

Pneumonia in the Hospitalized Patient: Use of Steroids

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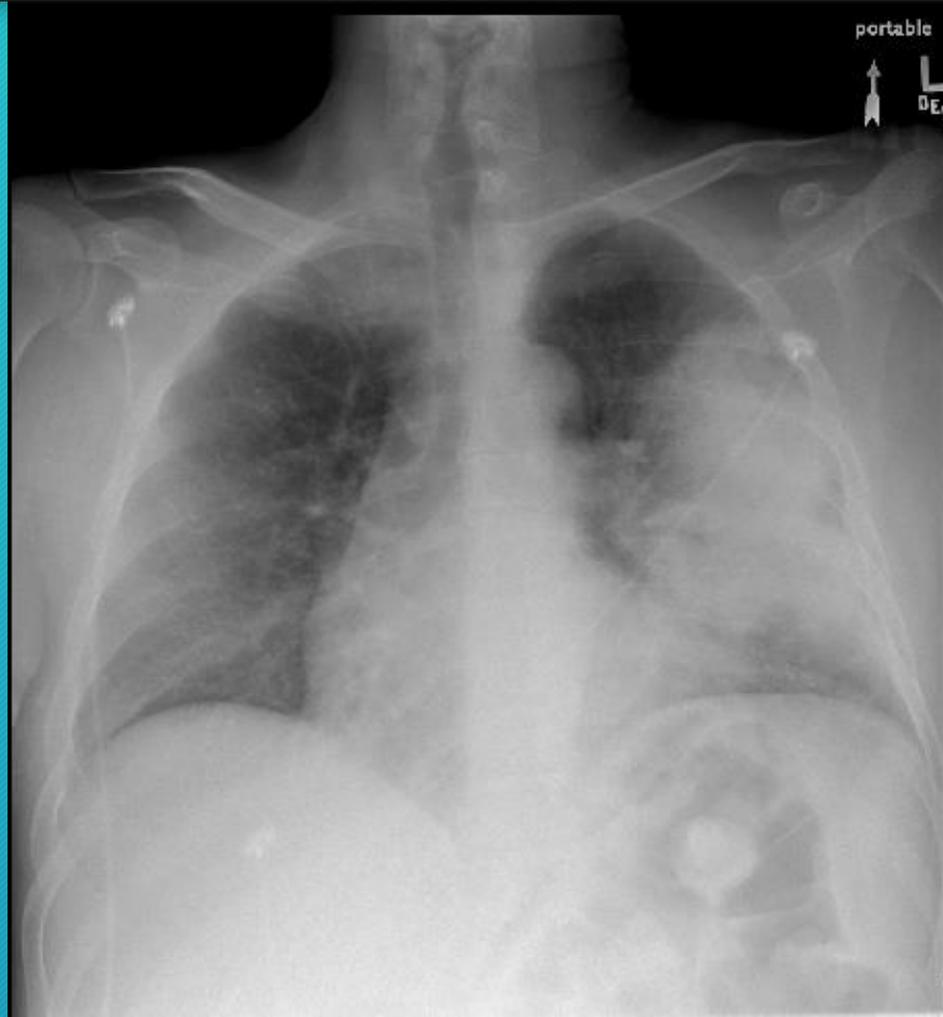
Facts About Pneumonia

- CAP is the 8th most common cause of death in the USA
- In 2006, 1.3 million hospitalizations for pneumonia.
- 30 day mortality rate for CAP patients requiring hospitalization is about 12%.

Definition of Infectious Pneumonia

- Acute infectious process involving the parenchyma of the lung.
- Requires x-ray evidence or CT chest evidence to really call it pneumonia
- Pathogens gain access to the lung by micro aspiration, hematogenous spread, direct spread from contiguous focus.
- Despite current diagnostic tests, no pathogen was detected in the majority of patients diagnosed with pneumonia. (23% viral, 11% bacterial, 1% fungal)

