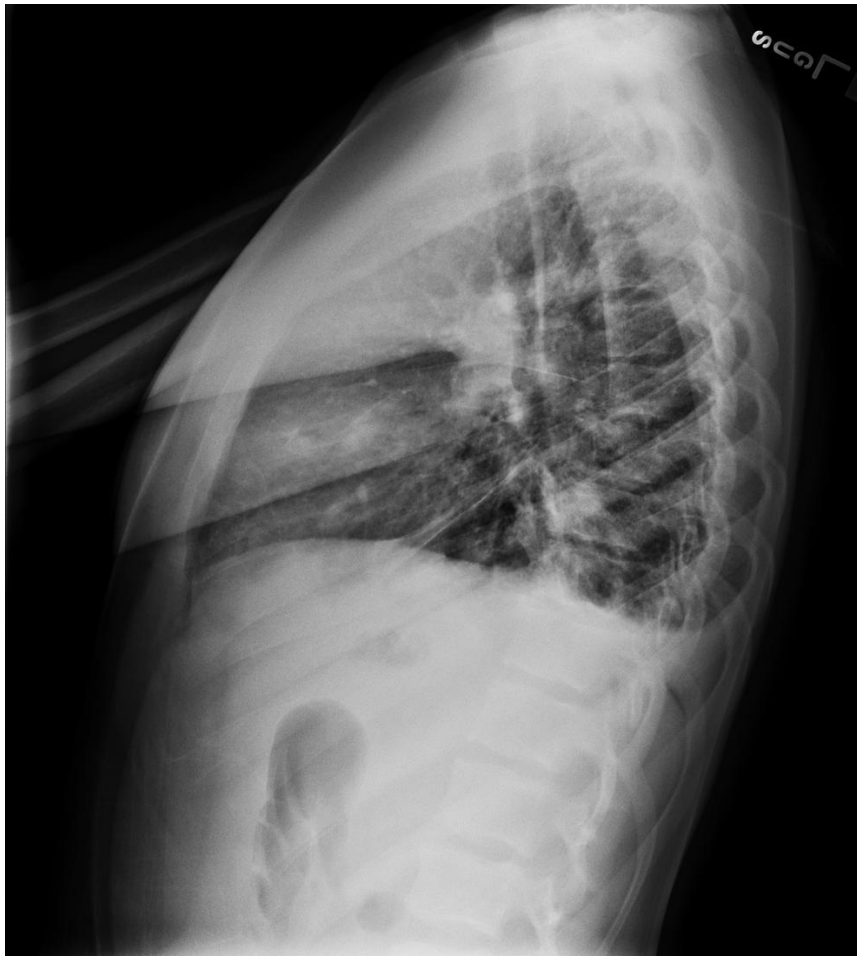
Staphyl pneum with empyema



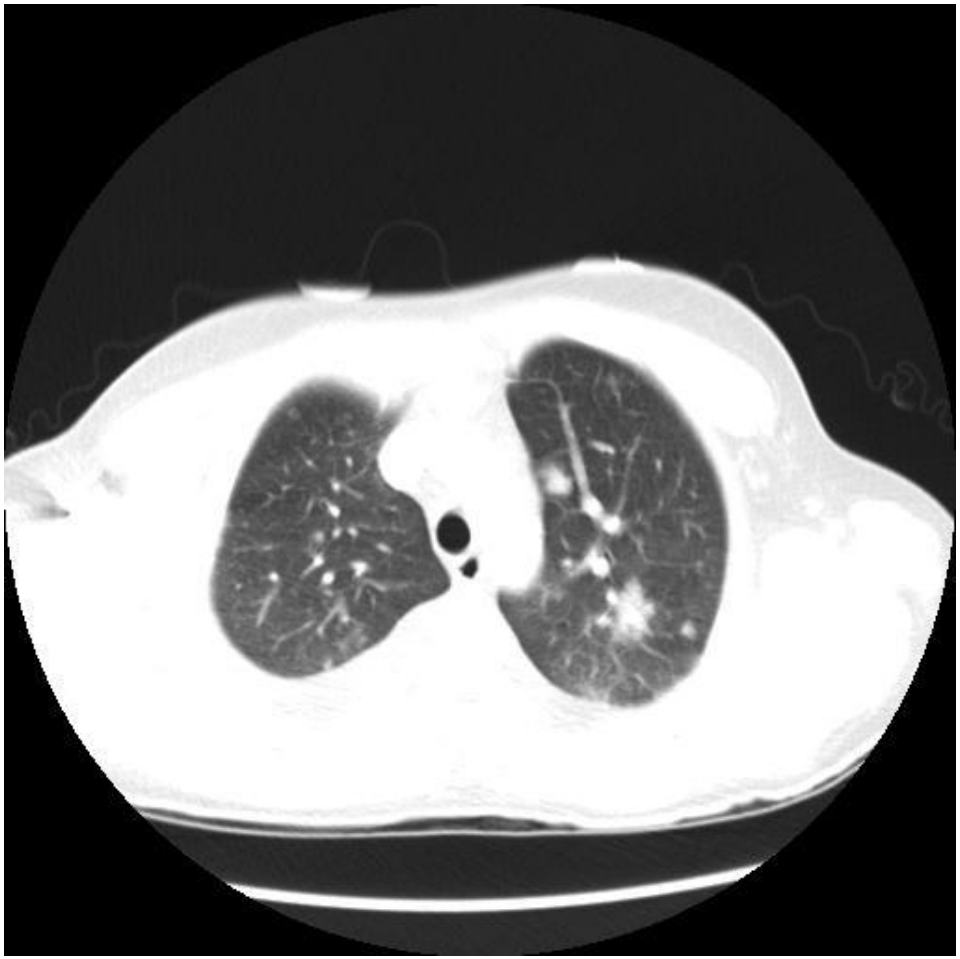
Posteroanterior chest radiograph of a 15-year-old with staphylococcal endocarditis and multiple septic emboli, revealing borderline cardiomegaly, multiple nodular infiltrates, and bilateral pleural effusions.



Lat/view



CT scan



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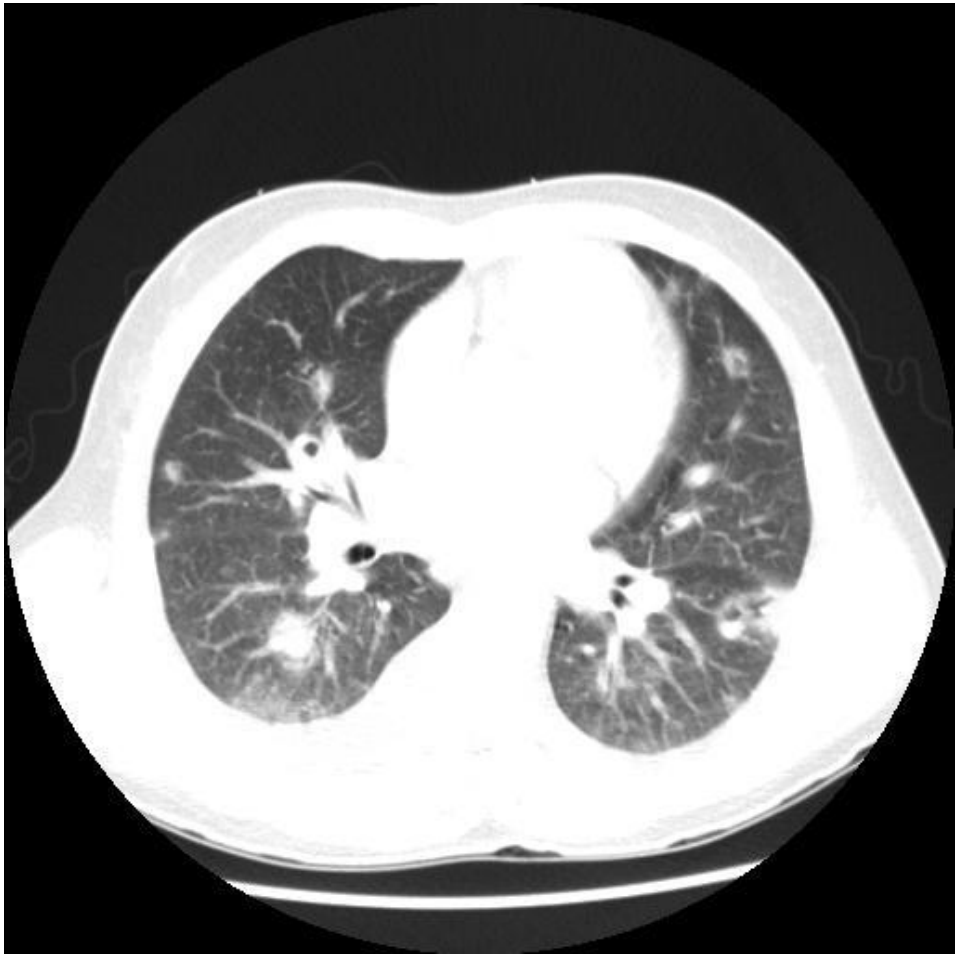

