CCM tutorial
-- pneumonia

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Definition of pneumonia

- Acute infection of the pulmonary parenchyma that is associated with at least some symptoms of acute infection, accompanied by the presence of an acute infiltrate on a chest radiograph, or auscultatory findings consistent with pneumonia

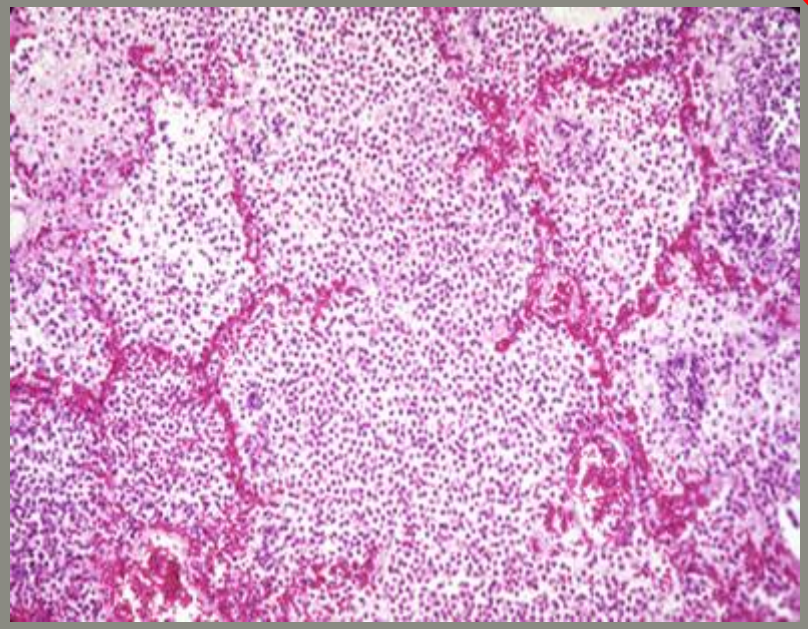
Bartlett. Clinical Infect Diseases 2000;31:347-82.

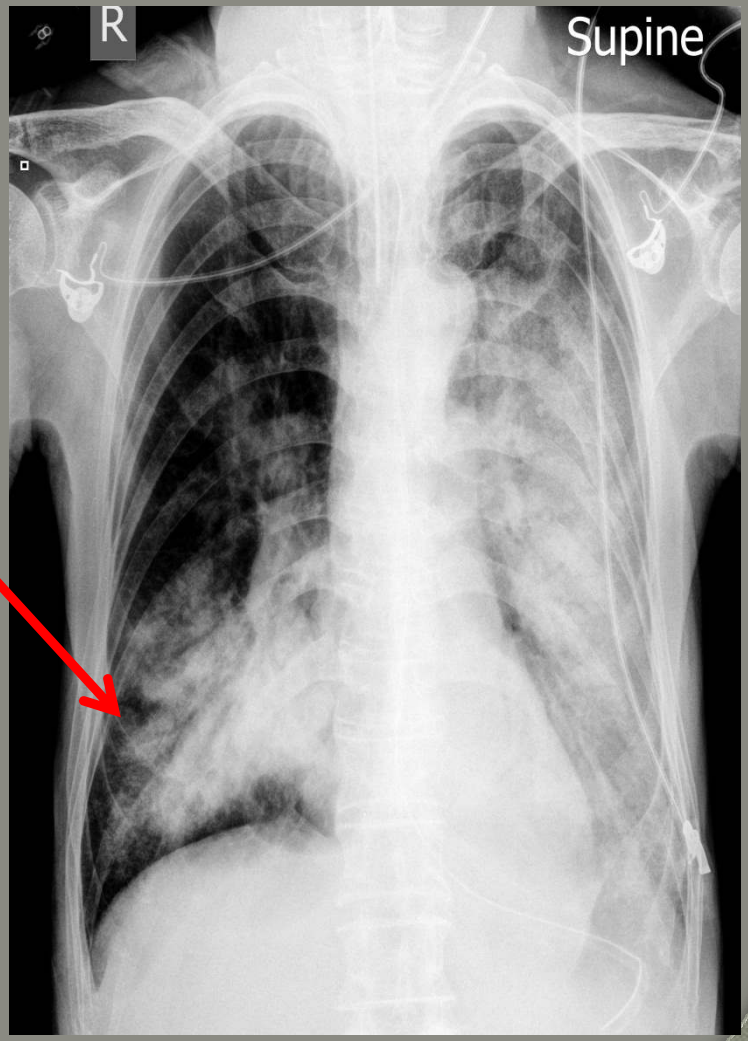
Patho-radiology of pneumonia

- Abnormal inflammatory condition of the lungs as response to noxious stimuli
- Typical pneumonia often characterized as inflammation of the parenchyma of lung (i.e. alveoli) and alveolar filling with fluid (consolidation and exudation)
- X-ray sign for consolidation: air-bronchogram

