PNEUMONIA

definition

- infection of the pulmonary parenchyma associated with recently developed radiological pulmonary shadowing

- classified :
  1- community acquired
  2- hospital-acquired
  3- occurring in immunocompromised hosts.

التشريح المرضي

- أنواع ذات الرئة :

- <u>ذات رئة فصية :</u>

التهاب على حساب العدلات في كامل الفص (العقديات الرئوية والكليبسيلا والمستدميات النزلية)

- *<u>ذات رئة وقصيات :</u>* بؤر متعددة من التكثف في الشدف والشديفات الرئوية (العنقوديات المذهبة والعصيات الزرق وسلبيات الغرام الأخرى).

- <u>ذات الرئة الخلالية</u> :

وذمة في الحاجز السنخي وعلى حساب الوحيدات (المفطورات الرئوية والفيروسات) .

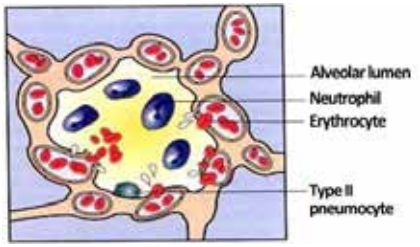
- <u>أي عامل ممرض ← أنماط نسيجية مختلفة</u>

Effects and patterns of microbial colonization:

where and how inflammation appears can be informative

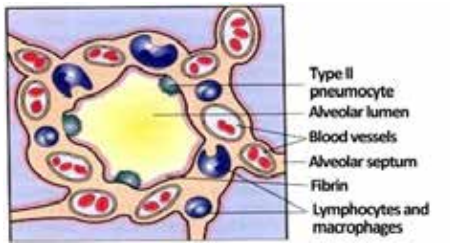
Alveolar

- In alveolar **lumen**
- Purulent exudate of RBCs and PMNs



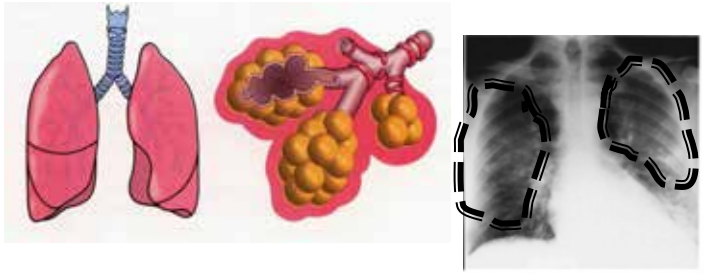
Interstitial

- Mostly in alveolar **wall**
- Mononuclear WBCs
- Fibrinous exudate



Lobar pneumonia

- lobar distribution
- "typical" CAP
- *S. pneumo, H. flu.*



Bronchopneumonia

- patchy distribution
- aspiration, intubation, bronchiectasis
- *Staph, enterics, Pseudomonas*

Atypical pneumonia

- diffuse infiltrate w/ perihilar concentration
- *Mycoplasma, Chlamydophila, Legionella*
- Respiratory viruses, e.g. influenza

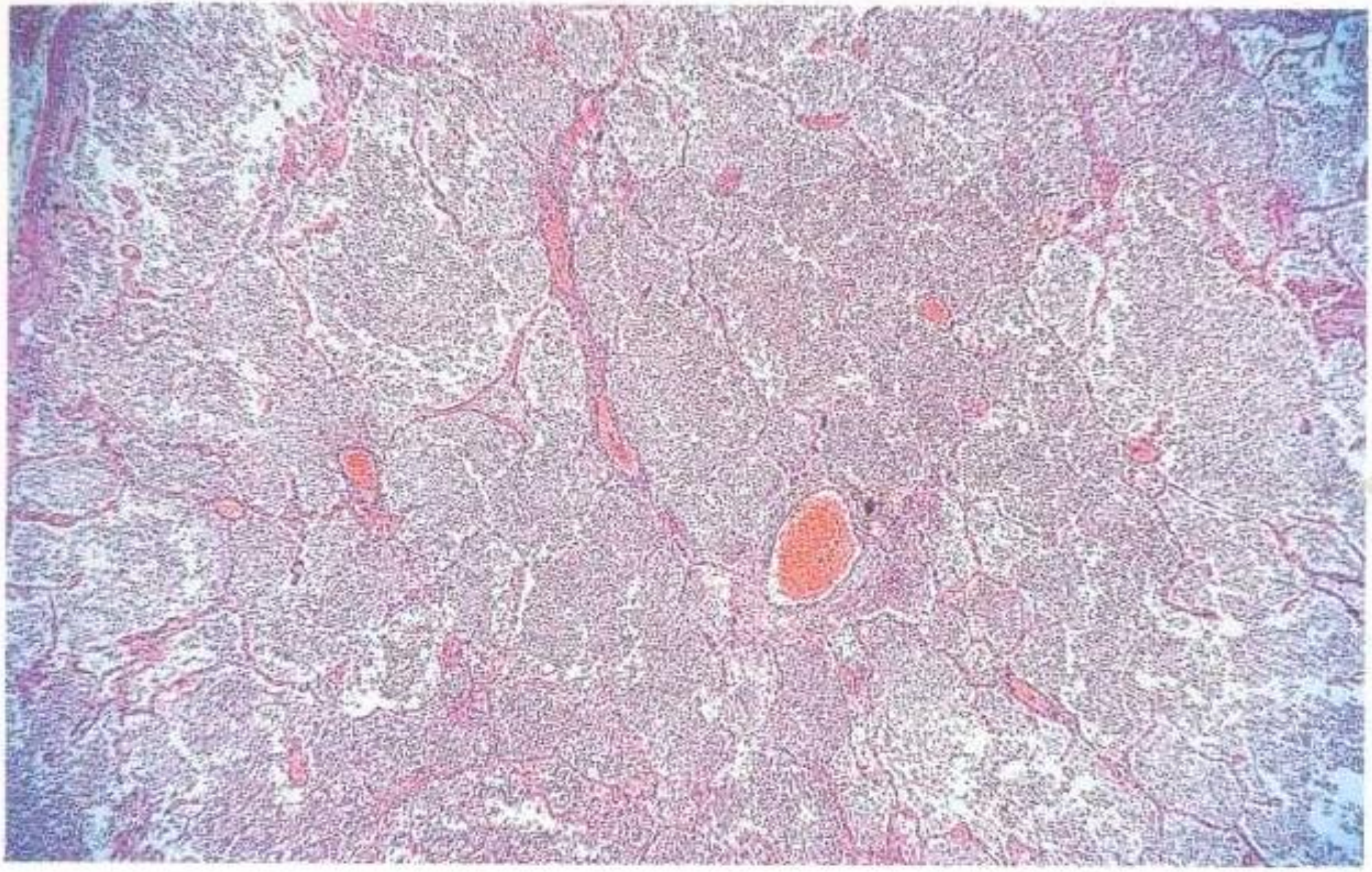


Fig. 141 Consolidation in pneumonia: histopathology.

Normal lung defences

- cough reflex, reflex closure of the glottis
- tracheobronchial mucociliary transport
- alveolar macrophages
- inflammatory immune system response

الفيزيولوجيا المرضية

- طرق وصول العوامل الممرضة للرئتين :

١- الامتداد المباشر
٢- الانتشار الدموي
٣- استنشاق العوامل الدقيقة إلى الطرق الهوائية السفلية
٤- استنشاق محتويات البلعوم الفموي

- إعادة تفعيل عوامل ممرضة في حالة هجوع

- الجزيئات الهوائية الجافة > ١٠٠ ميكرو مم لاتستنشق
- الجزيئات الهوائية > ١٠ ميكرو مم تلتقطها البشرة التنفسية
- معظم الجزيئات تلتقط في القصبات الرئيسية
- فقط الجزيئات مع قطر < ٥ ميكرو مم تصل للأسناخ
- معظم الجراثيم قطرها ١ميكرو مم
- معظم الجراثيم تصل إلى الفصوص السفلية

الآليات الفيزيولوجية المرضية الرئيسية لذات الرئة

الآلية	العامل الممرض
انتشار دموي	العنقوديات المذهبة انتان دم
الطريق الهوائي	المفطورات الرئوية، الكلاميديا الرئوية، الليجيونيلا الحموية، المتفطرة السلية، الغبار
استنشاق المفرزات البلعومية	العقديات الرئوية، المستدميات النزلية، الجراثيم سلبية الغرام، اللاهوائيات.
إعادة تفعيل عوامل ممرضة هاجعة	المتفطرة السلية، متكيسة الرئوي الكاريني (P. jiroveci)

الفيزيولوجيا المرضية

- شروط حدوث ذات الرئة بالطريق الهوائي :

- أن تكون الجزيئات الهوائية قادرة على البقاء في الهواء لفترة طويلة
- حجمها < ٥ ميكرو مم
- تتغلب على دفاعيات المضيف

risk factors impairing lung defences

- Smoking
- toxic inhalation
- aspiration
- mechanical obstruction,intubation
- pulmonary edema
- hypoxemia
- Acidosis
- immunosuppression
- Splenectomy
- Uremia
- DM
- malnutrition
- elderly age

pathogenesis

- **aspiration of upper airway organisms:**
  S. *pneumoniae, S. pyogenes, Mycoplasma, H. influenzae, M. Catarrhalis*

- **inhalation of infectious aerosols:**
  Mycoplasma, TB, influenza, Legionella,Histoplasma, C. psittaci, Q fever

- **other: hematogenous**
  (S. aureus, Fusobacterium), direct (trauma)

Pneumonia is common and serious

- **5.6 million cases** in US in 2011[1]
- **2nd leading cause of hospitalization** in US (1.1 million admissions in US)[1]

~20% of patients with pneumonia require hospitalization

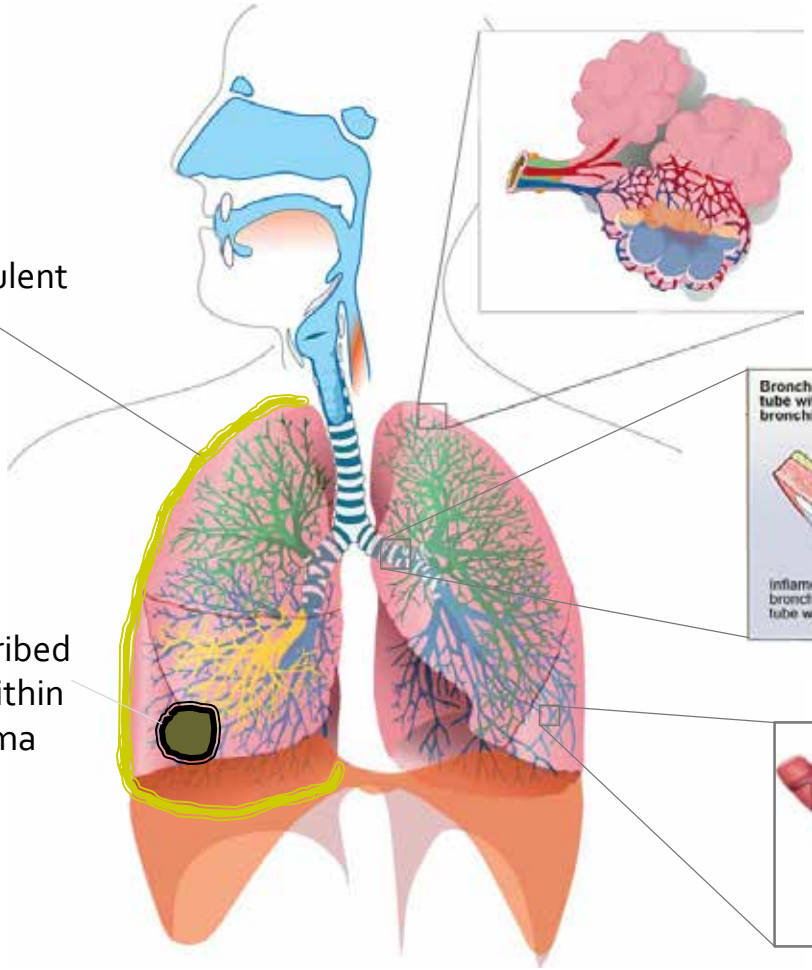
- **6th leading cause of death** in US in 2011 (~**60,000 deaths**)[1]

~10% of patients with pneumonia die

Variations in rates of disease:

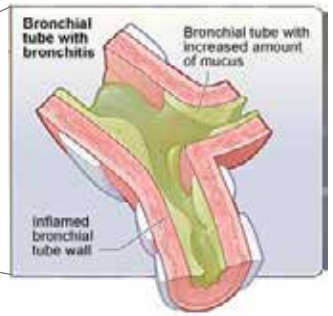
- Higher rates in winter months
- More common in men
- More common in African Americans compared to Caucasians
- More common in children and older adults (overall rate for 18-49 yo is ~5 per 1000 overall rate for >65 yo is **75 per 1000**)

Lower respiratory and pleural disease



Pneumonia -- infection of alveoli (viral or bacterial)
vs. ***Pneumonitis*** *-- immune-mediated inflammation of alveoli*

Empyema: purulent exudate in the pleural cavity



Bronchitis -- inflammation of bronchi, may be **immune-mediated**, e.g. asthma, COPD, or **infectious** (usually viral but can be bacterial)

Abscess: circumscribed collection of pus within the lung parenchyma

Bronchiolitis: inflammation of bronchioles (often viral but can be bacterial)