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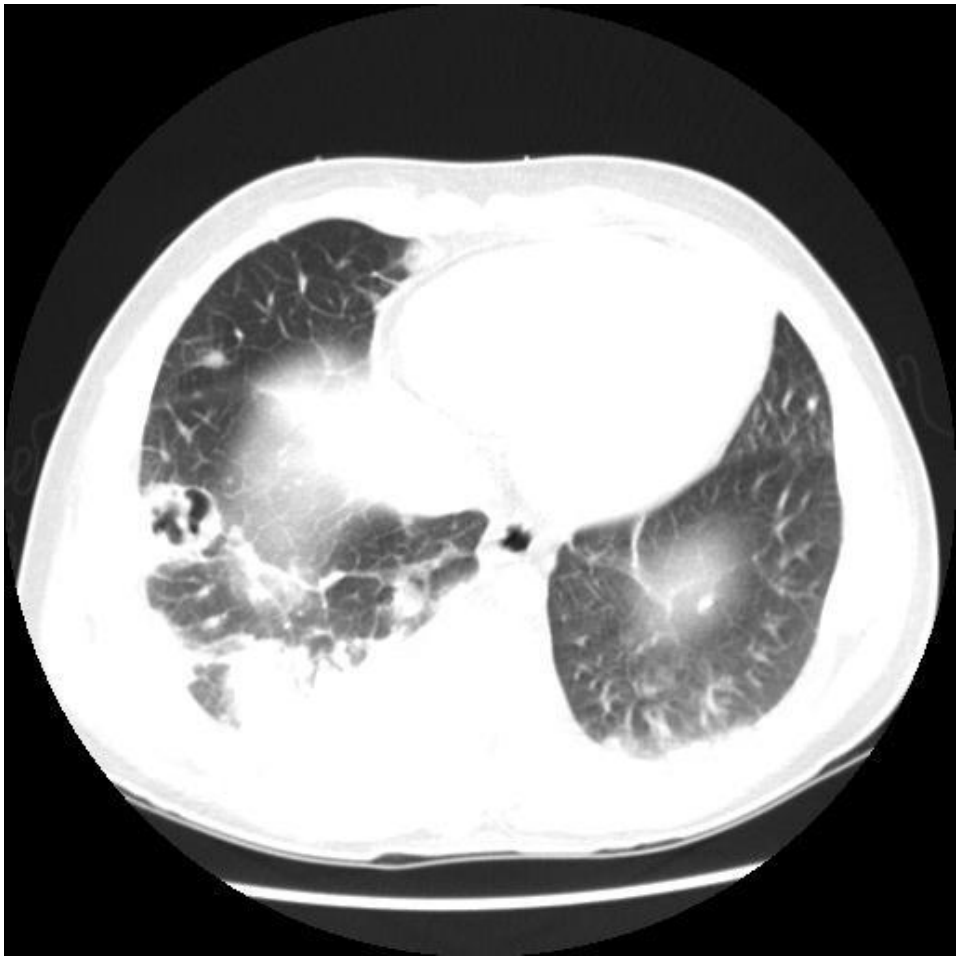
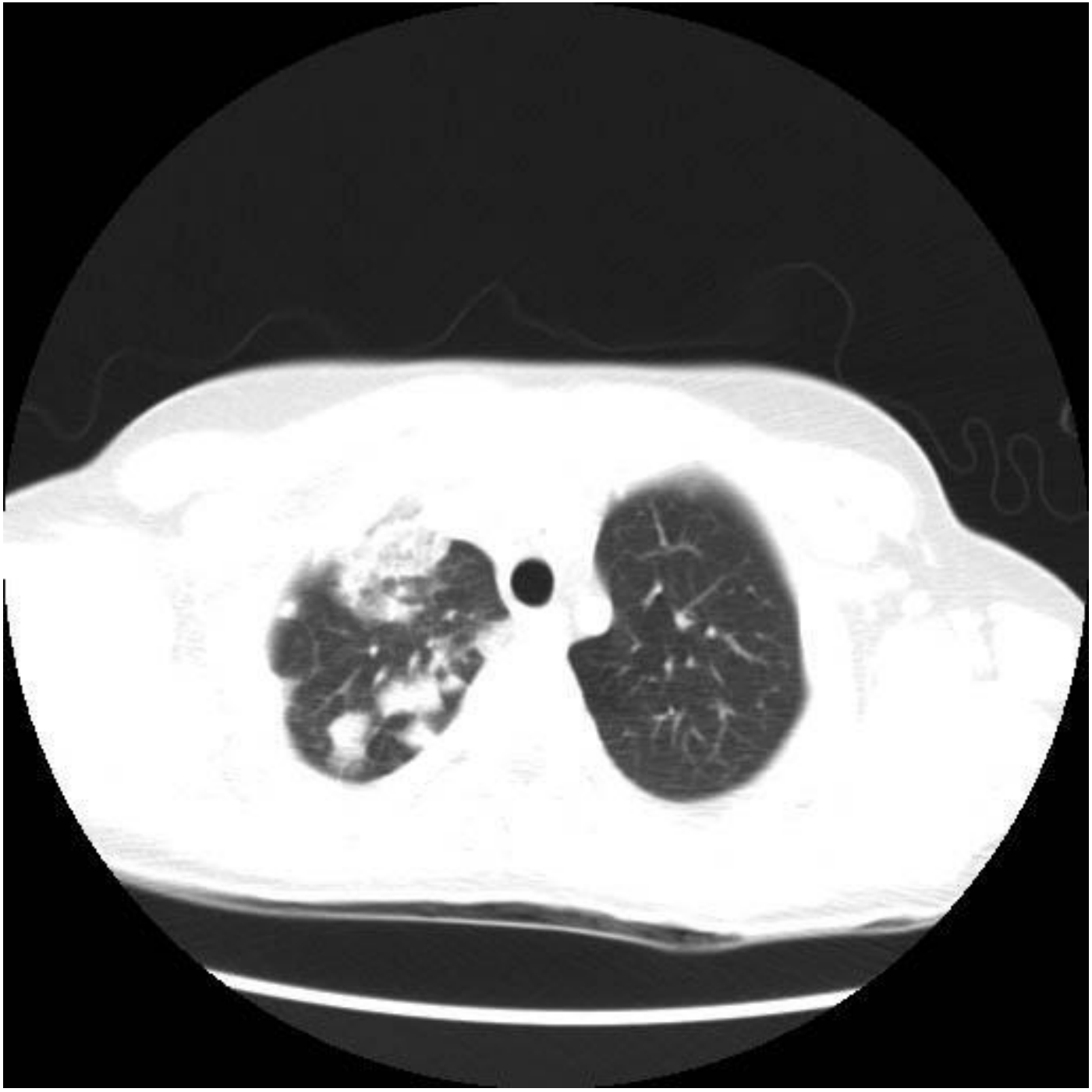
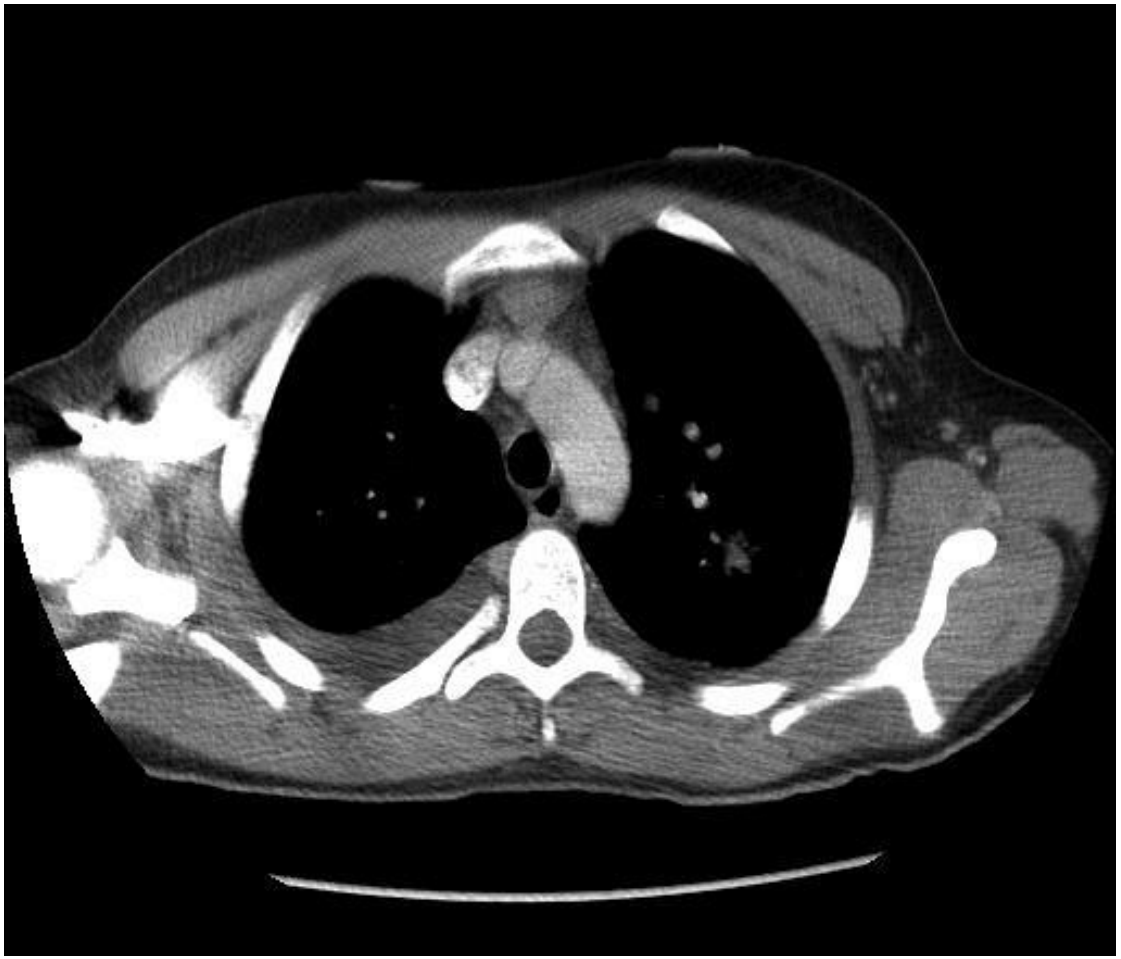
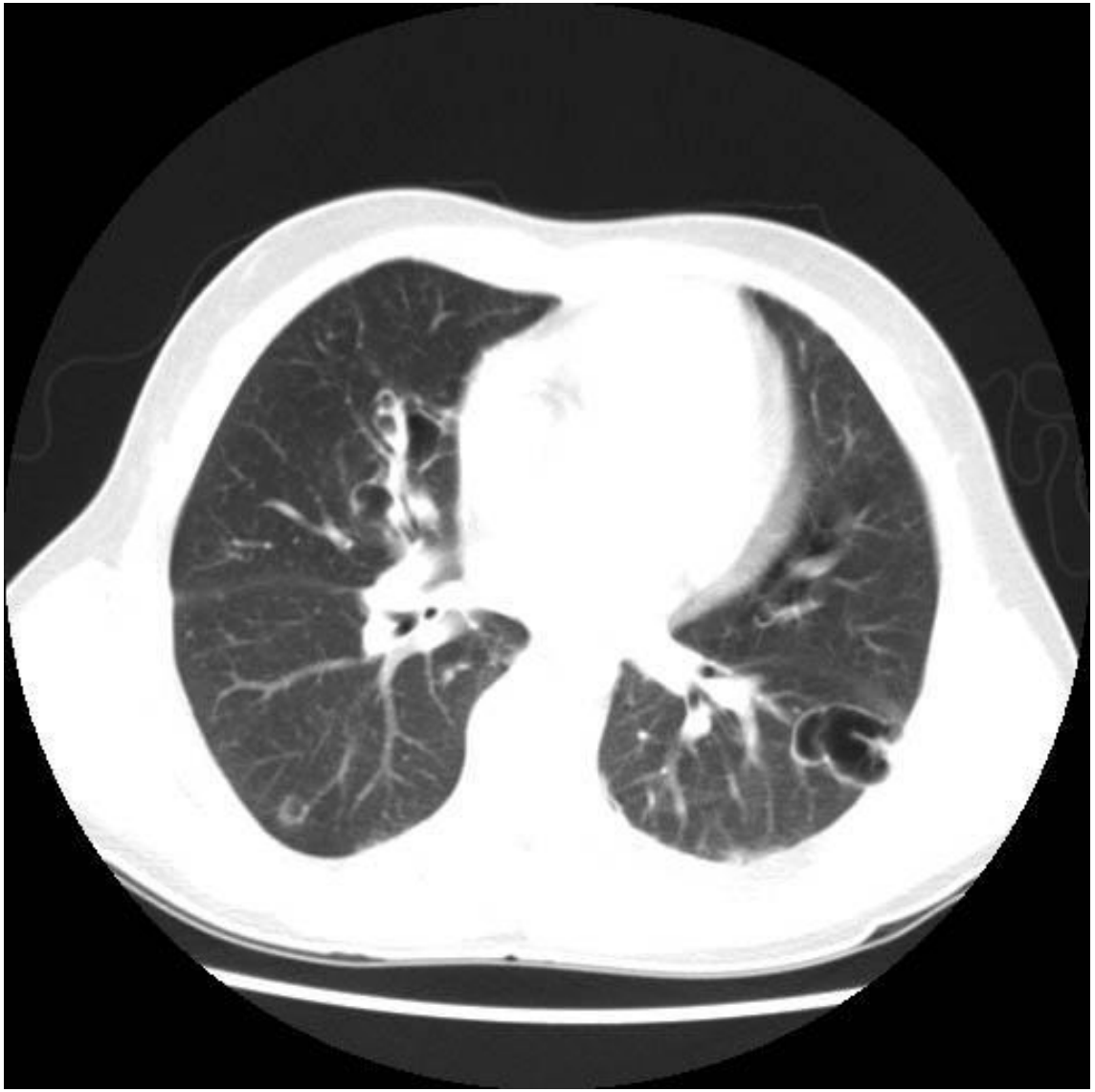


