Best Practices in the Diagnosis and Treatment of Community-Associated Lower Respiratory Tract Infection

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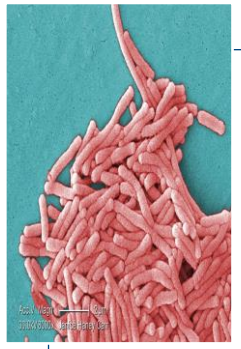
Learning Objectives

1. Identify key changes in the management of community-acquired pneumonia (CAP) following publication of the 2019 guidelines
2. Discuss the four moments of antibiotic decision making for patients with suspected CAP
3. Determine appropriate empiric therapy for patients presenting with CAP based on patient- and institution-specific factors
4. Identify areas of opportunity for antimicrobial stewardship interventions in CAP

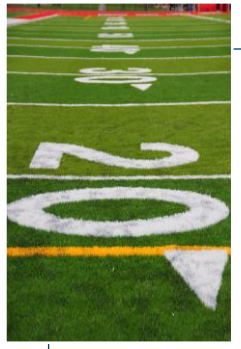
Controversies in CAP Management



Atypical Coverage

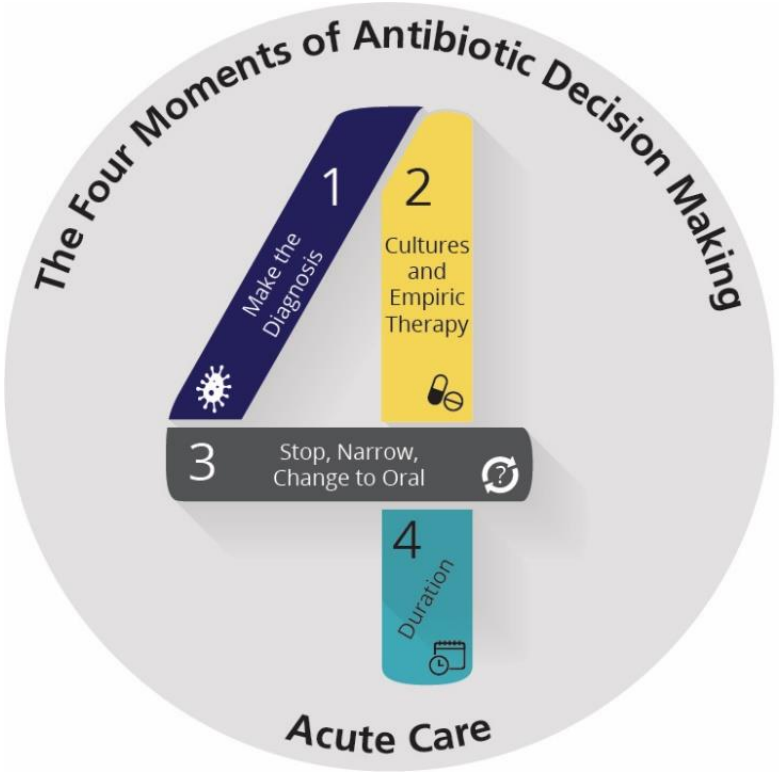
Risk Factors for Resistance

Corticosteroids



Duration

The Four Moments of Antibiotic Decision Making



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2. Have I ordered appropriate cultures before starting antibiotics? What empiric therapy should I initiate?
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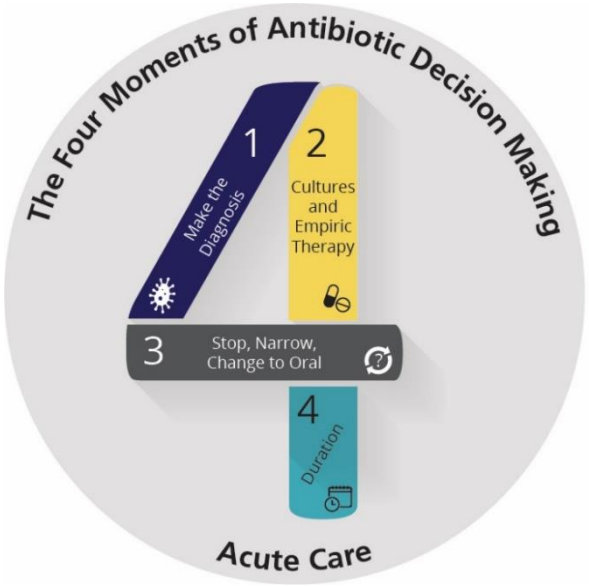
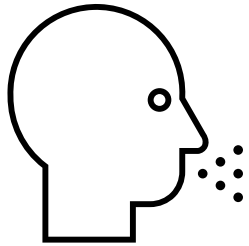
4. What duration of antibiotic therapy is needed for my patient's diagnosis?

