

PNEUMONIA CAP TO HAP AND EVERYTHING IN-BETWEEN

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 - ▶ No Disclosures

OBJECTIVES

- ▶ 1) Review IDSA/ATS guidelines
- ▶ 2) Discuss the role of pneumonia severity scores
- ▶ 3) Identify high risk features for treatment failure

BY THE NUMBERS

- ▶ 4-5 million CAPs/year
- ▶ 20/100,000 people
- ▶ 25% require hospitalization
- ▶ Nosocomial pneumonia – 250,000/yr
- ▶ 18% of nosocomial infections

Outpatient

- ▶ *Streptococcus pneumoniae*
- ▶ *Mycoplasma pneumoniae*
- ▶ *Haemophilus influenzae*
- ▶ *Chlamydophila pneumoniae*
- ▶ Respiratory viruses

Inpatient (non-ICU)

- ▶ *S. pneumoniae*
- ▶ *M. pneumoniae*
- ▶ *C. pneumoniae*
- ▶ *H. influenzae*
- ▶ *Legionella* species
- ▶ Aspiration
- ▶ Respiratory viruses

Inpatient (ICU)

- ▶ *S. pneumoniae*
- ▶ *Staphylococcus aureus*
- ▶ *Legionella* species
- ▶ Gram-negative bacilli
- ▶ *H. influenzae*

CHOICES

- ▶ 1) Macrolides – Azithromycin, Clarithromycin
- ▶ 2) Sulfamethoxazole / Trimethoprim
- ▶ 3) Fluoroquinolones – Ciprofloxacin, Levofloxacin, Moxifloxacin
- ▶ 4) Amoxicillin / Clavulanate
- ▶ 5) Doxycycline

IDSA/ATS guidelines: Recommended empiric antibiotics for community-acquired pneumonia in adults

Outpatient treatment

1. Previously healthy and no use of antimicrobials within the previous three months:

A macrolide (azithromycin, clarithromycin, or erythromycin)

OR

Doxycycline*

2. Presence of comorbidities such as chronic heart, lung, liver, or renal disease; diabetes mellitus; alcoholism; malignancies; asplenia; immunosuppressing conditions or use of immunosuppressing drugs; or use of antimicrobials within the previous three months (in which case an alternative from a different class should be selected):

A respiratory fluoroquinolone (moxifloxacin, gemifloxacin, or levofloxacin [750 mg])

OR

A beta-lactam (first-line agents: high-dose amoxicillin, amoxicillin-clavulanate; alternative agents: ceftriaxone, cefpodoxime, or cefuroxime)

PLUS a macrolide (azithromycin, clarithromycin, or erythromycin)*

3. In regions with a high rate (>25 percent) of infection with high-level (MIC \geq 16 mcg/mL) macrolide-resistant *Streptococcus pneumoniae*, consider use of alternative agents listed in (2) above.

Inpatients, non-ICU treatment

A respiratory fluoroquinolone (moxifloxacin, gemifloxacin, or levofloxacin [750 mg])

OR

An antipneumococcal beta-lactam (preferred agents: cefotaxime, ceftriaxone, or ampicillin-sulbactam; or ertapenem for selected patients)[†] **PLUS** a macrolide (azithromycin, clarithromycin, or erythromycin)*^Δ

Inpatients, ICU treatment

An antipneumococcal beta-lactam (cefotaxime, ceftriaxone, or ampicillin-sulbactam) **PLUS** azithromycin

OR

An antipneumococcal beta-lactam (cefotaxime, ceftriaxone, or ampicillin-sulbactam) **PLUS** a respiratory fluoroquinolone (moxifloxacin, gemifloxacin, or levofloxacin [750 mg])

OR

For penicillin-allergic patients, a respiratory fluoroquinolone (moxifloxacin, gemifloxacin, or levofloxacin [750 mg]) **PLUS** aztreonam

Special concerns

If *Pseudomonas aeruginosa* is a consideration:

An antipneumococcal, antipseudomonal beta-lactam (piperacillin-tazobactam, cefepime, imipenem, or meropenem) **PLUS** either ciprofloxacin or levofloxacin (750 mg)

OR

The above beta-lactam **PLUS** an aminoglycoside **PLUS** azithromycin

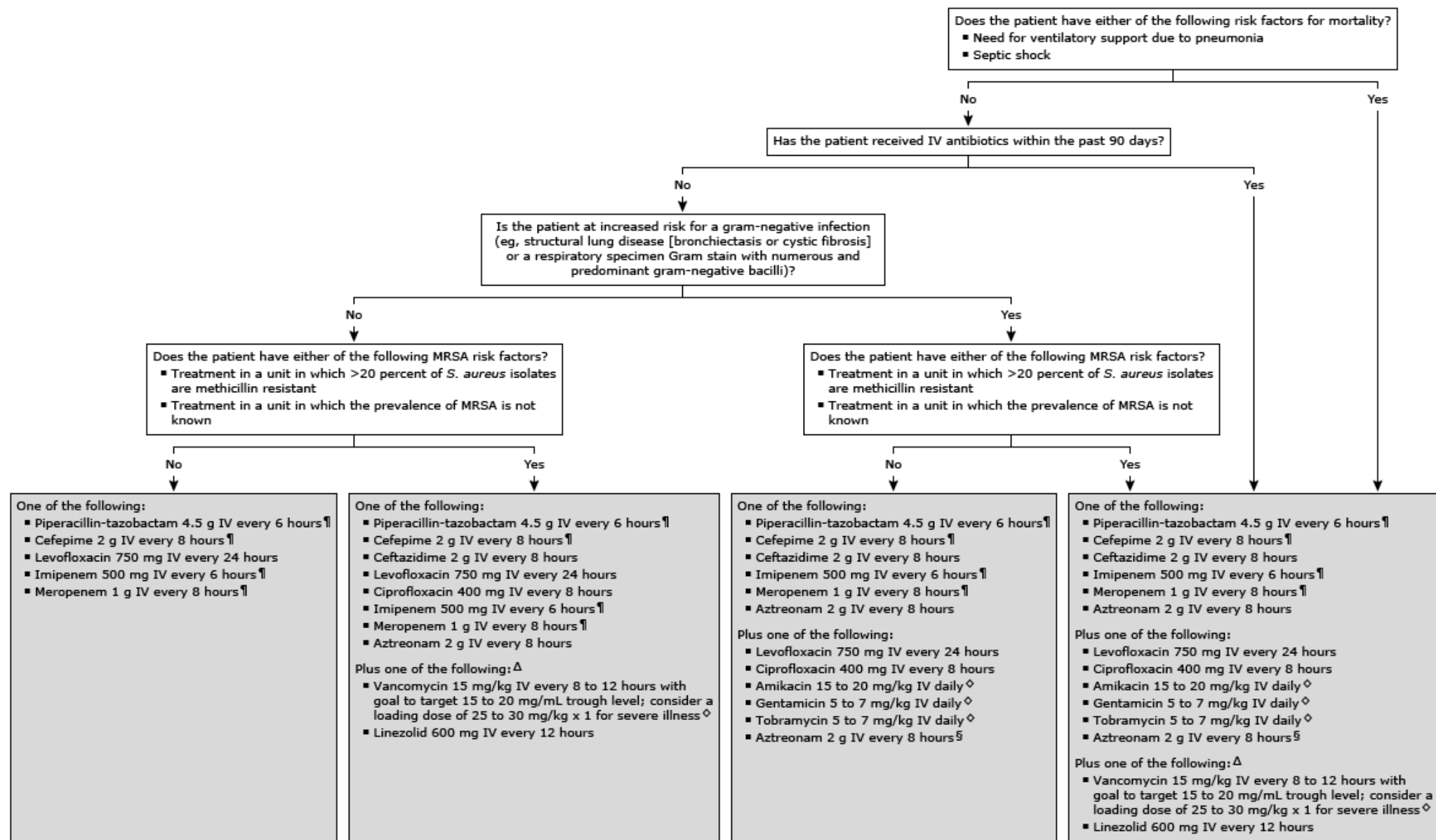
OR

The above beta-lactam **PLUS** an aminoglycoside **PLUS** a respiratory fluoroquinolone (moxifloxacin, gemifloxacin, or levofloxacin [750 mg]); for penicillin-allergic patients, substitute aztreonam for above beta-lactam