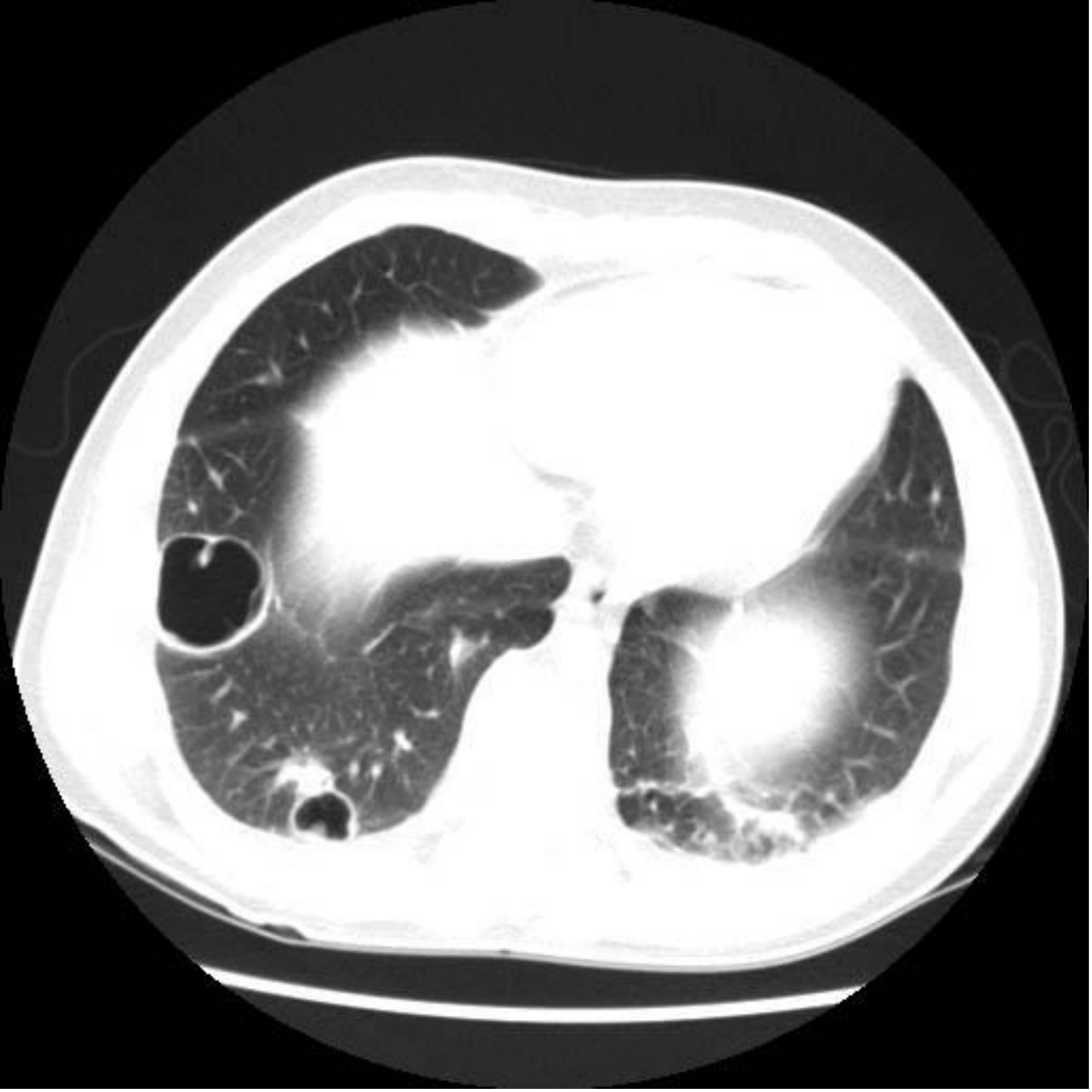


T scan of the thorax (mediastinal windows) .