The Four Moments of Antibiotic Decision Making



1. Does my patient have an infection that requires antibiotics?

Moment 1: Diagnosing CAP

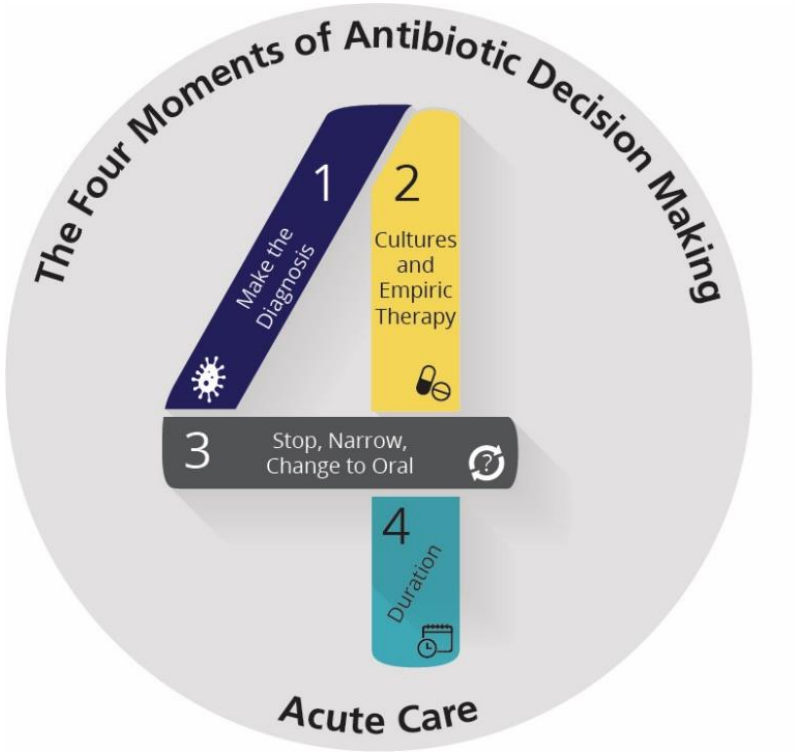


- Common signs and symptoms:
  - Cough and/or sputum production (90%)
  - Fever (>90%)
    - Less common in older patients
  - Chills (50%)
  - Tachypnea (45%)
  - Pleuritic chest pain (30%)
  - Crackles during chest auscultation

- If common signs and symptoms are present, obtain chest x ray
  - No infiltrates – indicates pneumonia not present
  - Presence of infiltrate without respiratory symptoms is unlikely to be CAP

Metlay JP et al. Am J Respir Crit Care Med. 2019 Oct 1;200(7):e45-e67.

The Four Moments of Antibiotic Decision Making



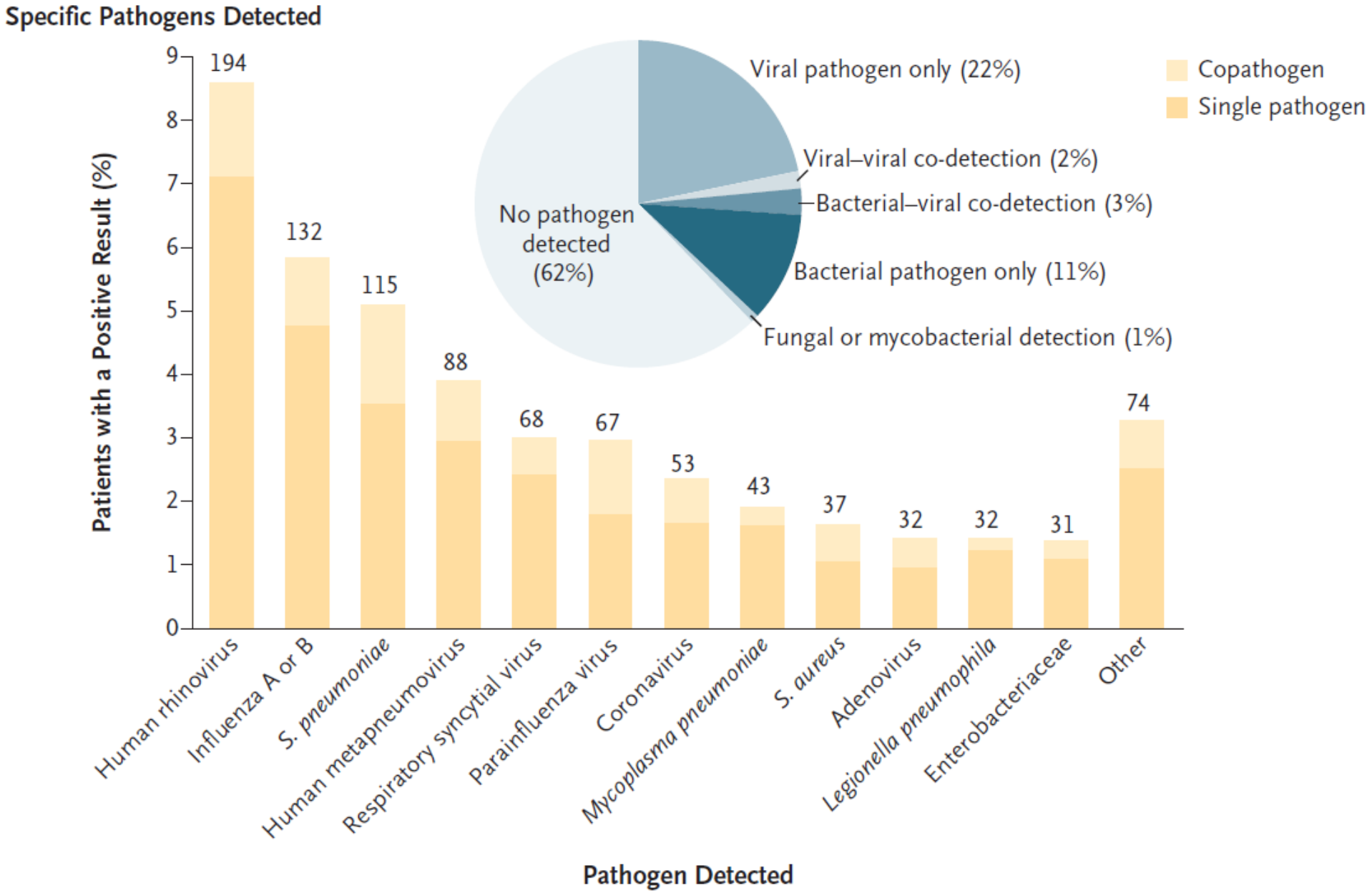
1. Does my patient have an infection that requires antibiotics?
2. Have I ordered appropriate cultures before starting antibiotics? What empiric therapy should I initiate?