Typical pneumonia

Air-bronchogram

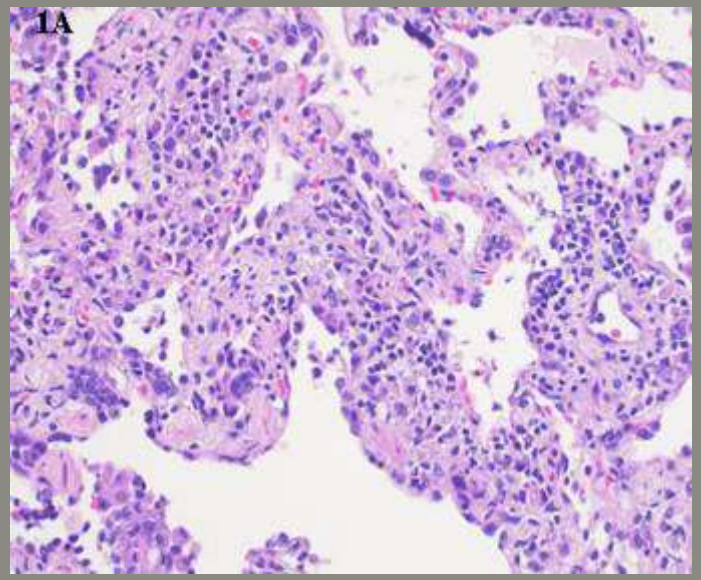


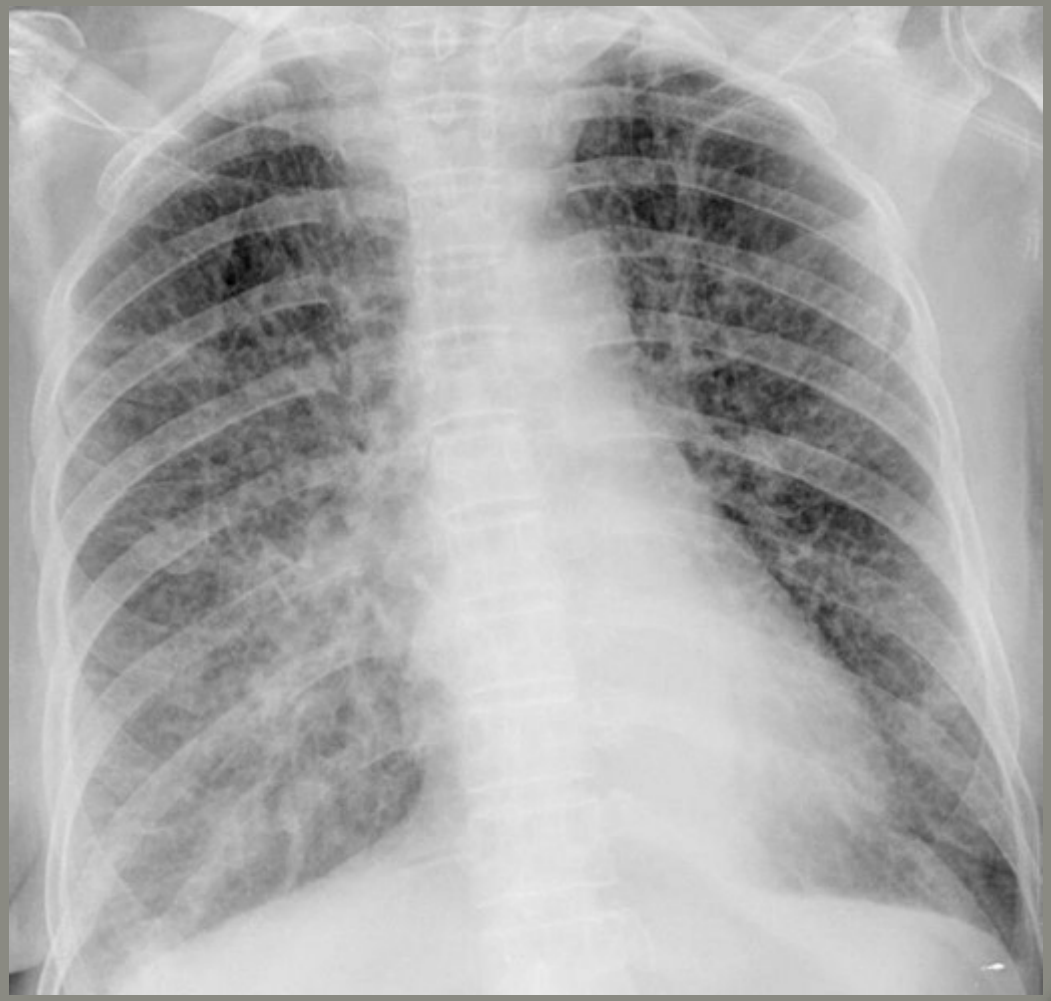


Atypical pneumonia

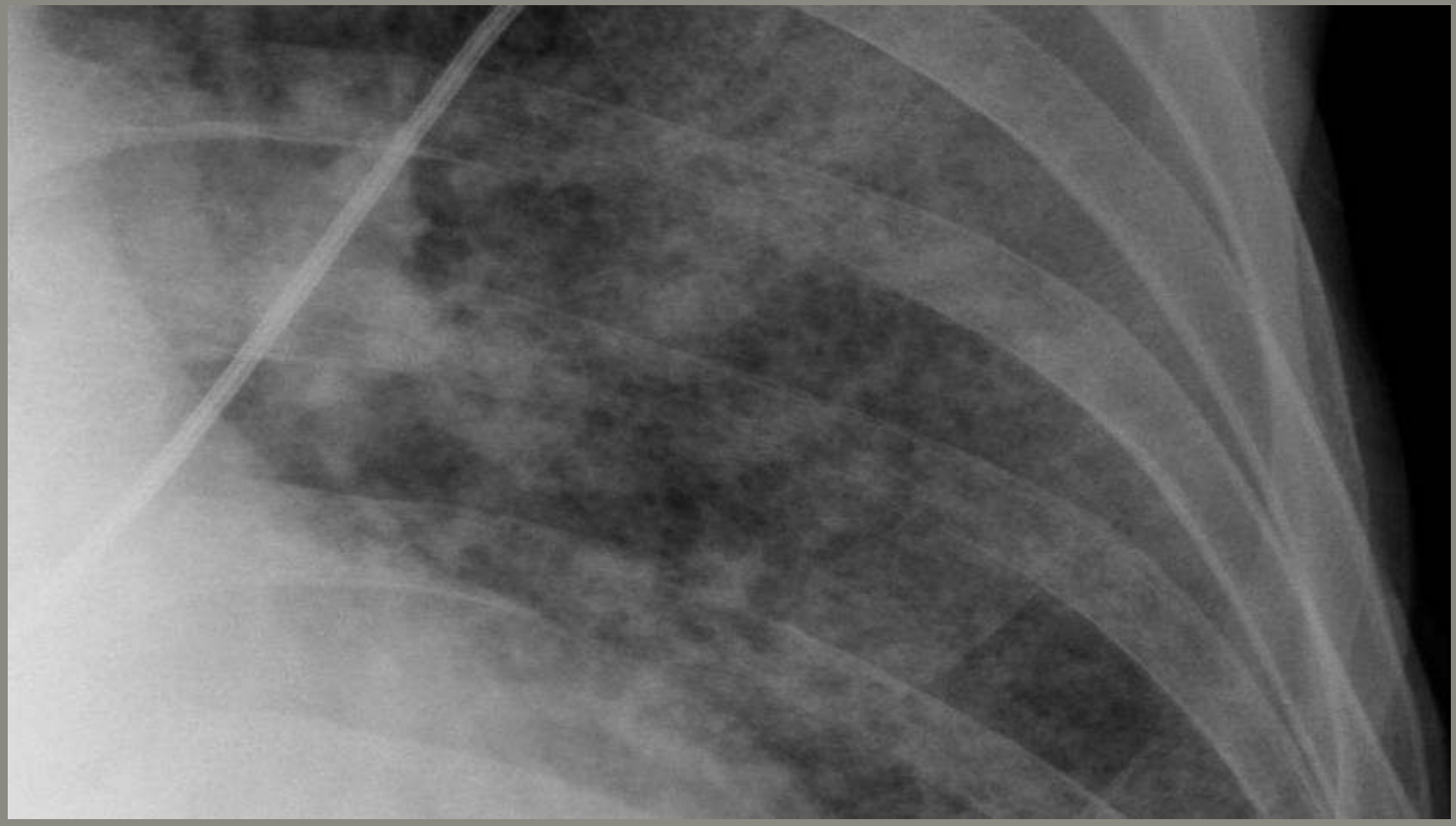
Interstitial pattern

- Ground-glass
- Reticular shadow
- Fine nodules

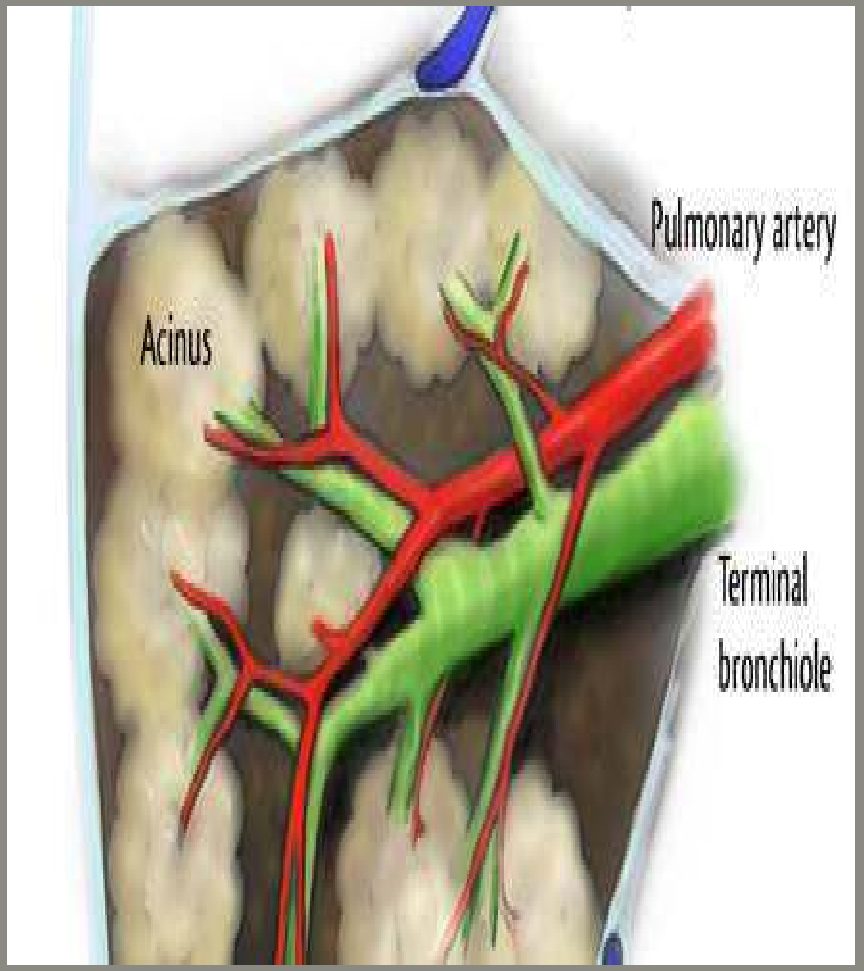




Closer Look

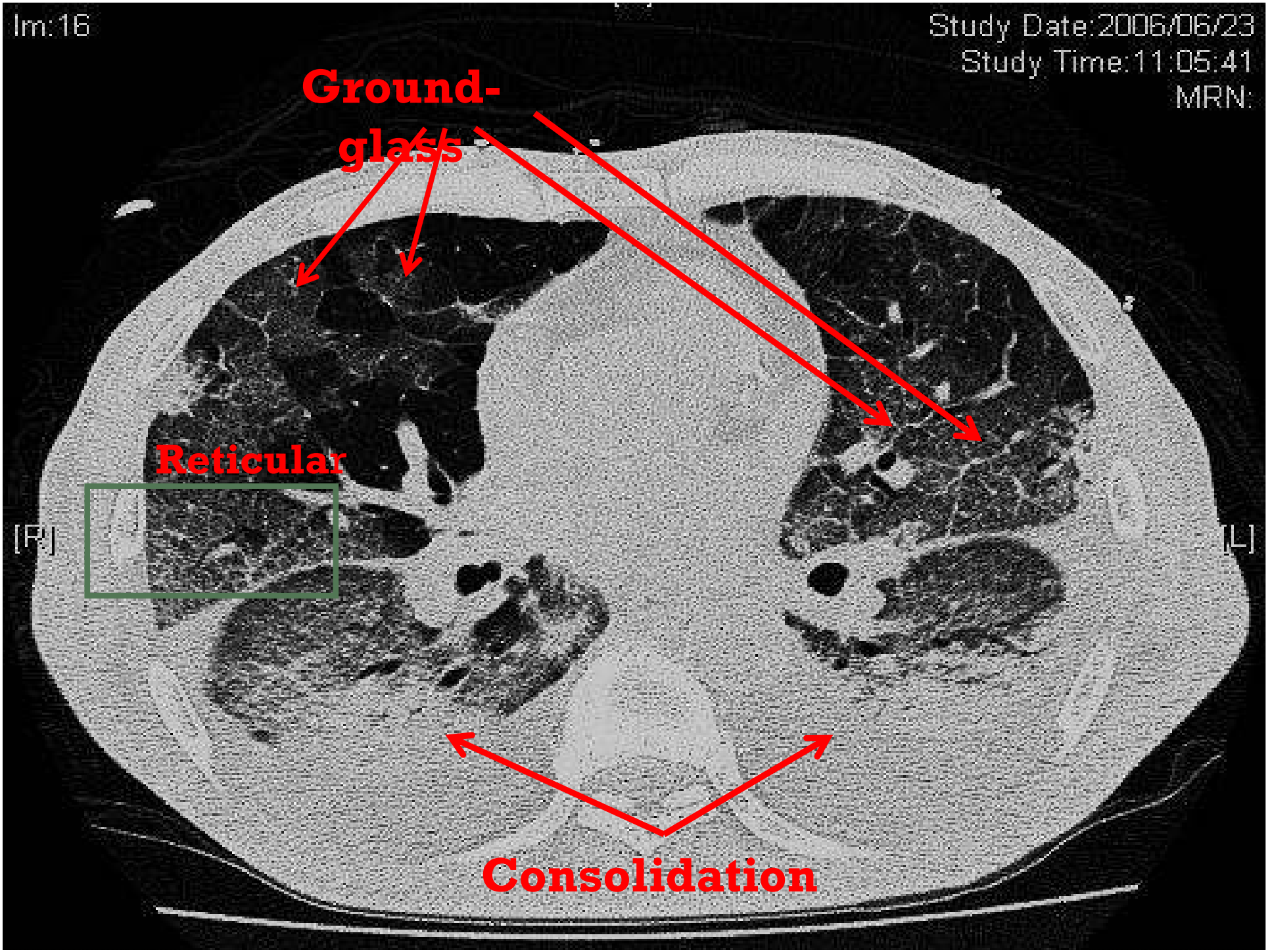


What reticular shadow means



- Fluid or cells accumulate in the intralobular septum

1. Pulmonary fibrosis
2. Prolonged interstitial pneumonitis
3. Nodular thickening: seen in sarcoidosis & lymphangitis carcinomatosis


Im:16
Study Date:2006/06/23
Study Time:11:05:41
MRN:
Ground-glass
Reticular
[R]
[L]
Consolidation

Comparison

Typical pneumonia

- No age limitation
- Purulent sputum
- Extra-pulmonary presentation less
- Consolidation
- Expansion in volume
- Pleural effusion +/-
- Causes: bacteria

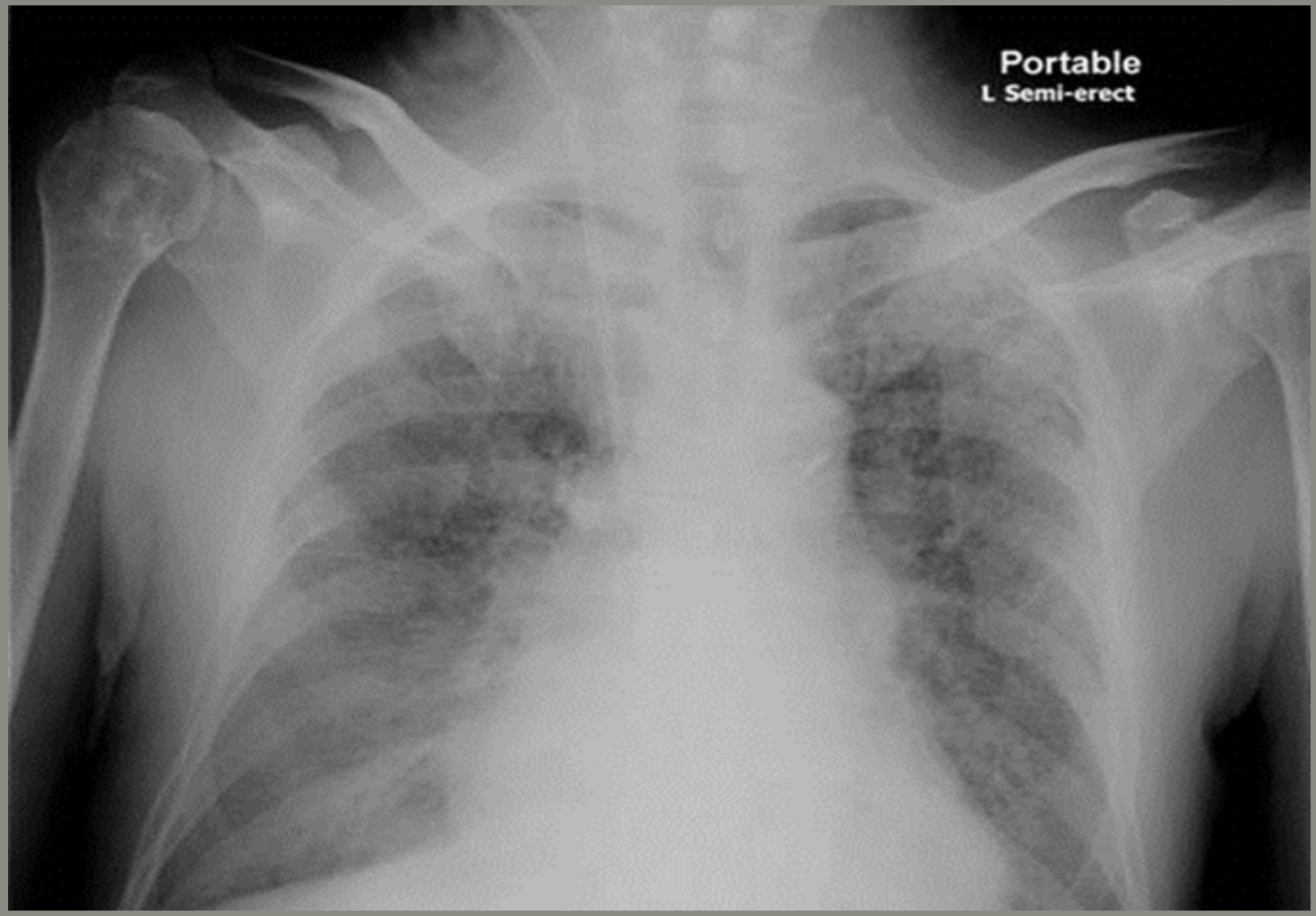
Atypical pneumonia

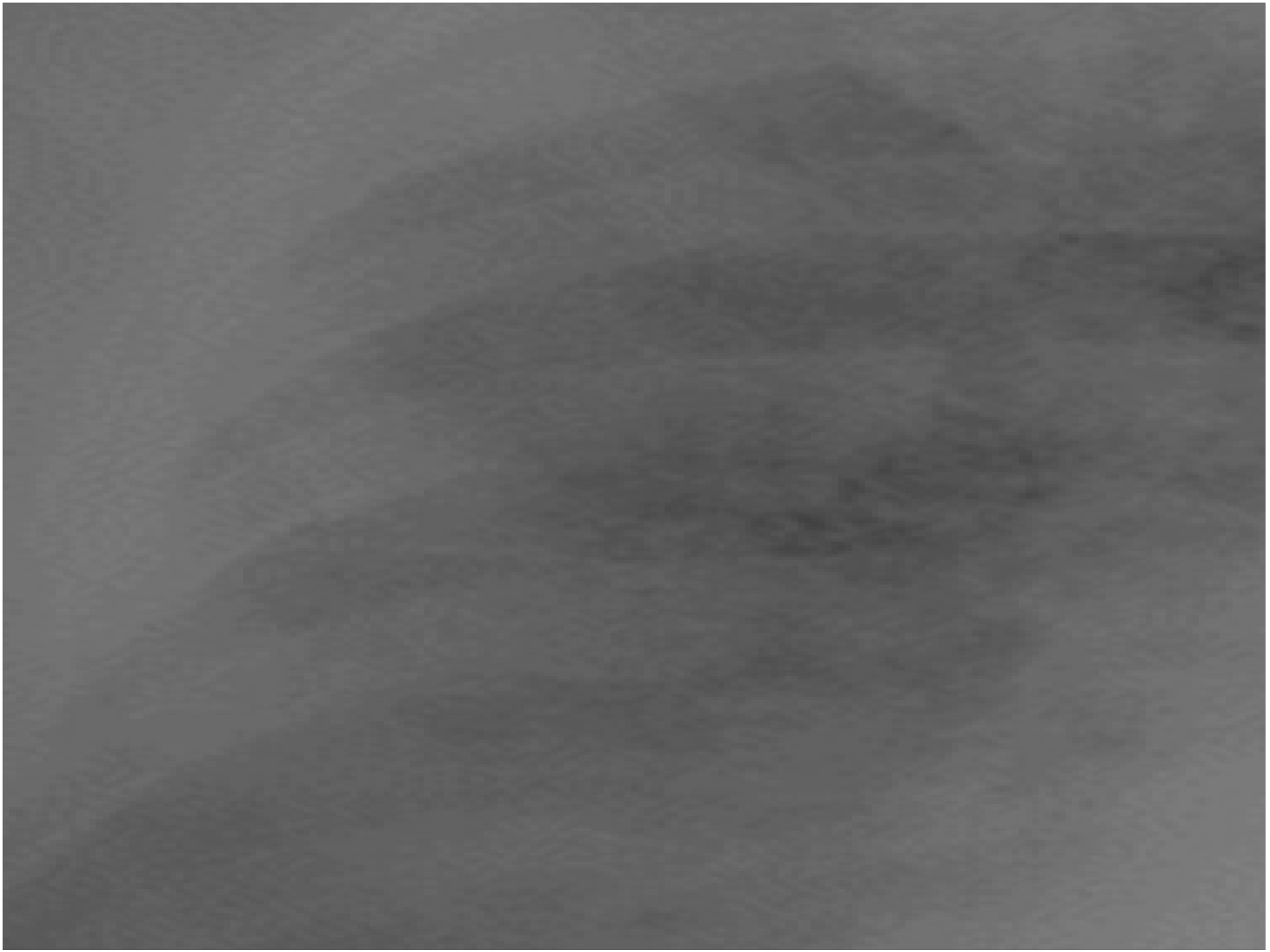
- Affect young adults
- Unproductive cough
- Hematological, neurological, GI
- Ground-glass
- Reticular shadow
- Nil pleural effusion
- Atypical bacteria, virus, fungus