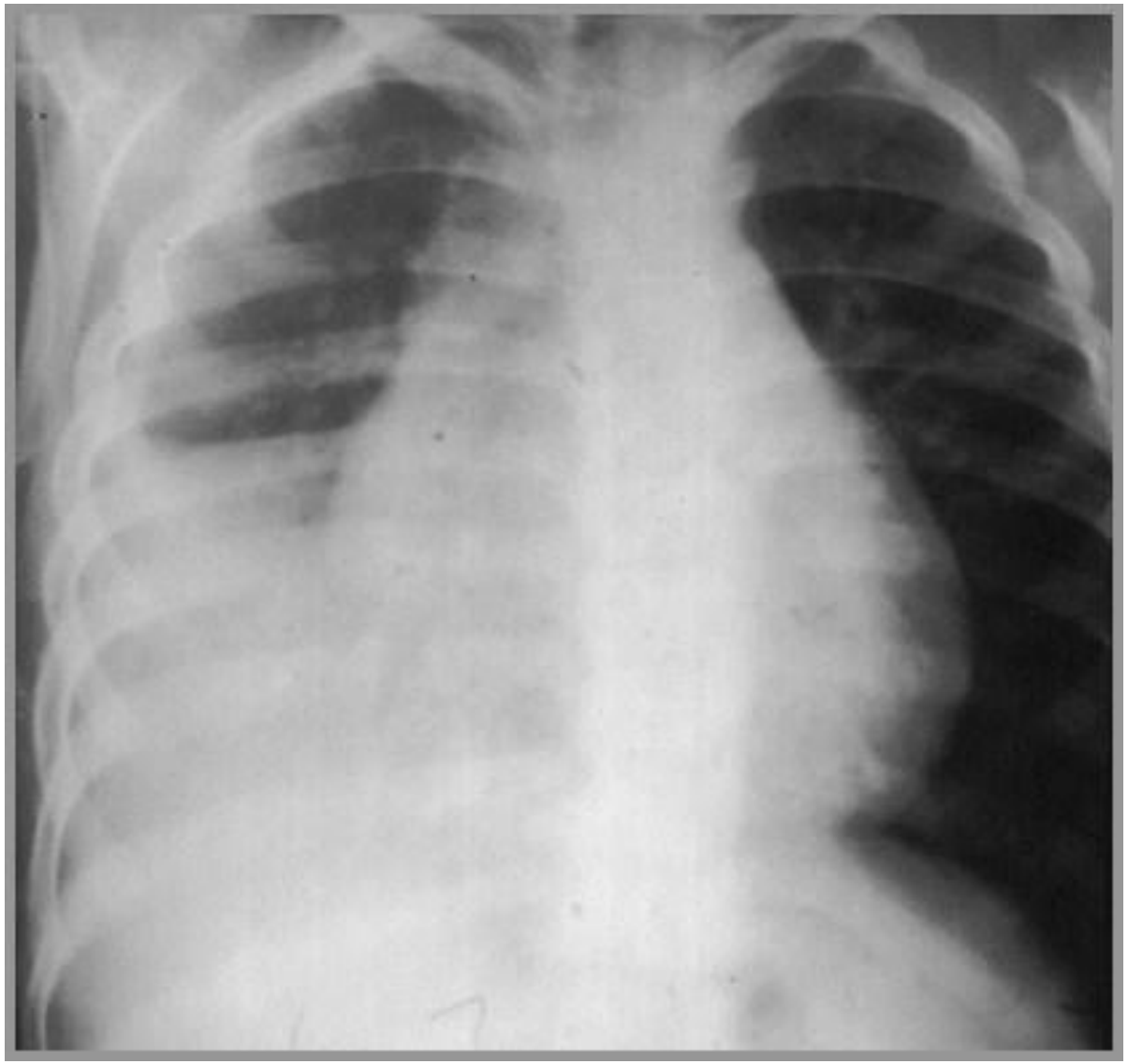


follow up

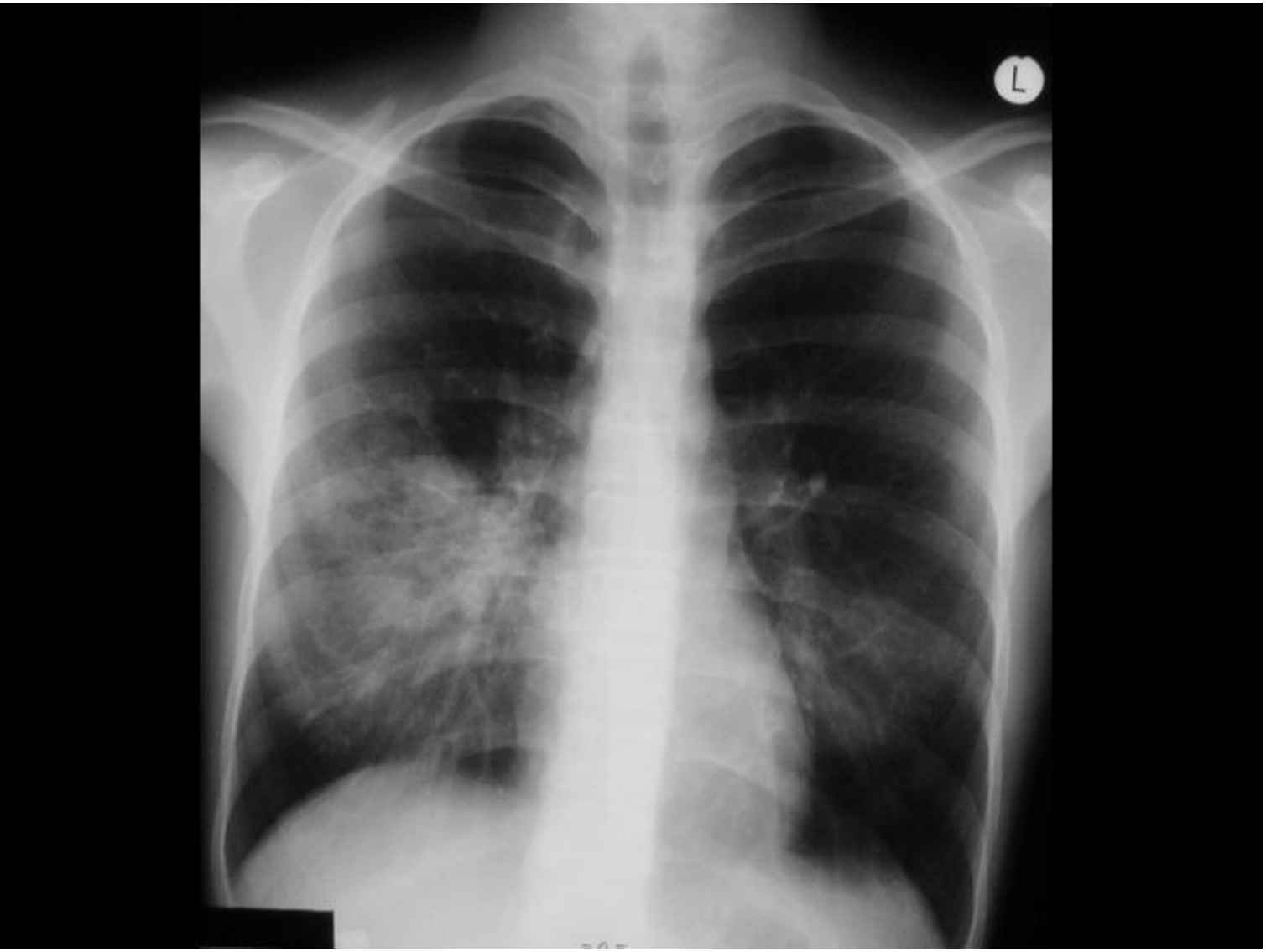


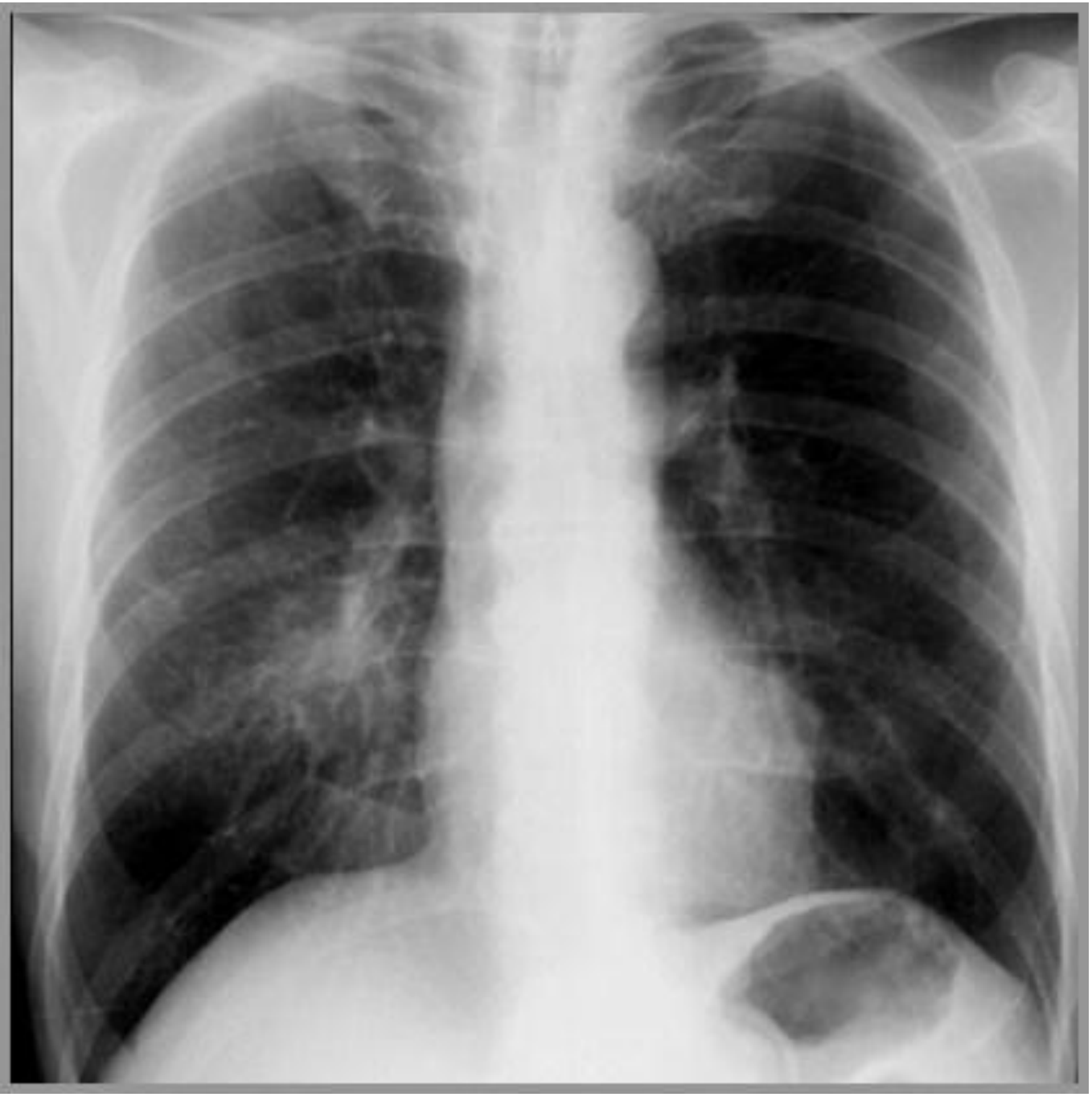


Cavitating clebsiella pneum



Mycoplasma





Klebsiella

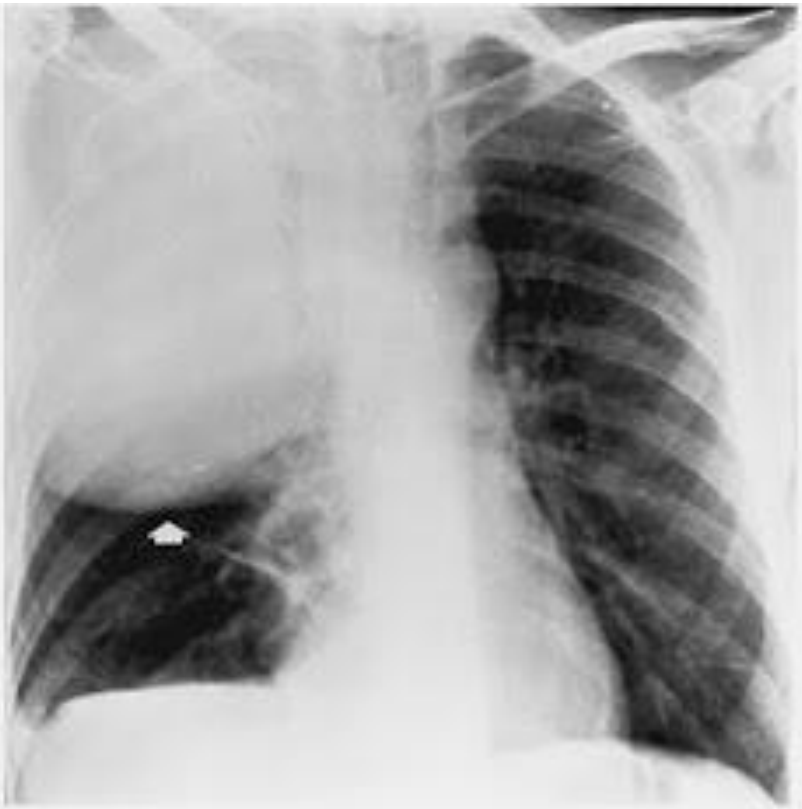


FIG C 15-1. *Klebsiella* pneumonia. Downward bulging of the minor fissure (arrow) due to massive enlargement of the right upper lobe with inflammatory exudate.

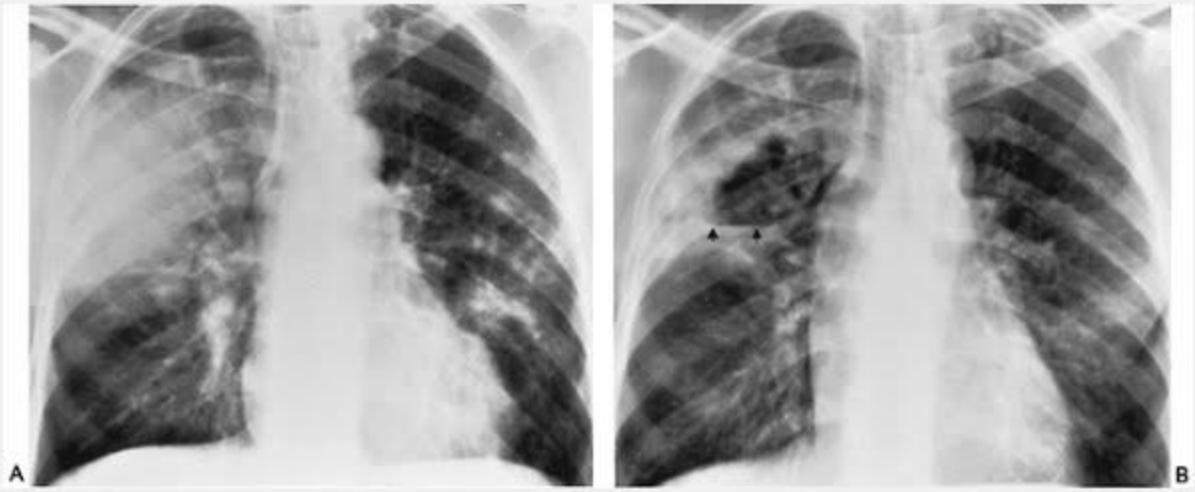


FIG C 1-4. *Klebsiella* pneumonia. (A) Air-space consolidation involving much of the right upper lobe. (B) Progression of the necrotizing infection produces a large abscess cavity with an air-fluid level (arrows).