What is the most common cause of community acquired pneumonia?

a. Atypical bacteria like *Mycoplasma pneumoniae*
b. Streptococcus pneumoniae
c. Viruses
d. Well now probably COVID….

CAP Pathogens

Old School	New School
Streptococcus pneumoniae	*Streptococcus pneumoniae*
Haemophilus influenzae	Viruses
Mycoplasma pneumoniae	
Staphylococcus aureus	
Chlamydia pneumoniae	
Moraxella catarrhalis	
Legionella spp.	



Jain S, et al. N Engl J Med 2015; 373:419

Diagnostic Tests

Test	Notes
Blood cultures	• Recommended for patients who are moderately to severely ill or with chest imaging findings of an abscess or parapneumonic effusion
Sputum Gram-stain and culture	• Recommended for making the diagnosis of CAP
Respiratory viral panel	• Provides an alternate explanation for the presentation
Streptococcus pneumoniae urinary antigen	• Recommended, if available, to assist with narrowing antibiotic therapy
Legionella urinary antigen	• Consider for patients with moderate to severe illness, smokers, or patients over 50 years of age • Only detects *L. pneumophilia* serogroup 1 (70–80% of Legionella infections)
Bronchoscopy	• Severely ill or immunocompromised patient not responding to therapy and no clear etiology

CAP Diagnostics – Procalcitonin?

- Procalcitonin is a calcitonin-related gene released by both immune and parenchymal cells as a host response to a bacterial infection
  - ↑ PCT levels in bacterial vs. viral or non-infectious causes
  - Typically appears 4-6 hours after inflammatory insult
  - Magnitude of PCT level thought to correlate with severity/resolution of infection
- May be elevated in other disease states: renal dysfunction, trauma, severe burns, major surgery, acute pancreatitis, and subarachnoid hemorrhage

Mesiner M et al. Intensive Care Med 2000;26:S212-6.

Procalcitonin IRL

- Higher procalcitonin strongly correlates with increased probability of bacterial infection but there is not a well validated threshold for discriminating viral and bacterial pathogens
- Sensitivity of procalcitonin to detect bacterial infection ranges from 38-91%

New Guideline Recommendation: PCT alone should not be used to justify withholding antibiotics in patients with clinically confirmed CAP

Self WH, et al. Clin Infect Dis 2017;65:183-190.

Metlay J, et al. Am J Respir Crit Care Med 2019;200:e45-67.

Beta-Lactam (BL) Monotherapy?
To Cover Atypicals or Not to Cover Atypicals

- CAP-START was designed for non-ICU patients and those unlikely to have *Legionella*
- Study had very low identification of atypical pathogens (e.g., Mycoplasma 0.4-1.8%)
- 90-day mortality endpoint – best choice?
- 38.7% of patients in the BL monotherapy arm still received atypical coverage during their hospitalization

…guideline verdict?

Garin N, et al. JAMA Intern Med 2014;174:1894-1901.

Eljaaly K, et al. BMC Infect Dis 2017;17:385.

Postma D, et al. N Engl J Med 2015;372:1312-1323.