If CA-MRSA is a consideration:

Add vancomycin or linezolid

Empiric treatment of hospital-acquired pneumonia (not ventilator-associated pneumonia)*



IV: intravenous; MRSA: methicillin-resistant *Staphylococcus aureus*; HAP: hospital-acquired pneumonia; VAP: ventilator-associated pneumonia.

* The recommendations in this algorithm are generally in keeping with the 2016 Infectious Diseases Society of America/American Thoracic Society guidelines for the management of HAP and VAP. These regimens are intended for the initial treatment of patients with HAP in whom the microbiologic cause has not yet been identified. For patients with VAP, refer to the separate UpToDate algorithm. The doses above are intended for patients with normal renal function; dosing will need to be adjusted for patients with renal dysfunction.

Risk factors for MDR pathogens and/or increased mortality in patients with hospital-acquired pneumonia

Risk factors for increased mortality:
<ul style="list-style-type: none">▪ Ventilatory support for HAP▪ Septic shock
Risk factor for MDR <i>Pseudomonas</i>, other gram-negative bacilli, and MRSA:
<ul style="list-style-type: none">▪ IV antibiotics within the past 90 days
Risk factors for MDR <i>Pseudomonas</i> and other gram-negative bacilli:
<ul style="list-style-type: none">▪ Structural lung disease (bronchiectasis or cystic fibrosis)▪ A respiratory specimen Gram stain with numerous and predominant gram-negative bacilli
Risk factors for MRSA:
<ul style="list-style-type: none">▪ Treatment in a unit in which >20 percent of <i>Staphylococcus aureus</i> isolates are methicillin resistant▪ Treatment in a unit in which the prevalence of MRSA is not known

MDR: multidrug resistant; HAP: hospital-acquired pneumonia; MRSA: methicillin-resistant *S. aureus*; IV: intravenous.



CAP

- ▶ “an acute infection of the pulmonary parenchyma in a patient who has acquired the infection in the community.”

HAP

- ▶ “is pneumonia that occurs 48 hours or more after admission and did not appear to be incubating at the time of admission.”

VAP

- ▶ “is a type of HAP that develops more than 48 to 72 hours after endotracheal intubation.”

HCAP

- ▶ “a pneumonia that occurs in a nonhospitalized patient with extensive healthcare contact, as defined by one or more of the following:
 - ▶ • Intravenous therapy, wound care, or intravenous chemotherapy within the prior 30 days
 - ▶ • Residence in a nursing home or other long-term care facility
 - ▶ • Hospitalization in an acute care hospital for two or more days within the prior 90 days
 - ▶ • Attendance at a hospital or hemodialysis clinic within the prior 30 days

RISK STRATIFICATION

CAP – leading cause of sepsis

Clinical prediction rules for severity

- Pneumonia Severity Index
- CURB-65 score
- Severe community-acquired pneumonia score
- SMART-COP

Pneumonia Severity Index

- ▶ 1) Complex and requires a calculator
- ▶ 2) Only scoring system with randomized trials
- ▶ 3) Derived from the Pneumonia Patient Outcomes Research Team (PORT) study
 - ▶ 14,199 adults – 5 institutions
 - ▶ ICD-9 code
- ▶ 4) Validated – 38,039 inpatient with ICD-9
 - ▶ - 2287 outpatients
- 5) Age, coexisting conditions, physical exam

Pneumonia Severity Index

- ▶ Low risk – Class 1 and 2
- ▶ Low/Medium – Class 3
- ▶ High – Class 4 and 5

Pneumonia Severity Index

PSI class and mortality in the Pneumonia PORT validation cohort

Class	Points	Mortality, percent
I	No predictors	0.1
II	≤70	0.6
III	71 to 90	0.9
IV	91 to 130	9.3
V	>130	27.0

PSI: Pneumonia Severity Index; PORT: Patient Outcomes Research Team.