Differential diagnosis

- Sputum retention
- Acute exacerbation of COPD
- Pulmonary edema
- Pulmonary embolism
- Radiation Pneumonitis
- Chemical pneumonitis
- Inhalational pneumonitis

“Special form of pneumonia”





Miliary TB

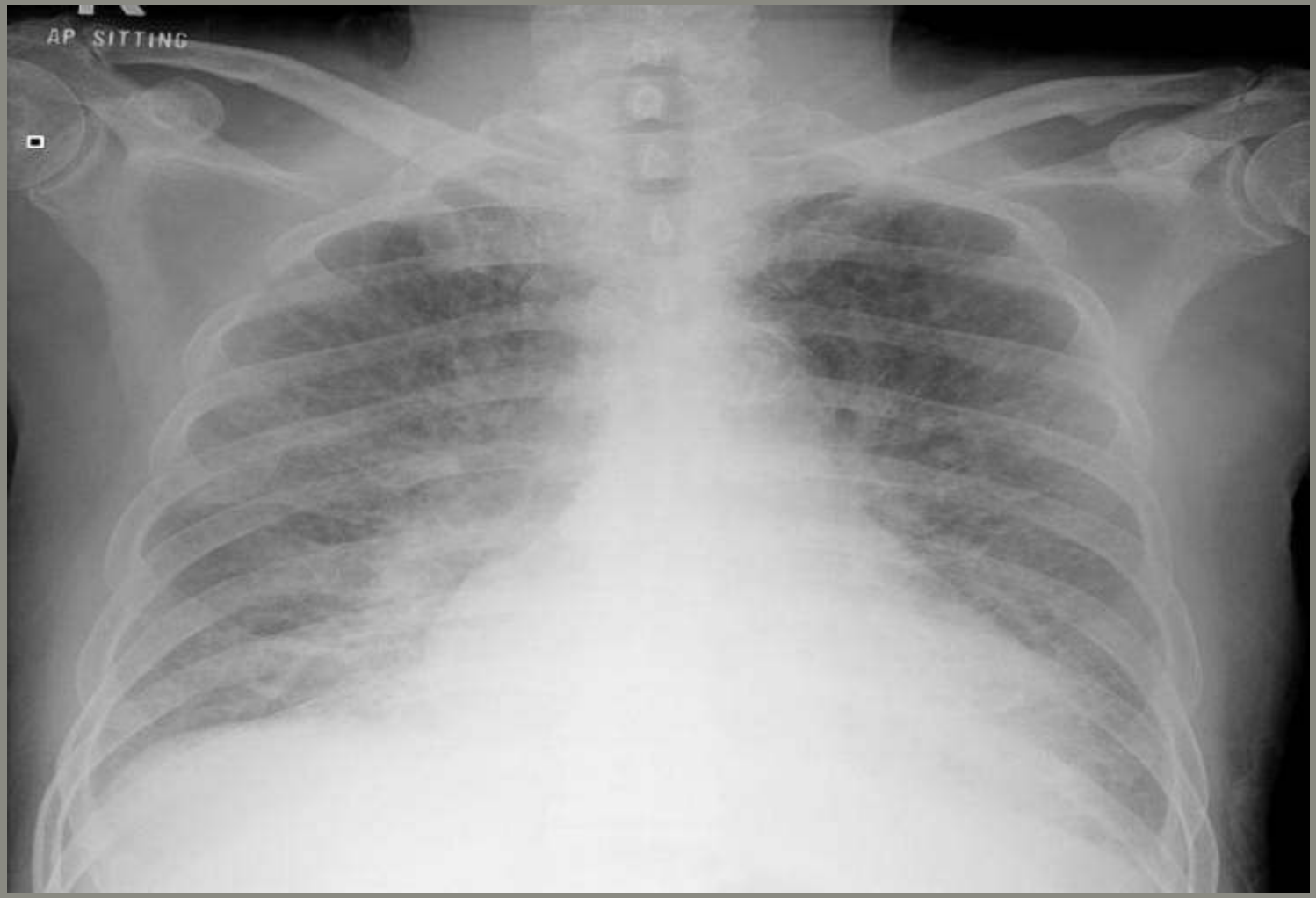
- Millet-like (mean 2 mm; range, 1-5 mm) seeding of TB bacilli in the lung
- This pattern is seen in 1-3% of all TB cases
- ~ 50% of cases are undiagnosed ante-mortem
- 20-30% sputum smear +ve
- May be associated with cavitating primary focus of infection

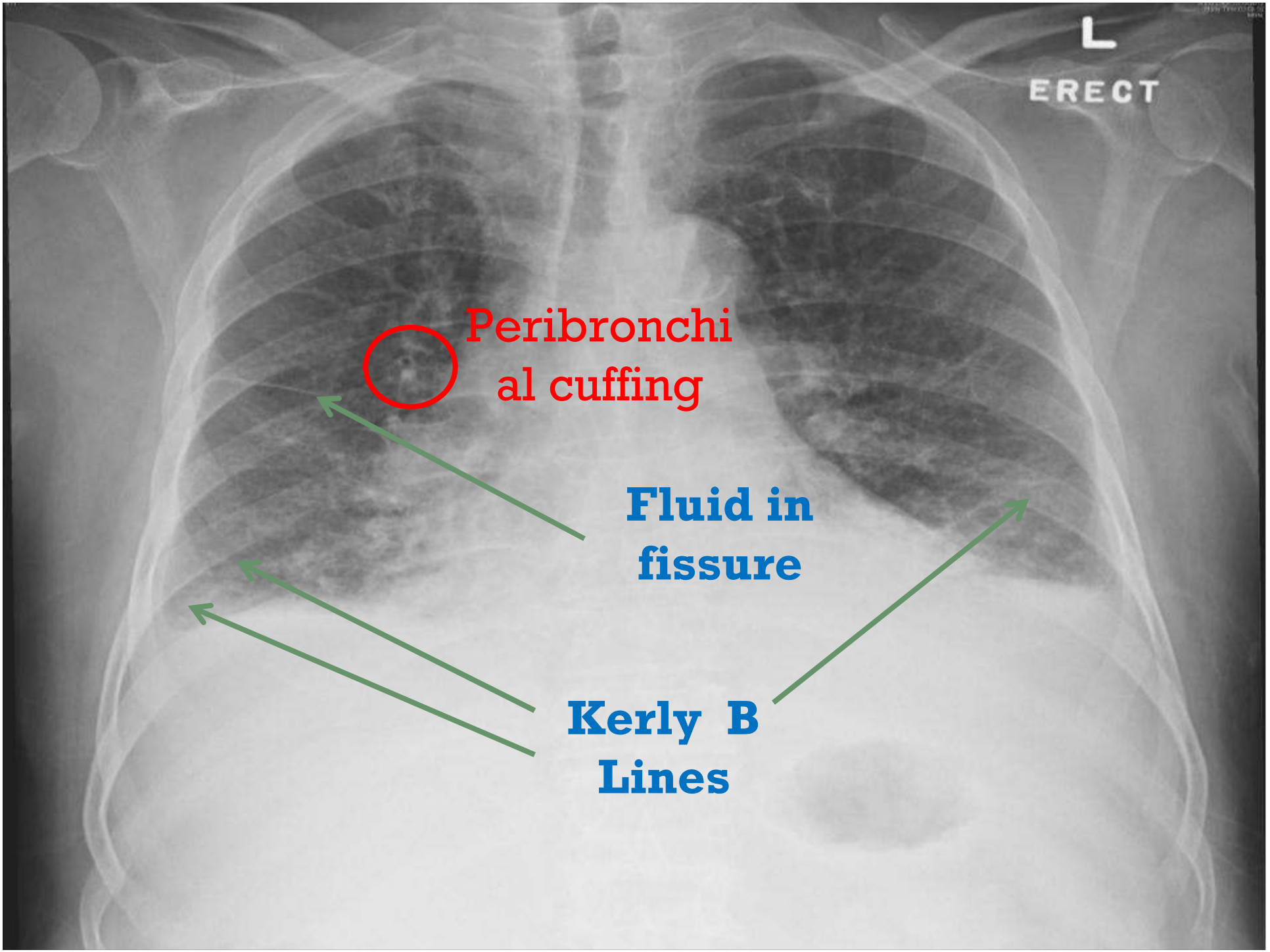
Miliary shadow

- Diffuse numerous nodules ≤ 3mm, caused by

1. Miliary TB
2. Viral (VZV)
3. Granulomatous disease
   - Histoplamosis/ blastomycosis/ cryptoccus
4. Hypersensitivity pneumonitis
5. Metastasis (Thyroid, RCC, Pancreas, Breast, Melanoma, lymphangitis carcinomatosis)
6. Pneumoconiosis

Need airborne precaution?




L
ERECT
Peribronchi
al cuffing
Fluid in
fissure
Kerly B
Lines

CXR features of CHF

- Pre-existing cardiomegaly (Often)
- Stage 1 → Pulmonary venous hypertension
  - Upper lobe pulmonary venous diversion
  - Veins diameter > 3mm at the 1st/ 2nd intercostal space
- Stage 2 → Interstitial oedema
  - Kerley B Lines (Visible interlobular septa, after being filled by fluid, more obvious at basal)
  - Peribronchial cuff
  - Stage 3 → pulmonary oedema
    - Fluid accumulates in alveolar/ pleural space

衞生署

衞生防護中心乃衞生署轄下執行與特別防及控制的專業部門

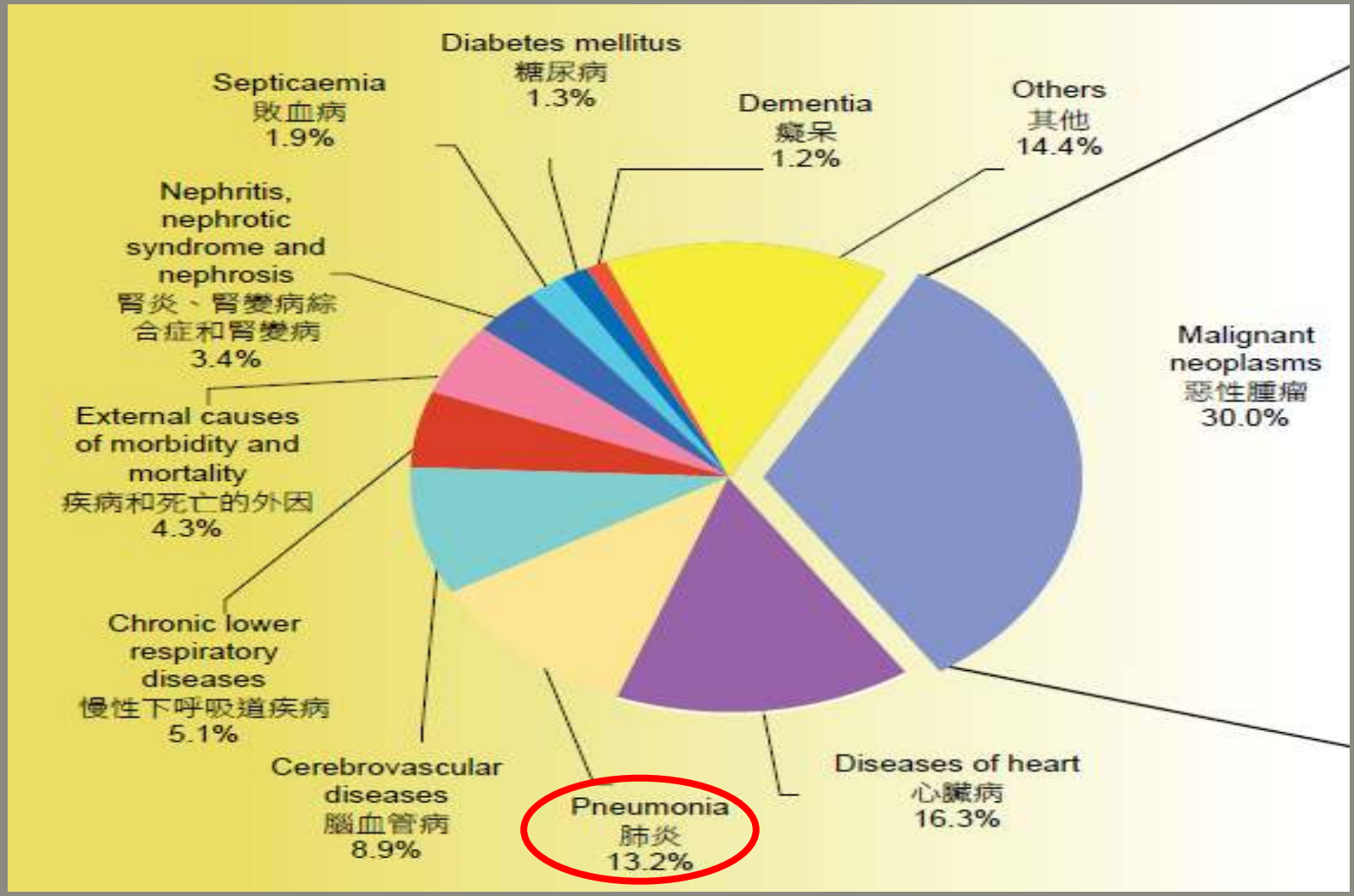
主要死因的死亡人數(根據ICD第十次修訂本)：2001 - 2010
死因排序是根據二零一零年的死亡數字。