IDSA Empiric CAP Therapy Recommendations

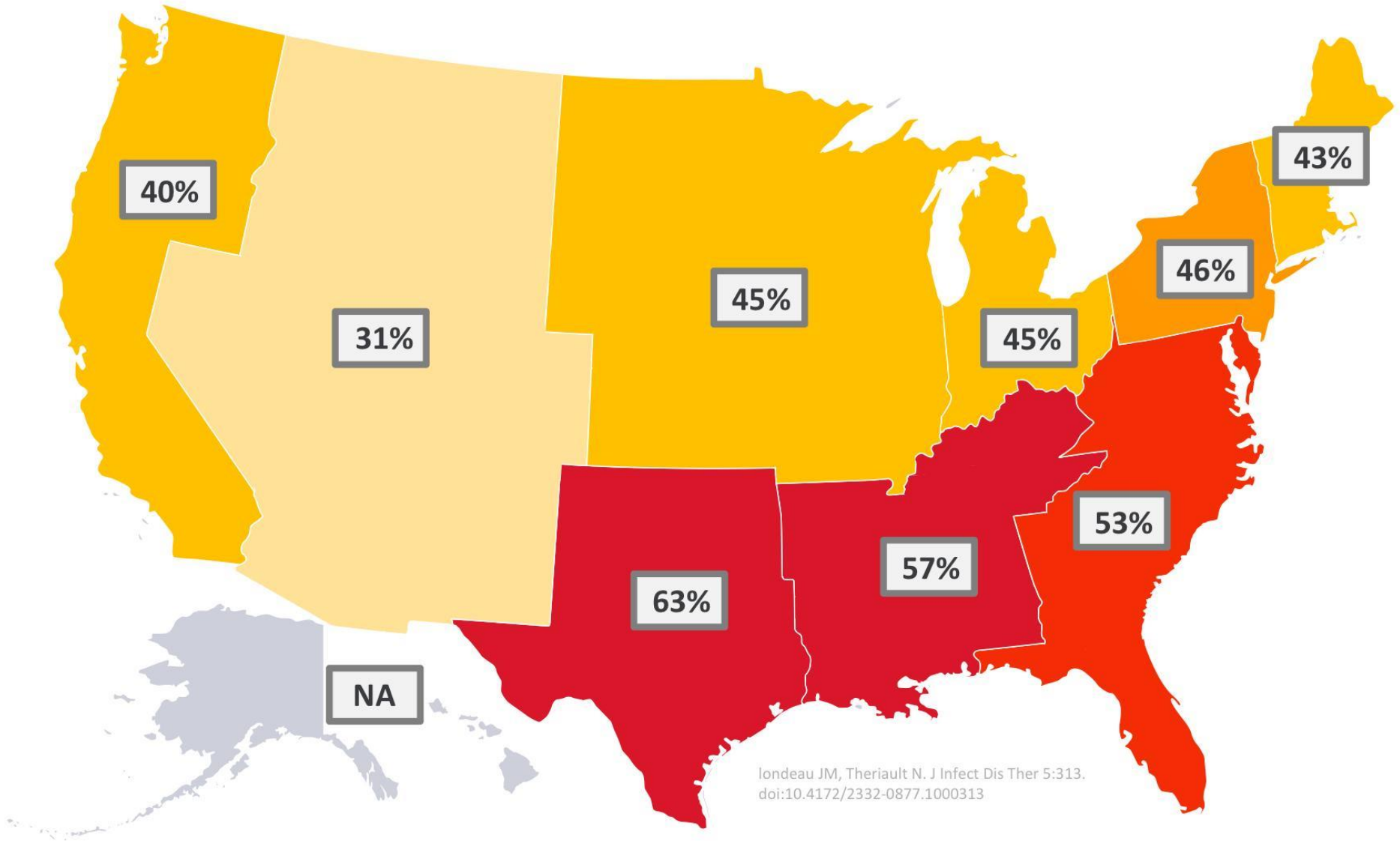
Healthy outpatients without comorbidities	Outpatients with comorbidities (e.g., chronic heart, lung, liver or renal disease; diabetes, malignancy)	Inpatients (non-severe) without risk factors for MRSA or *P. aeruginosa*	Inpatients (severe) without risk factors for MRSA or *P. aeruginosa*
• Amoxicillin 1g TID, or • Doxycycline 100 mg BID, or • A macrolide (e.g., azithromycin 500 mg on day 1 then 250 mg daily) in areas with macrolide resistance <25%	• Amoxicillin/clavulanate OR a cephalosporin (e.g., cefpodoxime) PLUS a macrolide or doxycycline, or • Respiratory fluoroquinolone*	• Beta-lactam (ampicillin/sulbactam, ceftriaxone) PLUS macrolide (or doxycycline) • Respiratory fluoroquinolone*	• Beta-lactam PLUS macrolide • Beta-lactam PLUS Respiratory fluoroquinolone*

Atypical coverage lives on!

*Reserve for severe PCN allergy

Metlay J, et al. Am J Respir Crit Care Med 2019;200:e45-67.

Azithromycin resistance for *S. pneumoniae*



Iondeau JM, Theriault N. J Infect Dis Ther 5:313.
doi:10.4172/2332-0877.1000313

FDA Drug Safety Communication: FDA updates warnings for oral and injectable fluoroquinolone antibiotics due to disabling side effects

- Combo therapy of beta-lactam plus macrolide or monotherapy with respiratory fluoroquinolone both given strong recommendations with high quality of evidence
- Weigh the risks and benefits, considering individual risk factors, when selecting

FDA Drug Safety Communication: www.fda.gov/drugs/drug-safety-and-availability/

Mandell L, et al. Clin Infect Dis 2007;44:S27-72.

What would you do?

A 72-year-old female presents from her long-term care facility to her local emergency department with concern for pneumonia. Her PMH is significant for HFrEF (EF 35%), type 2 diabetes, and CKD on hemodialysis MWF. She has no known drug allergies. What regimen would you start her on empirically?

A. Ceftriaxone
B. Ampicillin/sulbactam plus azithromycin
C. Piperacillin/tazobactam
D. Piperacillin/tazobactam plus vancomycin

RIP Healthcare-Associated Pneumonia (HCAP)

- Introduced in the 2005 American Thoracic Society (ATS)/Infectious Diseases Society of America (IDSA) guidelines for hospital-acquired, ventilator-associated and healthcare-associated pneumonia
- HCAP risk factors:
  - Nursing home resident or other long-term care facility
  - Hospitalization of 2+ days in the last 90 days
  - Receipt of home infusion therapy
  - Chronic dialysis
  - Family member with known resistant pathogen
- 2016 HAP/VAP Guidelines – turf dealing with HCAP to the CAP Guideline revisions

Niederman MS, et al. Am J Respir Crit Care Med 2005;171:388-416.

Kalil A, et al. Clin Infect Dis 2016;63:e61-e111.