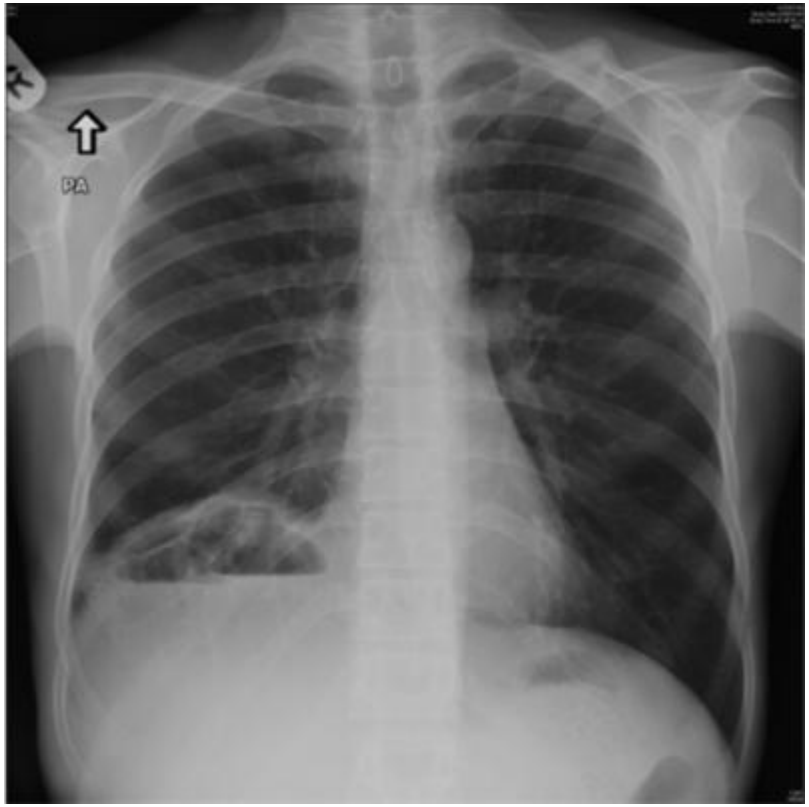
Klebsiella pneumonia

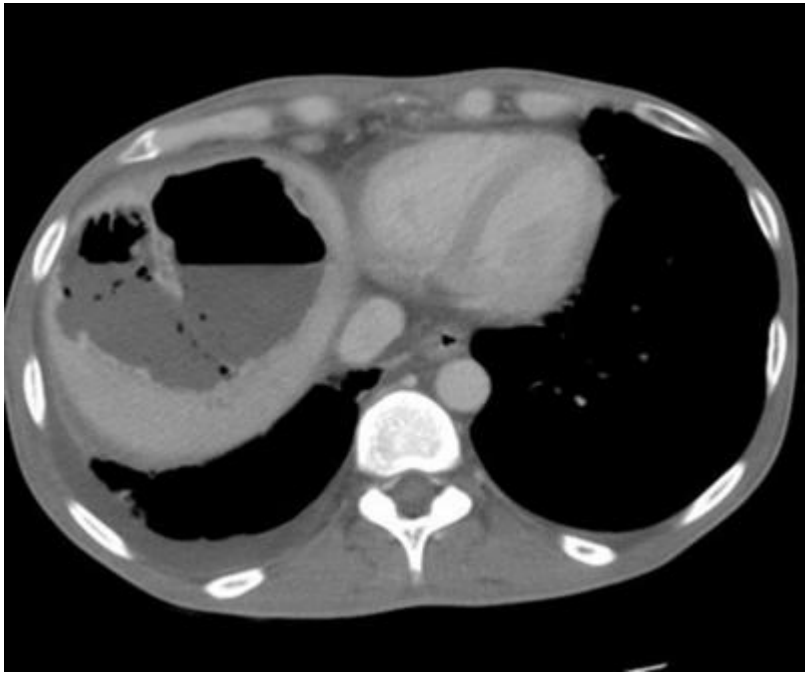
Pathogenesis

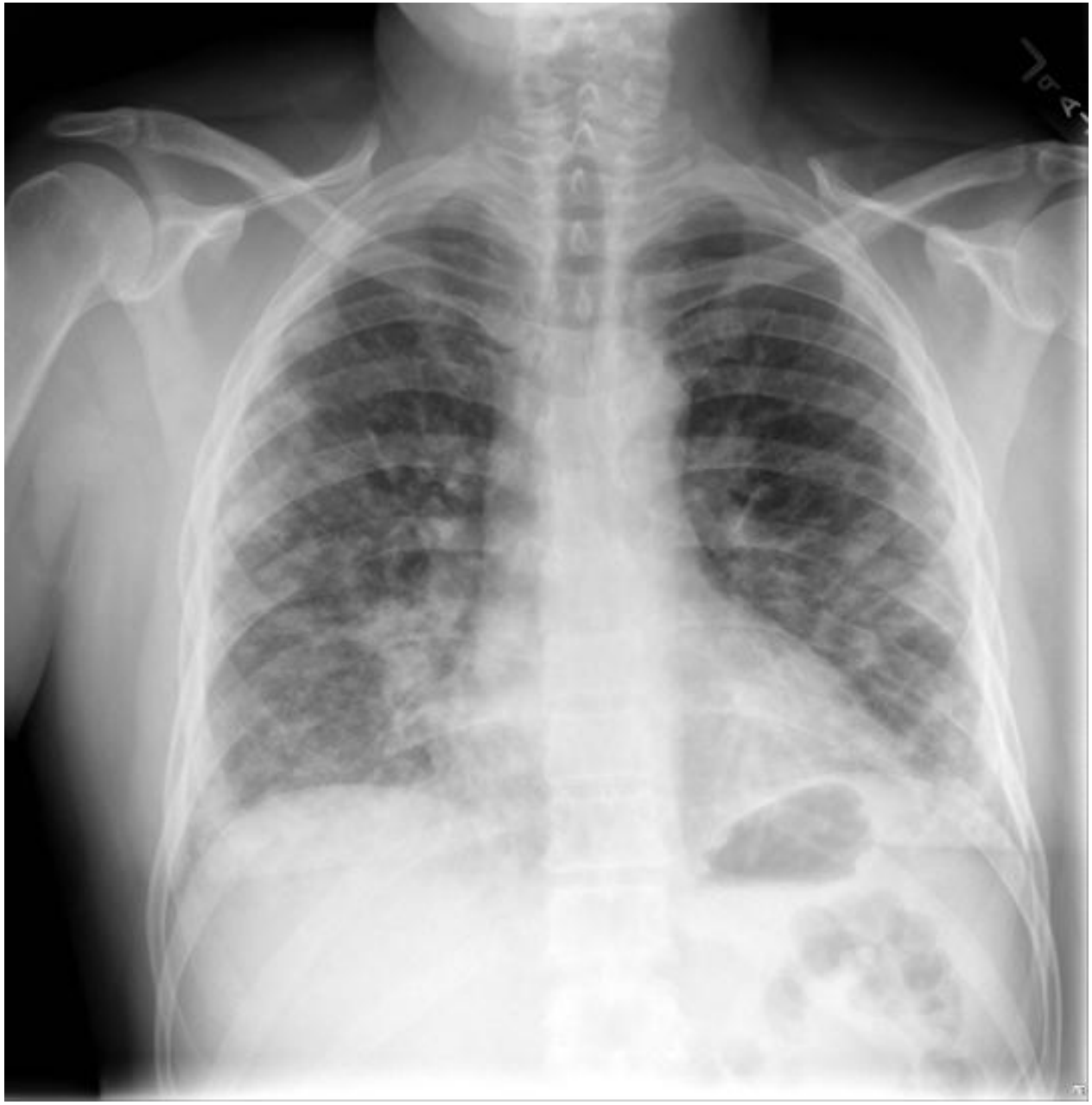
- colonize the mouth and throat
- carried to the lung by inspired air or a ball of aspirated mucous
- Capsule is key for pathogenesis
- *K, pneumoniae* causes death of lung tissue and rapid formation of lung abscesses.
- Bloodstream infections, causing abscesses of other tissues, release of endotoxin and shock.
- Without antimicrobial treatment – lung permanently damaged and death may occur

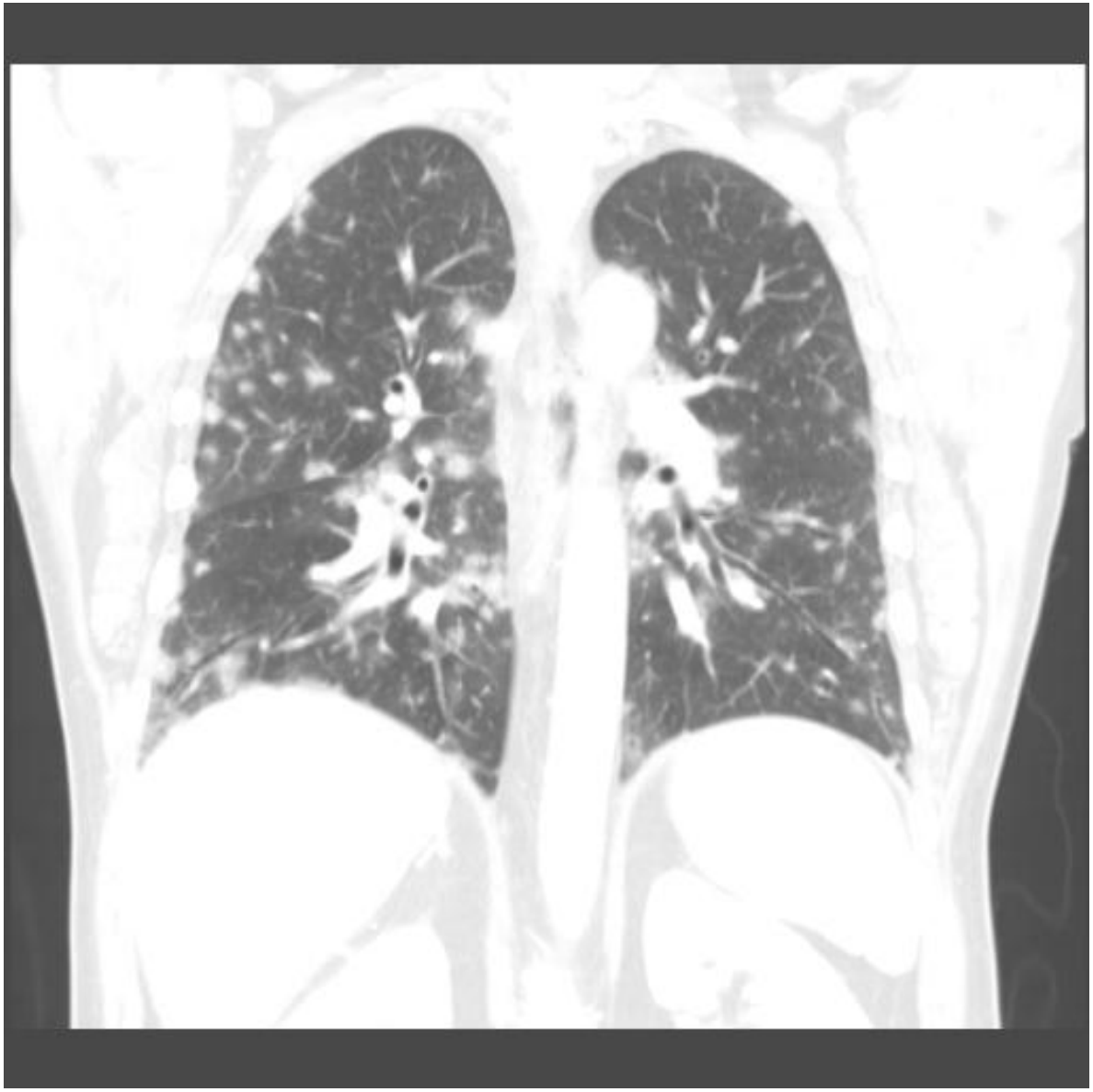
- A 45 years old male with 5 years history of type 2 diabetes mellitus
- 2 weeks history of high grade fever, chills, malaise, dysuria, and upper and lower abdominal pain.
- obstructive symptoms, in the form of dribbling and acute urinary retention.
- dehydrated , heart rate 124/mint, B.P 110/67 and temperature 39.5C^{o}. On abdominal examination, there was right hypochondial and suprapubic tenderness, with hepatomegaly. Shifting dullness was positive. Digital rectal examination showed extremely tender boggy prostate.
- WBC 30,000; neutrophils, 80%; MCV 84 fL; MCH, 27 pg; platelets, 548 X10.e9 /L and hemoglobin, 11.85 g/dl (12–16). ESR, 32 mm/h (0-20).
- Urine ananlysis revealed wbcs too numerous to count; urine culture and culture from EPS showed heavy growth of Klebsiella pneumoniae.
- Blood culture from both aerobic and anaerobic vials showed growth of extended-spectrum beta-lactamase (ESBL) producing Klebsiella pneumoniae.
-

Scan showing right hepatic lobe abscess involving segment VII and segment VII

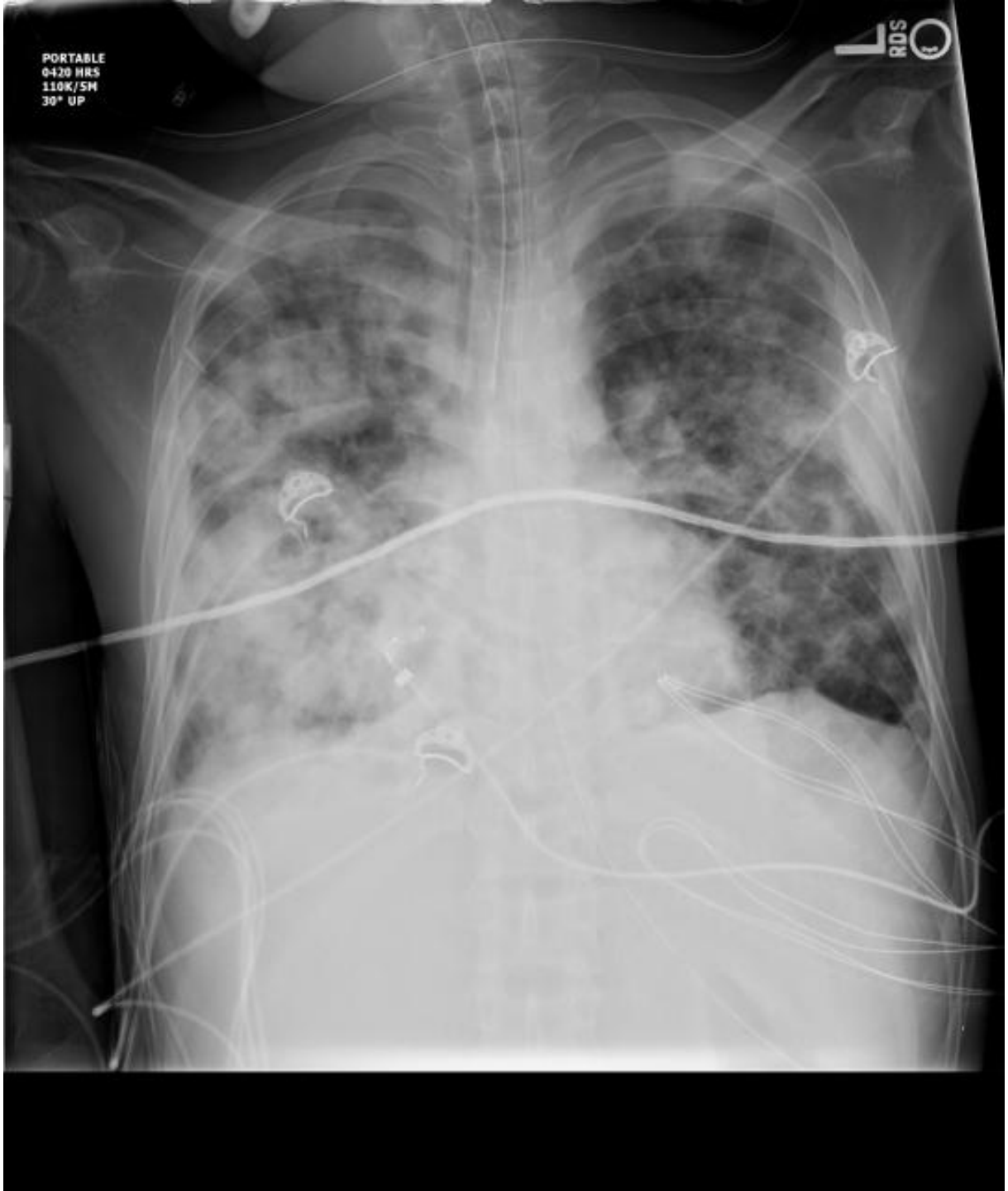








- The CT demonstrates multifocal opacities with some cavitation on the larger lesions. There seems to be a peripheral and lower-lobe predominence. This could represent atypical pneumonia (legionella, mycoplasma, chlamydia), fungal pneumonia (cocciodomycosis, histoplasmosis, aspergillosis), miliary tuberculosis, metastatic lesions or carcinomatosis, septic emboli, or viral pneumonia.
- After a significant inpatient workup the final diagnosis was Human Metapneumovirus. All others were ruled out and viral testing revealed this culprit.