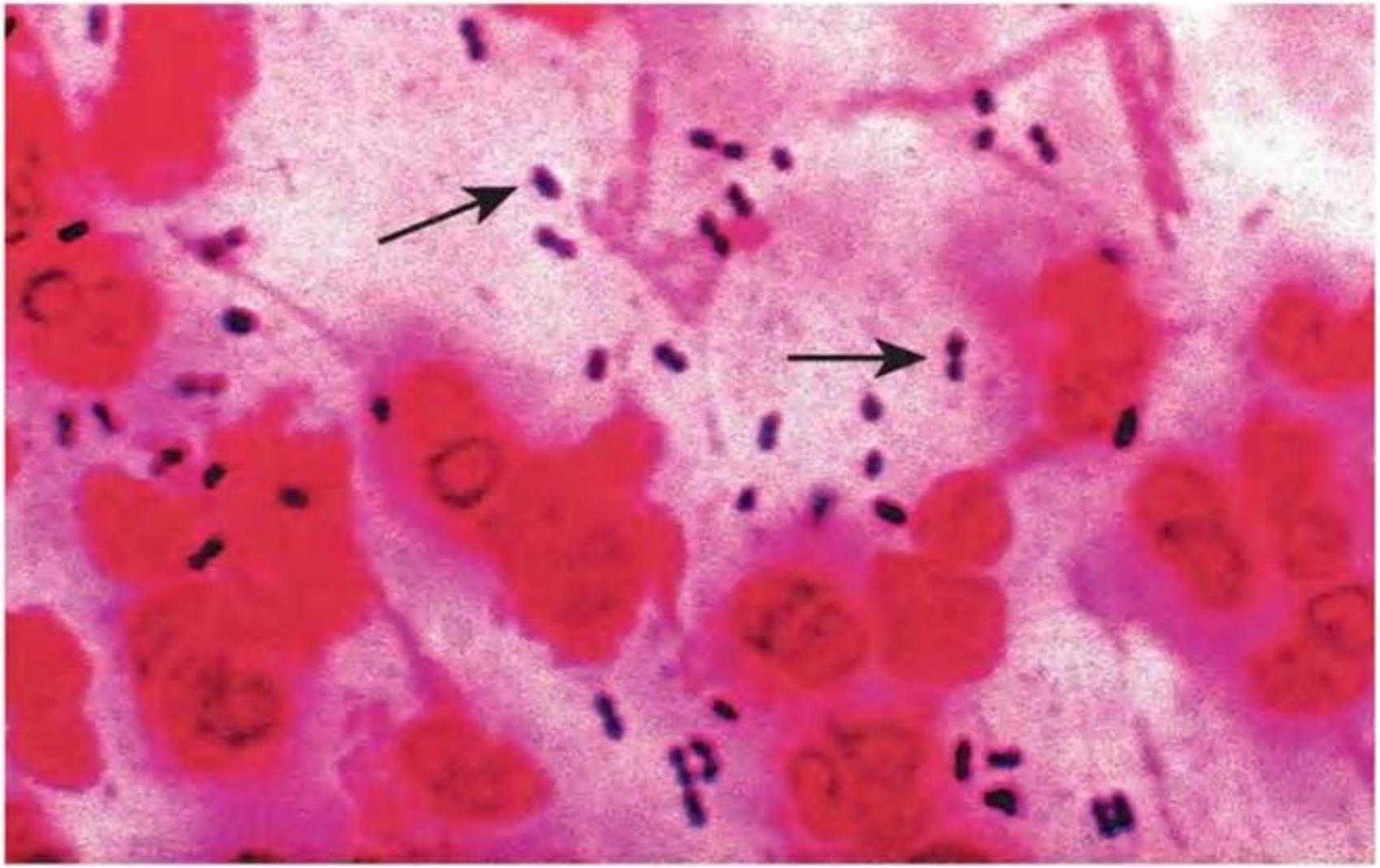
Community-acquired pneumonia (CAP)

- 5-11/1000 adults suffer from CAP each year
- sixth leading cause of death.
- much higher in the very young and very old
- *Strep. pneumoniae* remains the most common infecting agent
- Viral infections are an important cause of CAP in children

prognosis

- mortality of CAP in hospitalized patients is 14%
- mortality is less than 1% for patients who do not require hospitalization
- mortality increases to 20% to 50% in patients who require intensive care unit
- defining an etiologic agent is much more challenging

Gram stain of sputum showing Gram-positive diplococci characteristic of *Strep. pneumoniae*



الوبائيات

- نسبة الحدوث الحقيقية غير معروفة
- ٢٠-٥٠ % استشفاء
- نسبة حدوث CAP :٢-١٥ /١٠٠٠ شخص/سنة
- أسباب ذات الرئة خفيفة الشدة :
  المفطورات الرئوية ، الكلاميديا الرئوية ، الفيروسات .
- أسباب ذات الرئة الشديدة (استشفاء):
  العقديات الرئوية ، المستدميات النزلية ، المفطورات الرئوية .
  (غير شائعة :سلبيات الغرام ،العنقوديات المذهبة و اللوجيونيلا والفيروسات) .
- أسباب ذات الرئة الخطيرة (عناية مشددة) :
  العقديات الرئوية ، اللوجيونيلا ، المستدميات النزلية ، سلبيات الغرام ، والعنقوديات المذهبة ، المفطورات الرئوية والفيروسات .
- ذات الرئة بالعصيات الزرق :
  معالجة سابقة بالصادات ،توسع القصبات والداء الكيسي الليفي وcopd الشديد .
- صعوبة عزل العامل الممرض .

العوامل المؤثرة في حدوث ذات الرئة المتعلقة بالعمر

- العاملان الممرضان الأكثر شيوعاً حتى عمر السنتين :
العقديات الرئوية &الفيروسات التنفسية المخلاوية

- العامل الأساسي > السنتين &الشباب : المفطورات الرئوية

- تقدم العمر يزيد من شدة ونسبة حدوث ذات الرئة
(١٨-٤٤ / ١٠٠٠ من المسنين)

- الجراثيم لدى المسنين :
المستدميات النزلية ،العنقوديات المذهبة ، الرئويات ، العقديات ، سلبيات الغرام ،اللاهوائيات ، موراكسيلا ، اللوجيونيلا ، الكلاميديا ، عوامل متعددة

Previously well infant
1 RSV
2 Adenovirus and other viruses
3 Bacterial

Previously ill infant
1 Staphylococcus
2 *E. coli* and Gram-negative bacteria
3 Viruses and opportunistic organisms

Children
1 Viruses
2 Pneumococcus
3 Mycoplasma
4 Others

Previously fit adults
1 Pneumococcus
2 Mycoplasma
3 *H. influenzae*
4 Viruses
5 Staphylococcus
6 *Legionella*
7 Others

Previous respiratory illness; elderly and debilitated
1 Pneumococcus
2 *H. influenzae*
3 Staphylococcus
4 *Klebsiella* and Gram-negative organisms

If no response think of:
TB, *Mycoplasma, Legionella,* carcinoma

Severely immunocompromised and AIDS
1 Pneumocystis pneumonia
2 Cytomegalovirus
3 Adenovirus
4 Herpes simplex
5 Bacteria (*Legionella,* Staphylococcus, Pneumococcus)
6 Opportunistic mycobacteria; tuberculosis

Hospital-acquired pneumonia
1 Gram-negative bacteria (*Pseudomonas, Klebsiella, Proteus*)
2 Staphylococcus
3 Pneumococcus
4 Anaerobic bacteria, fungi
5 NB aspiration pneumonia
6 Others

Factors that predispose to pneumonia

- Cigarette smoking
- Upper respiratory tract infections
- Alcohol
- Corticosteroid therapy
- Old age
- Recent influenza infection
- Pre-existing lung disease
- HIV
- Indoor air pollution

تأثير العادات الشخصية

- **الكحول** ← استعمار البلعوم الفموي بسلبيات الغرام - ضعف منعكس السعال & اضعاف النقل الهدبي والمناعة الخلوية ← زيادة نسبة وشدة CAP (الرئويات)

- **التدخين** ← CAP بالرئويات & اللوجيونيلا & الانفلونزا (النقل الهدبي ، المناعة الخلطية والخلوية ،انجذاب الرئويات والمستدميات في البلعوم الفموي)

تأثير الأمراض المرافقة

- أكثر الأمراض حدوثاً مع CAP هو **COPD**
- **COPD شديد أو توسع قصبي** ← ذات رئة بالمستدميات النزلية & العصيات الزرق
- **الكحولية & التخدير العام & الصرع & GERD** ← الاستنشاق ← ذات الرئة باللاهوائيات
- **الداء السكري ونقص العدلات** ← عنقوديات & سلبيات الغرام
- **الكورتيزون** ← عنقوديات مذهبة ، نوكارديا ، لوجيونيلا ، رشاشيات والمتكيس الرئوي الكاريني

أثير الأمراض المرافقة

- **الداء السكري والفشل الكلوي** ← ذات رئة عنقودية بالعنقوديات المذهبة والمستدميات النزلية والعصيات الزرق
- **العلاج السابق بالصادات** ← سلبيات الغرام (العصيات الزرق)
- قصور القلب الاحتقاني & الأمراض الكلوية والكبدية المزمنة & اختلاطات الداء السكري & عته & الحوادث الوعائية الدماغية & نقص المناعة & الإيدز ← زيادة حدوث CAP وزيادة معدل الوفيات
- **استعمال مضادات الحموضة ← زيادة حدوث CAP**

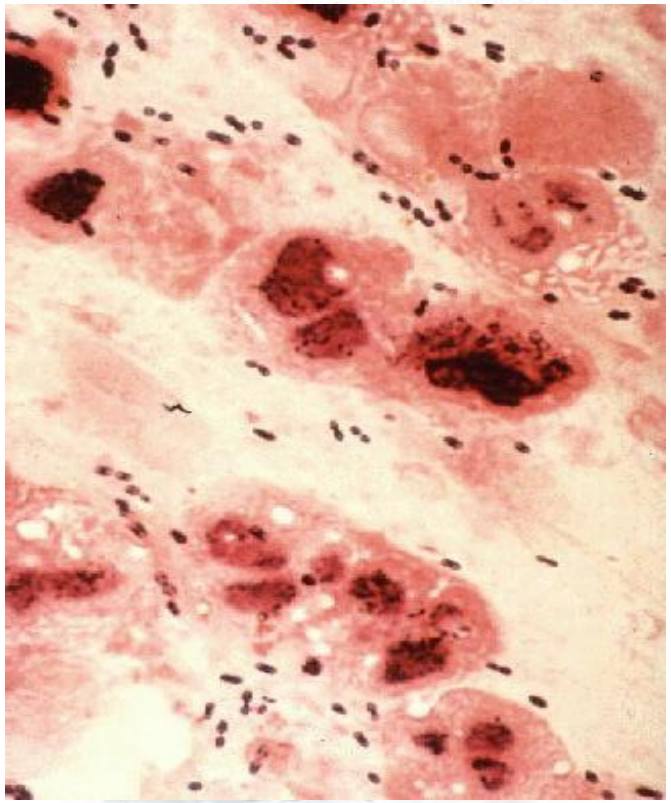
الاعتبارات الجغرافية والمهنية

- الجنود & عمال المناجم ← زيادة حدوث CAP بالرئويات
- التعرض للحيوانات ← داء الببغاء
- التماس مع القوارض ← **الطاعون** Yersinia pestis
- المناطق الريفية ← التولاريميا Francisella tularensis
- التعرض للأغنام والكلاب و القطط ← (**حمى Q**) C. burnetii
- التوقيت الزمني مهم في ذات الرئة بالرئويات والمستدميات النزلية
- جنوب شرق آسيا : فيروسات الكورونا ← ذات رئة شديدة **(SARS)**

Clinical Features of Typical vs. Atypical Pneumonia

Clinical Feature	Typical	Atypical
Organisms involved	*S. pneumoniae*, *H. influenzae*, Endemic oral flora	*Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, Viral, *Legionella*
Onset	Sudden	Subacute
Cough	Productive	Dry
Chest Pain	Pleuritic (some cases)	Uncommon
Other Symptoms	Chills, rigors, SOB, nausea, diarrhea	Headache, myalgia
Temp > 38°C	Common	Uncommon
HR > 110	Common	Uncommon
Consolidation Signs	Common	Uncommon
WBC count	Increased, Neutrophilia	Normal or slightly Increased
CXR	Unilateral, Localized, Alveolar	Bilateral, diffuse, Interstitial +/– , Alveolar

Typical CAP presentation



History
- Previously healthy with sudden onset of fever and shortness of breath

Physical signs and symptoms
- fever
- tachycardia
- tachypnea
- productive cough with purulent sputum and possible hemoptysis
- pallor and cyanosis
- localized:
  - dullness to percussion
  - decreased breath sounds
  - crackles , ronchi , egophony ("E" -to-"A" change)

Investigations
- CXR showing lobar consolidation
- CBC showing leukocytosis w/ left shift
- Sputum sample contains neutrophils, RBCs; Gram stain may be positive depending on organism

Clinical features

- fever, rigors, shivering and vomiting
- appetite is usually lost and headache is common
- breathlessness and cough(dry, but later accompanied by the expectoration of mucopurulent sputum)
- Pleuritic chest pain may be a presenting feature
- Upper abdominal tenderness (lower lobe pneumonia)

الصورة السريرية

- حمى ، تدهور بالحالة العامة & أعراض تنفسية (سعال +زلة)
- لدى المسنين :
الأعراض والعلامات ▼ أو تغير بالحالة العقلية ،سلس بولي ، انكسار معاوضة قلبية ، تسرع قلب ± زلة
- حمى > ٣٨,٥ + عرواءات ← صورة الصدر
- مظاهر خاصة في اللوجيونيلا و الرئويات والمفطورات الرئوية
- لدى الولدان علامات غير نوعية :
انخفاض حرارة ، اختلاجات ، تنفس بطيء .
- الفحوص المخبرية والشعاعية ← فشل في تحديد العامل الممرض
- البداية التدريجية والعلامات الفيزيائية القليلة ← اصابة فيروسية

Consolidation Signs

- dullness to percussion
- increased tactile and vocal fremitus
- Bronchial breath sounds, crackles
- the history, physical examination, radiographs, and sputum examination are neither sensitive nor specific for identifying the microbiologic cause .

