Pneumonia: Breathe Again!

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Learning Objectives

1. Monitor the health of patients who have weakened immune systems to mitigate risk factors that increase their risks of developing pneumonia.

2. Provide appropriate vaccines for prevention of pneumococcal pneumonia and influenza per current guidelines.

3. Prescribe appropriate empiric therapy for CAP based on suspected pathogen and local susceptibility patterns.

4. Identify risk factors for multidrug-pathogens in patients who have HAP or VAP.

5. Prescribe appropriate antibiotic therapy for HAP or VAP based on risk factors for multidrug-resistant pathogens, predominant pathogens in the clinical setting and local susceptibility patterns.
Audience Engagement System

**Step 1**

**Step 2**

**Step 3**

Agenda

- Community acquired pneumonia
- Hospital and ventilator acquired pneumonia
- Pneumococcal vaccinations

Featuring cases, questions, US and world history and more!

Image source: https://commons.wikimedia.org/wiki/File:Spanish_flu_hospital.png
Before we begin

If you do not have access to one of these on your phone, tablet, or computer, please download the following (both are free):
- MDCalc Medical Calculator
- CDC PneumoRecs

A little history

- The Spanish Flu: the 1918 Flu Pandemic
- It's not in Kansas, anymore: American mobilization
- Wilson’s press declaration: censoring the flu’s spread
- A bad time to be young and healthy: reverse epidemiology
- The race of a lifetime: a bacterial vaccine
- End of the day: disease non-battle injury
The 315th Regiment, “Philadelphia’s Own”

- Private Tadeusz (Ted) Kowalski
- 20 years of age
- From Pottsville, PA
- Miner for the Reading Anthracite Company
- Working since 12
- WWI: Volunteered to serve
- Joined 315th Regiment at Camp Meade
- Healthy, except chronic cough
- Occasional smoker

The 315th Regiment, “Philadelphia’s Own”

- July 1918, embark for France at Hoboken
- Joins Western Front
- Serves through Meuse-Argonne offensive
- Cramped quarters, suboptimal sanitation
- Fevers, chills, aches
- Improves then worsens
- Medic notes fevers, chills, shakes, sweating, racking cough productive of sputum
Audience Engagement System (AES) Question 1

You see Private Kowalski’s great, great grandson, DC2 Teddy Kowalski, Navy Reservist, in clinic. He’s 20 years of age, generally healthy, and presents with symptoms of community acquired pneumonia. He’s had no recent antibiotics. What would be the ISDA/ATS recommended empiric therapy?

A. Doxycycline
B. Respiratory fluoroquinolone
C. Antipseudomonal β-lactam
D. β-lactam in combination with a macrolide
Definitions and statistics

- Acute lower respiratory tract infection
- Fever, chills, cough, tachypnea, abnormal breath sounds
- Guidelines require abnormal radiograph
- 920K global deaths among children annually
- Eighth leading cause of death in the US (along with influenza)
- Fourth leading cause of death globally (COPD is third)
- Among the working, increases healthcare costs by up to $31K to $113K per year

Community-acquired pneumonia (CAP) guidelines

- 2007 IDSA/ATS Consensus CAP Guidelines most current
- Following guidelines lowers mortality
- What has happened since then?
  - Increasing pneumococcal vaccine coverage
  - Increasing epidemiologic data
  - Increasing numbers of immunocompromised patients
  - Increasing age of population
  - Trials of imaging modalities, steroids, and other treatments
Thoughts

• CT scan discordant with clinicians read of patient and plain film 40% of the time; almost one third dx as CAP: no infiltrate on CT
• Rhinovirus and influenza are top two detected causes of CAP; streptococcus pneumonia is third
• BUT, for those hospitalized, time to antibiotics is still important
• Increasing evidence for use of lung ultrasound for diagnosis
• Increasing evidence on use of steroids for treatment

Ultrasound

Evolving evidence
• Emergency Department (adults): 92% sensitive, 93% specific (17 studies, n = 5108)
• Children: 96% sensitive, 95% specific (12 studies, n = 1510); CXR 87% sens, 98% spec
• French study, n = 23 with CT proven pneumonia, 23 with positive US, 12 with positive CXR