死因	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010
1. 惡性腫瘤 (ICD10：C00-C97)	11406	11658	11510	11791	12310	12093	12316	12456	12839	13076
2. 心臟病 (ICD10：I00-I09, I11, I13, I20-I51)	4703	4969	5311	5866	5868	5619	6372	6777	6414	6636
3. 肺炎 (ICD10：J12-J18)	3026	3194	3877	3676	4291	4201	4978	5486	5312	5814
4. 腦血管病 (ICD10：I60-I69)	3130	3218	3462	3416	3434	3302	3513	3691	3443	3423
5. 慢性下呼吸道疾病 (ICD10：J40-J47)	2114	2075	2102	2123	2261	1924	2096	2103	1912	2093
6. 疾病和死亡的外因+ (ICD10：V01-Y89)	1844	2068	2044	2243	2150	1961	1854	1766	1938	1864
7. 腎炎，腎變病綜合症和腎變病 (ICD10：N00-N07, N17-N19, N25-N27)	1053	1055	1184	1182	1261	1287	1347	1419	1448	1493
8. 敗血病 (ICD10：A40-A41)	424	467	572	615	701	676	737	797	736	826
9. 癡呆 (ICD10：F01-F03)	252	289	256	276	283	288	317	495	638	767
10. 糖尿病 (ICD10：E10-E14)	676	574	783	728	602	511	506	548	492	522
其他原因	4677	4749	5322	5405	5522	5553	5927	5992	5875	6185
綜合所有原因	33305	34316	36423	37321	38683	37415	39963	41530	41047	42699

註:
表內的死亡數字是根據「已登記」死亡人數編製。
括號內顯示了該類疾病分類的編碼。

Consistently, the third leading cause of deaths

Situation in Hong Kong




孫明揚染退伍軍人症
蘋果日報
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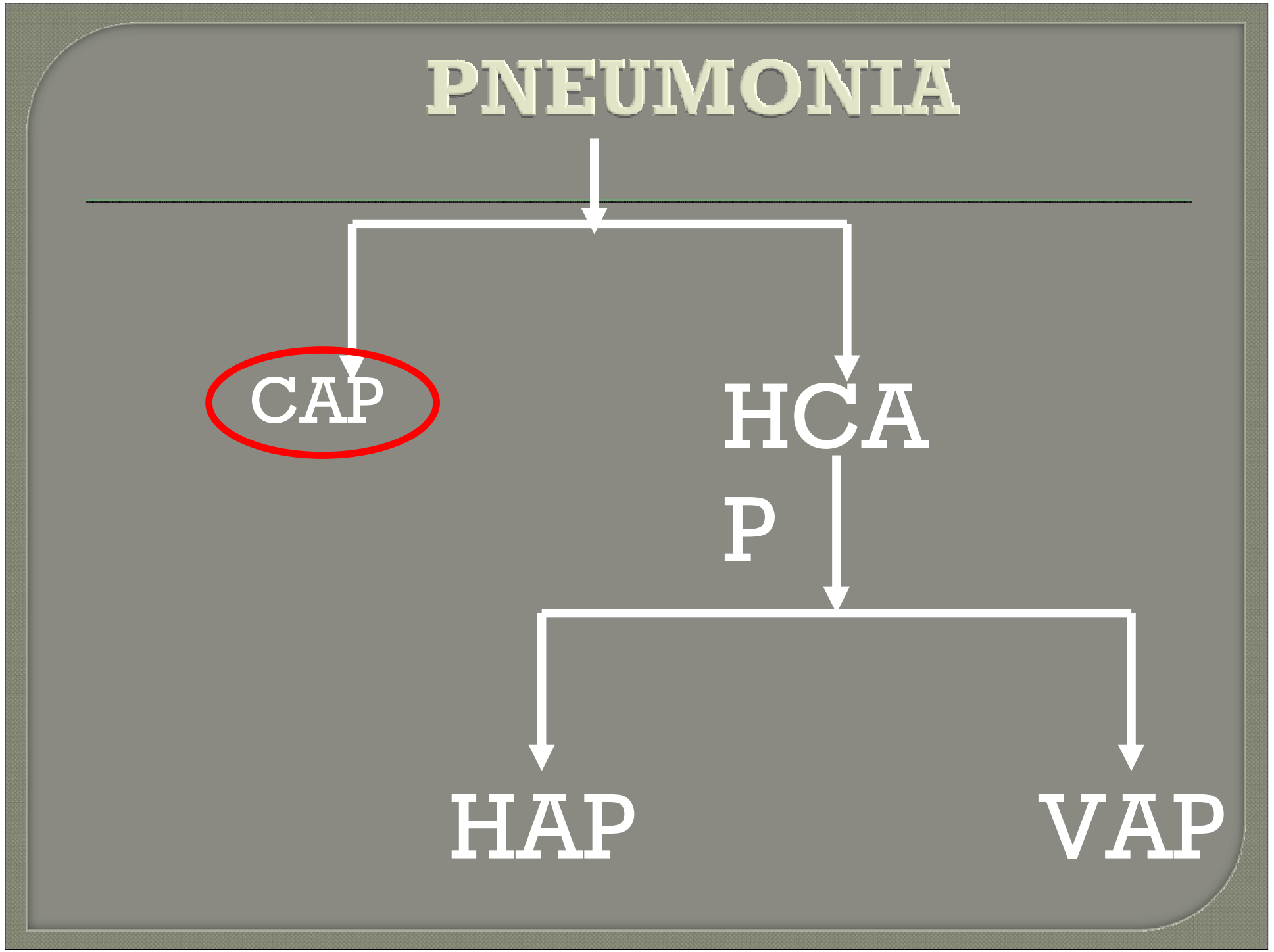
東方互動
退伍軍人症
特別服務台
Special Help Desk for
Legionnaires' Disease


衞生防護中心
Centre for He ection
Centre


楊啟彥


PNEUMONIA
CAP
HCA
P
HAP
VAP

Epidemiology of CAP

- The annual incidence rate is 6/1000 in the 18-39 age group in Britain
- This rises to 34/1000 in people aged 75 years and over
- Admission to hospital is needed in 20-40% of patients with CAP
- About 5-10% of all hospitalized CAP patients require ICU admission
- The overall CAP mortality is 5-10%
- ICU cases mortality 30-60%

Risk Factors for CAP

- **Demographics**
  - **Age, alcoholism, smoking**
- **Social Factors**
  - Infirmary, old age home
- **Chronic lung conditions**
  - Asthma/ COPD
  - Bronchiectasis
  - Obstructive lesion in airways
- **Immunocompromized state**
  - DM
  - Chronic steroid
  - Hyposplenism
  - Acquired/ congenital immunodeficiency
- **Therapeutics related**
  - Inhaled corticosteroid
  - Proton pump inhibitor

Aetiology

- Bacteria
  - Pneumococcus, H influenzae, Moraxella, Klebsiella, streptococcus species, CA-MRSA
- Virus
  - Influenza, parainfluenza, adenovirus, RSV, Rhino
- Mycobacteria
- Fungus
  - Candida, Aspergillus, Coccidiomycetes, PCP
- Parasite
  - Protozoa, Strongyloides
- Unclassified
  - Chlamydia, mycoplasma, rickettsia

Pathogens in at-risk group

- Alcoholism
  - Klebsiella, pneumococcus, anaerobic oral flora
- COPD and/or Smoking
  - Pneumoccus, H. influenza, Moraxella, Pseudomonas (in advanced disease)
- Structural lung disease
  - GNB, Pseudomonas, Burkholderia, Staphylococcus
- Impaired airway protection
  - Oral anaerobes, GNB
- HIV
  - PCP, Pneumococcus, TB, CMV, Candidiasis

Lam, chu. Medical Bulletin 2008; 13: 17-19

Epidemiological links	Organisms
Air conditioning, cooling towers, travel and hotel, mist machine, hospital	*Legionella pneumophila*
Cattle, sheep, goats	*Coxiella burnetii*
Windstorm in endemic area (e.g. California)	*Coccidioides immitis*
Homeless, prison	Tuberculosis
Military camp	*Streptococcus pneumoniae, Chlamydophila pneumoniae,* adenovirus, *Mycoplasma penumoniae*
Nursing home	Influenza A or B, *Chlamydophila pneumoniae,* Respiratory Syncytial Virus, *Streptococcus pneumoniae*
Bat caves	*Histoplasma capsulatum*
Turkeys, chickens, ducks, birds	Influenza A, *Chlamydophila psittaci*
Rabbits	*Francisella tularensis*
Health care worker	Tuberculosis, HIV, Influenza A or B, SARS
Thailand/SE Asia	*Burkholderia pseudomallei*
Alcoholism	*Streptococcus pneumoniae, Klebsiella pneumoniae, Staphylococcus aureus,* anaerobes

HK, nil pathogen in 44% of 439 cases

- 49% with 1 , 5.7% with 2, 1.8% with 3 pathogens identified in same episode
- Pneumococcus 16.9%
- Hemophilus 8.9%
- Other GNB 9.8%
- Flu A + Flu B + ParaFlu 12.2%
- Mycoplasma 8.9%
- TB 1.1% !!

Yeung, PMH

Management of CAP

- Triage site of care according to severity
- Select appropriate case to admit ICU
- Cover pathogens according to clinical profiles and local experience
- Organ support for failure
- Watch out of drug resistance
- Tackle complications promptly
- Controversy

Pneumonia Severity Index for Adult CAP

Age	years old 1 point per year
Female?	Yes -10
Nursing home resident?	Yes +10
Neoplastic disease history?	Yes +30
Liver disease?	Yes +20
CHF?	Yes +10
Cerebrovascular disease?	Yes +10
Renal disease?	Yes +10
Altered mental status?	Yes +20
Respiratory rate > 29?	Yes +20
Systolic blood pressure < 90?	Yes +20
Temperature < 35C (95F) or > 39.9C (103.8F)?	Yes +15
Pulse > 124?	Yes +10
pH < 7.35?	Yes +30
BUN > 29?	Yes +20
Sodium < 130?	Yes +20
Glucose > 249 (US) or > 13.8 (SI) ?	Yes +10
Hematocrit < 30%?	Yes +10
Partial pressure of Oxygen < 60?	Yes +10
Pleural effusion on x-ray?	Yes +10

http://www.mdcalc.com/psi-port-score-pneumonia-severity-index-adult-cap/

PSI risk categories

- Class I: all factors NEG → 0.1% died
- Class II: score < 70 → 0.6% died
- Class III: score 71-90 → 2.8% died
- Class IV: score 91-130 → 8.2% died
- Class V: score >130 → 29.2% died

30-day mortality

Medisgroup study 1989

BTS CURB-65 criteria

- CURB variables :
  - C-Confusion
  - U-Urea(>7 mmol/L)
  - R-Respiratory rate (>30)
  - B-Blood pressure (<90 sys or <60 diastolic)
- Age > 65
- Mortality: Score 0 → 0.7%; Score 1 → 3.2%; Score 2 → 13%; Score 3 → 17%; Score 4 → 41.5%; Score 5 → 57%

Lim et al. Thorax 2003; 58: 377-382

BTS 2004 recommends

- Score 0 or 1
  - Low risk patients, may treat at OPD
- Score 2
  - Raised risk of death, consider in-patient
  - Needs clinical judgement
- Score 3 or more
  - Severe pneumonia, need urgent in-patient

Comparing different predictors tool

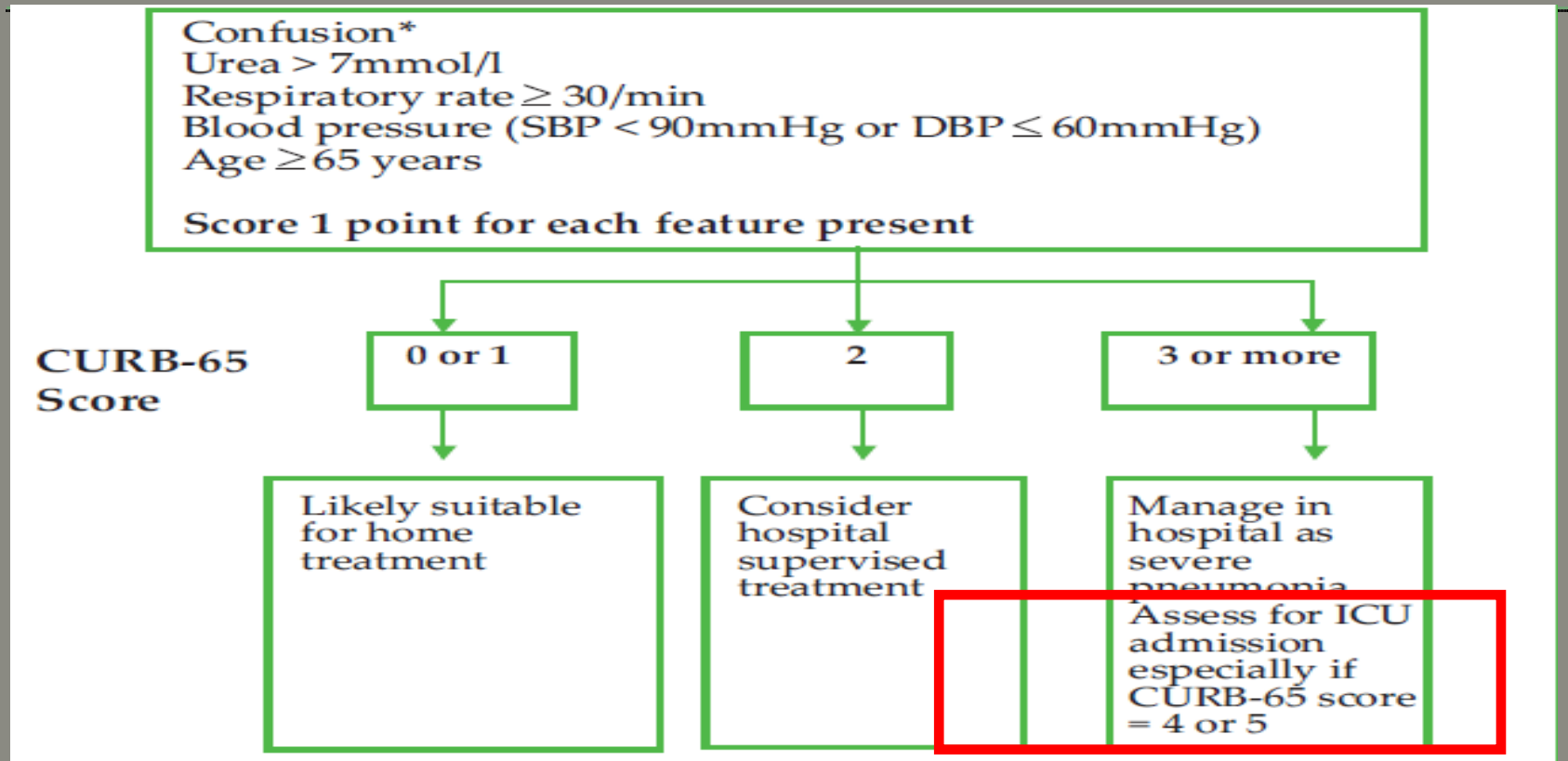
Table 1 Pooled performance characteristics of severity scores for predicting mortality in community-acquired pneumonia