التقييم السريري لل CAP

- سعال & حمى & تسرع تنفس وقلب & خراخر رئوية : ٢٠- ٥٠ % ← CAP
- تكثف رئوي سريري موجود في > ثلث الحالات
- السعال & الألم : ٠
- بطء القلب غير المناسب ← ذات الرئة باللوجيونيلا والمفطورات
- الآفات الجلدية ← مفطورات & تدرن & العصيات الزرق
- كشف الاختلاطات

general investigations

- routine labs:
  determine prognosis and need for hospitalization

- ABGs:
  assess adequacy of gas exchange and ventilatory insufficiency in more severe cases, oxygen saturation is sufficient in most

- sputum culture and Gram stain, blood cultures, pleural fluid cultures, serology/viral cultures (epidemiology)

Microbiological investigations in patients with CAP

- **Sputum:**
  - direct smear by Gram and Ziehl-Neelsen stains.
  - Culture and antimicrobial sensitivity testing

- **Blood culture:**
  frequently positive in pneumococcal pneumonia

- **Serology:**
  - acute and convalescent titres for *Mycoplasma*, *Chlamydia*, *Legionella*, and viral infections.
  - Pneumococcal antigen detection in serum or urine

- **PCR: *Mycoplasma* can be detected from swab of oropharynx**

التقييم الجرثومي

- **عزل العامل الممرض & توجيه المعالجة :**
  المرضى المقبولين بالمشفى & العناية المشددة

- **فحص القشع :**
  سريع وسهل ،العينة المقبولة (٤٠%)، التلوث (<١٠ خلايا ، <٢٥ كرية بيضاء) ،عدم امكانية زرع اللاهوائيات،
  - تلوين غرام (نوعية =٨٠%، حساسية :٦٠% للرئويات) ،
  مقارنة الزرع & تلوين غرام

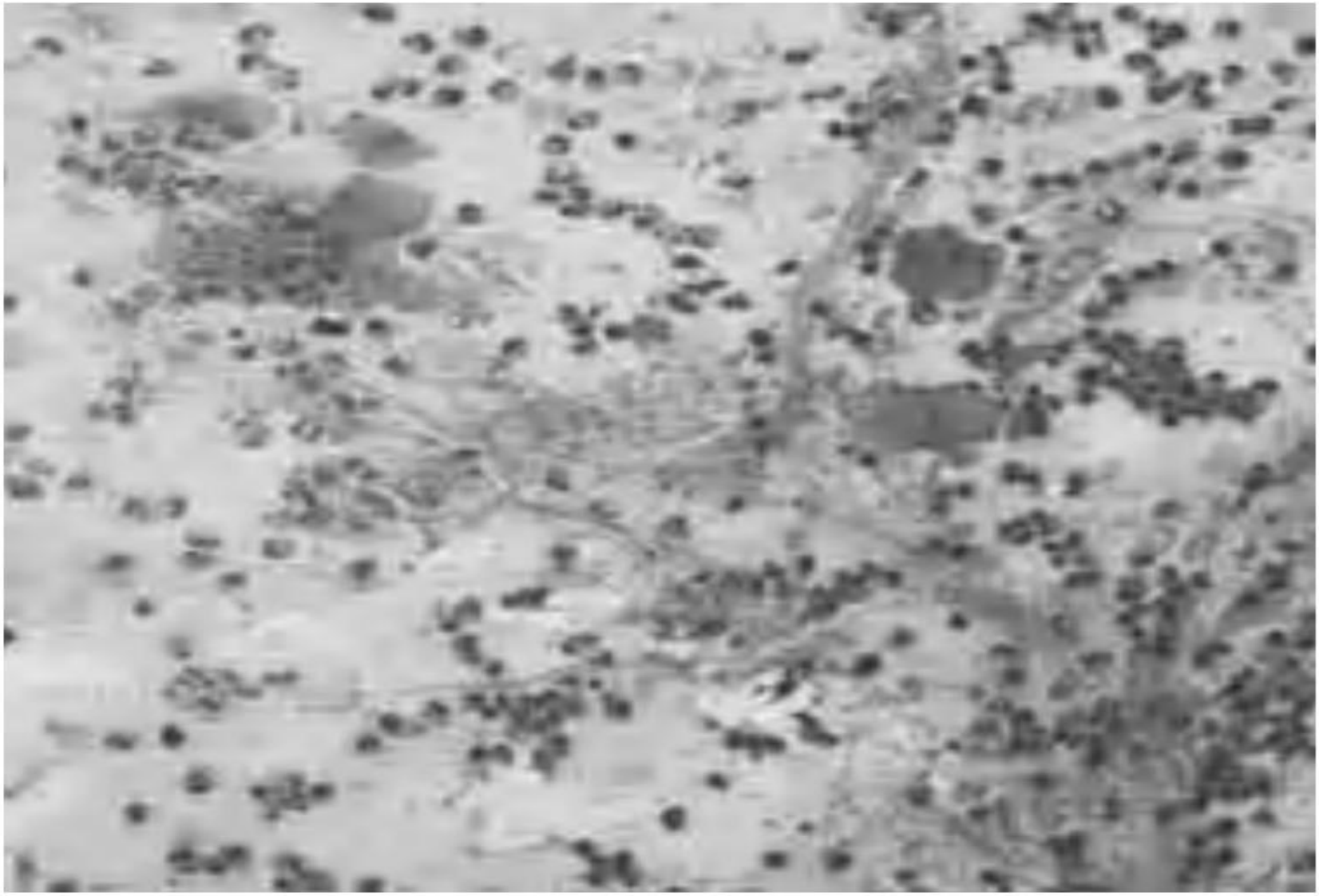
- **تلوين غرام للرشافة الرغامية : حساسية جيدة ونوعية قليلة**

- **زرع الدم & سائل الجنب : المرضى المقبولين بالمشفى ،**
  (حساسية :٢٠% لزرع الدم)

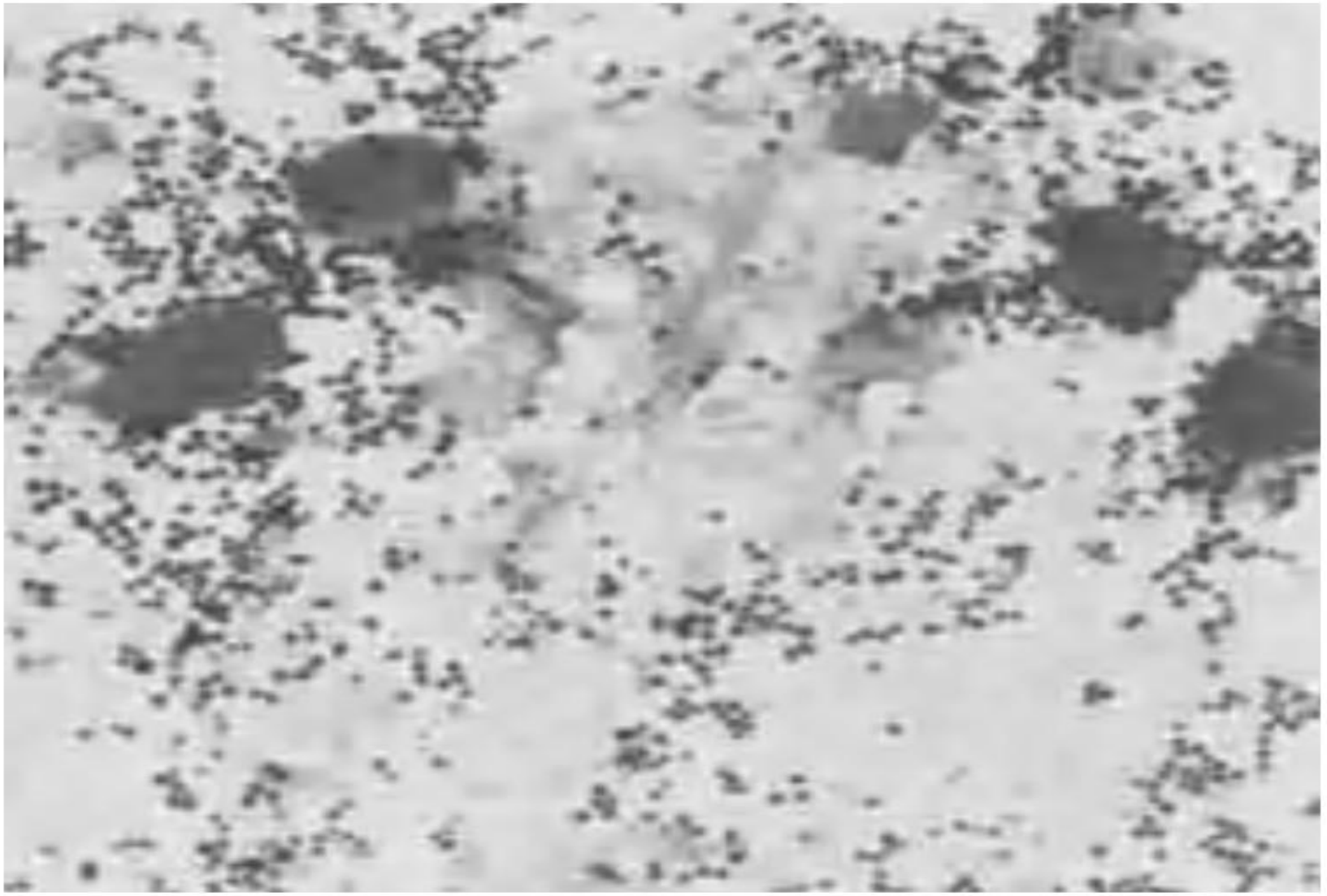
- **كشف المستضدات الجرثومية :**
  quellung reaction في القشع (الرئويات) لاتكس .....،
  PCR (لوجيونيلا ومفطورات)في القشع & البول
  (الرئويات:حساسية ٥٠-٨٠%ونوعية ٩٠% & اللوجيونيلا
  حساسية ٦٠-٨٠% ونوعية ٩٥%)

- **الاختبارات المصلية :ارتفاع > ٤ أضعاف ، غير مفيدة**

Gram stain of sputum at low power showing many polymorphonuclear leukocytes and a few squamous epithelial cells



Gram stain of sputum from a patient with staphylococcal pneumonia



التقييم الجرثومي:الاجراءات الغازية

- **التنظير القصبي :**
  -مرضى CAP شديدة أو معندة ،الحساسية أفضل والنوعية نفسها (تدرن &الفطور)

  -الغسالة القصبية السنخية المصغرة : زرع جرثومي وفطري وللسل والفيروسات

- **الفرشاة المحمية & الغسالة القصبة السنخية :**
  حساسية ونوعية ٦٠-٩٠%
  (النوعية الأفضل للفرشاة والحساسية الأفضل للغسالة)

- **الرشافة عبر الأنبوب الرغامي :حساسية >٨٠% ،نوعية<٣٥%**

- **الرشافة الرئوية عبر جدار الصدر :**
  حساسية ٣٥-٨٢ % ، الافات الرئوية الخبيثة

- **خزعة الرئة عبر القصبات :نوكارديا & لوجيونيلا**

- **خزعة الرئة المفتوحة : الانتانات الانتهازية**

CXR

Shows :