If interested in learning more about lung US: https://litfl.com/lung-ultrasound-pneumonia/
**Hospitalize?**

Free download: “Calculate by QxMD,” or “MDCalc Medical Calculator”

**CURB-65**
- Confusion
- Urea nitrogen >19mg/dl (7mmol/L)
- Respiratory rate ≥ 30
- BP systolic < 90 or diastolic ≤ 60mmHg
- Age ≥ 65

**PSI**
- Age
- Female
- Nursing home
- Liver
- Renal
- Cerebrovasc
- CHF
- AMS
- RR > 29
- SBP < 90
- T <35 or ≥40
- Pulse > 124
- pH < 7.35
- BUN >29
- Na <130
- Gluc > 249
- Hct < 30
- PaO2 < 60
- Pleural effusion

**AES Question 2**

Teddy returns, not improving. He admits that he lost his pills while on maneuvers and only took one day’s worth. That was five days ago. He doesn’t seem altogether right. Your assessment:

**Age:** 20  
**PMH:** No known disease  
**Alert but confused**  
**Respiratory rate:** 32  

**Heart rate:** 102, BP: 104/56  
**Temperature:** 104.2  
**Lung exam:** crackles, right posterior dullness, decreased breath sounds over base (suspect effusion)

What is the CURB-65 or PSI recommended disposition?

A. Restart outpatient therapy
B. Hold him for observation (inpatient, non-ICU care)
C. Send him to the field hospital for more intense care (inpatient, ICU care)
**Antibiotics**

- **Outpatient**
  - No comorbidities
    - Macrolide OR Doxycycline
  - Comorbidities
    - FQ OR β-lactam + macrolide

- **Inpatient**
  - FQ OR β-lactam + macrolide
  - ICU
    - β-lactam AND Azithromycin OR FQ
  - Non ICU
    - FQ OR β-lactam + macrolide
  - CA-MRSA
    - Add vancomycin or linezolid
  - Pseudomonas
    - Antipneumococcal/antipseudomonal β-lactam + FQ OR AG/azithromycin OR AG/FQ

**Steroids**

- Corticosteroids ↓ mortality in adults with severe pneumonia
  - RR 0.58, 95% CI 0.4 to 0.84
  - NNT to prevent one death 18, 95% CI 12 to 49
- Corticosteroids ↓ early clinical failure rates (combined death, radiographic progression, clinical instability) in adults with severe and non-severe pneumonia
- Corticosteroids reduce early clinical failures and time to cure in children
- Dosing variable
  - Average 40-50mg prednisone equivalents
  - Dosed one to ten days (most frequently seven days)
- Hyperglycemia more common in adults with corticosteroids, no significant difference in secondary infection
- Studies excluded patients with HIV
AES Question 3

You visit Teddy at the hospital; he’s doing better. Overhead, a rapid response is called. It is Teddy’s aunt, Elsinore, a retired Air Force air traffic controller five days out from a coronary artery bypass. She is 67 and has multiple comorbidities. She is found tachypneic and febrile and has diffuse crackles. Imaging reveals consolidation. She is intubated, and the rapid response team leaves to answer another call. The ICU team looks expectantly at you.

What is the recommended antibiotic treatment?

A. Single agent broad spectrum coverage
B. Single agent broad spectrum coverage + MRSA coverage
C. Two agent broad spectrum coverage + MRSA coverage

Hospital acquired pneumonia (HAP)
Ventilator acquired pneumonia (VAP)

Ventilator Associated Pneumonia
Occurs ≥ 48 hours after endotracheal intubation

Hospital Acquired Pneumonia
Occurs ≥ 48 hours after admission
Not incubating at time of admission

2016 IDSA/ATS Clinical Practice Guidelines

• In choosing therapeutic agents
  – First preference: use results of non-invasive sampling
  – Second preference: use results of local antibiograms
  – Third preference: use empiric regimens
• Seven days is sufficient