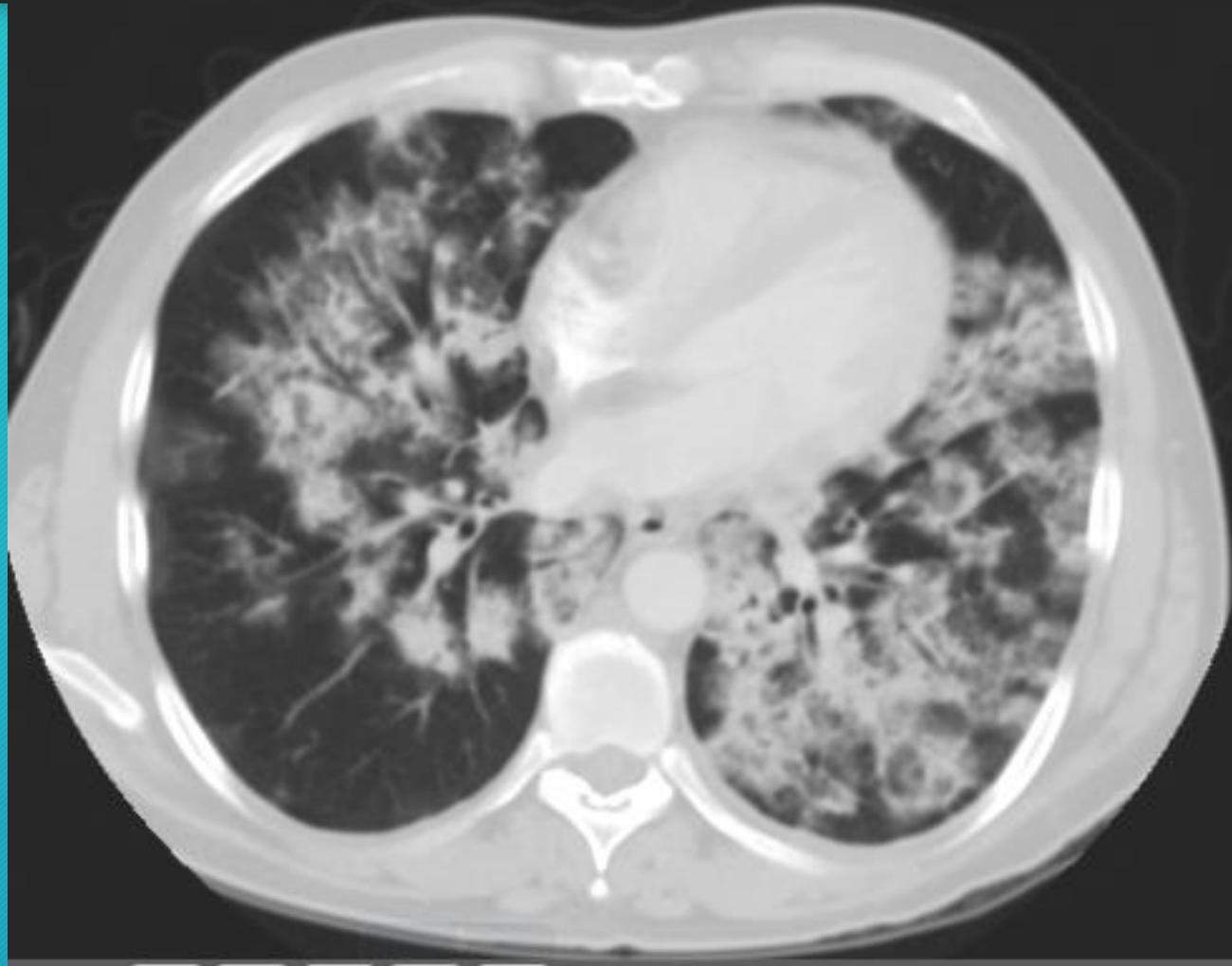
Community Acquired LUL Pneumonia



Causes of Radiographic Pneumonia

- Viral infections
- Bacterial infections
- Fungal infections
- Drugs reactions
 - Amiodarone, methotrexate, cancer immunotherapies
- Inhalational exposures
 - Crack cocaine
- Inflammatory causes
 - Systemic vasculitis, BOOP, eosinophilic pneumonia, sarcoidosis
- Pulmonary edema
- Pulmonary embolism with infarct