- **Distribution**
- **extent of infiltrate +/– cavitation**

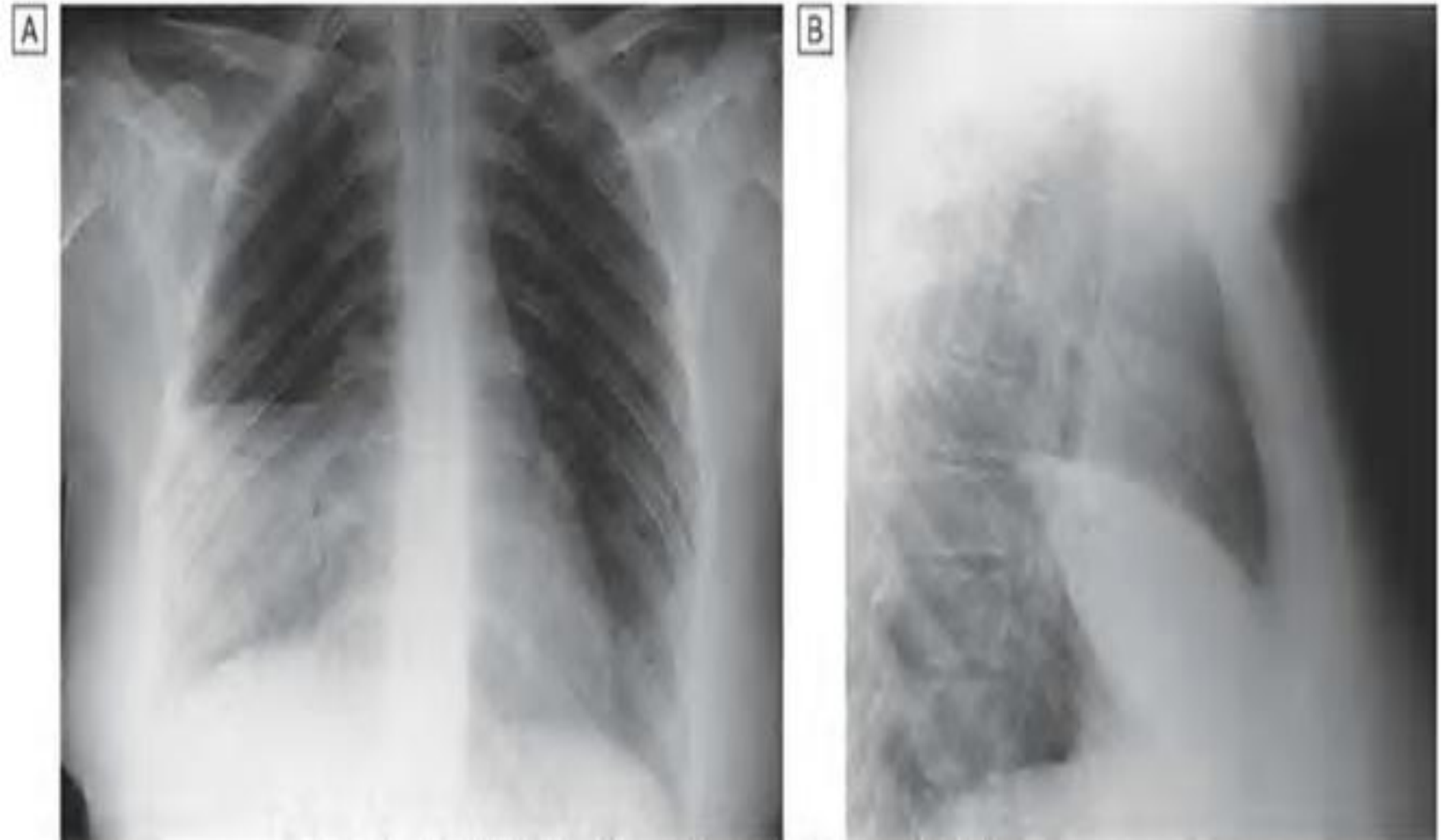
False negative chest radiographs

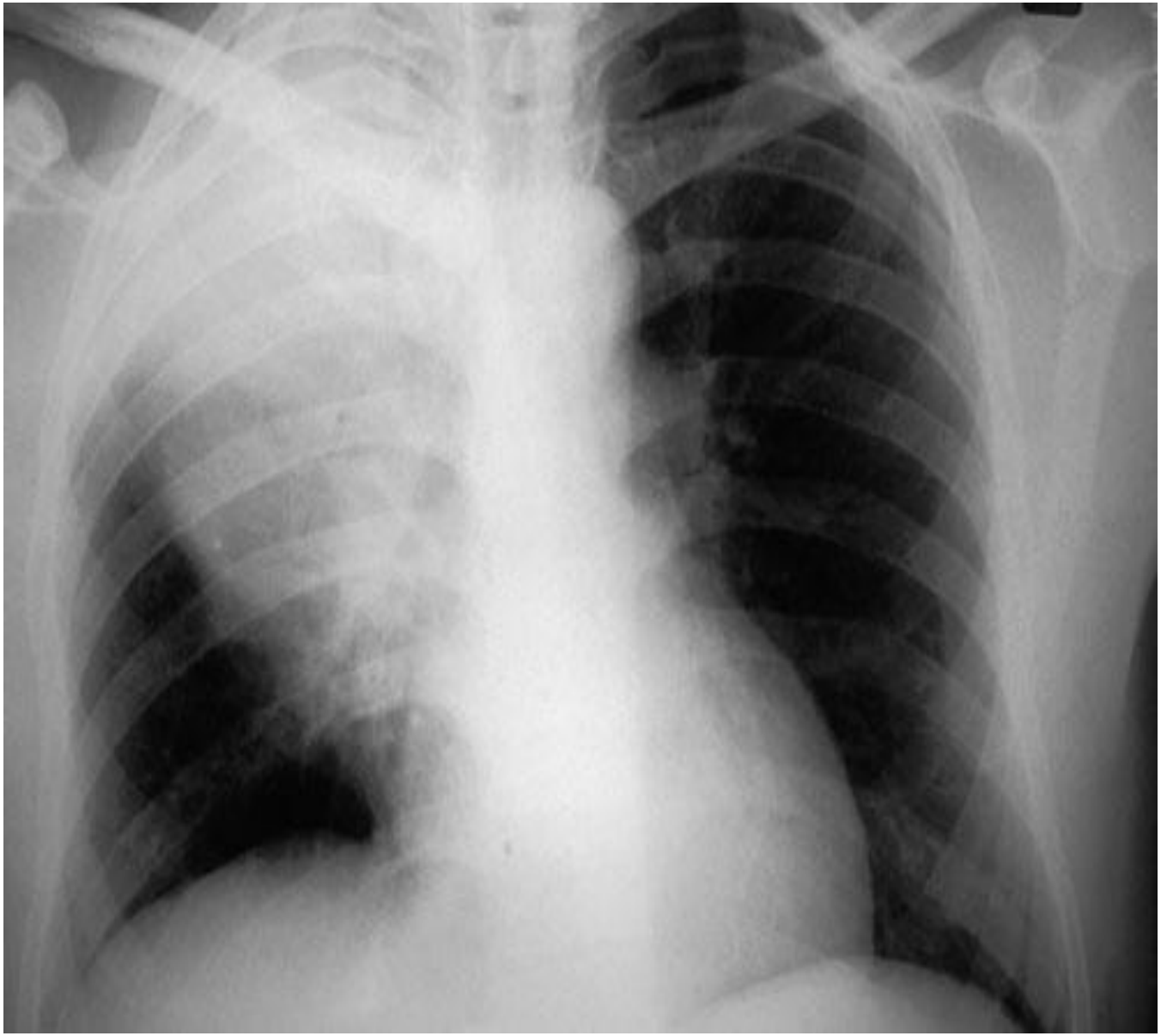
- an infection very early in the course (<24 hours)
- neutropenia
- dehydration
- Pneumocystis carinii pneumonia.

العوامل التي تؤثر على حساسية صورة الصدر

- النفاخ الرئوي
- البدانة
- المرحلة الباكرة من CAP
- نقص المحبيات

Pneumonia of the right middle lobe





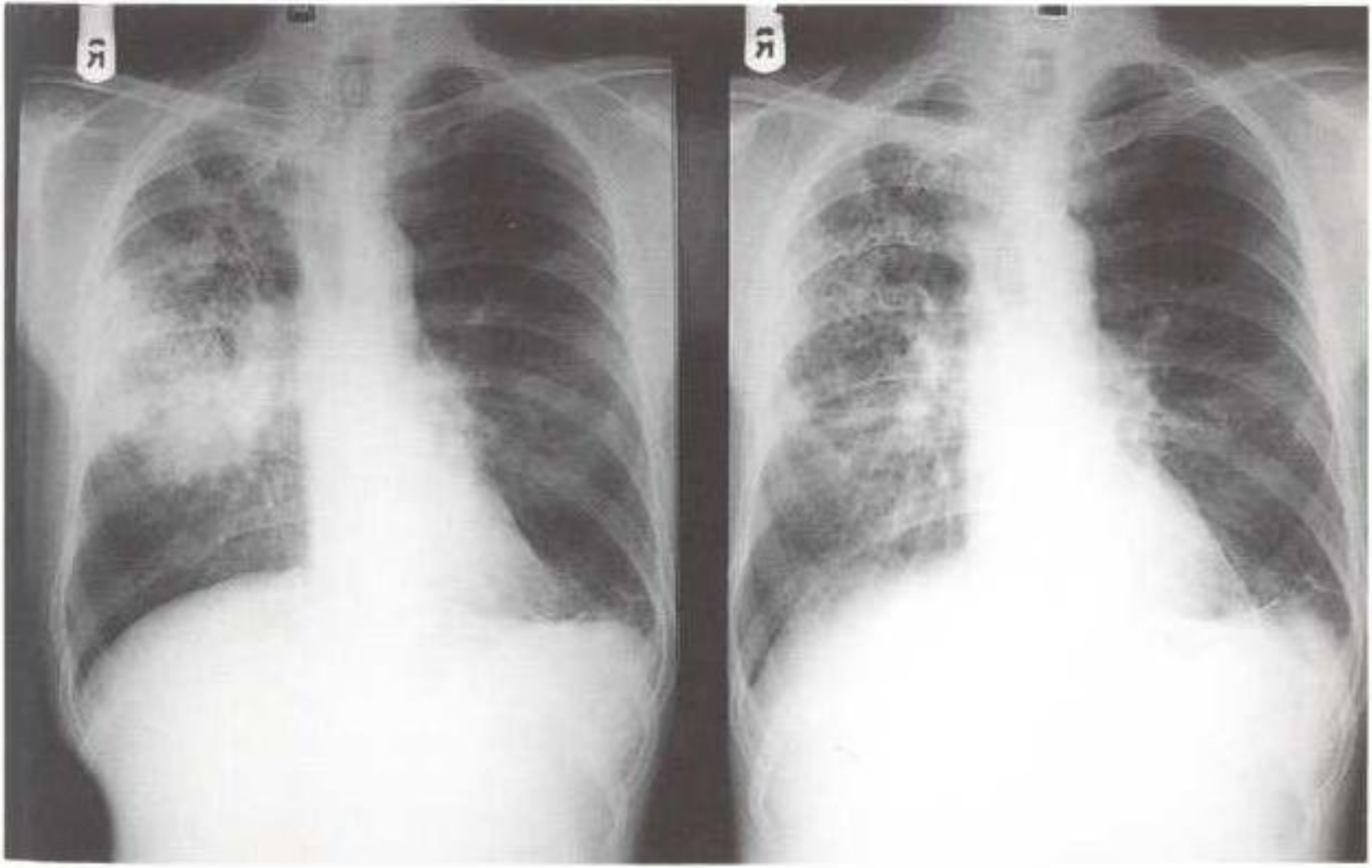
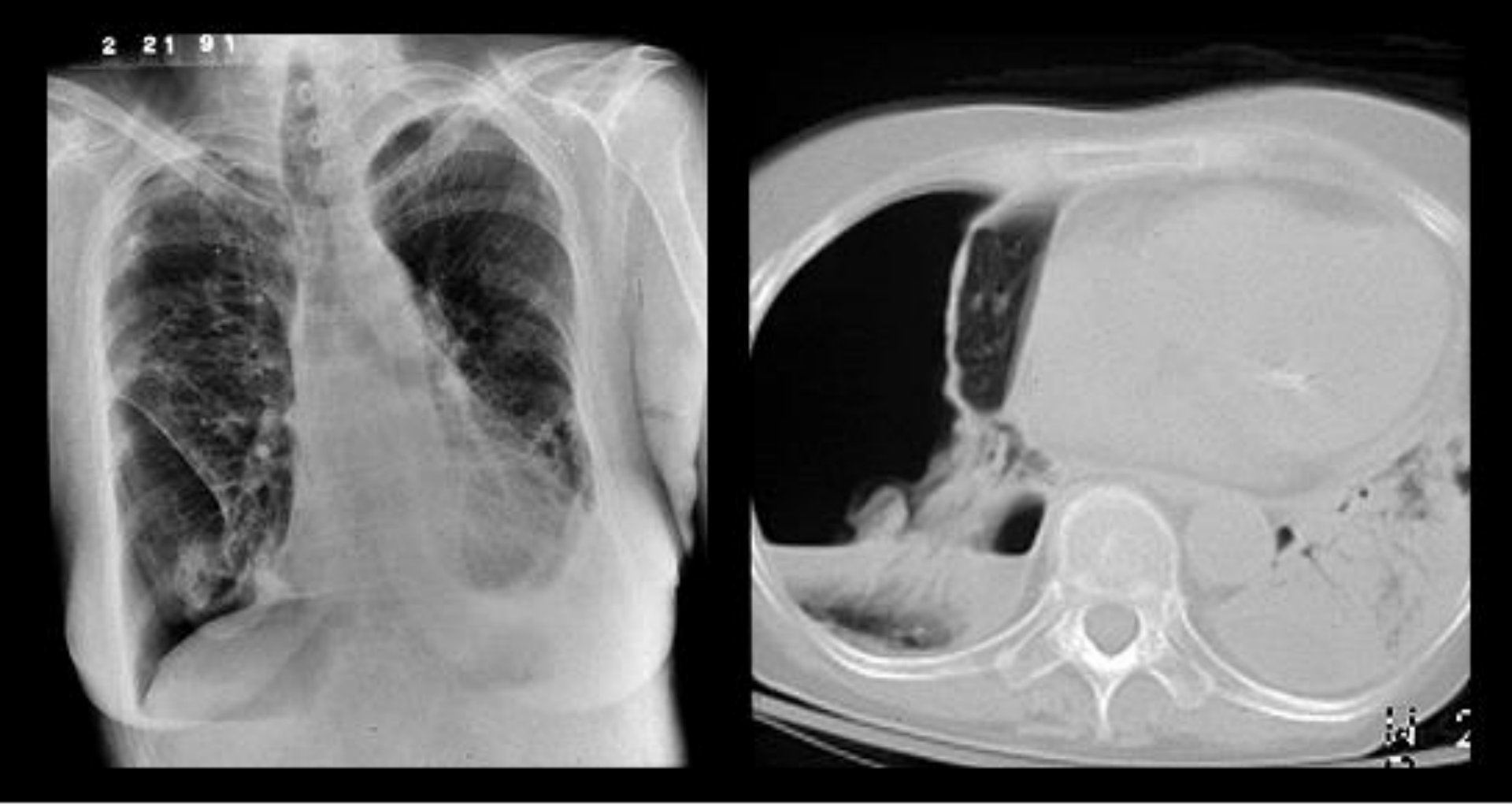


Fig. 140 Bronchopneumonia at onset and during convalescence.



Atypical pneumothorax Chronic atypical pneumothorax in patient with known rheumatoid arthritis, bibasilar pulmonary fibrosis, and left pleural effusion. Chest radiograph (left panel) shows right infero-lateral collection of intrapleural gas with an atypical concave pleural edge toward the chest wall and the costophrenic sulcus. CT scan (right panel) shows right basilar hydropneumothorax and the collapsed right lower lung with a thickened visceral pleura. Courtesy of Paul Stark, MD.

bronchoscopy +/– washings

For :

- **severely ill patients unresponsive to treatment**
- **the immunocompromised**

Differential Diagnosis

- acute bronchitis
- effusion (can be due to pneumonia)
- PE
- CA
- pulmonary edema
- bronchiectasis
- hypersensitivity pneumonitis
- BOOP
- drug-induced pneumonitis
- chronic eosinophilic pneumonia

criteria for hospitalization

- demographic factors: elderly, nursing home residents
- co-existing illness:
  neoplasm, CHF, cerebrovascular disease,
  chronic liver/renal disease
- physical examination:
  altered mental status, tachypnea, tachycardia,
  hypotension,extremes of temperature
- laboratory findings:
  hyponatremia, acidemia, hyperglycemia, hypoxemia,
  azotemia,decreased hematocrit
- radiographic findings: pleural effusion

Community-Acquired Pneumonia Severity-of-Illness Scoring System: Assignment of Points*

Patient Characteristics	Number of Points
Demographic factors	
Age	
Men	Age in years
Women	Age in years minus 10
Nursing home resident	Age plus 10
Coexisting illnesses (definitions listed below)	
Neoplastic disease†	30
Liver disease‡	20
Congestive heart failure§	10
Cerebrovascular disease#	10
Renal disease¶	10
Physical examination findings	
Altered mental status**	20
Respiratory rate >30/min	20
Systolic blood pressure <90 mHg	20
Temperature <35°C (95°F) or >40°C (104°F)	15
Pulse rate >125/min	10
Laboratory and roentgenographic findings	
Arterial pH <7.35	30
Blood urea nitrogen >30 mg/dL (11 mmol/L)	20
Sodium <130 mmol/L	20
Glucose >250 mg/dL (14 mmol/L)	10
Hematocrit <30%	10
Partial pressure of arterial oxygen <60 mmHg	10
Pleural effusion	10

Table 9–11. PORT risk class 30-day mortality rates and recommendations for site of care.

Number of Points	Risk Class	Mortality at 30 days (%)	Recommended Site of Care
Absence of predictors	I	0.1–0.4	Outpatient
≤ 70	II	0.6–0.7	Outpatient
71–90	III	0.9–2.8	Outpatient or brief inpatient
91–130	IV	8.2–9.3	Inpatient
≥ 130	V	27.0–31.1	Inpatient

CURB-65 Rule Severity of Illness Scoring System for Community-Acquired Pneumonia

Confusion : new mental confusion
Urea >7 mM/L
Respiratory rate >30 breaths per minute
Blood pressure: Diastolic BP <60 mmHg or systolic blood pressure <90 mmHg
Age ≥65 years of age
Group 1: 0 or 1 of the above—mortality low—1.5%. Likely suitable for treatment at home.
Group 2: 2 of the above—mortality—9.2%. Hospitalization for treatment.
Group 3: 3 or more of the above—mortality—22%. Likely requires admission to ICU.