RIP Healthcare-Associated Pneumonia (HCAP)

- **HCAP risk factors were not shown to predict high prevalence of antibiotic-resistant pathogens in most settings**
  - Meta-analysis of 24 studies (n=22,456) found that the discriminatory ability of HCAP definition for resistant pathogens was low (AUC, 0.70; 95% CI, 1.9-2.63)
- **HCAP risk factors led to a significant increase in use of broad spectrum agents without improving patient outcomes**
  - Cohort of patients admitted to 150 VA hospitals compared outcomes of guideline-concordant HCAP treatment vs non-guideline concordant HCAP therapy actually associated with higher 30-day mortality after controlling for confounders (OR 1.51; 95% CI 1.20-1.90)
  - Trends in antibiotic prescribing across 95,511 VA hospitalizations demonstrated a 15% increase in vancomycin use and 11% increase in piperacillin/tazobactam use with a decrease of 7% of ceftriaxone and 6% of azithromycin (P<0.001 for all) in the 5 years following the HCAP guidelines

Chalmers JD, et al. Clin Infect Dis 2014;58:330-9.

Attridge RT, et al. J Crit Care 2016;36:265-71.

Jones B, et al. Clin Infect Dis 2015;61:1403-10.

Sensitivity/Specificity/PPV/NPV

- Sensitivity and specificity: Characteristics of a test, **independent of prevalence**
  - **SeNsitive = SNout = rule out**
  - **SPecific = SPin = rule in**
- Positive predictive value (PPV) and negative predictive value (NPV): Clinical relevance of a test, **dependent on prevalence**
  - **As prevalence decreases, the PPV decreases because there will be more false positives for every true positive**
  - **As prevalence decreases, the NPV increases because there will be more true negatives for every false negative**

Performance of Prediction Tools

HCAP Risk Factors	Prevalence (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Micek (St. Louis)	50.7	88	53.7	66.1	81.3
Shorr (St. Louis)	45.2	86.9	48.6	58.2	81.7
Kollef (US Database)	34	54.5	75.1	49.3	78.8
Schreiber (D.C.)	31.6	78.3	56.2	45.2	84.9

Drug Resistance in Pneumonia (DRIP) Prediction Score

Major Risk Factors (2 points each)	Minor Risk Factors (1 point each)
Antibiotic use within previous 60 days Residence in long-term care facility Tube feeding Prior infection with a drug-resistant pathogen (1 yr)	Hospitalization within 60 days Chronic pulmonary disease Poor functional status Gastric acid suppression Wound care MRSA colonization (1 year)

>/= 4 points
Prevalence 33%
PPV 0.68
NPV 0.90

Webb B, et al. Respir Med 2015;109:1-10.

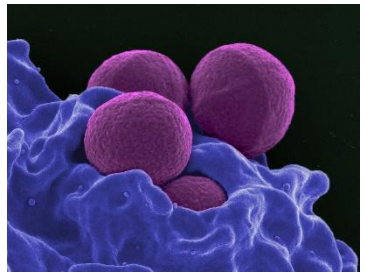
Webb B, et al. Antimicrob Agent Chemother 2016;60:2652

So when to broaden?

- Add empiric coverage of MRSA or *P. aeruginosa* in adults with CAP if *locally validated* risk factors for either pathogen are present
- Strongest individual risk factors-
  - prior isolation of these organisms, especially from the respiratory tract
  - and/or recent hospitalization and exposure to parenteral antibiotics
- "While we understand that clinicians would prefer a simple rule that does not require incorporating site specific data, the current evidence available does not permit endorsement of a simple and accurate rule to determine which patients with CAP should be covered for MRSA and/or *P. aeruginosa*"

Metlay J, et al. Am J Respir Crit Care Med 2019;200:e45-67.

So when to broaden?



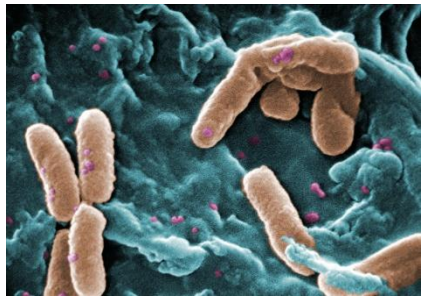
- Strongest individual risk factors per guidelines
  - Prior isolation of these organisms, especially from the respiratory tract
  - and/or recent hospitalization and exposure to parenteral antibiotics
- GLIMP: Methicillin-resistant *S. aureus* (MRSA)
  - Global Initiative for MRSA Pneumonia: Multicenter, international cohort (222 hospitals in 54 countries)
  - 3193 patients hospitalized with CAP who had microbiologic tests within 24h of admission
  - Prevalence of MRSA pneumonia = 3%
  - Risk factors for MRSA pneumonia
    - **Previous MRSA colonization or infection (OR 6.21, 95% CI 3.25-11.85)**
    - Recurrent skin infections (OR 2.87, 95% CI 1.10-7.45)
    - Severe pneumonia* (OR 2.39, 95% CI 1.55-3.68)
- Recent study out of Chicago showed 1.2% of patients with CAP had MRSA within 72h of admission, rate was higher in ICU patients requiring MV

*ICU admission, mechanical ventilation, vasopressors/inotropes in first 24h of admission

Aliberti S et al. Lancet Infect Dis 2016;16:1364-76
Rhodes NJ et al. Antimicrob Agents Chemother 2003;67:e0102322..

Image Credit: NIH NIAID

So when to broaden?