Treatment of HAP

- Not at increased risk for mortality
  - Not at increased risk for MRSA
    - Piperacillin-tazobactam
    - Cefepime
    - Levofloxacin
    - Imipenem
    - Meropenem
  - At increased risk for MRSA
    - Piperacillin-tazobactam
    - Cefepime or ceftazidime
    - Levofloxacin or ciprofloxacin
    - Imipenem
    - Meropenem
    - Vancomycin or linezolid
    - AND
Treatment of HAP

High risk for mortality

Choose two agents, only one of which can be a β-lactam

- Piperacillin-tazobactam
- Cefepime or ceftazidime
- Levofloxacin or ciprofloxacin
- Imipenem
- Meropenem
- Amikacin or gentamicin or tobramycin
- Vancomycin or linezolid

OR

OR

OR

OR

OR

AND

Treatment of VAP

Column A
- Vancomycin
- Linezolid

Column B
- Piperacillin-tazobactam
- Cefepime or ceftazidime
- Imipenem or Meropenem
- Atreonam

Column C
- Ciprofloxacin or Levofoxacin
- Amikacin or Gentamicin or Tobramycin
- Colistin or Polymyxin B
Treatment of VAP

Column A

Vancomycin

Linezolid

Cover for MRSA if one of the following are present:

- Patient has risk factors for antimicrobial resistance:
  - Prior abx use within 90 days
  - Septic shock
  - ARDS
  - Hospitalized ≥ 5 days prior to VAP
  - Need for acute renal replacement therapy prior to VAP
- Patient treated in unit where > 10-20% of S. aureus isolates are MRSA
- Patients in units with unknown MRSA prevalence

If RF for MRSA absent, regimen with piperacillin-tazobactam, cefepime, levofloxacin, imipenem, or meropenem sufficient for presumptive MSSA

Treatment of VAP

Column B

Piperacillin-tazobactam

Cefepime or Ceftazidime

Imipenem or Meropenem

Aztreonam

Double cover for P. aeruginosa and gram-negative bacilli if the following present:

- Patient has risk factors for antimicrobial resistance:
  - Prior abx use within 90 days
  - Septic shock
  - ARDS
  - Hospitalized ≥ 5 days prior to VAP
  - Need for acute renal replacement therapy prior to VAP
- Patient treated in unit where > 10% of gram-negative isolates resistant to monotherapy
- Patients in units with unknown antimicrobial susceptibility rates
AES Question 4

Elsinore sees you in follow up, along with her husband Larry, a retired Chief Master Sergeant. He is new to your practice, is 65 years old, and is open to vaccinations. You review his records and note he has not had any "pneumonia" vaccines. You schedule him for:

A. PCV13 now and PPSV23 one year later
B. PPSV23 now and PCV 13 one year later
C. PCV 13 only
D. PPSV23 only

Pneumonia then

- Discovered by Army Major George Sternberg in 1880
- Major threat to military operations during World War I
- Pneumococcal polysaccharide vaccines field tested by US Army
- 792,000 soldiers hospitalized for influenza or pneumonia, 25,000 deaths
- One in 67 soldiers died of influenza or pneumonia
Pneumonia now

• Streptococcus pneumoniae
  – Over 90 serotypes identified as of 2011
  – Polysaccharide capsule important in pathogenicity
• In children 6 or less
  • 7 serotypes common
  • 80% of invasive disease


PPSV23

• Pneumococcal Polysaccharide Vaccine
  – 1983 – 23 valent PPSV23 released
  – Replaced PPSV14 (not made anymore)

• Pneumovax 23 (Merck)
• Routinely given in Seniors (65 or greater)
PCV13

- Pneumococcal *Conjugate* Vaccine
- 2000 – 7 serotypes *conjugated* to CRM197 (nontoxic variant of diptheria)
- 2010 – 13 serotypes (7+ 6 new ones) *conjugated* to CRM197
- Typical use in *Children*

PCV13 vs. PPSV23

- *Conjugate* vs. *Saccharide*
- *Children* vs. *Senior*
- 13-valent vs. 23-valent

**Chronic Diseases**: Chronic heart disease, lung disease, Diabetes, smoking, liver disease, alcoholism, CSF leaks and cochlear implants
CAPiTA: is PCV13 effective for adults?