	Sensitivity	Specificity	PLR	NLR	DOR	AUROC
PSI						
≥III	98.2% (97.8–98.5%)	38.8% (38.4–39.2%)	1.4 (1.3 to 1.6)	0.08 (0.06 to 0.12)	18.1 (11.5 to 28.5)	0.88 (0.02
≥IV	91.4% (90.8–92.1%)	49.5% (49.2–49.9%)	1.9 (1.8 to 2.0)	0.2 (0.17 to 0.24)	9.6 (8.0 to 11.6)	0.82 (0.01
≥V	63.2% (62.1–64.3%)	83.6% (83.4–83.9%)	4.1 (3.7 to 4.5)	0.5 (0.44 to 0.58)	8.4 (7.2 to 9.8)	0.81 (0.01
CURB65						
≥1	98.6% (97.6–99.2%)	26.5% (26.5–27.4%)	1.2 (1.1 to 1.3)	0.10 (0.06 to 0.16)	13.6 (9.3 to 22.3)	0.86 (0.02
≥2	89.1% (87.1–90.8)	52.2% (51.3–53.1%)	1.7 (1.5 to 1.9)	0.21 (0.15 to 0.30)	8.3 (5.8 to 11.9)	0.81 (0.02
≥3	62.0% (59.3–64.6%)	80.8% (80.2–81.4%)	3.1 (2.7 to 3.5)	0.46 (0.40 to 0.54)	7.0 (5.8 to 8.3)	0.79 (0.01
≥4	29.0% (26.3–31.8%)	95.3% (95.0–95.7%)	5.4 (4.4 to 6.6)	0.73 (0.65 to 0.83)	7.8 (6.3 to 9.6)	0.80 (0.01
CRB65						
≥1	94.4% (94.2–94.6%)	38.3% (38.1–38.5%)	1.3 (1.2 to 1.5)	0.15 (0.10 to 0.22)	9.4 (5.8 to 15.3)	0.82 (0.03
≥2	72.7% (69.3–76.0%)	70.8% (69.8–71.8%)	2.4 (1.9 to 3.0)	0.39 (0.28 to 0.54)	6.3 (4.4 to 9.2)	0.78 (0.02
≥3	29.1% (28.8–29.5%)	90.9% (90.8–91.0%)	4.4 (3.6 to 5.5)	0.72 (0.66 to 0.79)	6.9 (4.9 to 9.5)	0.79 (0.02

- Overall performance similar for all three tools
- Best negative likelihood ratio for PSI low-risk group
- CURB-65/ CRB-65 performed best to identify high-risk groups

Thorax 2010; 65: 878-883

Lam, chu. Medical Bulletin 2008; 13: 17-19



*Defined as a Mental Test Score of 8 or less, or new disorientation in person, place or time.

The Abbreviated Mental Test (each question scores 1 mark, total 10 marks): Age, date of birth, time (to nearest hour), year, hospital name, recognition of two persons, recall address, date of First World War, name of monarch, count backwards 20→1

ATS/ IDSA guideline

- 1 major or 3 minor criteria for ICU care
- Major criteria:
  - Invasive mechanical ventilation
  - Septic shock in need of vasopressor
- Minor criteria:
  - Respiratory rate 30 or above per minute
  - PaO2/ FiO2 ratio 250 or less
  - Multi-lobar infiltrates on CXR
  - New onset confusion/ disorientation
  - Hypotension requiring aggressive IVF
  - Hypothermia < 36 Celsius
  - Thrombocytopenia: Platelet count <100
  - Leukopenia: total WCC <4
  - Uremia: Urea 7mmol/L or more

Clinc Infect Dis 2007;44 S2: 27-72

Adequate workup

- Blood cultures
  - +ve in 5-14% of pre-treated patients
  - Adequate volume and more than one
- Gram-stain and cultures
  - No evidence to favor lower tract specimen in terms of clinical response and survival
  - Lower tract sample more likely affect change of A/B
- Urine antigen
  - Sensitivity limited in Legionella and Pneumococcus
- Serology/ Molecular
  - Essentially for atypical pathogens

Tested for virus?

- Rapid antigen test
- Immuno-florescence test
- Polymerase Chain Reaction (PCR) method to detect genetic material
  - Reverse transcriptase (RT-PCR) for RNA virus
  - Direct PCR for DNA virus
  - Mycoplasma
  - Mycobacterial TB
  - Chlamydia
  - Flu/ ParaFlu/ Adeno/ RSV/ Metapneumo/ Rhino

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近月呼吸系統病原的病毒分離測試結果

日期	25/2-1/3	3/3-8/3	10/3-15/3	17/3-20/3
甲型流感	77	160	189	156
乙型流感	97	98	204	185
呼吸道合胞體病毒	35	49	70	60
腺病毒	20	29	36	45
副流感	27	40	40	33
鼻病毒	5	2	3	2
肺炎支原體	9	3	9	14

資料來源：衞生防護中心

伊院兒科三女嬰 染RSV

【本報訊】呼吸道合胞體病毒（RSV）近期非常活躍，不但學校有幼童集體感染，伊利沙伯醫院兒科病房也爆發，三名一歲大女嬰自八月廿四日起出現呼吸道感染，證實感染RSV，其中一名有長期病患的女嬰需深切治療，情況嚴重，其餘兩名女嬰一人隔離治療，情況穩定，另一人已康復。該病房已停收新症和加強感染控制措施。

傳染病專科醫生勞永樂表示，流感不活躍時，RSV爆發是意料之內，家長探病時可能將病毒帶入病房，加上醫院病房環境擠迫，醫護人員照顧嬰兒時，感染控制措施一鬆懈，可致病毒爆發。RSV進入呼吸道後，令呼吸道出現大量分泌物，嬰兒呼吸道幼細，易被分泌物阻塞，併發支氣管炎或肺炎，嚴重可致呼吸衰竭甚至死亡，對嬰兒殺傷力很大。

伊利沙伯醫院三名嬰兒感染呼吸道合胞體病毒。（林少權攝）

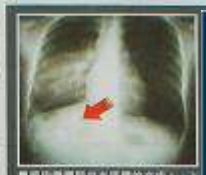
醫院偏肺病毒爆發 七病人隔離治療

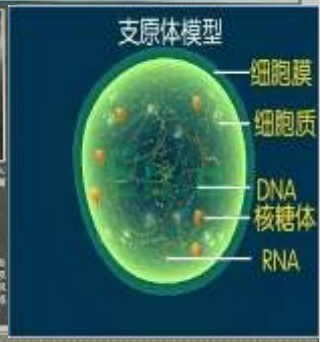
屯門醫院弱智科病房爆發人類偏肺病毒感染，病房已暫停接收新症，並實施有限度探訪及出院安排。目前七名病人正接受隔離治療，情況穩定，另一名染病職員則曾經休假，現已復工。

女職員疑感染

人類偏肺病毒於○一年首先被發現，一旦感染，病毒可入侵肺部、氣管及上呼吸道，出現近似感染流感的症狀。人類偏肺病毒一般影響兒童，部份病童或會出現中耳炎、腹瀉、嘔吐、出疹及發燒抽筋。資料顯示，有關的弱智科病房，先後有七名二十至四十六歲病人，及一名女職員發燒及呼吸道感染徵狀，其中四名病人對人類偏肺病毒測試結果呈陽性反應。

變種肺炎專襲年輕人 少女險死





Methods to obtain lower tract specimens

- Bronchoscopic
  - BAL
  - PSB
- Non-bronchoscopic
  - Tracheobronchial aspiration
  - Mini-BAL
- **Bronchoscopic sampling does not improve mortality**, length of hospital stay, duration of MV or length of ICU stay. However, it may lead to a narrower antimicrobial regimen and/or more rapid de-escalation of antimicrobial therapy

BAL

- A fiberoptic bronchoscope is directed to the area of concern within the lung, which is flushed with sterile fluid.
- Quantitative cultures are usually obtained
- The large volume of the specimen makes it useful for detecting nonbacterial pathogens.
- Sensitivity ranges from 42-93%
  Specificity 45-100%

Protected specimen brush

- Specialized catheter containing a brush
- When the area to be sampled is visualized in FOB, the brush is pushed through a plug and a sample obtained by gentle scraping.
- Sample is low volume, it is not appropriate for detection of non-bacterial pathogens.

Mini-BAL

- Non-Bronchoscopic BAL
- Telescoping catheter system protects the end of the catheter from contamination during insertion. The catheter is advanced approximately 30 cm and the inner cannula is then gently advanced until it meets resistance. Thirty mL of sterile saline is injected and suctioned.
- Usually the lower lobe is sampled
- Bleeding is a potential complication

Quantitative culture

- Different Thresholds for different sampling methods
  - 10^6 cfu/ml: tracheobronchial aspiration
  - 10^4 cfu/ml: BAL
  - 10^3 cfu/nl: PSB
- Quantitative cultures derived from nonbronchoscopic specimens tend to have a lower specificity than those derived from bronchoscopic specimens
- However, this is balanced by a higher sensitivity, resulting in comparable diagnostic accuracy
- Quantitative cultures do not appear to improve clinical outcomes. They may lead to more judicious use of antibiotics

Role of procalcitonin?

- Not use routinely to guide the decision of whether to initiate antibiotics in patients with suspected VAP
- May be helpful in the decision as to whether to discontinue antibiotic therapy
- Progressive increases in serum procalcitonin have been associated with septic shock and mortality

Adequate organ support for CAP as severe sepsis

Surviving sepsis campaign

Early goal-directed therapy

- Goal-directed resuscitation should begin immediately upon recognition of the syndrome and target:
  - CVP 8-12mmHg
  - MAP >65mmHg
  - Urine Output >0.5ml/kg/hour
  - Central Venous Oxygen Saturation >70%
- Within first 6 hours, if SaCV is less than 70%, RBC transfusion or dobutamine infusion should be employed
- Either norepinephrine or adrenaline as vasopressor agents

Other SSC recommendation

- Crystalloid or colloid solutions are equally effective in resuscitation
- Appropriate cultures immediately
- Antibiotics should be given within first hour, but after cultures being obtained. De-escalate as appropriate
- Low-dose steroids if patients still need vasopressors after adequate IVF resuscitation
- Sedation with protocol and daily interruption
- Nutrition/ glycemic control

Initial resuscitation (first 6 hrs)

- Begin resuscitation immediately in patients with hypotension or elevated serum lactate >4 mmol/L; do not delay pending ICU admission (1C)
- Resuscitation goals (1C)
  CVP 8–12 mm Hg[a]
  Mean arterial pressure ≥ 65 mm Hg
  Urine output ≥0.5 mL·kg^{-1}·hr^{-1}
  Central venous (superior vena cava) oxygen saturation ≥70% or mixed venous ≥65%
  - If venous oxygen saturation target is not achieved (2C)
    Consider further fluid
    Transfuse packed red blood cells if required to hematocrit of ≥30% and/or
    Start dobutamine infusion, maximum 20 μg·kg^{-1}·min^{-1}

Diagnostic

- Obtain appropriate cultures before starting antibiotics provided this does not significantly delay antimicrobial administration (1C)
  Obtain two or more BCs
  One or more BCs should be percutaneous
  One BC from each vascular access device in place >48 hrs
  Culture other sites as clinically indicated
- Perform imaging studies promptly to confirm and sample any source of infection, if safe to do so (1C)

Antibiotic therapy

- Begin intravenous antibiotics as early as possible and always within the first hour of recognizing severe sepsis (1D) and septic shock (1B)
- Broad-spectrum: one or more agents active against likely bacterial/fungal pathogens and with good penetration into presumed source (1B)
- Reassess antimicrobial regimen daily to optimize efficacy, prevent resistance, avoid toxicity, and minimize costs (1C)
  - Consider combination therapy in *Pseudomonas* infections (2D)
  - Consider combination empiric therapy in neutropenic patients (2D)
  - Combination therapy ≤3–5 days and de-escalation following susceptibilities (2B)
- Duration of therapy typically limited to 7–10 days; longer if response is slow or there are undrainable foci of infection or immunologic deficiencies (1D)
- Stop antimicrobial therapy if cause is found to be noninfectious (1D)