- Same cohort as GLIMP
- Prevalence of *P. aeruginosa* – 4.2% (11.3% of patients with a positive culture for bacterial pathogens)
- Prevalence of antibiotic-resistant* *P. aeruginosa* – 2.0%
- Risk factors *P. aeruginosa* CAP
  - **Prior *Pseudomonas* infection/colonization (OR 16.10, 95% CI 9.48-27.35)**
  - Prior tracheostomy (OR 6.50, 95% CI 2.61-16.19)
  - Bronchiectasis (OR 2.88, 95% CI 1.65-5.05)
  - Invasive respiratory and/or vasopressor support (OR 2.33, 95% CI 1.44-3.78)
  - Very severe COPD, FEV_1 ≤30% (OR 2.76, 95% CI 1.25-6.06)

*resistant to at least one antibiotic with Pseudomonal coverage

Restrepo M, et al. Eur Respir J 2018;52 (epub)

Image Credit: Wiki Commons, CDC

How do I do this locally?

- ICD-10 codes for Pneumonia present on arrival along with risk factors of interest identified retrospectively across a health system
- Multivariable logistic regression used to determine risk factors associated with MRSA or *P. aeruginosa* CAP

Table 3. Logistic Regression Evaluation for Methicillin-Resistant *Staphylococcus aureus* in Community-Acquired Pneumonia.

Variable	Odds ratio	95% CI	*P* value
Empyema/Abscess	4.24	2.21-8.14	<0.0001
Alcohol use disorder	1.04	0.67-1.64	0.8
Illicit substance use	1.7	1.25-2.3	0.007
COPD/Tobacco use	1.26	1.01-1.55	0.04
Diabetes mellitus type II	1.13	0.9-1.42	0.3
HIV	2.55	0.6-10.79	0.2
Influenza	2.34	1.18-4.67	0.01
Bronchiectasis	1.27	0.46-3.48	0.6
Chronic kidney disease	0.89	0.67-1.2	0.9
End-stage renal disease	2.09	1.23-3.56	0.006

Abbreviation: COPD, chronic obstructive pulmonary disease.

Table 4. Logistic Regression Evaluation for *Pseudomonas aeruginosa* in Community-Acquired Pneumonia.

Variable	Odds ratio	95% CI	*P* value
Empyema/Abscess	3.36	1.43-7.87	0.005
Alcohol use disorder	0.32	0.13-0.79	0.01
Illicit substance use	0.8	0.5-1.3	0.4
COPD/Tobacco use	1.84	1.41-2.39	<0.0001
Diabetes mellitus type II	0.61	0.46-0.82	0.001
Influenza	0.73	0.23-2.32	0.6
Bronchiectasis	6.13	3.35-11.23	<0.0001
Chronic kidney disease	1	0.72-1.41	0.9
End-stage renal disease	1.06	0.47-2.39	0.9

Abbreviation: COPD, chronic obstructive pulmonary disease.

Lewis P. Annals of Pharmacotherapy 2020. DOI:10.1177/1060028020935106.

…and then when to pull back

- "De-escalation of antibiotic therapy at 48 hours in accord with microbiological results that do not yield MRSA or *P. aeruginosa* is safe and reduces duration of antibiotic treatment, length of hospitalization, and complications of broad-spectrum antibiotic therapy"
- MRSA nasal screening can assist!

Type of Pneumonia	No. Studies	Sensitivity, % (95% CI)	Specificity, % (95% CI)	PPV, %	NPV, %
All	22	70.9 (58.8-80.6)	90.3 (86.1-93.3)	44.8	96.5
CAP/HCAP	4	85 (59.7-95.6)	92.1 (81.5-96.9)	56.8	98.1
VAP	5	40.3 (17.4-68.4)	93.7 (77.1-98.4)	35.7	94.8

Pooled prevalence of MRSA pneumonia in meta-analysis ~ 10%

Carugati M, et al. Clin Microbiol Infect 2015;21:936
Viasus D et al., J Antimicrob Chemother 2016;73:547
Yamana H, et al. J Infect 2016; 73:314
Parente DM, et al. Clin Infect Dis. 2018;67(1):1-7.
Metlay J, et al. Am J Respir Crit Care Med 2019;200:e45-67.

Leveraging Technology to Assist

Sputum Culture	Moderate Growth of Normal Oral Flora
	Negative For Methicillin Resistant Staphylococcus aureus.
	Negative for Staphylococcus aureus.
	Negative for Pseudomonas aeruginosa.
Gram Stain	Few WBC Seen
	Few Epithelial Cells Seen
	Rare Gram Negative Rods
	Moderate Gram Positive Cocci
	Rare Gram Positive Rods
	Specimen Optimum for Culture

- **Total de-escalation ↑** from 39% to 73% ($p<0.001$)
- **Duration of anti-MRSA and antipseudomonal therapy ↓** from 7 to 5 days
- **Acute kidney injury ↓** from 31% to 14% ($p=0.003$)
- Subsequent culture with multidrug-resistant organism ↓ from 8% to 1% ($p=0.035$)
- No difference in CDI, length of stay, all cause mortality

Musgrove MA, et al. Open Forum Infect Dis. 2018;5(7):ofy162.