Data from: Fine MJ, Auble TE, Yealy DM. A prediction rule to identify low-risk patients with community-acquired pneumonia. *N Engl J Med* 1997; 336:243.

UpToDate®

VALIDATION

- ▶ 1) CAPITAL – 19 Canadian ED's
 - ▶ 1743 enrolled
 - ▶ 18% reduction in admission (class 1-3)
- ▶ 2) Prospective Assessment of the Safety of PSI
 - ▶ Mandell L, Ann Intern Med 2005, 142:215
 - ▶ PSI score < 90 (class 2/3) – outpatient vs inpatient (oral vs IV Levaquine)
 - ▶ Exclusions: PaO₂<60, sat < 90%, complicated pleural effusion...
 - ▶ Hard end points: treatment length, adverse events
- ▶ 3)EDCAP – 32 US ED's
 - ▶ Low risk (class 1-3) – 1901 without hypoxia
 - ▶ Statistically equal between classes – mortality, medical complications, ICU admits

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 radiograph	+10



CURB-65 SCORE

- ▶ 1) **C**onfusion
- ▶ 2) **U**rea > 20 mg/dl
- ▶ 3) **R**R > 30
- ▶ 4) **S**BP < 90
- ▶ 5) **A**ge > **65**

CURB-65 SCORE

- ▶ Lim WS, Thorax 2003;58:377
 - ▶ 718 pts
- ▶ 30 day mortality
 - ▶ - 0.7
 - ▶ - 2.1
 - ▶ - 9.2
 - ▶ - 14.5
 - ▶ - 40

CRB-65

- ▶ Bauer TT, J Intern Med 2006; 260:93.
 - ▶ 670 German patients
 - ▶ Outpatient – score 0
 - ▶ Inpatient – score 1+



DRUG RESISTANCE

- ▶ Risk factors
 - ▶ Age > 65
 - ▶ Abx use in the past 3 months
 - ▶ Alcoholism
 - ▶ Medical comorbidities
 - ▶ Immunosuppressive illness or therapy
 - ▶ Exposure to child in daycare

MACROLIDE RESISTANCE

- ▶ Use within the past 3 months
- ▶ > 25% resistance in the local community
- ▶ Pneumococcal bacteremia with MIC >1 mcg/ml
- ▶ Comorbidities – zithromycin preferred

FLUOROQUINOLONE RESISTANCE

- ▶ Prior use increases *S. Pneumoniae*
- ▶ Levofloxacin < Moxifloxacin < Gemifloxacin
- ▶ Treatment of patients with TB may delay diagnosis, increase resistance, and worsen outcomes

MRSA

- ▶ Vancomycin
- ▶ Linezolid
- ▶ Tigecycline
- ▶ Daptomycin

CAP TREATMENT

- ▶ Treatment duration 5-7 days
- ▶ Fluoroquinolone vs Beta-lactam + macrolide
- ▶ Macrolide + third generation cephalosporin decreased mortality and hospital stay compared to beta-lactam alone



QUESTION # 1

- 1) What is the drug of choice for the treatment of CAP in a low risk patient?
 - a) Augmentin
 - b) Levofloxacin
 - c) Clarithromycin
 - d) Amoxicillin

QUESTION #2

2) Which of the following is a risk factor for a multidrug resistant pathogen?

- a) Antibiotic use in the past 90 days
- b) Bronchiectasis
- c) Cystic Fibrosis
- d) All the above