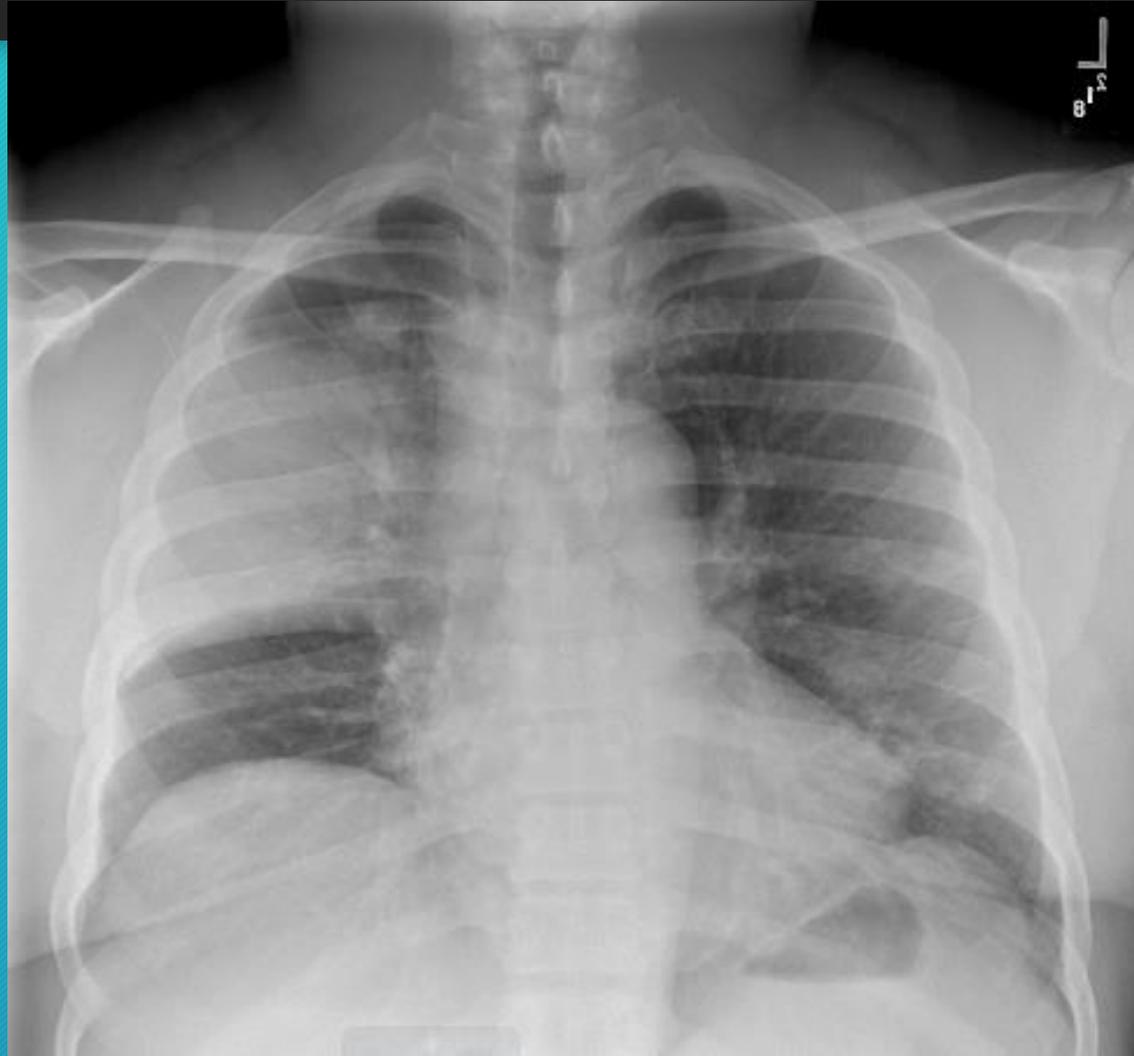
Community Acquired Bilateral Pneumonia



IDS Guidelines for Treatment of Inpatient Pneumonia

- General Floor Admission
 - Macrolide plus Ceftriaxone
 - Doxycycline plus Ceftriaxone
 - Fluoroquinolone
- ICU Admission
 - Macrolide plus Ceftriaxone
 - Fluoroquinolone plus Ceftriaxone
 - Underlying risk factors: add Vancomycin, add extended spectrum beta lactam

Community Acquired RUL Pneumonia



? Admit or Not ? General Medicine vs ICU

- CURB-65
 - Confusion, Bun >20 , RR ≥ 30 , BP systolic ≤ 90 or diastolic ≤ 60 , Age ≥ 65 yr
- Pneumonia Severity Index (PSI)
 - 20 different risk factors with point assignment and risk stratification I-V
- IDSA Guidelines Recommend ICU admission
 - RR ≥ 30 , PaO₂/FiO₂ ≤ 250 , multilobar infiltrate, confusion, BUN ≥ 20 , WBC < 4 , platelets < 100 , T < 36 , hypotension requiring fluid resuscitation

What is Happening at a Cellular Level in Pneumonia?

- Pathogen enters lungs and innate immune system fails to clear pathogen.
- Cytokine mediated systemic inflammatory response good and bad
 - Local inflammation impairs alveolar gas exchange
 - Systemic inflammation leads to other organ dysfunction
- Dysregulated immune response
- Antibiotics target the invading organism but not the immune system.
- **Can systemic steroids attenuate inflammatory response and improve outcome?**

CT Chest: RUL pneumonia



Is There a Role for Steroids in Conjunction with Antibiotics?

- Multiple studies have been done suggesting steroids may be beneficial.
 - Annals of Internal Medicine 2015
 - JAMA 2015
 - Chest Medicine 2016
 - JAMA 2017
 - Cochrane Database 2017.

Corticosteroid Therapy for Patients Hospitalized with Community Acquired Pneumonia.

- Systematic Review and Meta-analysis: 13 randomized controlled trials for total 2005 patients.
- Examine effect of adjunctive corticosteroid therapy on mortality, morbidity, and duration of hospitalization in CAP
- Various formulations of steroids used: 1 dose - 10 days
- All cause mortality 7.9% control group and 5.3% steroid group RR, 0.67 (CI 0.45-1.01)
 - Stratified to severe pneumonia 6 studies RR, 0.39 (CI 0.2-0.77)
- 5% Reduction in need for mechanical ventilation RR 0.45 (CI 0.26-0.79)
- 5% Reduction in risk for ARDS with steroids RR, 0.24 (CI 0.1-0.56)
- Reduction in length of hospitalization by 1 day (CI -1.79 to -0.21)

Effect of Corticosteroids on Treatment Failure Among Hospitalized patients with Severe CAP and High Inflammatory Response.