Source identification and control

- A specific anatomic site of infection should be established as rapidly as possible (1C) and within first 6 hrs of presentation (1D)
- Formally evaluate patient for a focus of infection amenable to source control measures (e.g. abscess drainage, tissue debridement) (1C)
- Implement source control measures as soon as possible following successful initial resuscitation (1C) (exception: infected pancreatic necrosis, where surgical intervention is best delayed) (2B)
- Choose source control measure with maximum efficacy and minimal physiologic upset (1D)
- Remove intravascular access devices if potentially infected (1C)

Antibiotics for severe CAP

Principles:

- As early as possible
- As broad as possible
- In light of local prevalence study
- Adequate workup
- As short as indicated (7-10days)
- De-escalation based on microbiology result and clinical response

ATS guideline 2011

Table 2. American Thoracic Society Guidelines for the Empiric Treatment of Community-Acquired Pneumonia

Patient Classification	Recommended Therapy
Group I: outpatients, no cardiopulmonary disease, no modifying factors	Newer macrolide* or doxycycline (if allergic to or intolerant of macrolides)
Group II: outpatient with cardiopulmonary disease and/or other modifying factors	β-lactam† plus macrolide or doxycycline‡ *or* antipneumococcal fluoroquinolone§ monotherapy
Group III: inpatients not in the ICU	
a. No cardiopulmonary disease, no modifying factors	IV azithromycin alone If macrolide allergic or intolerant, use doxycycline *or* antipneumococcal fluoroquinolone monotherapy
b. Cardiopulmonary disease and/or modifying factors	IV β-lactam‖ plus IV or oral macrolide or doxycycline‡ *or* IV antipneumococcal fluoroquinolone monotherapy
Group IV: ICU-admitted patients	
a. No risks for *Pseudomonas aeruginosa*	IV β-lactam¶ plus either IV azithromycin or IV fluoroquinolone
b. Risks for *P aeruginosa*	IV antipseudomonal β-lactam# plus IV ciprofloxacin *or* IV antipseudomonal β-lactam plus IV aminoglycoside plus either IV azithromycin or IV nonpseudomonal fluoroquinolone

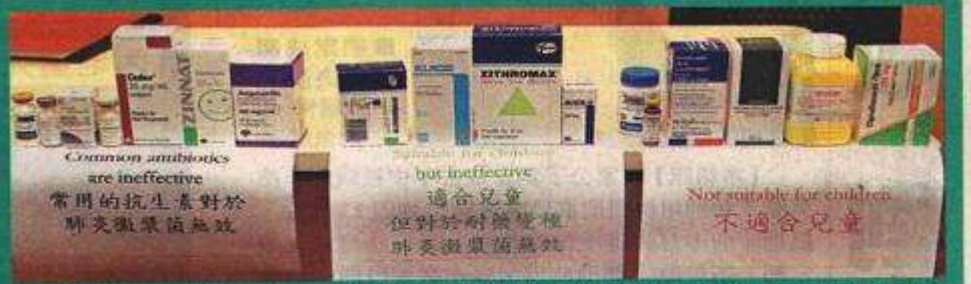
Essential problems in HK

- Increasing resistance rate of Mycoplasma to Macrolide
- Dominant resistant strain of pneumococcus to respiratory quinolones
- Severe CAP leading to ICU admission
  → coverage of Enterobacteriacea
  → increasing ESBL producer
- ? CA-MRSA

肺炎徵漿菌 專襲兒童無藥醫

被迫服帶毒性抗生素 或有副作用

■劉太女兒用到第八種抗生素才控制病情。



■圖左為一般常用抗生素；圖中適合兒童使用但對肺炎徵漿菌無效的抗生素；圖右為不適合兒童使用但有效治療肺炎徵漿菌的抗生素。 楊柏賢攝

【本報訊】專襲兒童的肺炎徵漿菌出現嚴重抗藥性，已到無藥可醫地步。香港大學發現，近八成感染肺炎徵漿菌的病人，對過往沿用的「大環內酯類」抗生素無效，感染的幼兒只能用對兒童有毒性的抗生素殺菌。專家呼籲當局要加強監察惡菌，並引入快速測試及早確診。 記者：梁麗兒

微生物學系2010年至去年，抽驗549名因下呼吸道感染在瑪麗醫院留醫的病人，他們多數患肺炎。其中91人感染肺炎徵漿菌，包括80名兒童及11名成人。測試顯示，近80%感染該菌的病人，對大環內酯類抗生素呈抗藥。病人包括一名四個月大及一名五個月大的嬰兒。

四環素令牙齒終身變灰

港大感染及傳染病中心總監何栢良表示，肺炎徵漿菌屬飛沫傳播疾病，常見於幼稚園、小學爆發，兒童感染後，會出現咳嗽、頭痛等與流感相似症狀。南韓、日本及內地近年都錄得該菌呈抗藥性上升。今次研究顯示其抗藥性程度，已打入本港十大抗藥惡菌之一。

過往20年一般使用大環內酯類抗生素治療肺炎徵漿菌感染，現只能改用其他抗生素如四環素、喹諾酮類等，但此類抗生素不適合兒童使用。其中四環素對8歲以下兒童帶毒性，高劑量及長期使用，牙齒會終身變啡黃及灰色；喹諾酮類則會致兒童關節痛及僵硬。但在無藥可醫情況下，病童也只能用藥。瑪麗醫院為例，近年每年都有病人感染該惡菌，有數名病童要使用四環素。

劉太的6歲女兒，去年11月因高燒及肺炎入住私家醫院，證實感染抗藥肺炎徵漿菌，但使用多種抗生素，病情也無好轉，更惡化至左肺積水，每日抽出約一罐可樂的積水。其後轉往瑪麗醫院，進行腹腔支氣管手術，累積住院15日，使用到第八種抗生素，即四環素才有效控制病情。她指，為救女兒一命，無奈要採用有毒性的抗生素，幸好女兒暫無副作用。

何栢良表示，感染此惡菌的症狀常見如發燒、咳嗽等，「有經驗嘅兒科專家都未必分辨到係流感，定係肺炎徵漿菌，快速測試就幫到手」。他促請當局加強監察惡菌感染走勢，並定期公佈。

76% community isolates of Mycoplasma are resistant to macrolides

Ho et al, 2013

CA-MRSA

- Coverage for CA-MRSA should be considered.
  - Non-Chinese ethnicity (e.g. Filipinos, Caucasian)
  - Patients with concurrent skin infection (e.g. abscess)
  - Patients with known exposure to CA-MRSA
  - Patients with chest X-ray suggestive of staphylococcal infection (e.g. cavitatory, peumatoceles)
  - Patients whose pleural fluid or brochial aspirate lavage show clusters of gram positive cocci
  - Patients presented with haemoptysis
- Intravenous linezolid is preferred and vancomycin is the alternative.

IMPACT 4th Edition, Hong Kong

CAP	*Usual organisms*	*Preferred regimens*	*Alternatives*
CAP, not hospitalised	*S. pneumoniae* *H. influenzae* *C. pneumoniae* *C. psittaci* (influenza A, *M. tuberculosis)*	PO Amoxicillin-clavulanate or ampicillin-sulbactam ± a macrolide *or* PO amoxicillin + a newer macrolide	
CAP, hospitalized in general ward	As above	IV/ PO Amoxicillin-clavulanate or ampicillin-sulbactam ± a macrolides	Cefotaxime or ceftriaxone ± a macrolides
CAP, hospitalized in ICU for serious pneumonia	As above + *Enterobacteriaceae*	IV Piperacillin-tazobactam or cefotaxime or ceftriaxone + a macrolide	Cefepime + a macrolide

Complication of severe CAP

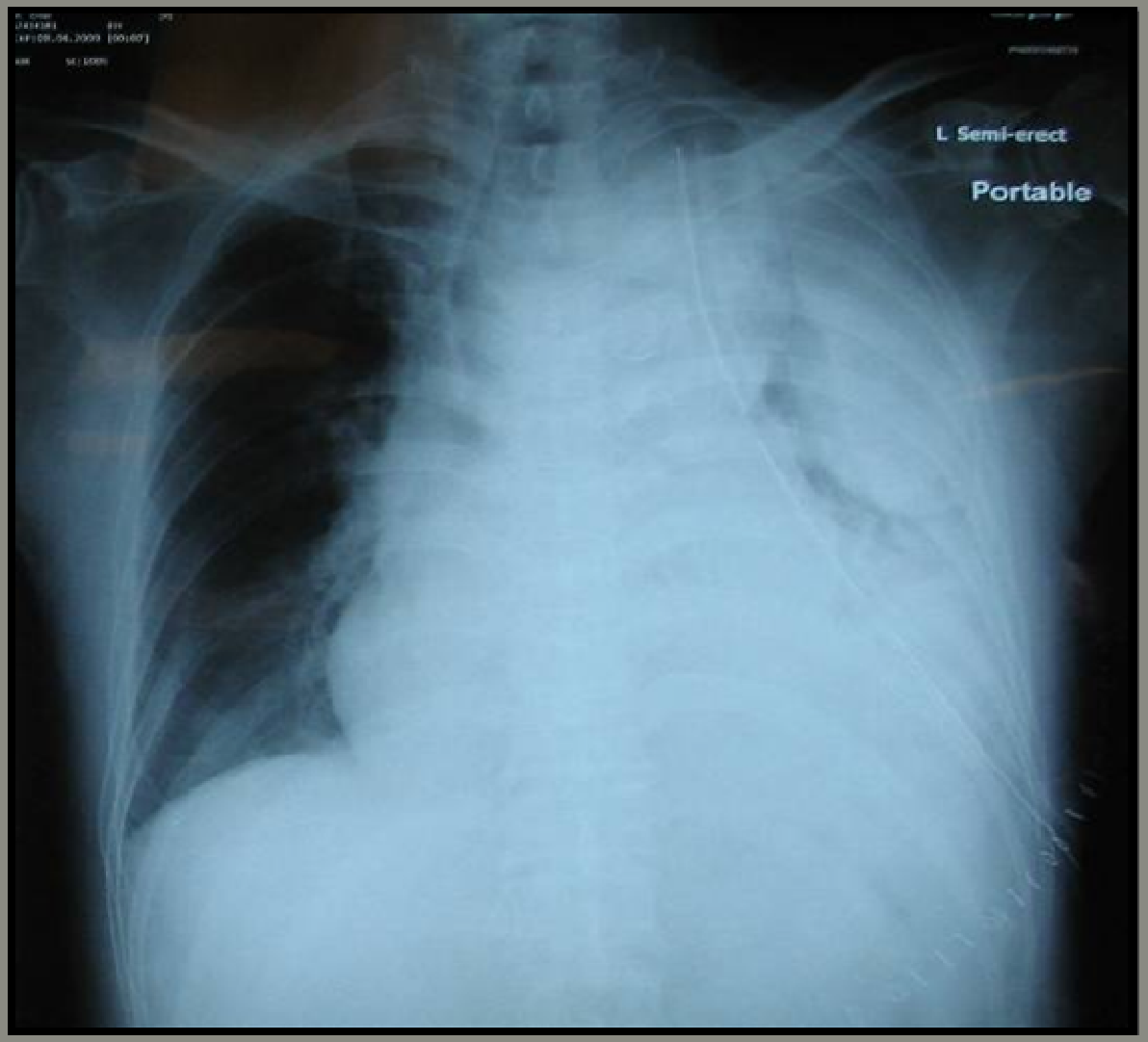
Complications of CAP

- Sputum retention
- Respiratory Failure/ ARDS
- Septic shock
- Multi-organ failure with DIC
- Metastatic infection
- Lung Abscess
- Complicated parapneumonic pleural effusion/ empyema
- Pneumothorax

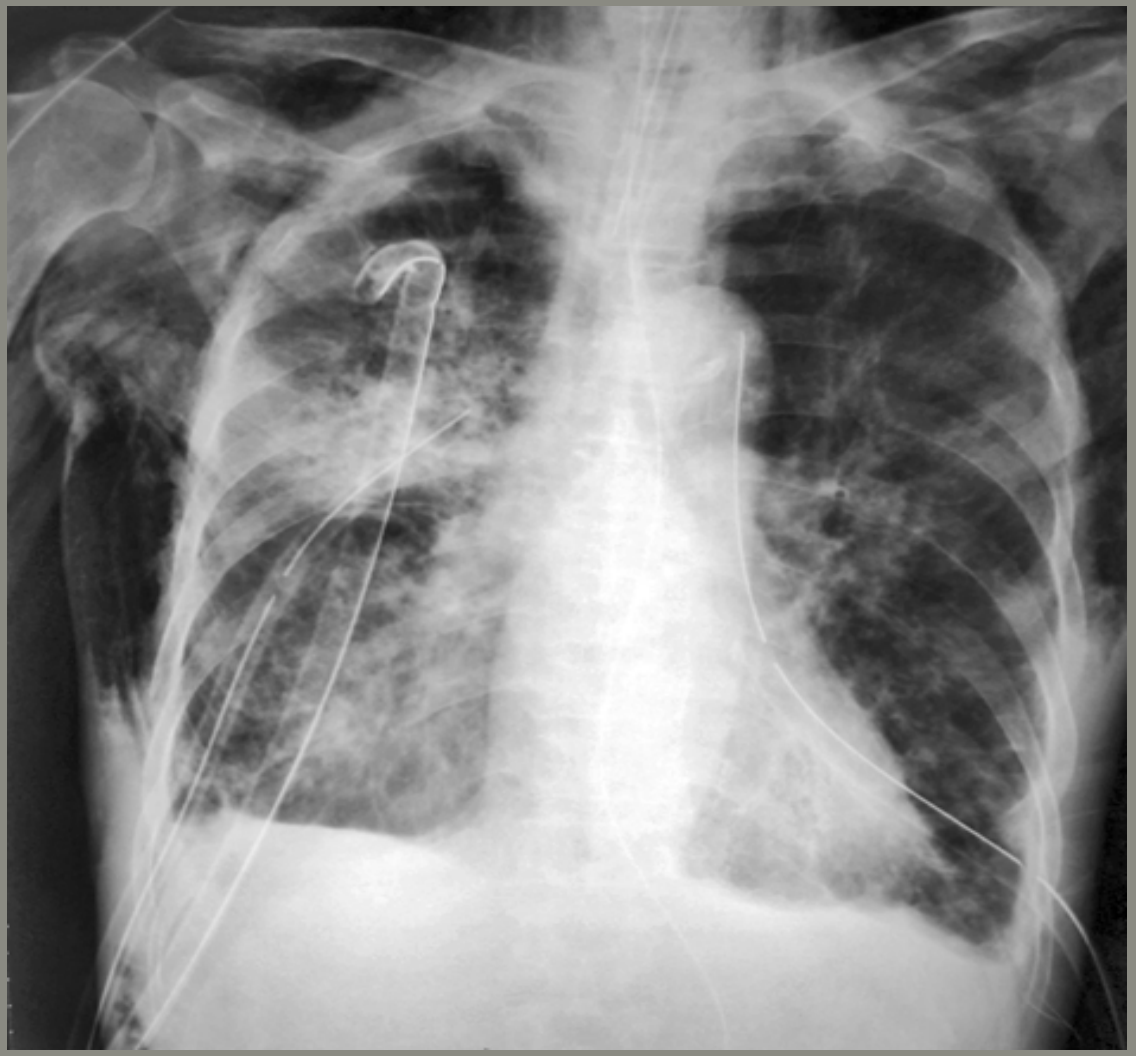
Why complication?