PORTABLE
0420 HRS
110K/5M
30° UP
RDS

- This is a multilobar pneumonia vs. ARDS (Acute Respiratory Distress Syndrome). AIDS patients can have the same bacterial causes of multilobar pneumonia that is present in other patient populations (*Streptococcus pneumoniae, Staphylococcus aureus, Haemophilus Influenza, Moraxella catarrhalis, Mycoplasma pneumoniae, Chlamydophila pneumoniae, Legionella pneumoniae*, etc.). If they are healthcare associated or hospital-acquired further drug-resistant bugs such as*Pseudomonas aeruginosa* and MRSA could be implicated. Infectious organisms specifically involved in immunocompromised hosts could include (among others):

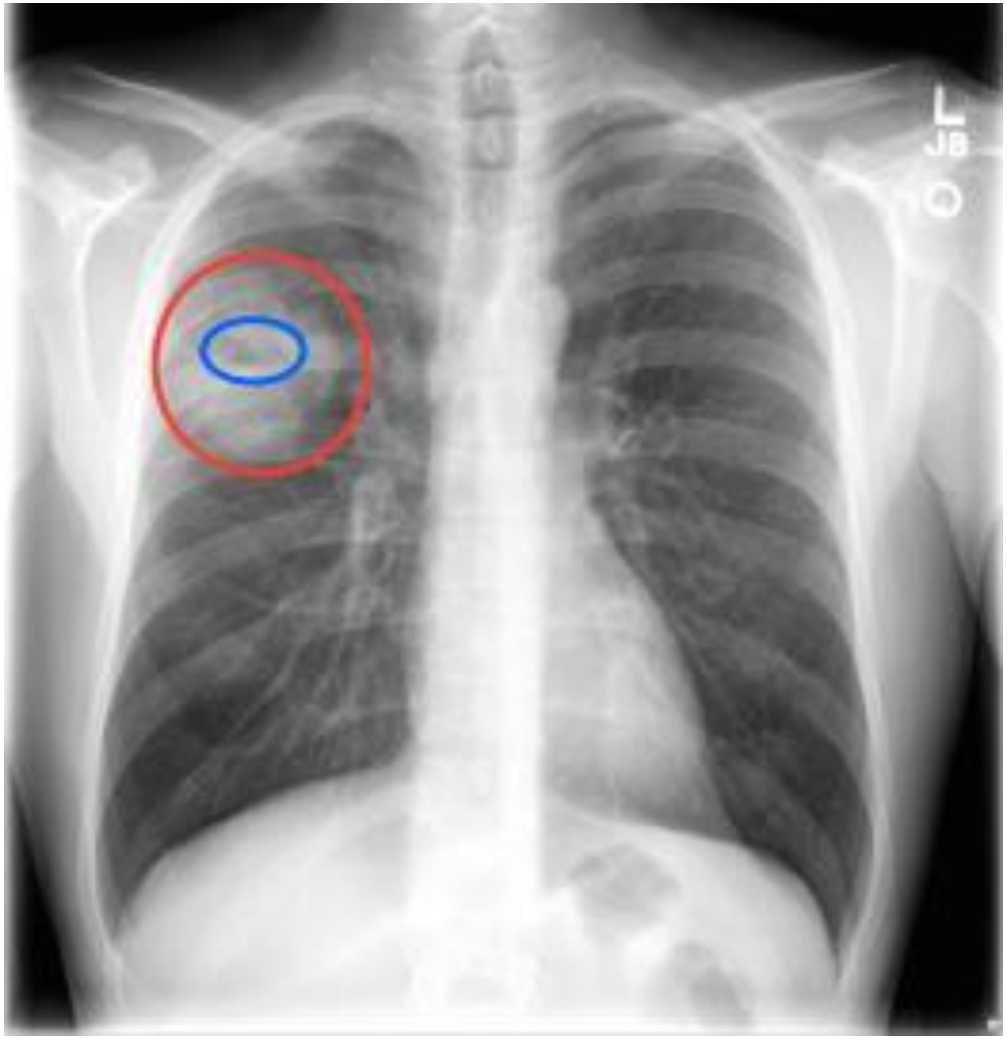
Multilobar infiltrates

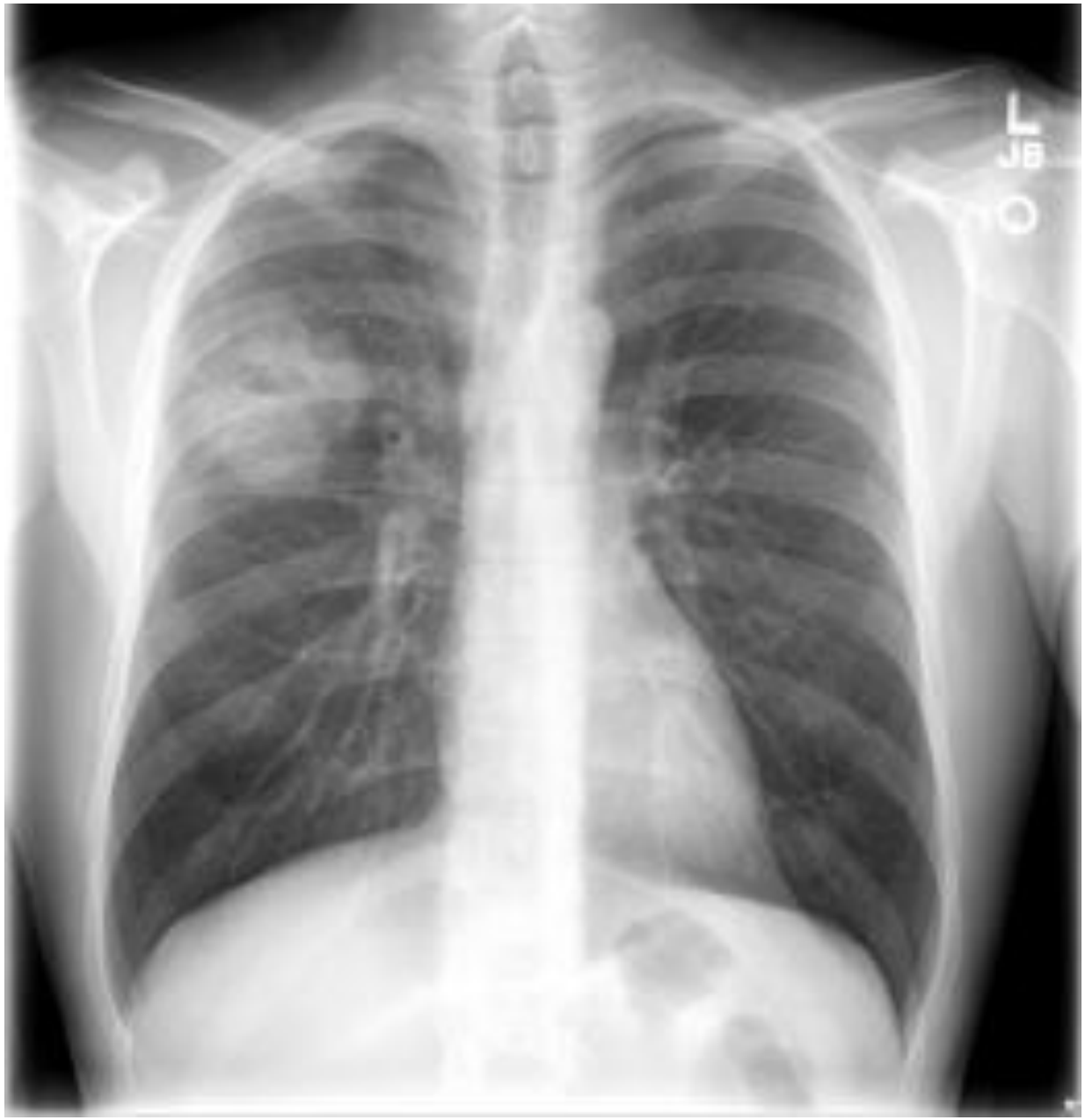
- *Pneumocystis Jiroveci* (PCP pneumonia)
- *Coccidioides* species
- Cytomegalovirus (CMV)
- Tuberculosis (TB)
- *Histoplasma* species
- *Aspergillus* species
- *Mycobacterium avium* complex (MAC)
- Influenza
- Herpes simplex virus (HSV)
- Varicella-zoster virus (VZV)
- *Legionella* species
- *Nocardia* species
- *Cryptococcus neoformans*
- Mucoraceae species
- *Strongyloides* species
- *Toxoplasma* species
- *Capnocytophaga* species

Non-infectious causes of multilobar infiltrates

- diffuse alveolar hemorrhage,
- cardiogenic pulmonary edema,
- ARDS,
- multilobar involvement of the Xray above could implicate certain pathogens in favor of others (for example, *Pneumocystis Jiroveci* is usually multilobar as opposed to *Streptococcus pneumonia* which usually will cause a dense, lobar pneumonia).
- CMV rather than a bat-wing ground-glass appearance of*Pneumocystis Jiroveci*. For further discussion on pneumonia radiographic findings in AIDS, please see radiopaedia.org discussion below:

Cavitary lesions in the lungs are gas or fluid filled compartments in an area of pathology, such as a consolidation or a mass. Interestingly, a specific set of pathologies are known to cause this specific finding. Cavitary lesions can be detected

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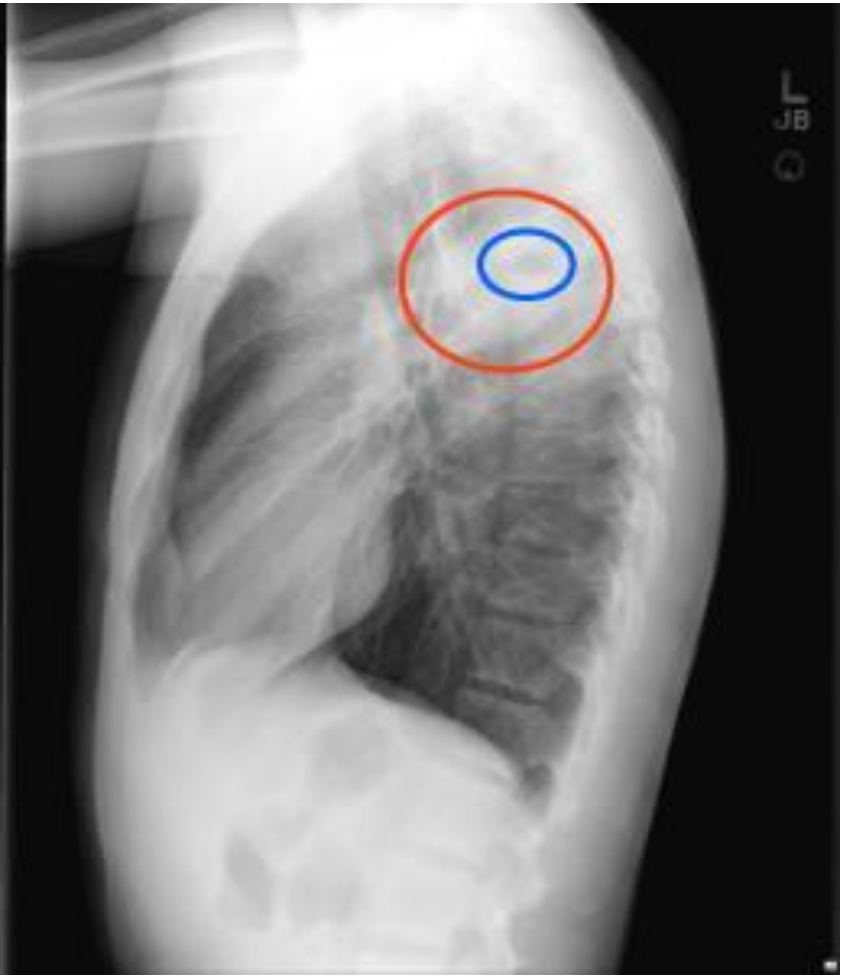
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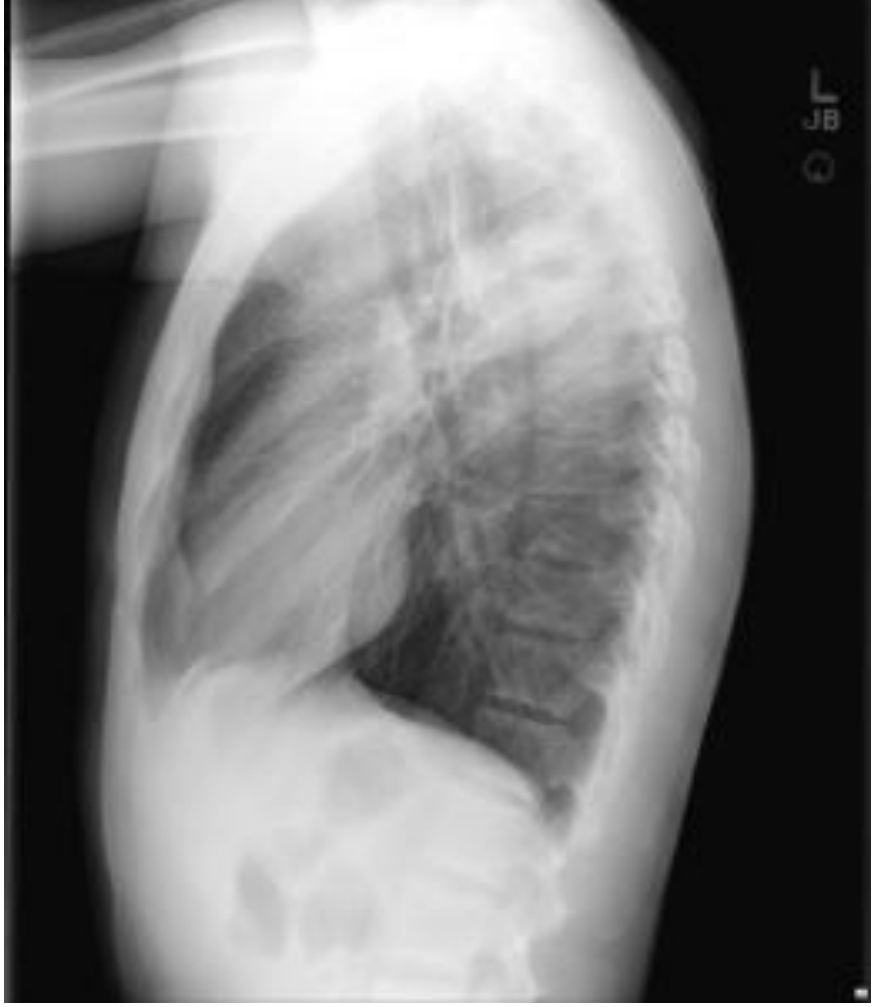
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ASPIRATION PNEUMONIA