- Randomized Clinical Trial, double blind, placebo controlled, multicenter
- Severe CAP and CRP > 150mg/L (convert to mmol/L multiply by 9.524)
- Methylprednisolone 0.5mg/kg q12 hr x 5 days vs placebo started within 36 hrs of hospitalization
- Primary outcome: treatment failure (composite outcome early and late)
 - Early treatment failure
 - Development of shock
 - Need for mechanical ventilation
 - Death within 72 hrs
 - Late treatment failure
 - Radiographic progression
 - Persistence of severe respiratory failure
 - Development of shock
 - Need for mechanical ventilation
 - Death between 72-120 hrs

Effect of Corticosteroids on Treatment Failure Among Hospitalized patients with Severe CAP and High Inflammatory Response.

- Secondary outcome:
 - in hospital mortality
- Less treatment failure in steroid group 13% vs 31% (P=.02)
 - Decrease in radiographic progression and late appearance of septic shock
- In hospital mortality rate same

Adjunct Prednisone Therapy for Patients with CAP: a Multicenter, Double-blind, Randomized, Placebo-Controlled Trial

- Prednisone 50mg day vs placebo for 7 days
- Primary endpoint was time to clinical stability
 - Stable vitals for 24hrs, normal mental status, normal oral intake, sats>90% RA
- Total of 785 patients studied
- Median time to clinical stability was shorter in prednisone group 3 days vs 4.4 days (CI 1.15-1.50, $p<0.0001$)
- No difference in pneumonia associated complications
- Higher incidence of in-hospital hyperglycemia needing insulin 19% vs 11%, CI 1.31-2.93, $p=0.001$)

Efficacy and Safety of Corticosteroids for Community-Acquired Pneumonia: A Systematic Review and Meta-Analysis

- 9 RCTs and 6 cohort studies including total of
- Mean steroid use 30mg day methylprednisolone 7 days
- Steroids did not have a statistically significant effect on mortality in CAP (RR, 0.72, CI 0.43-1.21)
- Steroids did not reduce mortality in patients with severe CAP
- Secondary outcomes
 - Steroids were associated with decrease risk of ARDS (RR 0.21, CI 0.08-0.59)
 - Steroids may help reduce LOS in hospital and ICU and time to clinical stability
- Steroids not associated with increased rates of adverse events

Effect of Oral Prednisone on Symptom Duration and Severity in Non-asthmatic Adults With Acute Lower respiratory Track Infection. A Randomized Clinic Trial.

- Assess oral steroids for acute lower respiratory track infections
- 40mg day for 5 days vs placebo
- 398 adults
- Primary outcomes were duration of cough or worse cough and severity of symptoms on days 2 and 4
- No difference in outcomes seen

Steroids in Management of Pneumonia

- Cochrane data base 2017: 17 RCTs for total of 2264 participants, 13 RCTs were adults and 4 RCTs children.
- Trials limited to inpatients with CAP
- Corticosteroids significantly reduced mortality in adults with severe pneumonia (RR 0.58, 95% CI 0.4-0.84)
- Corticosteroids did not significantly reduce mortality in adults with non-severe pneumonia
- Steroids shortened hospital length of stay by about 3 days
- NNT was 18 to prevent 1 death
- Adverse events included hyperglycemia

Recommendations from Uptodate

- Use steroids in patients with CAP who have significant inflammatory response with sepsis and respiratory failure
- Methylprednisolone 0.5mg/kg q 12 hrs or prednisone 50mg day x 5 days