- Host factors
  - Age extreme
  - Immunocompromized
  - Malnourished
  - Diseased lungs
- Disease factors
  - Severity: bacteremic, multi-lobar
  - Pathogens: pneumoccocus, pseudomonas, acinetobacter
  - Non-infectious conditions
- Treatment factors
  - Late antibiotics
  - Inadequate dosing
  - Resistance/ tolerance

Empyema



Pneumothorax



Controversy in CAP

Evidence to cover atypical pathogens?

- **Findings from 24 trials (5015 patients)**
  - Mortality: atypical vs. typical (RR 1.13; 95% 1.54)
  - Atypical arm:
    - → Insignificant trend towards clinical success
    - → Significant bacterial eradication most notably for ***Legionella***
    - → Not significant for *Pneumococcus*

- **Conclusions**

  No survival or clinical efficacy benefit to empirical atypical coverage in hospitalised CAP patients

Cochrane Library 2005

Is penicillin susceptibility Important?

Variable	All patients (n = 638)	By penicillin susceptibility			*P*
		Sensitive (n = 409)	Intermediate (n = 164)	Resistant (n = 65)	
Total mortality	14.4	12.2	18.3	18.5	.054
Mechanical ventilation	13	12	16.5	10.8	.673
Shock	16	15.4	17.1	16.9	.666
DIC	2	2.9	0.6	0	.038
Empyema	8.3	10	4.9	6.2	.041
Bacteremia	73.6	77.4	61.1	72.9	.022

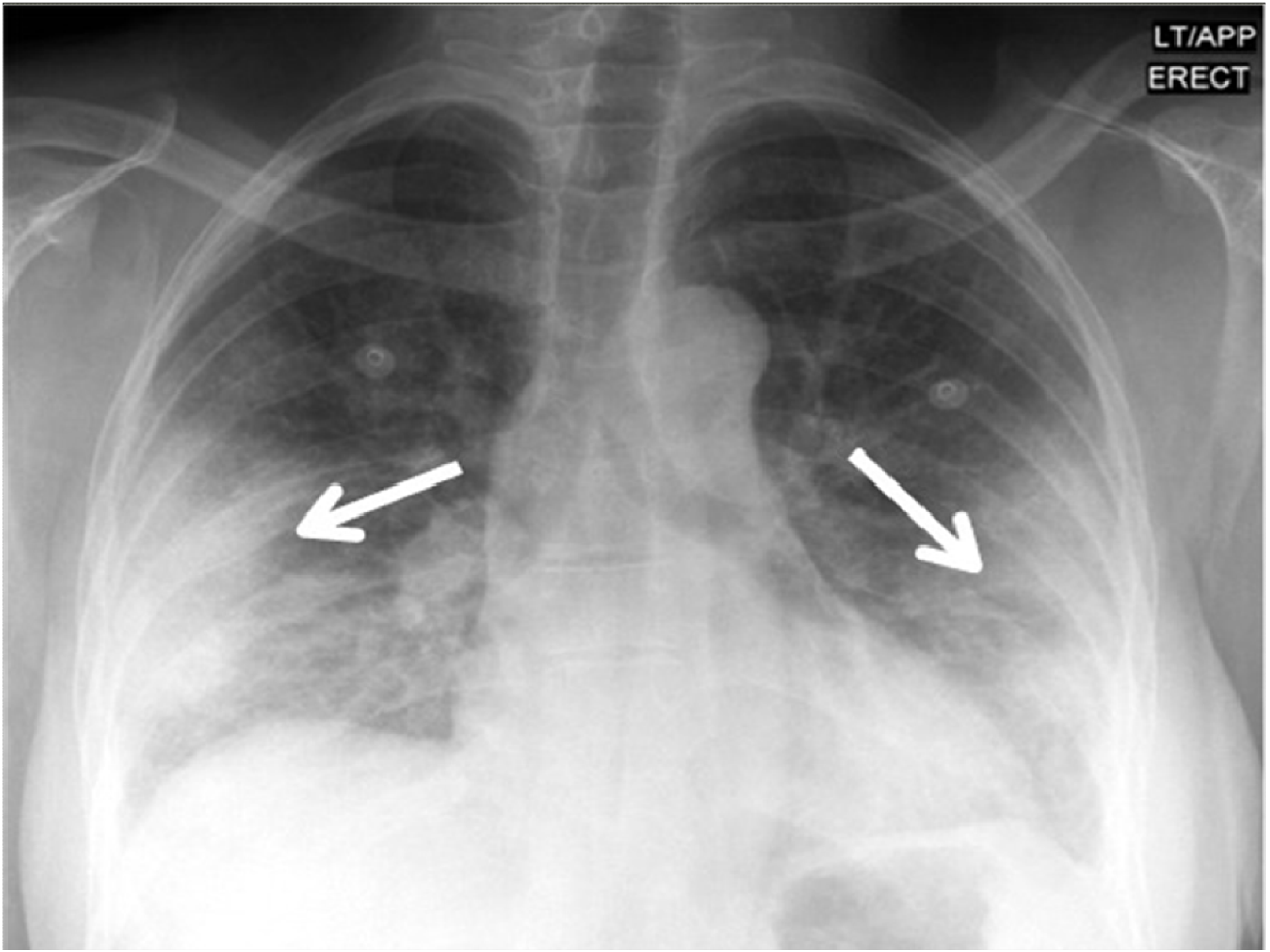
Aspa J et al, Clin Infect Dis 2004

CDC recommendation

- For severe pneumococcal CAP
  → always measure MIC in isolates
  → cut-off MIC to decide resistance
    Susceptible: < 1 mcg/ml
    Intermediate: >1 but < 2 mcg/ml
    Resistance: >4 mcg/ml
- Need validation in large-scale prospective trials
- Not for other sites

Case 1

- 30-year-old woman
- 2-day history of fever, cough and dyspnea. She had a recent URTI characterized by fever, sore throat, myalgias and arthralgias
- In distress with a pulse of 120/min, respiratory rate 38/min, blood pressure 95/60 mmHg, and temperature 39.0^0C.
- Oxygen saturation was 75% with the patient breathing room air.


LT/APP
ERECT

- Her CXR showed bilateral lung air-space consolidation.
- She was immediately intubated and transferred to the ICU
- Required high FiO_2 and 12 cm H_2O of PEEP to maintain acceptable oxygenation.

- What is your plan of management?

Management

- Nursed in isolation room with NEG pressure
- Arrange appropriate sampling (Nasopharyngeal aspirate or bronchial aspirate) for RT-PCR and viral culture.
- Commence Tamiflu prior to results.
- Empirical antibiotics for typical and atypical pneumonia are to be given.

Progress

- NPA for RT-PCR for inflenza A (H1N1) was positive
- What treatment would you give to this patient?

Antivirals

- Oseltamivir (Tamiflu), Zanamivir (Relenza)
- Both are neuraminidase inhibitors
- Both have activity against influenza A and B
- Oseltamivir is administered orally
- Zanamivir has been given iv and intranasally via a Diskhaler

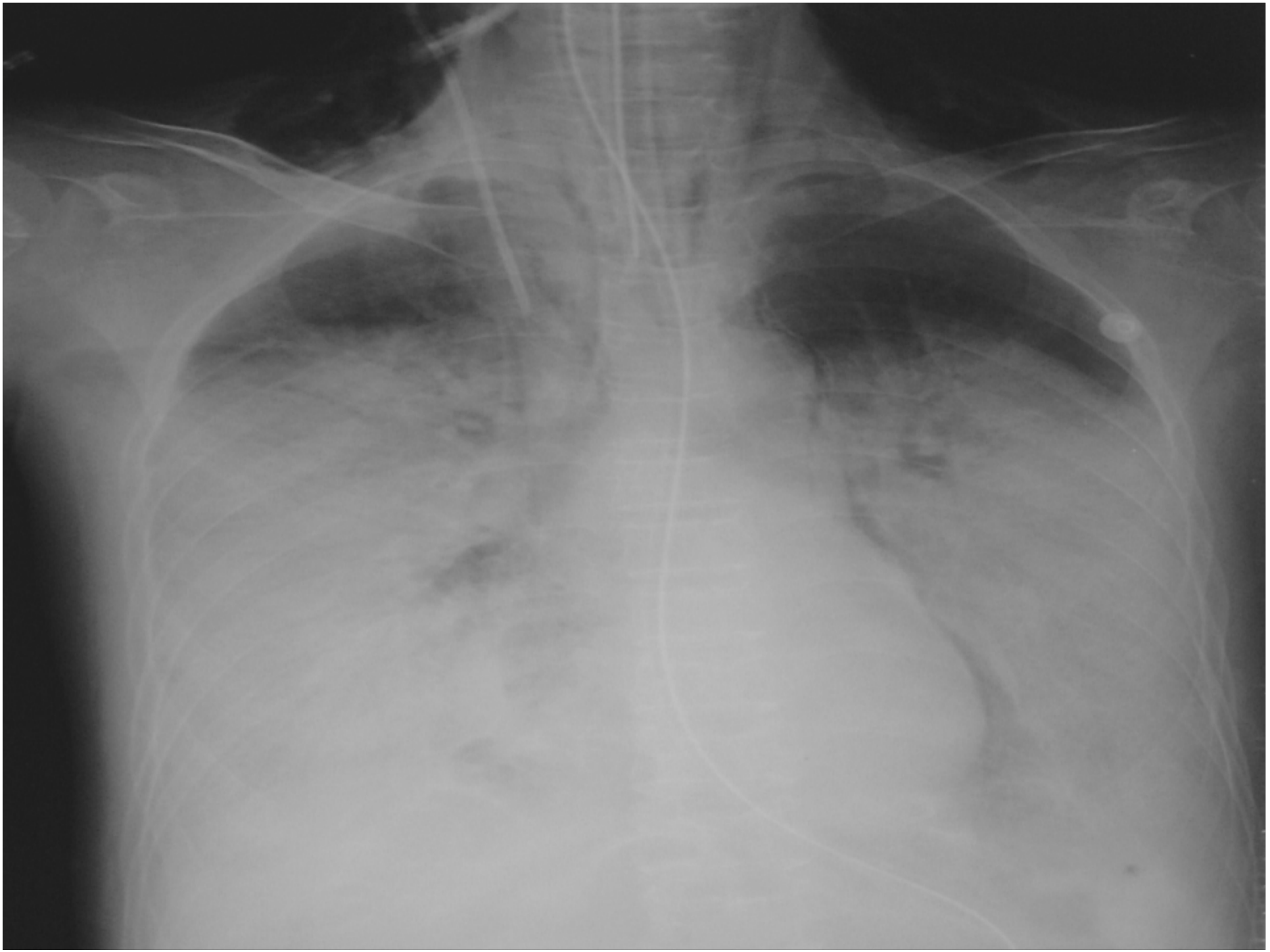
- Zanamivir for nebulization have not been approved by the FDA.
- Relenza Inhalation Powder should only be used by using the Diskhaler device provided.

Progress

- Gram stain of tracheal secretion indicated Gram-positive cocci in clusters
- The patient was started on linezolid

- On the third hospital day she developed tachycardia and hypotension not responsive to fluid replacement.
- There were worsening in hypotension and hypoxemia

- Serial CXRs……



- CXR compatible with ARDS

- Her antibiotic were continued, norepinephrine and vasopressin were started, and she was treated aggressively for sepsis.
- She developed renal insufficiency and metabolic acidosis.

Laboratory

- Na 142
- K 4.1
- Cl 105
- HCO_3 6
- Creatinine 168

- ABG
  - pH 7.24
  - PO_2 96mmHg (12.8kPa)
  - PCO_2 14 mmHg (1.8 kPa)

What is the most likely cause of the metabolic disorder in this patient?

Interpretation

- High anion-gap metabolic acidosis.
- Causes of acidosis:
  - Sepsis/ septic shock induced lactic acidosis
  - Renal failure
  - Drugs: Linezolid

Case 2

- 52-year-old engineer visited GP for URTI symptoms
- He was found during the intake process to have oxygen saturation in the mid-80% range.