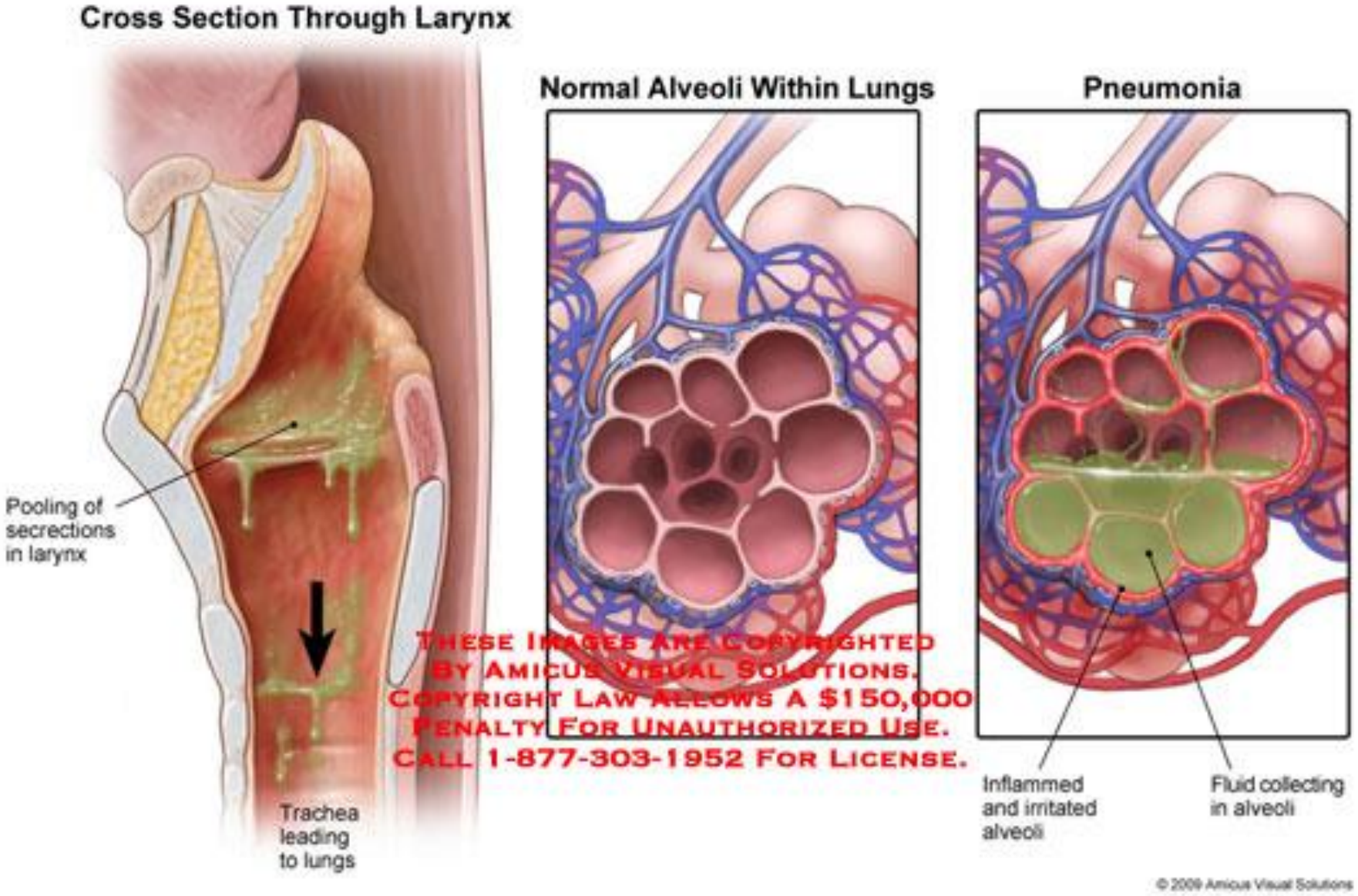
- When should aspiration pneumonia be suspected?

  Recommendation: There is no agreed definition. Aspiration pneumonia should be suspected in those with CAP which either:

1 follows an episode of witnessed aspiration; or

2 occurs in the presence of risk factors for aspiration, including reduced consciousness level and dysphagia due to mechanical or neurological upper digestive tract dysfunction

Aspiration Pneumonia



ASPIRATION PNEUMONIA

Hospital ward, admitted from home	ICU or admitted from nursing home
Oral or i.v. β-lactam/β-lactamase inhibitor or Clindamycin or i.v. cephalosporin + oral metronidazole or moxifloxacin	Clindamycin + cephalosporin or Cephalosporin + metronidazole

HAP (Hospital acquired pneumonia)

- VAP
- Nosocomial pneumonia
- HCAP

- NOSOCOMIAL PNEUMONIA

  AFTER the patient has been to the hospital for ≥48 hours (either intubated=VAP or not)

MAIN FOCUS

- HCAP (HEALTH CARE ASSOCIATED PNEUMONIA)

- MDR (MULTI DRUG RESISTANT BACTERIA)

  Pseudomonas aeruginosa, acinetobacter spp., staphylococcus aureus

DEFINITIONS

HEALTH CARE ASSOCIATED PNEUMONIA (HCAP)

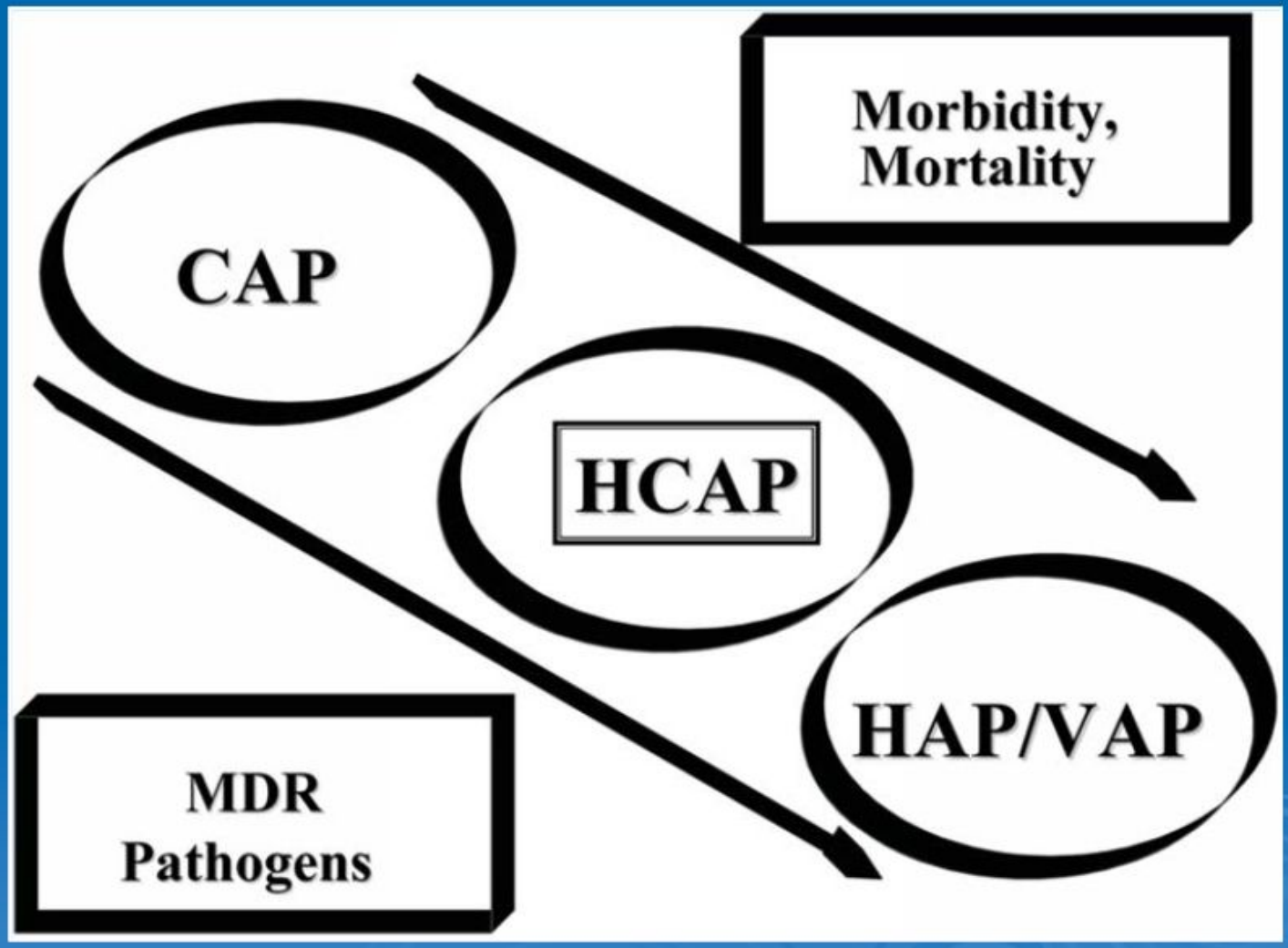
- Patients who have been hospitalized in an acute care hospital for ≥2 days within 90 days of infection
- Patients who reside in a nursing home or long-term care facility
- Patients who have received recent IV antibiotic therapy, chemotherapy or wound care within the 30-day period preceding the current infection
- Patients who have attended a hospital or hemodialysis clinic

HCAP *vs* CAP

Pathogen	No. (%) of patients with indicated infection		*P* value
	CAP (n = 208)	HCAP (n = 431)	
MRSA[c]	25 (12.0)	132 (30.6)	<0.001
Streptococcus pneumoniae	85 (40.9)	45 (10.4)	<0.001
Pseudomonas aeruginosa	10 (4.8)	110 (25.5)	<0.001
MSSA[c]	28 (13.5)	60 (13.9)	0.874
Haemophilus species	36 (17.3)	18 (4.2)	<0.001
Other nonfermenting gram-negative rods[a]	4 (1.9)	43 (10.0)	<0.001
Other *Enterobacteriaceae*[b]	5 (2.4)	39 (9.0)	0.002
Klebsiella species	7 (3.4)	28 (6.5)	0.103
Escherichia coli	12 (5.8)	18 (4.2)	0.372
Legionella species	7 (3.4)	1 (0.2)	0.017