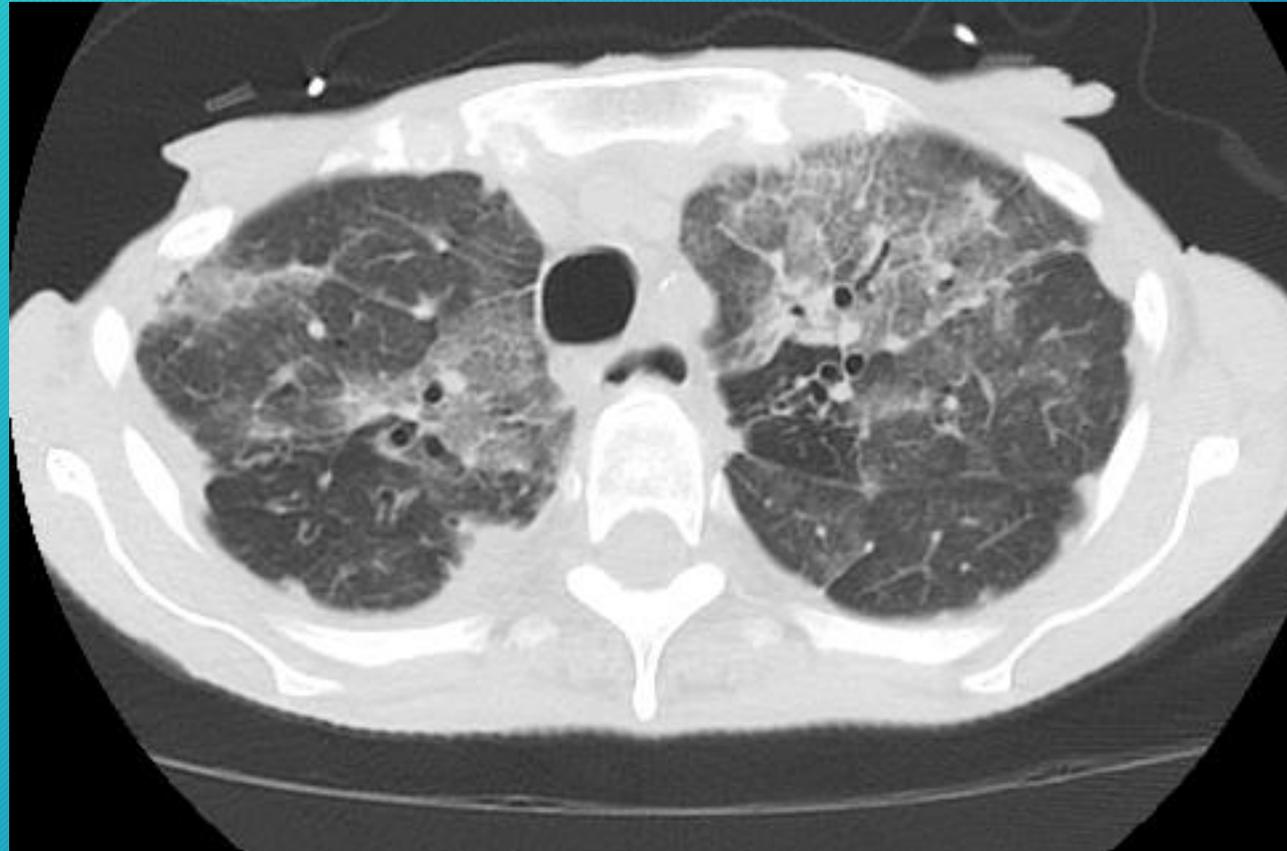
Why Do Steroids Help in Severe CAP?

- Contain an over active immune system that is destroying lung parenchyma
- Steroids are anti inflammatory and are down regulating pro inflammatory cytokines such as IL-6 and IL-8.
- Steroids help to upregulate anti-inflammatory cytokines such as IL-10.
- Relative adrenal insufficiency is treated
- Maybe this is not infectious but mimicking infectious pneumonia

Things to Consider that are Steroid Responsive

- Eosinophilic Pneumonia
- Cryptogenic organizing pneumonia
- Hypersensitivity Pneumonia
- Pulmonary Vasculitis
- ILD