Treatment of CAP

- Most patients are treated at home,with only about **25% needing hospital admission.**

• outpatient:
macrolides (e.g. erythromycin)

• outpatient with COPD (recent systemic steroids)
antibiotics/hospitalization:
quinolones with enhanced activities against S. *pneumoniae*
(e.g. levofloxacin) or macrolides or (cefuroxime)

• hospitalized patients:
IV/PO quinolones (e.g. levofloxacin) or
IV/PO macrolides plus IV/PO second/third generation cephalosporins (e.g. ceftriaxone)

• severe hospitalized patients (ICU):
IV quinolones (e.g. levofloxacin) plus third generation cephalosporins)
or IV macrolides plus third generation cephalosporin

Table 3. European Respiratory Society/European Society for Clinical Microbiology and Infectious Diseases antibiotic guideline options for CAP

Outside hospital	Amoxicillin Tetracycline
Hospitalised	
Nonsevere	Aminopenicillin ± macrolide Aminopenicillin/β-lactamase inhibitor ± macrolide Non-antipseudomonal cephalosporin Cefotaxime or ceftriaxone ± macrolide Levofloxacin Moxifloxacin Penicillin G ± macrolide
Severe	
No *Pseudomonas* risk	Non-antipseudomonal cephalosporin III + macrolide Moxifloxacin or levofloxacin ± non-antipseudomonal cephalosporin III
Pseudomonas risk	Antipseudomonal cephalosporin + ciprofloxacin Antipseudomonal cephalosporin + macrolide + aminoglycoside[#] Acylureidopenicillin/β-lactamase inhibitor + ciprofloxacin Acylureidopenicillin/β-lactamase inhibitor + macrolide + aminoglycoside[#] Carbapenem[¶] + ciprofloxacin Carbapenem[¶] + macrolide + aminoglycoside[#]

Evidence does not clearly support one regime as better than another so a choice is provided. Decision will depend on local circumstances. [#]: gentamicin, tobramycin or amikacin; [¶]: meropenem is preferred.

Antibiotic treatment for CAP*

Uncomplicated CAP

- Amoxicillin 500 mg 8-hourly orally

If patient is allergic to penicillin

- Clarithromycin 500 mg 12-hourly orally *or*
  Erythromycin 500 mg 6-hourly orally

If *Staphylococcus* is cultured or suspected

- Flucloxacillin 1-2 g 6-hourly i.v. *plus*
- Clarithromycin 500 mg 12-hourly i.v.

If *Mycoplasma* or Legionella is suspected

- Clarithromycin 500 mg 12-hourly orally or i.v. *or*
  Erythromycin 500 mg 6-hourly orally or i.v. *plus*
- Rifampicin 600 mg 12-hourly i.v. in severe cases

Severe CAP

- Clarithromycin 500 mg 12-hourly i.v. *or*
  Erythromycin 500 mg 6-hourly i.v. *plus*

- Co-amoxiclav 1.2 g 8-hourly i.v. *or*
  Ceftriaxone 1-2 g daily i.v. *or*
  Cefuroxime 1.5 g 8-hourly i.v. *or*
  Amoxicillin 1 g 6-hourly i.v. *plus* flucloxacillin 2 g 6-hourly i.v.

Complications of pneumonia

- Para-pneumonic effusion-common
- Empyema
- Retention of sputum causing lobar collapse
- DVT and pulmonary embolism
- Pneumothorax, particularly with *Staph. aureus*
- Suppurative pneumonia/lung abscess
- ARDS, renal failure, multi-organ failure
- Ectopic abscess formation (*Staph. aureus*)
- Hepatitis, pericarditis, myocarditis, meningoencephalitis
- Pyrexia due to drug hypersensitivity

Common Organisms in Pneumonia

Community Acquired		Nosocomial	HIV-associated	Alcoholics
Healthy Adults	**Elderly/Comorbidity/ Nursing Home**			
S.Pneumoniae *Mycoplasma* *Chlamydia* *H. Influenzae* Viral	*S. Pneumoniae* *H. Influenzae* gram-negative bacilli *S. Aureus* Chlamydia Oral anaerobes *Legionella*	enteric gram-negative rods *Pseudomonas* *S. Aureus* Oral anaerobes *Legionella*	*Pneumocystis Carinii* *TB*	*Klebsiella* Enteric gram-negative rods *S. Aureus* Anaerobes (aspiration)

Community Acquired Pneumonia

Microbiology

- *S. pneumoniae*: 20-60%
- *H. influenzae*: 3-10%
- *Chlamydia pneumoniae*: 4-6%
- *Mycoplasma pneumonaie*: 1-6%
- Legionella spp. 2-8%
- *S. aureus*: 3-5%
- Gram negative bacilli: 3-5%
- Viruses: 2-13%

40-60% - NO CAUSE IDENTIFIED

2-5% - TWO OR MORE CAUSES

Streptococcus pneumoniae

- most common bacterial pneumonia
- at risk: secondary complication to a viral RTI

clinical presentation

- abrupt onset with fever, rigor, pleurisy, and **"rusty"sputum**
- watch for meningeal involvement

❑ CXR: classically causes a **lobar consolidation**

labs

- sputum: PMNs and gram-positive oval-shaped diplococci
- leukocytosis (10,000-30,000 is common, but may be leukopenic on admission)

treatment

- penicillin G (erythromycin if penicillin allergic; vancomycin,ceftriaxone or cefotaxime if resistant) x 7-10 days

❑ prevention: Pneumovax (give once only)

Staphylococcus aureus

- sudden onset bronchopneumonia

- at risk:
  - secondary complication of influenza
  - infection or in hospitalized patient with underlying disease, severe diabetes
  - drug abusers
  - immunocompromised

clinical presentation

- high fever, chills, progressive dyspnea
- cyanosis
- cough
- pleuritic pain
- quite toxic-appearing

complications

- cavitation (necrotizing pneumonia)
- pneumothorax
- empyema
- pneumatoceles in children

Cavitating staphylococcal pneumonia

treatment:

- cloxacillin or vancomycin (if penicillin allergic) x 7-10 days and drain any empyema

Mycoplasma pneumoniae

- most common atypical pneumonia; "walking pneumonia"
- at risk: young adults (especially 5-15 years old)
- incubation: 12-14 days (insidious onset)

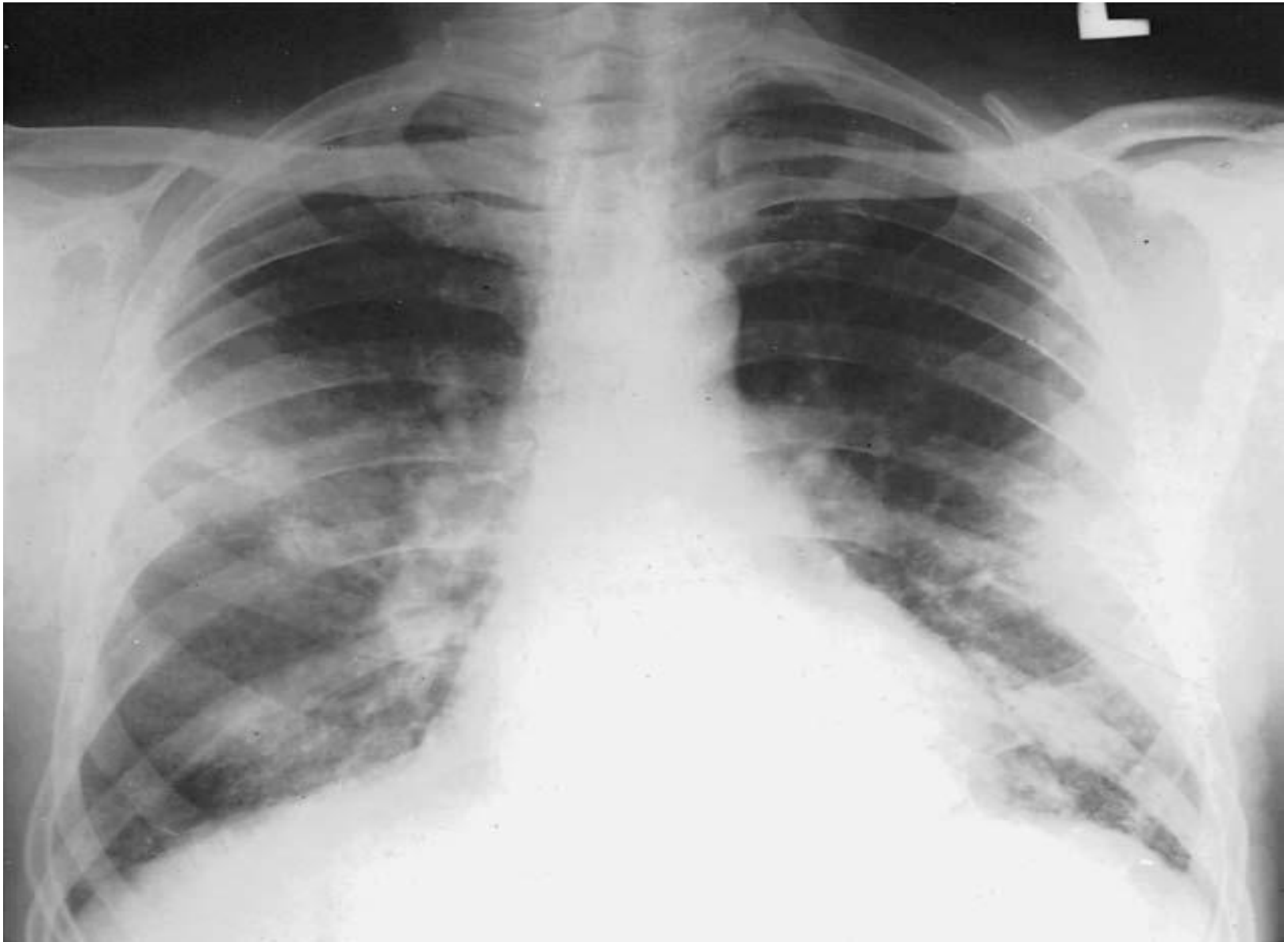
clinical presentation

- constitutional illness with fever, persistent hacking cough +/– scant sputum
- chills uncommon

❑ extrapulmonary features:
- headache
- diarrhea
- non-exudative pharyngitis
-skin (e.g. erythema multiforme)
-arthralgia, myalgia
- hemolytic crises
- bullous myringitis
- CNS (e.g. myelitis, Guillain-Barré syndrome, meningoencephalitis)

❑ CXR:
classically worse than clinical presentation; usually bilateral, patchy air-space diseas

Bilateral patches of micronodular shadowing :*Mycoplasma* pneumonia



labs

- **sputum:**
  more mononuclear cells and fewer PMNs than bacterial pneumonia, but mycoplasma not visualized

- complement fixation shows significant titre rise in up to 80%, anti-I **(IgM) increased in 50%**

- cold agglutinins

- WBC not significantly increased (PMNs slightly elevated)

treatment

- Macrolide
- newer generation quinolones
- doxycycline x 10-14 days

Legionella pneumophila

- Legionnaire's disease; found in contaminated water, air conditioners
- at risk:
  smokers, age > 65, male, immunocompromised, chronic lung disease, cancer, chronic heart and kidney disease
- incubation: 2-10 days

clinical presentation

- **initial nonrespiratory symptoms:**
  malaise, fever, GI symptoms, delirium, renal failure

- **subsequent respiratory symptoms:**
  cough, chills, dyspnea, pleuritis, bronchopneumonia, blood-streaked mucoid sputum

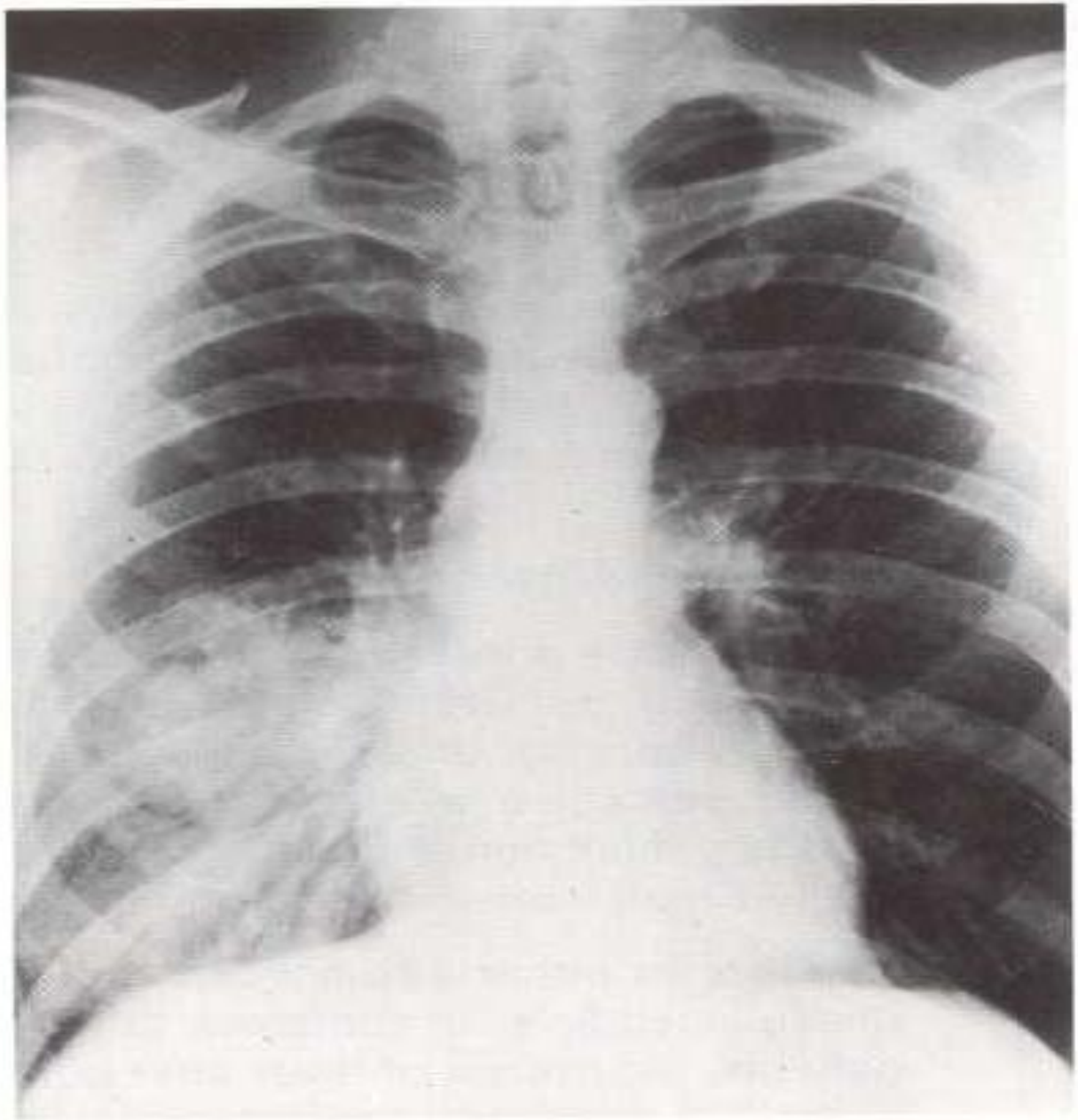


Fig. 145 Legionnaires' pneumonitis.