- **639 culture-positive patients with pneumonia**
- **HCAP → 40% "immunosuppression"**

PNEUMONIA



MICROBIOLOGY OF HAP

Core pathogens

- streptococcus pneumoniae, haemophilus influenzae, methicillin-sensitive staph. Aureus, and sensitive gram negative enterobacteriaee (escherichia coli, klebsiella spp., enterobacter spp., proteus spp., serratia marcescens)

MDR

- Pseudomonas aeruginosa, acinetabacter spp., MRSA

RISK FACTORS FOR MDR

- Current hospitalization ≥ 5 days
- Recent antibiotic treatment within the past 90 days
- Immunosuppression (disease or treatment – corticosteroids, chemotherapy)
- Admission to a unit with a high rate of MDR
- HCAP

HOSPITAL ACQUIRED PNEUMONIA

- What changed?
- MDR pathogens
- BEFORE: hospitalization for ≥ 5 days
- Empiric treatment should cover MDR pathogens in any patient with risk factors regardless of the time of onset of infection

DIAGNOSTIC STRATEGIES

- Clinical strategy

- New or progressive pulmonary infiltrate + clinical symptoms-signs (fever >38° C, leukocytosis, purulent secretions)
- Semiquantitative cultures of endotracheal aspirations or sputum – Gram stain
- Therapy started in a timely fashion
- More patients are been treated than they should
- Re-evaluation in 3 days based upon culture results and the clinical response of the patient
- D/D: congestive heart failure, atelectasis, pulmonary embolism, drug reactions, alveolar hemorrhage, ARDS

DIAGNOSTIC STRATEGIES

- Microbiological strategy

-Quantitative cultures of LRT (BAL, PSB, endotracheal aspiration)

-Effort to discriminate between colonization and infection

-Fewer patients are been treated – false negative cultures

-Should be obtained before the start of antibiotic treatment

-BAL, PSB, endotracheal aspirations: bronchoscopic or blind techniques

DIAGNOSTIC STRATEGIES

- Microbiological strategy

-Endotracheal aspirations > 10^6 cfu/ml

Sensitivity 76±9% Specificity 75±28%

-BAL > 10^4 cfu/ml

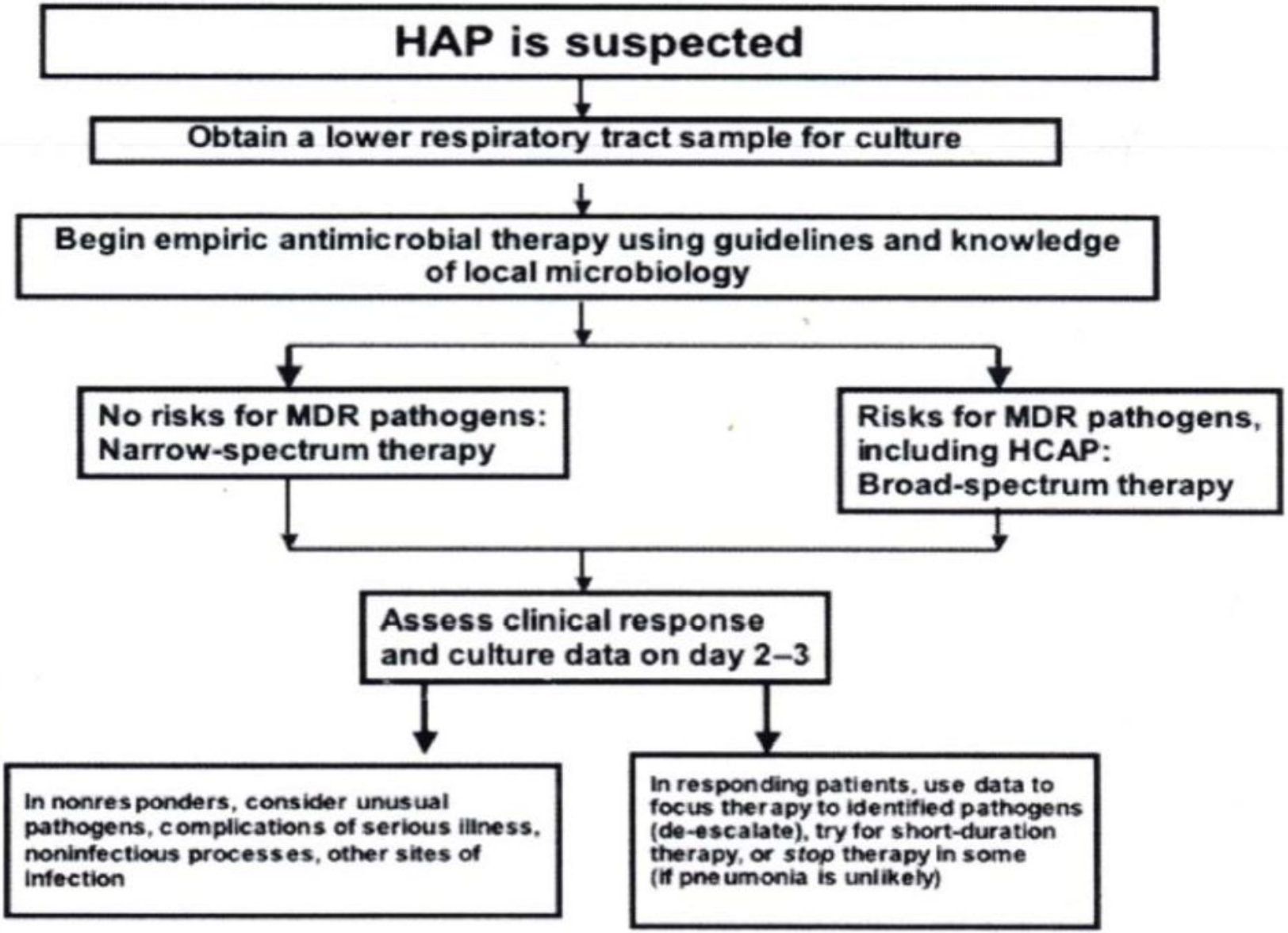
Sensitivity 73±18% Specificity 82±19%

-PSB > 10^3 cfu/ml

Sensitivity 66±19% Specificity 90±15%

-Blind techniques show similar sensitivity and specificity

-The choice is based upon local expertise, experience, availability and cost


HAP is suspected
Obtain a lower respiratory tract sample for culture
Begin empiric antimicrobial therapy using guidelines and knowledge of local microbiology
No risks for MDR pathogens: Narrow-spectrum therapy
Risks for MDR pathogens, including HCAP: Broad-spectrum therapy
Assess clinical response and culture data on day 2–3
In nonresponders, consider unusual pathogens, complications of serious illness, noninfectious processes, other sites of infection
In responding patients, use data to focus therapy to identified pathogens (de-escalate), try for short-duration therapy, or *stop* therapy in some (if pneumonia is unlikely)

ALGORITHMS FOR INITIAL EMPIRIC TREATMENT

- Narrow- or broad-spectrum
- Narrow-spectrum if the patient has pneumonia that started in the first 4 days of hospitalization, there are no other risk factors for MDR and HCAP is not present
- All other patients should receive broad-spectrum initial antibiotic treatment

INITIAL EMPIRIC TREATMENT FOR HAP AND VAP IN PATIENTS WITHOUT RISK FACTORS FOR MDR, EARLY-ONSET AND ANY SEVERITY

- Streptococcus pneumoniae
- Haemophilus influenzae
- Methicilin-sensitive staphulococcus aureus
- Antibiotic sensitive enteric gram negative bacilli
  - Escherichia coli
  - Klebsiella pneumoniae
  - Enterobacter species
  - Proteus species
  - Serratia marcescens

- Ceftriaxone or
- Levofloxacin, moxifloxacin or
- Ampicillin-sulbactam or
- Ertapenem

INITIAL EMPIRIC TREATMENT FOR HAP, VAP AND HCAP IN PATIENTS WITH LATE-ONSET OR WITH RISK FACTORS FOR MDR, AND ANY SEVERITY

- Core pathogens +
- MDR pathogens
  Pseudomonas aeruginosa
  Klebsiella pneumoniae (ESBL)
  Acinetobacter spp.

  Methicillin-resistant Staphylococcus aureus (MRSA)

- Antipseudomonal cephalosporins (cefepime, ceftazidime) or
- Antipseudomonal carbapenems (imipenem, meropenem) or
- Antipseudomonal β-lactam with β-lactamase inhibitor (piperacillin-tazobactam)

AND

- Antipseudomonal quinolone (ciprofloxacin or levofloxacin) or
- Aminoglycoside (amikacin, gentamycin or tobramycin)

AND

- Linezolid or vancomycin

ALGORITHMS FOR INITIAL EMPIRIC TREATMENT

- If the patient has recently been treated with antibiotics, then the empiric treatment should include an agent from a different antibiotic class
- Take into consideration the local microbiology patterns
- The initial antibiotic treatment is most likely to be appropriate when given based upon a protocol adjusted to the local resistance patterns

MONOTHERAPY OR COMBINATION?

- The combination is suggested for patients in whom an MDR pathogen is suspected in order to increase the possibility for appropriate empiric treatment
- Mainly for neutropenic patients or those with pseudomonas aeruginosa bacteremia
- Monotherapy when:

  - No risk factors for MDR

  - in severe VAP that has initially been treated with combination when no MDR is isolated from the cultures

DURATION OF TREATMENT

- All clinical parameters have improved within the first 6 days of the onset of appropriate antibiotic treatment
- Extending the duration of treatment for ≥14 days increased the colonization with gram negative enterobacteriae and mainly Pseudomonas during the 2nd week

DURATION OF TREATMENT

- A duration of antibiotic treatment of 8 days versus 14 days did not show any difference in the outcome (higher percentage of relapse with the shorter duration was observed when the causative agent was Pseudomonas or Acinetobacter)

DURATION OF TREATMENT

- THEN 14-21 days
- NOW 7 days

IN NO RESPONDERS

- Re-check the culture results
- New cultures (mainly using invasive methods)
- Diagnostic tests in order to exclude unusual pathogens (fungi, mycobacterium, viruses, immunosuppression)
- Other diagnosis (atelectasis, congestive heart failure, pulmonary infarction, chemical pneumonitis, alveolar hemorrhage)
- Different focus of infection (central vein catheter, sinus, urinary tract, colitis due to antibiotics)
- Complication of pneumonia (abscess, empyema)
- Drug fever
- Open lung biopsy ???
- In no responders a modification of empiric treatment and diagnostic re-evaluation no further than the 3rd day

RETHINKING THE CONCEPTS OF CAP AND HCAP

CAP

- Community-acquired pneumonia admitted to hospital during 2 years consecutively in Germany
- Of 388406 pts, 81% were 60 years or older
- 28.4% were 80-89 years old

EPIDEMIOLOGICAL DATA

- The population aged > 85y.o X2 by 2030
- 1.5 million residents in 16000 nursing homes in USA
- 90% > 65y.o
- Mean age 80 years
- More females
- Heterogeneous population with varying levels of nursing intensity

EPIDEMIOLOGICAL DATA

- Pneumonia or LRTI is the second most common cause of infection among nursing home residents
- 0.3-2.5 episodes per 1000 resident care-days
- Pneumonia is the leading cause of death in nursing homes

EPIDEMIOLOGICAL DATA

- Compared to older adults in the community, nursing-home residents:
  - develop pneumonia 10 times more frequently [1]
  - hospitalization rate 30 times higher [2]
  - Mortality rate significantly higher than for CAP in the elderly population[3]

PROGNOSIS

- **Preinfection functional status**
- Dementia
- Activities of daily living (ADL)
- Change in mental status

- **Functional impairment is the most relevant determinant of the risk for drug-resistant pathogens**