- Community acquired pneumonia Immunization Trial in Adults (CAPiTA)
- 84,946 adults 65 years or older (vaccine naïve)
- Randomized, double-blind trial
  – PCV13 vs. placebo
  – Followed for 4 years

<table>
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<th>PCV13 (42,240)</th>
<th>Placebo (42,256)</th>
<th>% Vaccine Efficacy</th>
<th>P Value</th>
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<td>90</td>
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<td>60</td>
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<td>28</td>
<td>75%</td>
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There are apps for that!

PneumoRecs VaxAdvisor
Centers for Disease Control and Prevention

PneumoVaccines
Joshua Steinberg, MD

AES Question 5

Larry’s and Elsinore’s friend, Jamal asks for you to be his doctor (your reputation is sky-rocketing based on your awesome pneumonia care). Jamal is 65 years of age, has type 2 diabetes, and would like to get his vaccinations done. After discussion, he would like any vaccines you recommend. You review his records and he has had one “pneumonia” vaccine (PPSV23) in 2017. It is September. You schedule him for:

A. PCV13 and influenza only
B. PPSV23 and influenza now and PCV 13 one year later
C. PCV 13 and influenza now and PPSV23 one year later
D. PCV 13 and influenza now and PPSV23 three years later
**Influenza vaccine**

**Benefit in preventing CAP**
- 2018 Song, PLoS One: Fewer cases of pneumonia when vaccine effective against circulating strains
- 2018 Heo, Hum Vaccin Immunother: Six meta-analyses report 25 to 53% effectiveness in preventing hospitalization due to pneumonia or influenza in the elderly

**Unsure benefit in those who later develop CAP**
- 2015 Li, J Hosp Med: small reduction in length of stay for CAP, no effect on inpatient survival
- 2011 Tessmer, Eur Respir J: less severe disease, improved survival at six months
- 2011 Manzur J Am Geriatr Soc: no difference in severity of CAP, length of stay, mortality in cohort ≥ 65 years of age
- 2007 Spaude, Arch Intern Med: improved inpatient survival

**Manufacturing influenza vaccine**

- Annual composition of vaccine varies based on circulating strains
- Once strains selected, six months to market
- WHO recommendations for 2019-2020
  - A/Brisbane/02/2018 (H1N1)pdm09-like virus
  - A/Kansas/14/2017 (H3N2)-like virus
  - B/Colorado/06/2017-like virus (B/Victoria/2/87 lineage)
  - B/Phuket/3073/2013-like virus (B/Yamagata/16/88 lineage)- quadrivalent only
- Egg-based, cell-based, and recombinant manufacturing techniques
Administering influenza vaccine

• 2019 ACIP recommendations
  – all persons 6 months and older without contraindications should receive influenza vaccine by end of October with an age appropriate vaccine
  – prioritize high risk groups
  – two doses for children 6 months to 8 years of age, 4 weeks between doses

The end of the story:
• 500 million infected globally
• 50 million deaths globally
• 675K deaths US
• Life expectancy fell 12 years
• Toll worsened by censorship
• Worse spread as a consequence of war

Today
• Routine influenza vaccination
• Antiviral medications
• Stockpiles of pandemic strain vaccines

https://commons.wikimedia.org/wiki/File:1919_‐_World_War_I_Victory_Parade_‐_Marching_Band_and_Veterans_Marching:_2_‐_Allentown_PA.jpg
Practice Recommendations

- Pneumonia is diagnosed clinically and radiographically
- Local microorganism epidemiology and susceptibility patterns should guide treatment
- Empiric regimens should be based on risk factors and severity of disease
- HAP and VAP are diagnosed if pneumonia develops 48 hours after hospitalization or ventilation, respectively
- Influenza and pneumococcal vaccination save lives
- If ≥ 65 y.o., immunocompetent, and vaccine naïve, give PCV13 first and then PSV23 in one year

Questions
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