labs

- sputum: gram-negative coccobacillary organisms stain poorly
- immunofluorescent serology, Legionella urine antigen, BAL

treatment

- **macrolide, quinolone +/– rifampin**

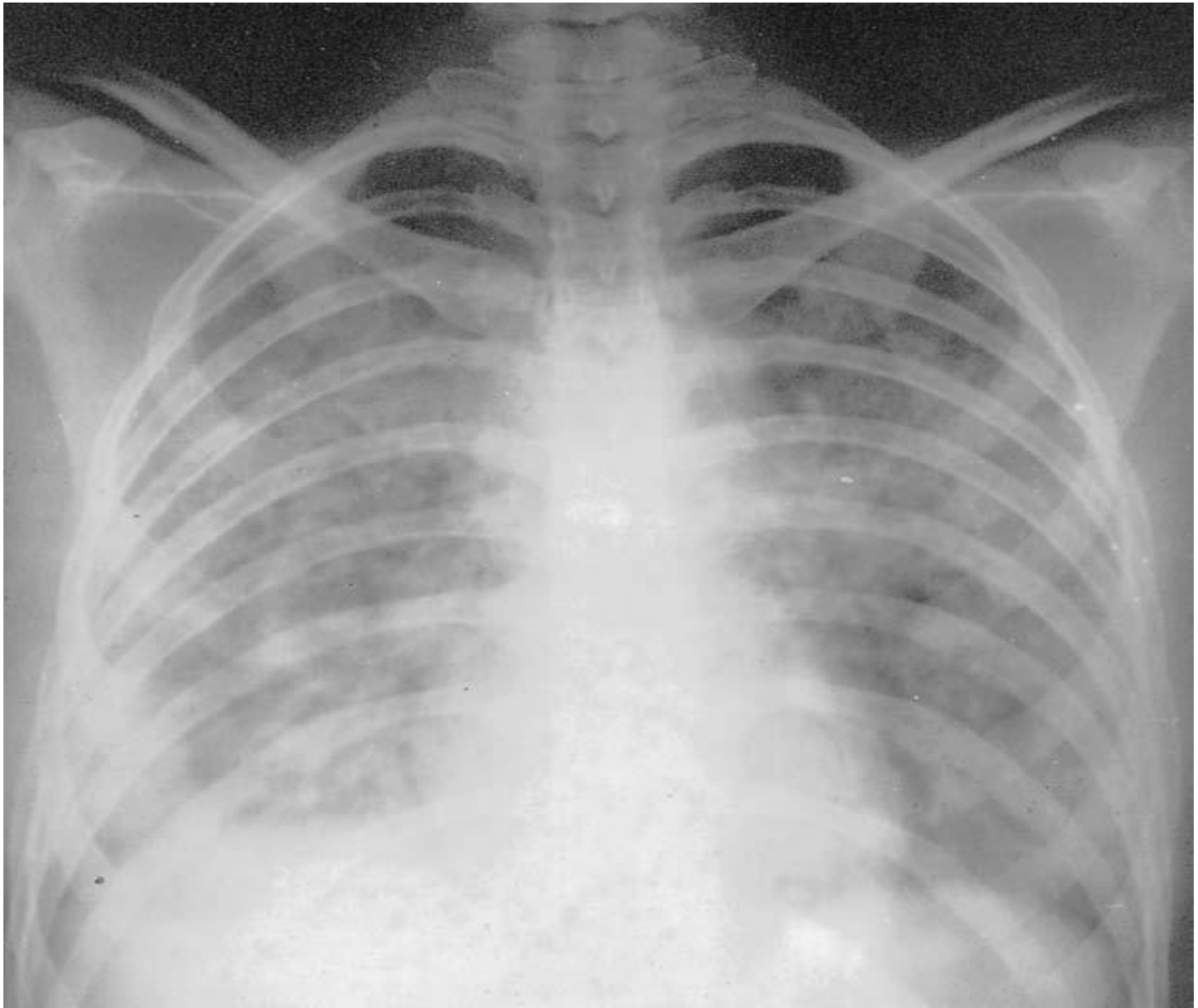
Viral pneumonia

- most common cause of pneumonia in children (mostly RSV)
- < 10% of adult pneumonia (mostly influenza virus)
- at risk: influenza pneumonia in elderly; chronic heart, lung, or renal disease
- influenza predisposes to superimposed bacterial pneumonia, especially pneumococcal or S. *aureus*

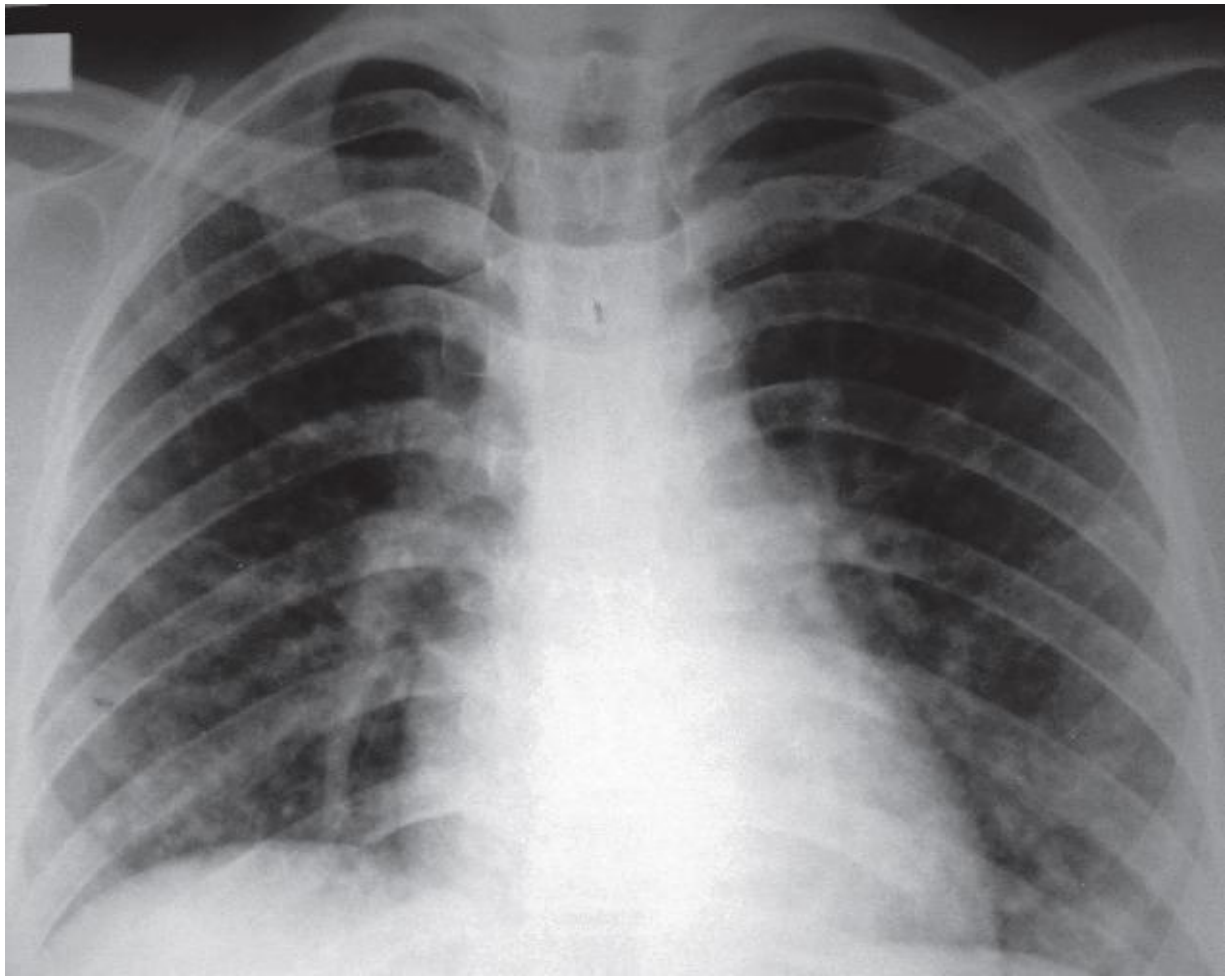
Laps

- CXR: worse than clinical presentation
- sputum: more monocytes, fewer PMNs than bacterial pneumonia

severe viral pneumonia



Posteroanterior plain chest radiograph of a patient with Varicella - *zoster virus (VZV) pneumonia shows diffuse* micronodular interstitial lung pattern bilaterally



treatment

- **Oseltamivir and zanamivir :**
  -reduce the replication of influenza viruses
  -Oseltamivir is given **orally**, whereas zanamivir is only available by **inhalation**.
  -These drugs have to be **given within 48 hours** of the onset of symptoms to be effective.
  -They **reduce the duration** of illness by about 1 day and they may
- **reduce complications** in at-risk patients with severe influenza.
  -They can also be given for **post-exposure** prophylaxis in at-risk adults not protected by vaccination.

- **if immunocompromised :**
  amantadine (for influenza A) or ribavirin (for RSV)

❑ **prevention: annual influenza vaccination**

Hemophilus influenzae

- ❑ at risk: children, smokers, associated with COPD exacerbations
- ❑ encapsulated and unencapsulated strains cause lung infections

clinical presentation

- similar to pneumococcal pneumonia, **lobar** pneumonia

❑ sputum: gram-negative coccobacilli

treatment

- (lots of penicillin resistance)
- cephalosporin (second generation)
- TMP/SMX
- quinolones
- amoxicillin-clavulina

Moraxella catarrhalis

at risk:

- **common in smokers**
- **COPD patients**
- **diabetics**
- **patients with malignancies**
- **alcoholics**
- **patients on steroids; rare in normal adults**

clinical presentation

- typical pneumonia

❑ CXR: **lobar consolidation**

❑ sputum: gram-negative cocci, singly or in pairs

treatment

- tetracycline or doxycycline
- TMP-SMX
- Cephalosporins
- Macrolides
- fluoroquinolones

Enteric gram-negative rods (including Pseudomonas aeruginosa) pneumonia

- at risk:
  hospital/nursing home
  (50-70% of nosocomial pneumonias)

- bilateral bronchopneumonia

- complications: septic shock with
  bacteremia, abscess

Pseudomonas
pneumonia

treatment

- cephalosporin (third generation) +/– aminoglycoside or ciprofloxacin
- *Pseudomonas aeruginosa :* usually requires penicillin/cephalosporin + aminoglycoside sensitive to organism

Klebsiella pneumoniae

- at risk:: alcoholics

- clinical presentation:
  explosive onset of fever, prostration; similar to pneumococcus; bloody sputum ("red currant jelly")

- complications:
  rapid cavitation, abscess, high mortality

Labs

- CXR: classically **lobar consolidation** with bulging fissure
- sputum: large gram-negative encapsulated rods

treatment:

- cephalosporin and aminoglycoside
- adequate drainage of empyema

Anaerobic pneumonia

- **at risk:**
  those who cannot protect airway with risk of aspiration (i.e. inhibited airway reflexes, seizures, alcoholics)

- **clinical presentation:**
  gradual onset, foul-smelling sputum

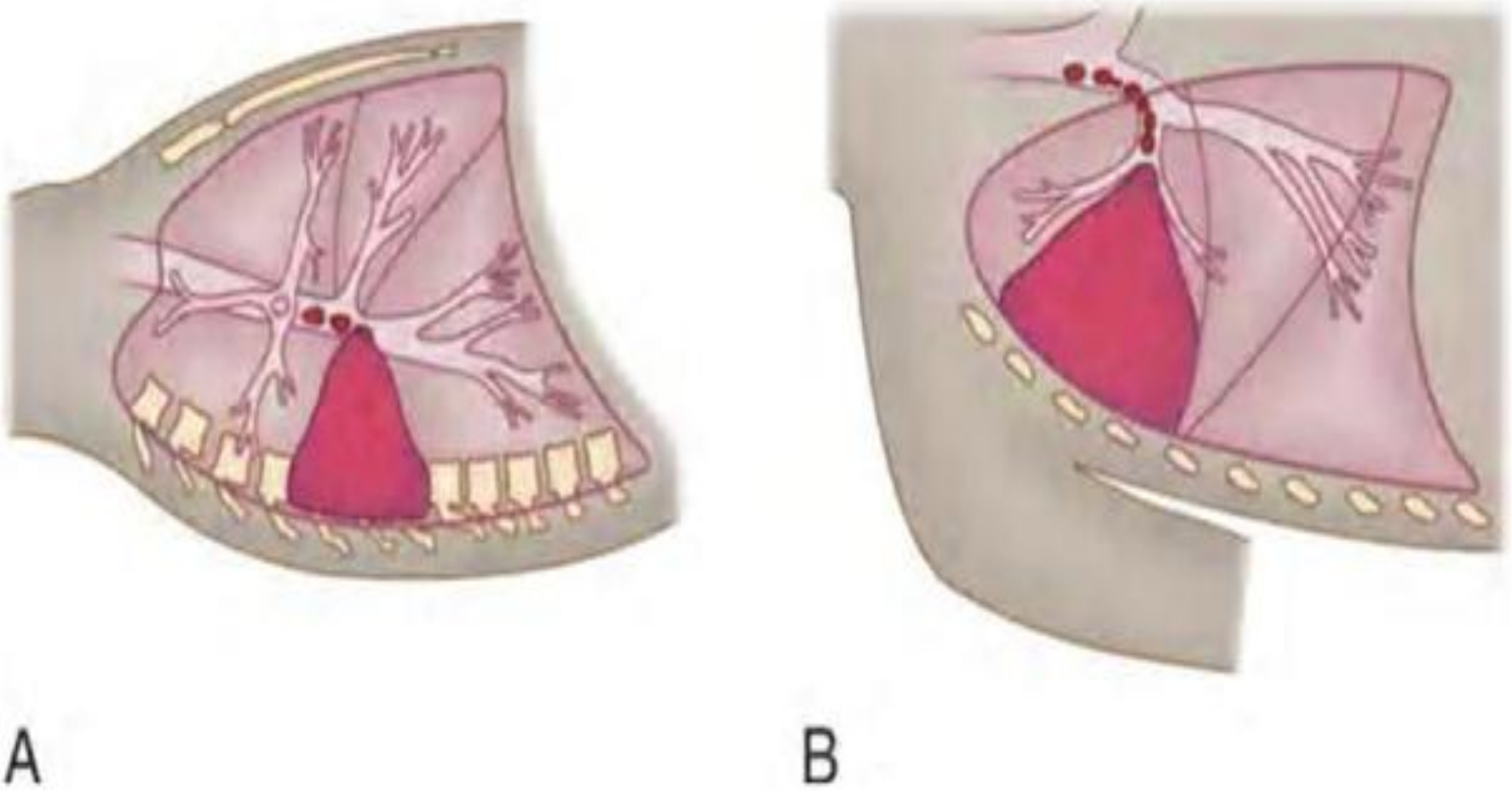
- **complications: necrotizing pneumonia with abscess formation; empyema**