Aspiration Events and Aspiration Pneumonia

Aspiration Event

- Macroaspiration of gastric contents leading to chemical irritation of the lung parenchyema
- Can progress quickly to respiratory failure followed by rapidimprovement ≤48 hours of the event
- Chest X-rays can look very concerning! BUT
- **Most aspiration events do not develop into bacterial pneumonia**
- Antibiotics do not prevent subsequent aspiration pneumonia
  - Patients who received prophylactic antibiotics following an aspiration event were no less likely to require transfer to the ICU, and were more likely to require escalation of antibiotic therapy during hospitalization

Dragan V et al. Prophylactic Antimicrobial Therapy for Acute Aspiration Pneumonitis. Clin Infect Dis. 2018;67:513-18

Aspiration Pneumonia

- Worsening pulmonary signs and symptoms after initial improvement following an aspiration event
- Occurs ~48 hours after the aspiration event
- Risk factors: bowel obstruction, enteral feeds, PPIs/H2 blockers, poor dentition, gingival diseases, loss of consciousness, older age, and esophageal motility disorder
- Treat as CAP or HAP depending on duration of hospitalization
  - For patents initially stated on antibiotics early, If rapid improvement in clinically status occurs, antibiotics can be discontinued
- **Targeted anaerobic coverage not needed**

Anaerobic Coverage

- Should I add additional anaerobic coverage to standard CAP therapy in patients with suspected aspiration pneumonia?
  - Not routinely!
    - Only if lung abscess or empyema suspected
    - **Lung abscess**
      - Result of chronic aspiration often in people with poor dentition and episodes of loss of consciousness
      - Mixed aerobic and anaerobic infection

Are steroids routinely used in your practice for patients with CAP?

A. Yes, for all patients admitted for CAP
B. Yes, only for patients admitted for CAP in the ICU
C. Yes, only for patients with septic shock secondary to CAP
D. No, didn’t even know that was a thing

Roid Rage

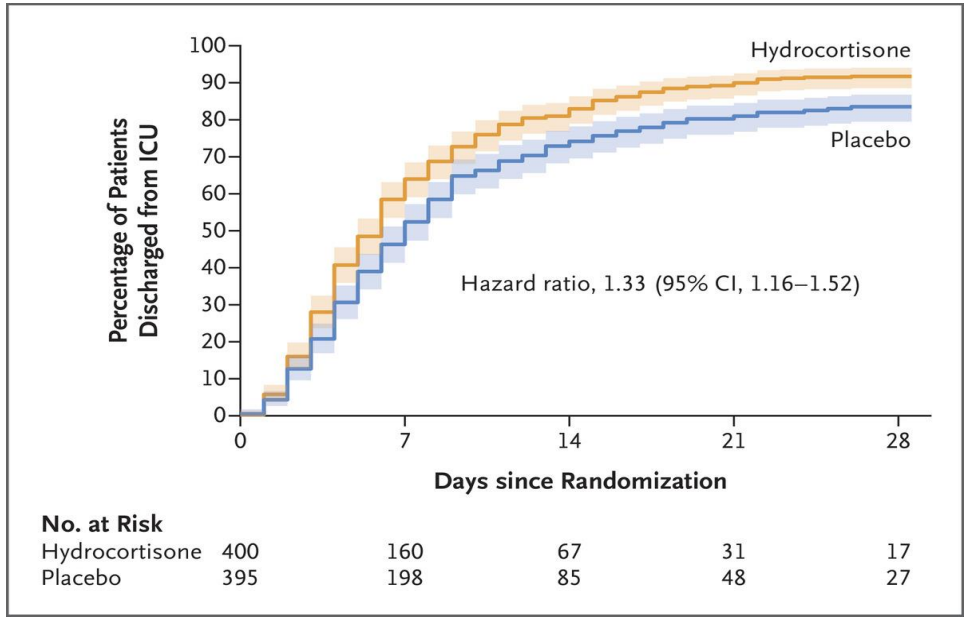
- Severe CAP → Excessive inflammatory response → steroids!
- Two large RCTs (Torres, Blum) have shown benefit in time to resolution of fever and clinical stability but not mortality, length of stay or organ failure
- Many, many meta-analyses have been done – some do show a mortality benefit in severe CAP
- Adverse effects of corticosteroids include hyperglycemia and possible higher secondary infection rates

Guideline Take Home: Corticosteroids are not routinely recommended in adults with CAP or severe influenza pneumonia. Use in CAP with refractory septic shock as per Surviving Sepsis Campaign

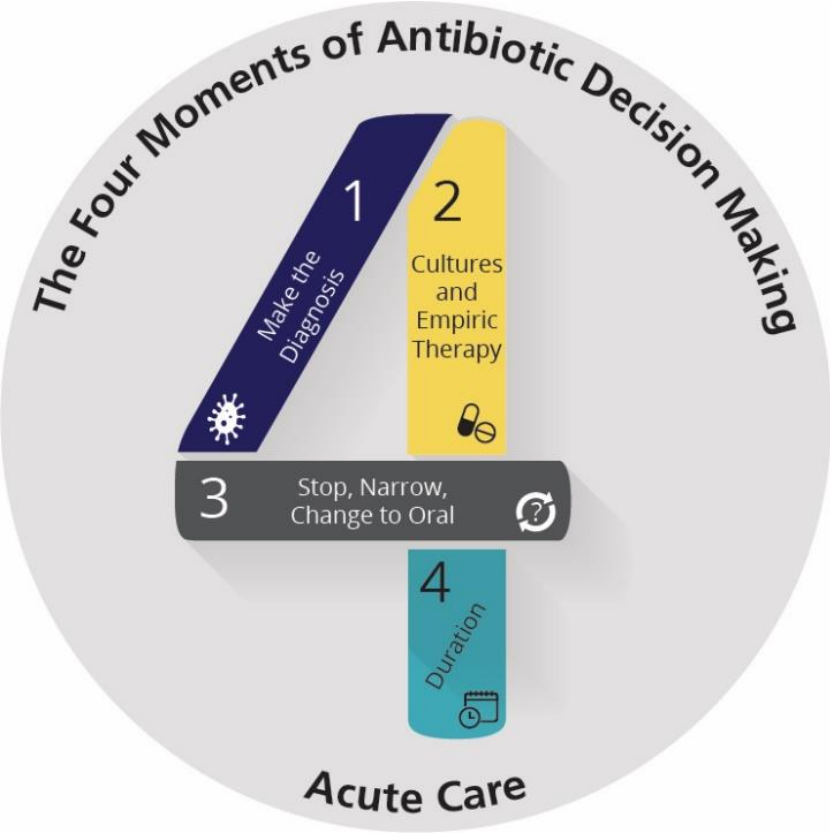
Torres A, et al. JAMA 2015;313:677-86.
Blum CA, et al. Lancet 2015;385:1511-8.
Briel M, et al. Clin Infect Dis 2018;66:346-54.