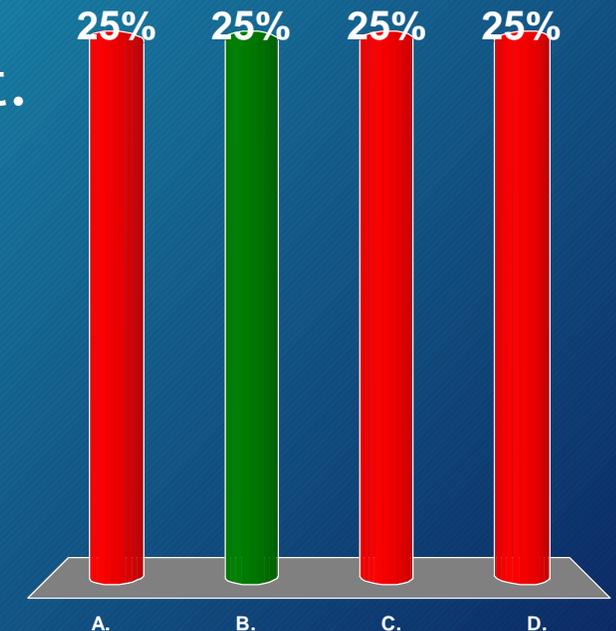
Ct Chest: Diffuse bilateral infiltrates



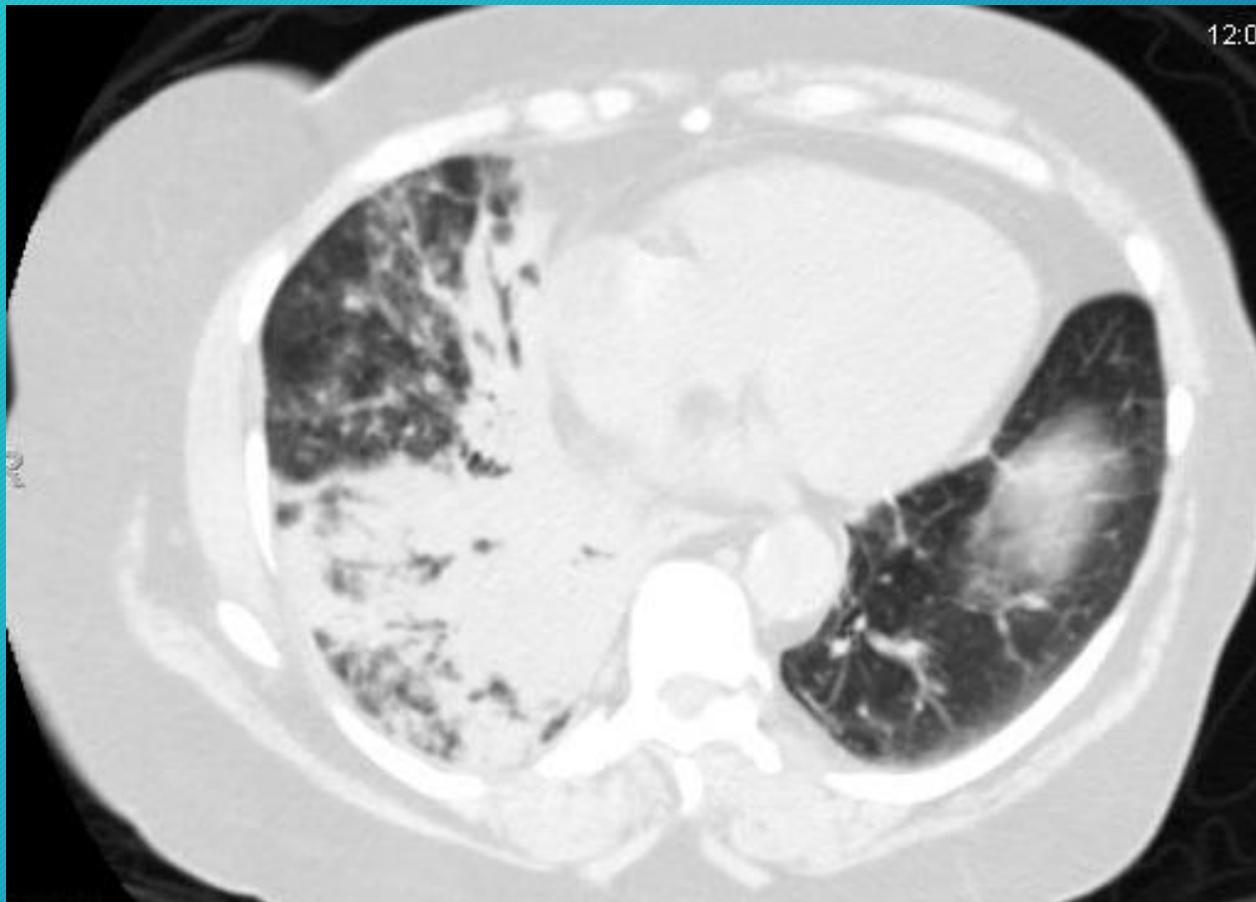
Question #1

- 63 yr old female with no significant past medical history presents with 2 day hx of cough, fevers, and dyspnea. She feels tired and looks sick. Temp 102, RR 25, BP 100/70, WBC 3.5, BUN 30, ABG shows pAO₂ 60, sats 89% and CXR shows dense infiltrate in RLL and RML. Which of the following are correct in regards to best management of this patient?

- A. Patient should be treated for pneumonia as an outpatient.
- B. Patient may benefit from treatment with methylprednisolone 0.5mg/kg q 12.
- C. Patient should be treated with fluoroquinolone plus vancomycin
- D. The most common pathogen identified on admission to hospital is streptococcus pneumoniae.