Labs

- **CXR:**
  dependent areas of lung involved; usually infiltrates inferior segment of right upper lobe or apical segment of lower lobe

- **sputum: tends to be a polymicrobial infection**

(A), aspiration occurs into the superior segment of the lower lobe. With patient lying on the side (B), aspiration occurs into the posterior segment of the upper lobe.



treatment

- high dose penicillin G or clindamycin

Pneumocystic carinii

- **at risk:**
  patients on immunosuppressants (e.g. transplant recipients) or chemotherapy, AIDS when CD_4 count < 200

- **clinical presentation: atypical, concurrent opportunistic infections**

Labs

- **CXR :**
  - **diffuse interstitial infiltration**
  - **often isolated to upper lobes**

- **sputum:**

  Giemsa stain; lower yield in patients on prophylaxis; diagnosis may require BAL or transbronchial biopsy

Pneumocystis pneumonia: typical chest X-ray appearance. Note the sparing at the apex and base of both lungs.

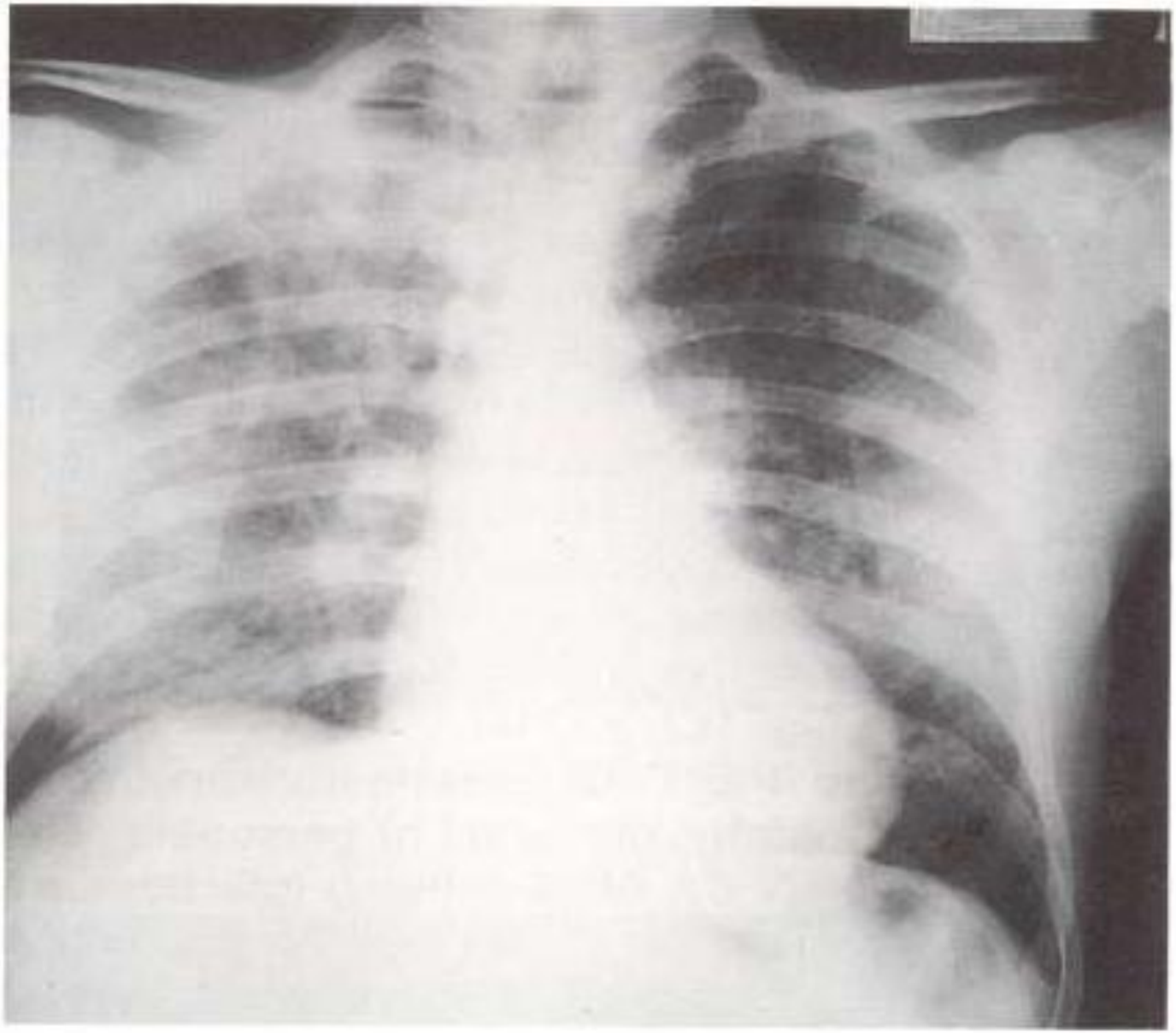


Fig. 161 Chest radiograph: *Pneumocystis carinii* pneumonitis.

treatment

- TMP-SMX, pentamidine, TMP-dapsone, clindamycin-primaquin,atovaquone
- add corticosteroids if PaO_2 < 70 mm Hg or $AaDO_2$ > 35 mm Hg

❑ <u>prevention</u>:
in AIDS, after an episode of PCP or when CD_4 count < 200 use TMP-SMX, TMP-dapsone, or pentamidine

Common clinical features of community-acquired pneumonia (CAP)

Organism	Clinical features
Streptococcus pneumoniae	Most common cause. Affects all age groups, particularly young to middle-aged. Characteristically rapid onset, high fever and pleuritic chest pain; may be accompanied by herpes labialis and 'rusty' sputum. Bacteraemia more common in women and those with diabetes or COPD
Mycoplasma pneumoniae	Children and young adults. Epidemics occur every 3-4 years, usually in autumn. Rare complications include haemolytic anaemia, Stevens-Johnson syndrome, erythema nodosum, myocarditis, pericarditis, meningoencephalitis, Guillain-Barré syndrome
Legionella pneumophila	Middle to old age. Local epidemics around contaminated source, e.g. cooling systems in hotels, hospitals. Person-to-person spread unusual. Some features more common, e.g. headache, confusion, malaise, myalgia, high fever and vomiting and diarrhoea. Laboratory abnormalities include hyponatraemia, elevated liver enzymes, hypoalbuminaemia and elevated creatine kinase. Smoking, corticosteroids, diabetes, chronic kidney disease increase risk
Chlamydia pneumoniae	Young to middle-aged. Large-scale epidemics or sporadic; often mild, self-limiting disease. Headaches and a longer duration of symptoms before hospital admission. Usually diagnosed on serology
Haemophilus influenzae	More common in old age and those with underlying lung disease (COPD, bronchiectasis)
Staphylococcus aureus	Associated with debilitating illness and often preceded by influenza. Radiographic features include multilobar shadowing, cavitation, pneumatocoeles and abscesses. Dissemination to other organs may cause osteomyelitis, endocarditis or brain abscesses. Mortality up to 30%
Chlamydia psittaci	Consider in those in contact with birds, especially recently imported and exotic. Malaise, low-grade fever, protracted illness, hepatosplenomegaly and occasionally headache with meningism
Coxiella burnetii (Q fever, 'querry' fever)	Consider in workers in dairy farms, abattoirs and hide factories (as amniotic fluid and placenta carry high risk). Risk of infection increases with age and male sex. Acute illness characterised by severe headache, high fever, hepatitis, myalgia, conjunctivitis. Chronic disease causes endocarditis, hepatomegaly
Klebsiella pneumoniae (Freidländer's bacillus)	More common in men, alcoholics, diabetics, elderly, hospitalised patients, and those with poor dental hygiene. Predilection for upper lobes and particularly liable to suppurate and form abscesses. May progress to pulmonary gangrene
Actinomyces israelii	Mouth commensal. Cervicofacial, abdominal or pulmonary infection, empyema, chest wall sinuses, pus with sulphur granules

Hospital-acquired pneumonia

- **pneumonia occurring at least 2 days after admission to hospital.**
- **leading cause of HAI-associated death**
- **ventilator-associated pneumonia (VAP)**
- **<u>Health care-associated pneumonia (HCAP):</u> the development of pneumonia in a person who has spent at least 2 days in hospital within the last 90 days**

Aetiology

more often attributable to :

- **Gram-negative bacteria (e.g. *Escherichia*, *Pseudomonas* and *Klebsiella* species)**
- ***Staph. aureus* (including meticillin-resistant)**
- ***Staph. aureus* (MRSA)**
- **anaerobes.**

19.50 Factors predisposing to hospital-acquired pneumonia

Reduced host defences against bacteria

- Reduced immune defences (e.g. corticosteroid treatment, diabetes, malignancy)
- Reduced cough reflex (e.g. post-operative)
- Disordered mucociliary clearance (e.g. anaesthetic agents)
- Bulbar or vocal cord palsy

Aspiration of nasopharyngeal or gastric secretions

- Immobility or reduced conscious level
- Vomiting, dysphagia, achalasia or severe reflux
- Nasogastric intubation

Bacteria introduced into lower respiratory tract

- Endotracheal intubation/tracheostomy
- Infected ventilators/nebulisers/bronchoscopes
- Dental or sinus infection

Bacteraemia

- Abdominal sepsis
- I.v. cannula infection
- Infected emboli

Clinical features and investigations

- purulent sputum (or endotracheal secretions)
- new radiological infiltrates
- unexplained increase in oxygen requirement
- a core temperature > 38.3°C
- leucocytosis or leucopenia.
- In mechanically ventilated patients, bronchoscopy-directed protected brush specimens or bronchoalveolar lavage (BAL)

Management

- Gram-negative cover is usually provided by:

- a third-generation cephalosporin (e.g. cefotaxime) with an aminoglycoside (e.g. gentamicin)
- Meropenem
- a monocyclic β-lactam (e.g. aztreonam) and flucloxacillin.

- **MRSA is treated with intravenous :** vancomycin or linezolid.

Ventilator-associated pneumonia (VAP)

- Sputum cultures should be obtained prior to starting antibiotics or if patient is failing therapy by endotracheal suction or invasive techniques. ET suction appears just as sensitive but less specific than invasive methods.
- **Empiric treatment MUST be narrowed as soon as sputum culture results are known.**
- If the patient is on antibiotic therapy or has recently been on antibiotic therapy, choose an agent from a different class.

Optimal treatment can likely be based on severity of illness as determined by the Clinical Pulmonary Infection Score (CPIS).

Calculating the Clinical Pulmonary Infection Score (CPIS)

	0 points	1 point	2 points
Temperature (°C)	36.5 to 38.4	38.5 to 38.9	≤ 36.4 or ≥ 39
Peripheral WBC	4,000 – 11,000	< 4,000 or > 11,000 *> 50% bands: add 1 extra point*	
Tracheal secretions	None	Non-purulent	Purulent
Chest X-ray	No infiltrate	Diffuse or patchy infiltrates	Localized infiltrate
Progression of infiltrate from prior radiographs	None		Progression (ARDS, CHF thought unlikely)
Culture of ET suction	No growth/light growth	Heavy growth *Same bacteria on gram stain: add 1 extra point*	
Oxygenation (PaO2/FiO2)	> 240 or ARDS		≤ 240 and no ARDS

EMPIRIC TREATMENT

If the CPIS is ≤ 6

- VAP is unlikely
- If VAP strongly suspected see treatment recommendations below
- If CPIS remains ≤ 6 after 3 days, antibiotics can be stopped in most cases

If the CPIS is > 6

Early-onset VAP (occurring within 72 hours of hospitalization and patient has not been hospitalized or resided in a nursing home, long-term care or rehabilitation facility in the past 3 months)

Etiology: *S. pneumoniae, H. influenzea, S. aureus*

- Ceftriaxone 1 g IV Q24H
  OR
- Severe PCN allergy: Moxifloxacin 400 mg IV Q24H

Late-onset VAP (all VAP that is not early-onset)

Etiology: *S. aureus, P. aeruginosa*, other Gram-negative bacilli

- Vancomycin (see dosing section, p. 150) PLUS [Piperacillin/tazobactam 4.5 g IV Q6H OR Cefepime 2 g IV OR Q8H] ± Gentamicin (see dosing section, p. 146)
  OR
- Severe PCN allergy: Vancomycin (see dosing section, p. 150) PLUS [Ciprofloxacin 400 mg IV Q8H OR Aztreonam 2 g IV Q8H] PLUS Gentamicin (see dosing section, p. 146)

Enterococci and candida species are often isolated from sputum in hospitalized patients. In general, they should be considered to be colonizing organisms and should not be treated with antimicrobials.