- He was referred to the A&E Department, where he was found to be hypotensive, with a systolic blood pressure of 85 mmHg and an oxygen saturation of 96% on 2 L/min oxygen via nasal cannula.
-
- A portable CXR performed

- He was admitted for further work-up.

At medical ward

- In medical ward he was requiring 100% oxygen via NRM to maintain his oxygen saturation in the upper 90% range.
- He also noted an unintentional 50-pound weight loss over a 2-month period, low-grade fevers and a 2-3 week of dry cough
- Known hypertension and bipolar disorder.
- His medications included paroxetine, hydroxyzine and felodipine.
- He was a lifelong nonsmoker and denied any history of alcohol or intravenous drug use.
- He was married and living with his wife.
- His travel and environmental and occupational exposure histories were unremarkable.

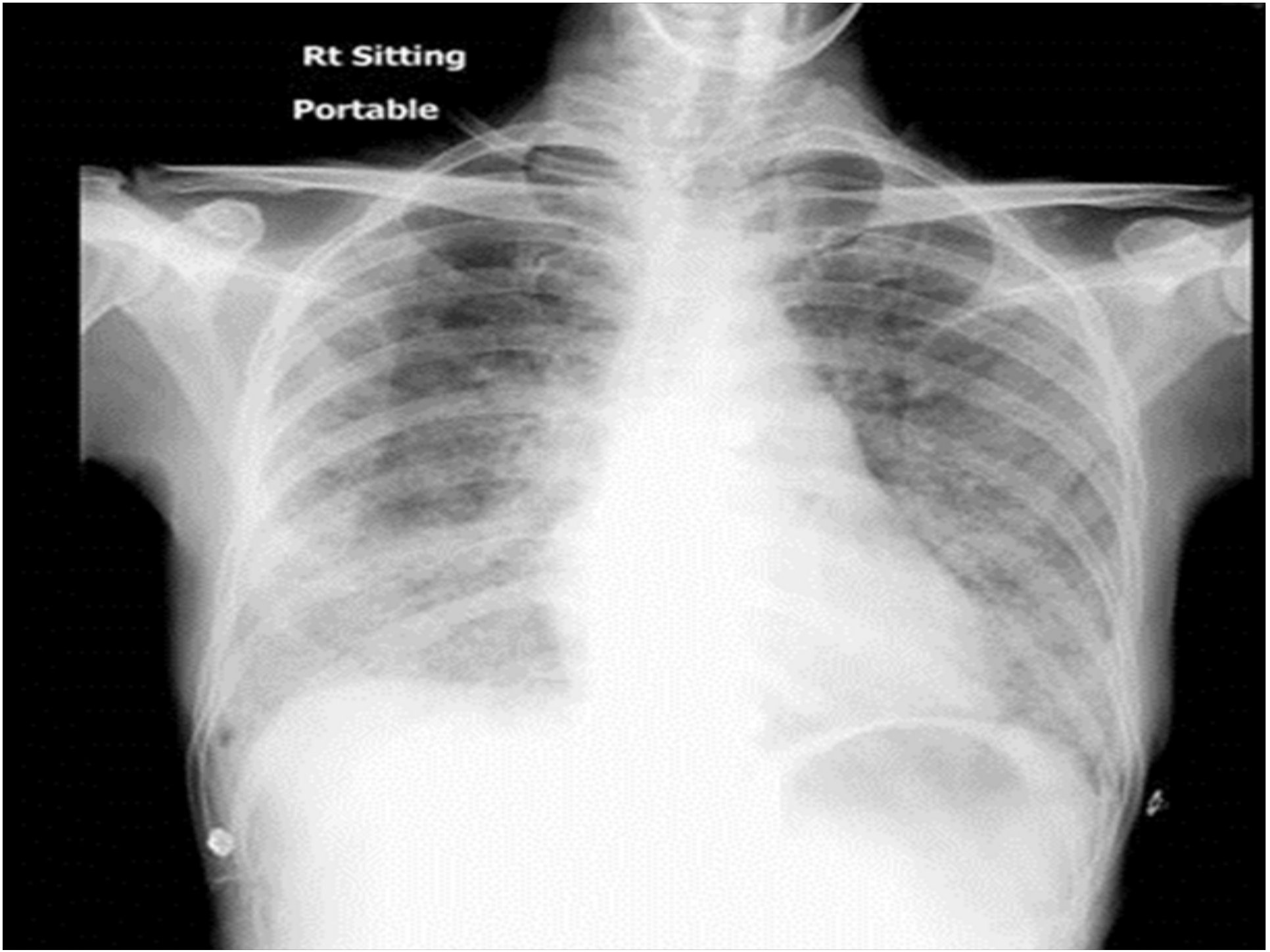
Physical Examination

- Vital signs
  - Temperature 35.4^{0}C
  - BP 90/59 , HR 70
  - RR 22
  - SpO2 100% with 100% nonrebreather mask
- Appeared chronically ill, mildly tachpneic
- Lung – crackles halfway up both lungs
- Heart - NAD

Laboratory Findings

- WBC 4.4 x 10^9 /L
  - N 3.65 L 0.48
- ESR 90
- Na 146; K 4.5
- Cl 110
- HCO3 23
- Urea 17.5
- Creat 254
- LDH 523
- Alb 24; Globulin 43

- ABG:
  - pH 7.36
  - PaCO2 35mmHg(4.6kPa)
  - PaO2 50mmHg(6.6 kPa)
  - HCO3 20
- Urine:
  - protein 1+
  - RBC 3-8


Rt Sitting
Portable

Progress

- The patient was started on empirical antibiotic coverage (ceftriaxone and azithromycin) for community-acquired pneumonia.

- Bronchoscopy was performed
- He was intubated for the procedure

- **Following the bronchoscopy, how would you manage this patient?**

Management after investigation

- Empirical trimethoprim/sulfamethoxazole and oral prednisone for P. jiroveci pneumonia.
- Testing for HIV status

Progress

- Several days later, his HIV ELISA was reported as positive. This was subsequently confirmed with western blot analysis.
- His absolute CD4+ count was 5 cells/ml and his HIV RNA was >1,000,000 copies/ml.

Progress

- He received parenteral treatment with cotrimoxazole and methylprednisolone.
- 2 weeks later, a skin rash developed over his body and was itchy.

- **What was the most likely cause for the skin rash and what was your management?**

Management of sulfa allergy

- **For mild to moderate disease**, acceptable alternative regimens include pentamidine, atovaquone, dapsone-trimethiprim, or clindamycin-primaquine for a similar duration.

- **For severe pneumonia** and a reported drug allergy to sulfa, **desensitization** is often proposed, given the marked benefit of trimethoprim/sulfamethoxazole in severe P. jiroveci pneumonia.

Progress

- Cotrimoxazole was stopped and replaced by pentamidine.
- His clinical and radiologic condition normalized

- HAART was started subsequently

- **What precautions and monitoring should be taken for patients on pentamidine therapy?**

Pentamidine-associated adverse events

- Hypoglycemia
- Hypotension (the drug should be given while the patient is supine, adequately hydrated, and administered over at least 60 minutes)
- Renal function and glucose, calcium, and electrolyte concentrations should be monitored
- Periodic monitoring of complete blood counts and liver function tests is also recommended.

Questions for discussion

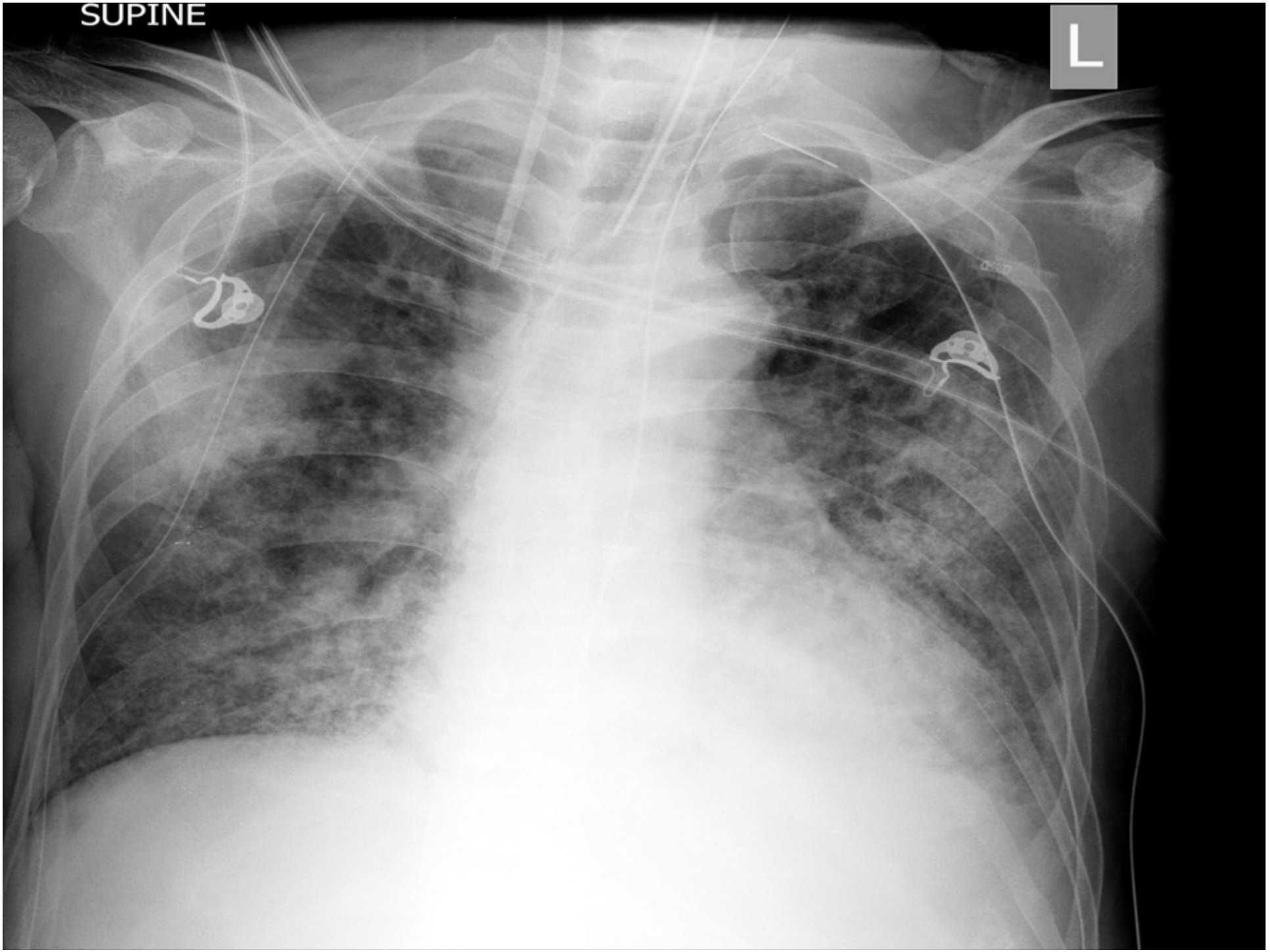
- Antiretroviral therapy in the ICU

Initiation of HAART: traditional view

- Defer ART until the acute respiratory illness has been treated in patients not already receiving ART (particularly in patients for whom PCP leads to the diagnosis of HIV infection)
- ART start times should therefore vary depending on the patient's individual clinical course, tolerance of the anti-PCP regimen

CDC July 2013

- In patients not on ART, ART should be initiated, when possible, within 2 weeks of diagnosis of PCP
- In a RCT of 282 patients with infections other than TB, (63% of whom had PCP), a significantly lower incidence of AIDS progression/ death by early HAART (12 days vs. 45 days)


SUPINE
L

Progress

- Bilateral pneumothorax and pneumomediastinum, with bilateral chest drains inserted
- 3 weeks later, the lungs were fully expanded but air leak persisted
- What are the strategies for ventilating a patient with significant air leak?

Strategy in managing air-leak

- Minimizing peak airway pressure in BPF and transpulmonary pressure (alveolar pressure – intrapleural pressue) in APF
- Lowest effective TV, minimal PEEP, least no of positive-pressure breaths
- Any negative suction through chest drain should be discontinued as early as possible
- Look out for hyperventilation due to auto-triggering

Etiologies

- APF (Alveolo-pleural fistula)
  - Communication between the pulmonary parenchyma distal to a segmental bronchus and the pleural space
- BPF (Broncho-pleural fistula)
  - Communication between the lobar or segmental bronchi and the pleural space

Differences between BPF and APF

	BPF	APF
Aetiology	•Postoperative •Blunt or penetrating trauma •Airway laceration following intubation	•Necrotizing infection •Iatragenic laceration of visceral pleura •Barotrauma from MV •Traumatic laceration of visceral pleural •Persisent spontaneous pneumothorax •Invasive tumor, chemotherapy and irradiation
Patho-physiology	•Gas shunted through a proximal fistula has not participated in gaseous exchange •Alveolar hypoventilation significant	•Gas shunted through a peripheral fistula participates in gaseous exchange to some extent •Alveolar hypoventilation usually not significantly compromised

When to close an APF?

- Repair is necessary when air leak persist for more than 7-14 days to avoid
  - infective complications
  - complications associated with prolonged immobilization
  - ventilatory failure.

Methods to close the fistula?

- Surgical repair
  - VAT
  - thoracotomy
- Chemical pleurodesis
- Endoscopic closure
  - Sealants injection
  - Devices placement eg endobrochial watanabe spigot, endobronchial valves, Amplatzer device

Strategies to prevent VAP

1. Keep the head of the patient's bed up to at least 30^0 unless contraindicated
2. Use antiseptic oral rinse to provide oral care to patients with ETT on regular basis
3. Perform hand hygiene before and after each respiratory care
4. Review sedation at least daily
5. Assess patient's readiness to wean or to extubate at least daily
6. Prevent condensate from entering patient's airway
7. Maintain proper care of the respiratory consumables and equipments
8. Conduct ongoing active VAP surveillance