Community Acquired RLL Pneumonia



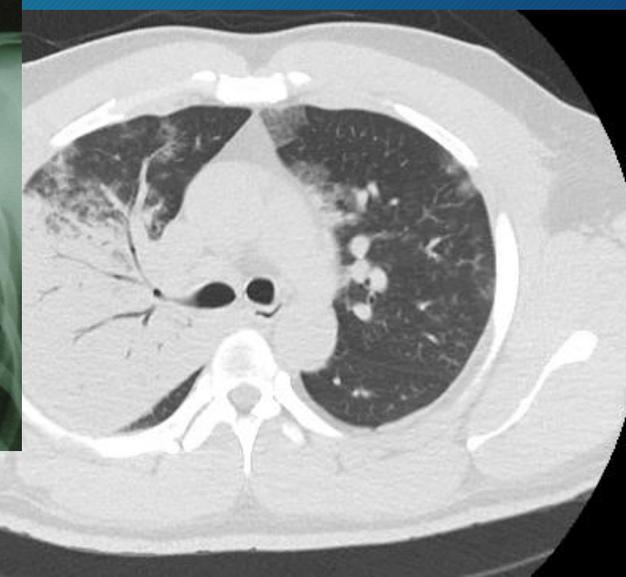
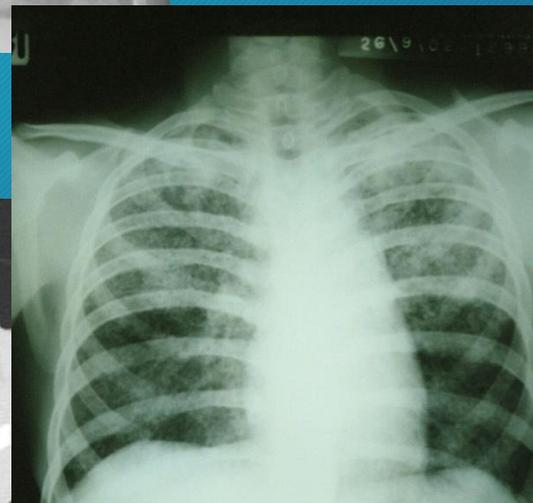
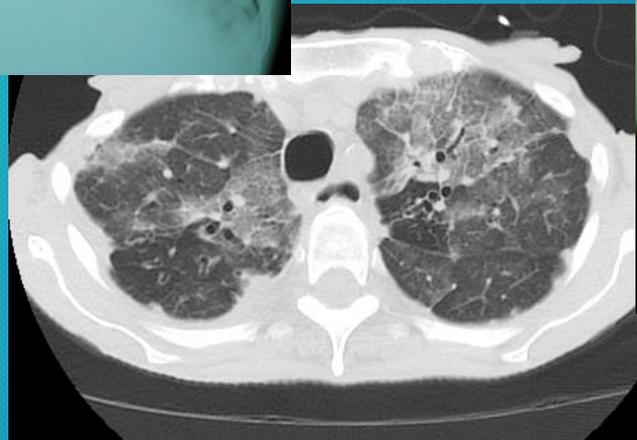
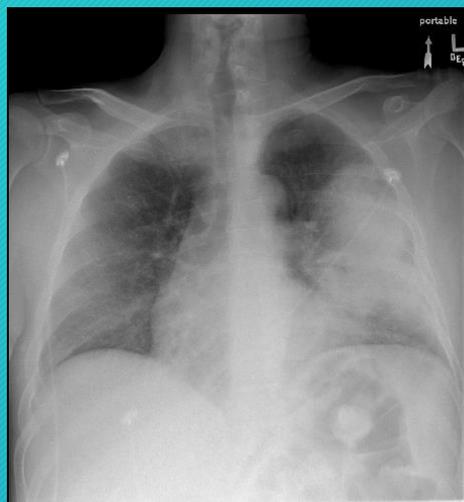
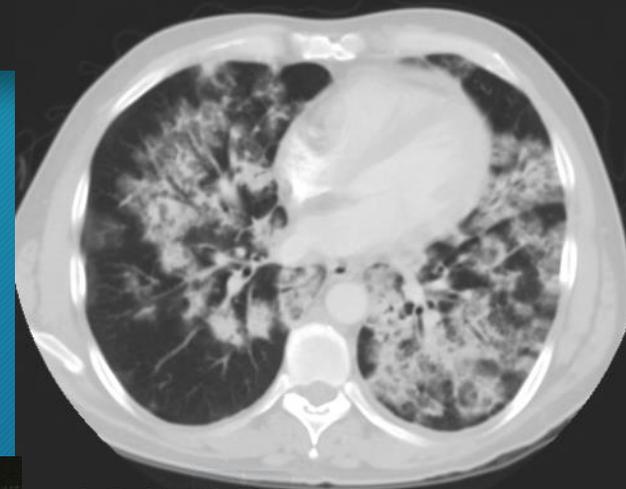
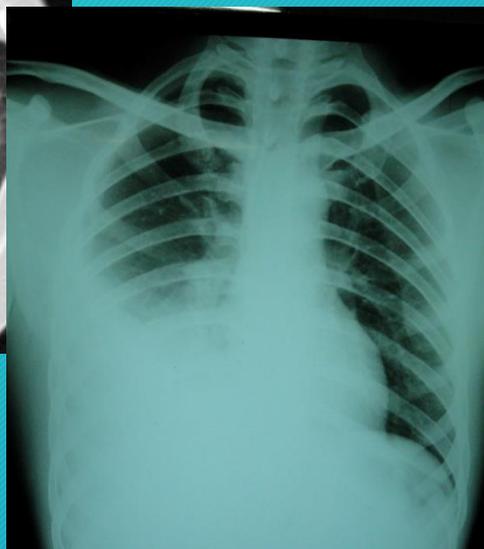
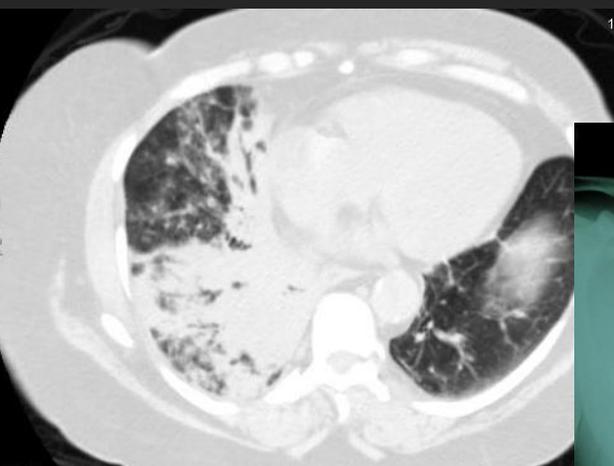
Question #1