If the patient is immunocompromised, consider adding Azithromycin 500 mg Q24H to Piperacillin/tazobactam, Cefepime or Aztreonam to cover *Legionella*

Duration

- **3 days** if CPIS remains ≤ 6 in patients with initial CPIS ≤ 6; VAP is unlikely
- **7 days** if the patient has clinical improvement
- If symptoms persist at 7 days consider alternative source and/or bronchoscopy with quantitative cultures
- VAP associated with *S. aureus* bacteremia should be treated for at least 14 days

Pneumonia in the immunocompromised patient

Causes of immune suppression-associated lung infection

	Causes	Infecting organisms
Defective phagocytic function	Acute leukaemia Cytotoxic drugs Agranulocytosis	Gram-positive bacteria, including *Staph. aureus* Gram-negative bacteria Fungi, e.g. *Candida albicans* and *Aspergillus fumigatus*
Defects in cell-mediated immunity	Immunosuppressive drugs Cytotoxic chemotherapy Lymphoma Thymic aplasia	Viruses Cytomegalovirus Herpesvirus Adenovirus Influenza Fungi *Pneumocystis jirovecii* (formerly *carinii*) *Candida albicans* *Aspergillus fumigatus*
Defects in antibody production	Multiple myeloma Chronic lymphocytic leukaemia	*Haemophilus influenzae* *Mycoplasma pneumoniae*

Clinical features

- fever, cough and breathlessness, but are less specific
- the onset of symptoms tends to be less rapid (*Pneumocystis jirovecii* and in mycobacterial infections)
- Cavitation may be seen with *N. asteroides*, mycobacteria and fungi.
- Pleural effusions suggest a pyogenic bacterial infection and are uncommon in *P. jirovecii* pneumonia.

Management

- **treatment should be based on an established aetiological diagnosis**

- **the causative agent is frequently unknown and broad-spectrum antibiotic therapy is required:**

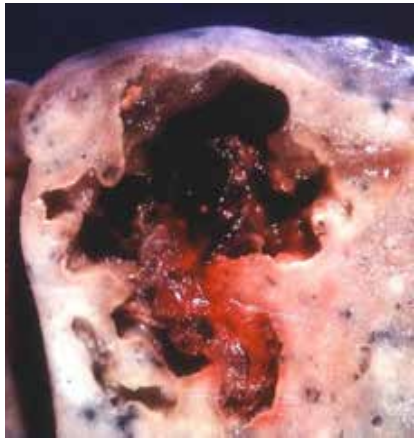
  - a third-generation cephalosporin, or a quinolone, plus an antistaphylococcal antibiotic, *or*
  - an antipseudomonal penicillin plus an aminoglycoside.

***antifungal or antiviral therapies may be added**

LUNG ABSCESS

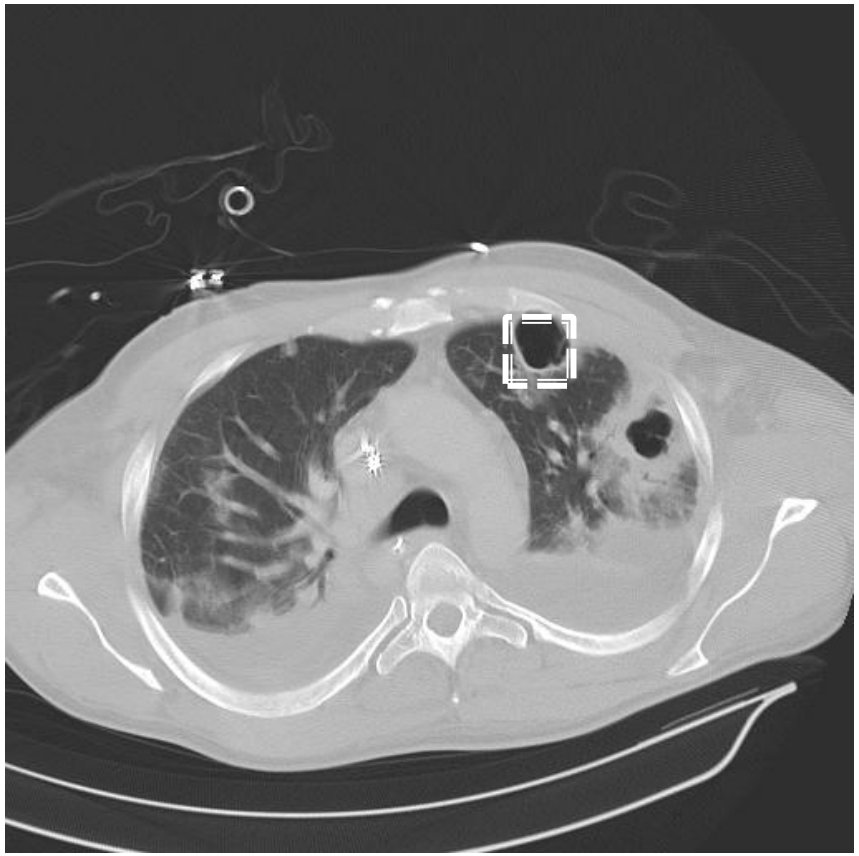
- a localized cavity with pus resulting from tissue necrosis, with surrounding pneumonitis

Complications of pneumonia



Abscess / cavitary lesion

- circumscribed focus of liquefactive necrosis within lung tissue
- associated with necrotizing *Staph* or *Strep* infections or Gram-neg rods (e.g. aspiration)



pathogenesis

- aspiration of upper airway anaerobic organisms
- inadequately treated pneumonia (especially S. *aureus*, *Klebsiella pneumoniae)*
- bronchial obstruction (tumour, foreign body)
- pulmonary infarction
- septic emboli

clinical presentation

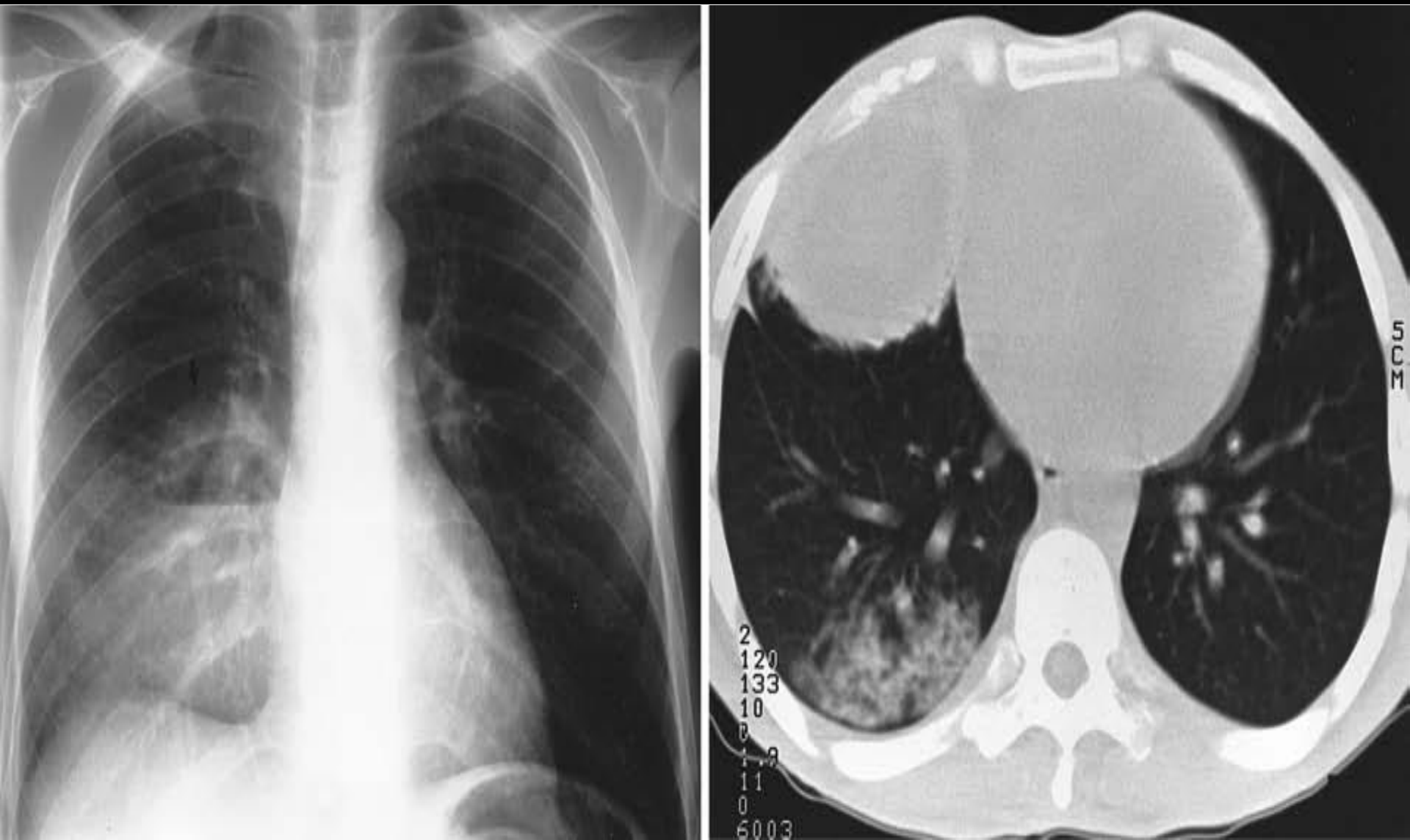
- acute or insidious with early symptoms like pneumonia
- purulent sputum, may be blood streaked
- putrid odor —> anaerobes
- weight loss, anemia, clubbing —> chronic abscess
- physical signs of consolidation

investigations

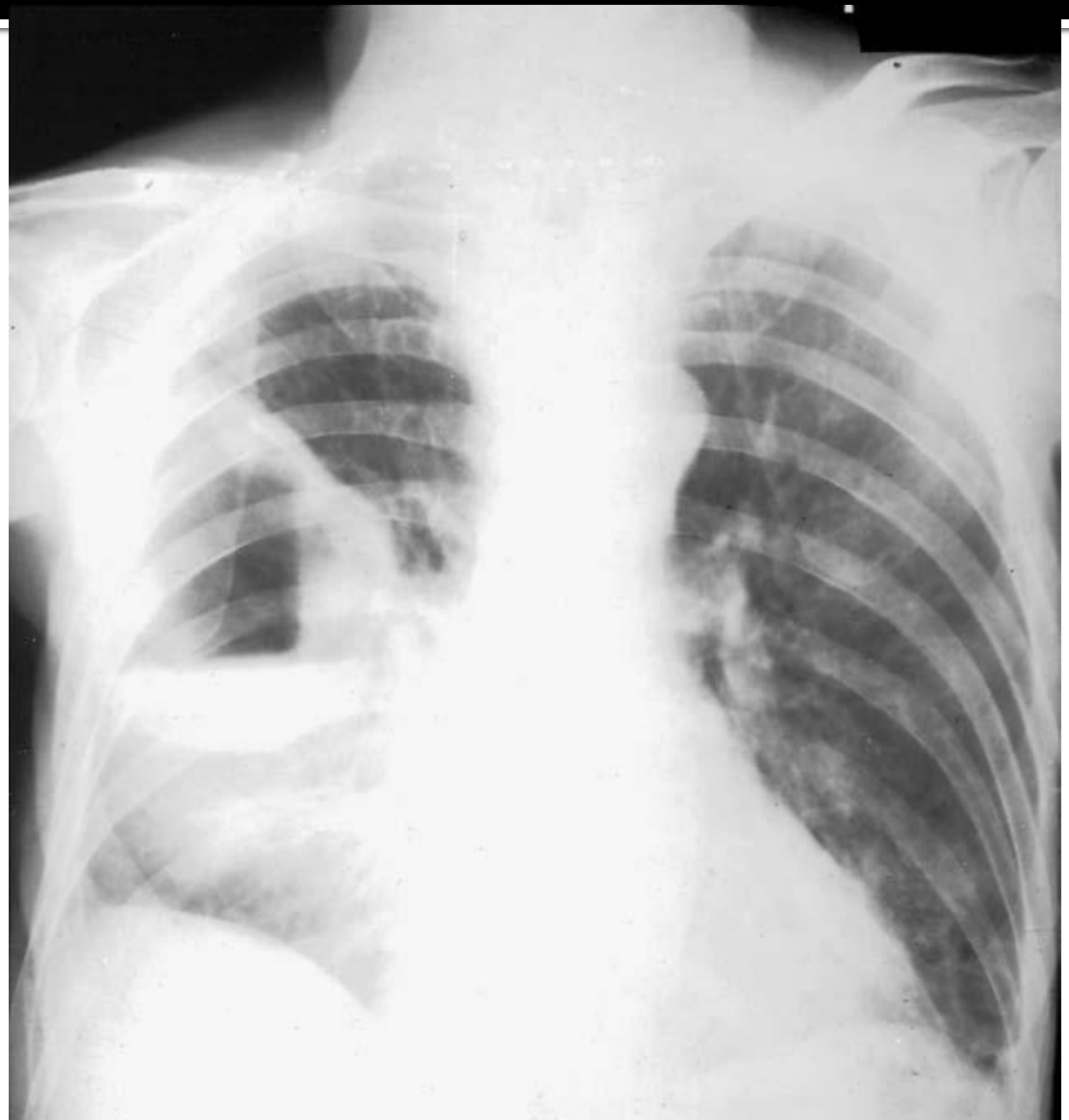
- **imaging:**
  CXR (thick-walled cavity with air-fluid level), CT, bronchoscopy

- **sputum:**
  transtracheal/transthoracic aspiration, culture and Gram stain

(a) Chest radiograph of a 34-year-old man with an eating disorder and suspected self-induced vomiting showing *Streptococcus anginosus abscess in the right middle lobe. (b) CT of* the same patient showing the middle lobe abscess but also pneumonic changes in the apical segment of the right lower lobe.



Large lung abscess in right mid zone following staphylococcal pneumonia. Pneumonic changes can be seen below the lesion and also in the left lower zone.



Left upper lobe lung abscess distal to bronchographic carcinoma in the left hilum

Differential Diagnosis

- cavitating CA
- bronchiectasis
- TB, coccidioidomycosis

Cavitating squamous carcinoma in the right lower zone. Note thick irregular wall and absence of any surrounding pneumonic change.

treatment

- antibiotics based on culture and sensitivity
- 4-6 weeks may be required
- co-amoxiclav 1.2 g 8-hourly + oral metronidazole 400 mg 8-hourly should be added
- Physiotherapy
- postural drainage
- surgical drainage and resection are rarely necessary