- **Correct Answer:**
 - B) based on current available data, steroids may be beneficial in the management of severe in-patient pneumonia.
- **Explanation:** Cochrane Data base 2017: Corticosteroids significantly reduced mortality in adults with severe pneumonia (RR 0.58, 95% CI 0.4-0.84). Reductions in mortality were not seen in non severe pneumonia.
- Per the IDS guidelines the patient has a score of 3 and should be admitted to the ICU
 - RR>30, PaO2/FiO2 <250, multilobar infiltrate, confusion, BUN>20, WBC<4, platelets<100, T<36, hypotension requiring fluid resuscitation
- Per IDS and ATS guidelines for antibiotics for CAP admitted to the ICU
 - Macrolide plus Ceftriaxone
 - Fluoroquinolone plus Ceftriaxone
 - Underlying risk factors: add Vancomycin, add extended spectrum beta lactam
- Most common pathogens identified on admission to a hospital are viruses but for the majority of cases no pathogen is identified.

Take Home Pearls

- Consider the use of steroids in patients admitted with severe CAP but as a general recommendation this should not be used in all patients admitted with community acquired pneumonia.
- Follow ID guidelines for antibiotics use so we are good stewards of antimicrobial use.
- Vaccinate everyone with flu vaccines and pneumococcal vaccine per guidelines as this intervention will be impactful on this potentially lethal disease.
- Expand your differential diagnosis to noninfectious causes of radiographic pneumonia.
- Better randomized controlled trials are needed to truly answer the question “Should steroids be used in the setting of CAP?”.

END



References

- Stern, A et al. Corticosteroids for Pneumonia. *Cochrane Database Syst Rev*. 2017 Dec 13; 12: CD007720
- Siemieniuk RA, Meade MO, Alonso-Coello P, et al. Corticosteroid therapy for patients hospitalized with community-acquired pneumonia: a systematic review and meta-analysis. *Ann Intern Med*. 2015; 163(7): 519– 528.
- Steroids Beneficial As Adjunctive Treatment for Community-Acquired Pneumonia. *American Family Physician*. 2016 Feb 1;93(3):227.
- Wan YD, Sun TW, Liu ZQ, Zhang SG, Wang LX, Kan QC. Efficacy and Safety of Corticosteroids for Community-Acquired Pneumonia: A Systematic Review and Meta-Analysis. *Chest*. 2016;149(1):209-19
- Tagami T, Matsui H, Horiguchi H, Fushimi K, Yasunaga H. Low-dose corticosteroid use and mortality in severe community-acquired pneumonia patients. *The European Respiratory Journal*. 2015;45(2):463-72
- Jain, S et al. Community-Acquired Pneumonia Requiring Hospitalization among U.S. Adults. *NEJM* 2015; 373:415-27.

References

- Infectious Diseases Society of America. Infectious Diseases Society of America/American Thoracic Society consensus guide-lines on the management of community- acquired pneumonia in adults. *Clin Infect Dis*. 2007;44 Suppl 2:S27- 72.
- American Lung Association. Trends in pneumonia and influenza and pneumonia morbidity and mortality; 2010.
- Niederman, M. In The Clinic. Community-Acquired Pneumonia. *Annals of Internal Medicine*. October 6, 2015.
- Blum CA et al. Adjunct Prednisone Therapy for Patients with Community acquired pneumonia: a multicentre, double-blind, randomized, placebo-controlled trial. *Lancet*. 2015;385 (9977): 1511-8.
- Torres A et al. Effect of corticosteroids on treatment failure among hospitalized patients with severe community-acquired pneumonia and high inflammatory response: a randomized clinical trial. *JAMA*. 2015;313:677-86.
- Hay, A et al. Effect of Oral Prednisone on Symptom Duration and Severity in Nonasthmatic Adults With Acute Lower respiratory Track Infection. A Randomized Clinic Trial. *JAMA*. 2017: 318(8): 721-30.

Pneumonia Severity Index

Pneumonia Severity Index Step 2: Risk factors and assigned points

Risk factors	Points
Demographic factors	
Age for a man	Age (in years)
Age for a woman	Age (in years) - 10
Nursing home resident	+10
Coexisting illnesses	
Neoplastic disease (active)	+30
Chronic liver disease	+20
Heart failure	+10
Cerebrovascular disease	+10
Chronic renal disease	+10
Physical examination findings	
Altered mental status	+20
Respiratory rate ≥ 30 /minute	+20
Systolic blood pressure < 90 mmHg	+20
Temperature $< 35^\circ\text{C}$ or $\geq 40^\circ\text{C}$	+15
Pulse ≥ 125 beats/minute	+10
Laboratory and radiographic 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 percent	+10
Partial pressure of arterial oxygen < 60 mmHg*	+10
Pleural effusion on chest x-ray	+10

0 to 50 Points: Class I 0.1% Mortality
51 to 70 Points: Class II 0.6% Mortality
71 to 90 Points: Class III 0.9% Mortality
91 to 130 Points: Class IV 9.3% Mortality
131 to 395 Points: Class V 27.0% Mortality

Risk class

Classes 1 and 2 - outpatient management

Class 3 - observation unit or short inpatient stay

Classes 4 and 5 - inpatient management