This Just In!

- Phase 3 RCT of patients with CAP in the ICU randomized to IV hydrocortisone for 4 or 8 days followed by a taper or placebo
  - ~45% of patients required mechanical ventilation
  - Most were PSI Class IV
- 25/400 (6.2%) in the hydrocortisone group and 47/395 (11.9%) in the placebo group had 28 day all-cause mortality (p=0.006)
- Similar rates of hospital acquired infections and GI bleeding between groups; hydrocortisone group had higher insulin requirements



The Four Moments of Antibiotic Decision Making



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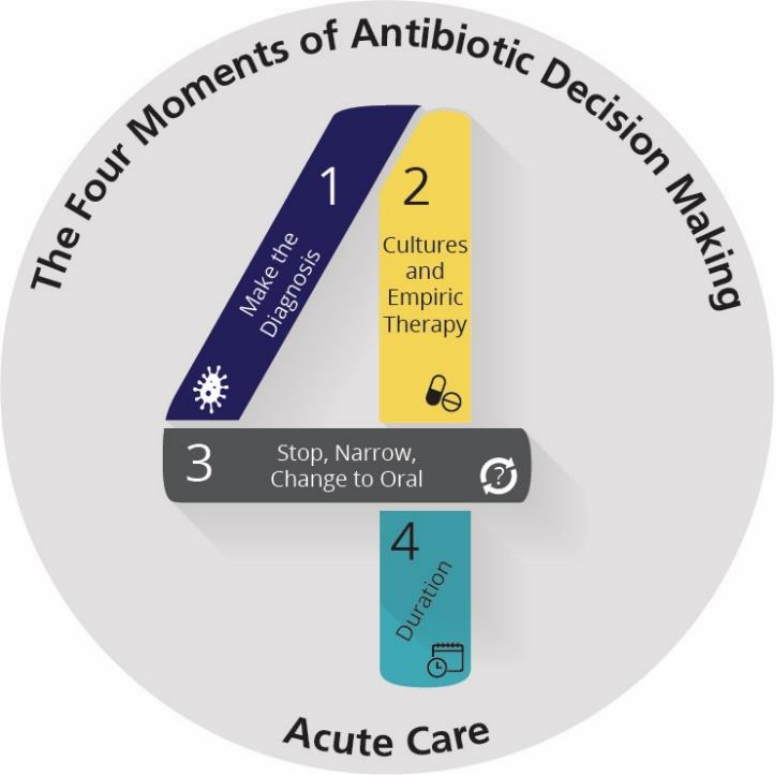
3. A day or more has passed. Can I stop antibiotics? Can I narrow therapy or change from IV to oral therapy?

IV-to-PO Conversions

- Convert your patient to oral antibiotics as soon as clinical improvement is observed and the patient is able to tolerate oral therapy.
- When can I narrow to amoxicillin?
  - If the sputum culture grows an amoxicillin or ampicillin-susceptible organism
  - If the streptococcal urinary antigen test is positive and the proportion of *S. pneumoniae* isolates in your hospital that are penicillin resistant is low
- If no results are positive, consider amoxicillin/clavulanate or an oral third generation cephalosporin
  - Respiratory fluoroquinolones should only be used in patient with severe penicillin allergies
- 3 days of azithromycin is sufficient given its long half life

The Four Moments of Antibiotic Decision Making



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How Low Can You Go?

- Antibiotic therapy should be continued until the patient achieves stability and “for no less than a total of 5 days”

  - Validated RCT of patients hospitalized with CAP
    - Treatment for a minimum of 5 days and stopping if afebrile x48 hours and no more than 1 sign of clinical instability vs duration determined by clinician
    - Median days of therapy in the intervention arm was 5 days vs 10 days in the control
    - No differences in clinical success at day 10 or 30, mortality or days until normal activity
    - 30 day readmissions higher in the control group

Criteria for Clinical Stability
Temp </= 37.8◦C
HR </= 100 BPM
RR </= 24 breaths/min
SBP >/= 90 mmHg
Arterial O2 sat >/= 90% on room air
Ability to maintain oral intake*
Normal mental status

*Important for PO switch but not duration of treatment

Uranga A et al. JAMA Intern Med. 2016;E1-E9.

5 Days of Antibiotics is Sufficient for CAP

- At least five randomized-controlled trials (RCTs) have shown that antibiotic treatment for 5 days is as safe and effective as longer treatment courses
  - One RCT even showed therapy as short as 3 days was sufficient
  - Data from bronchoscopy samples demonstrate 95% of patients with bacterial pneumonia eradicate pathogen after 3 days of therapy
- Two meta-analyses have also shown short courses of antibiotic therapy are effective for the treatment of CAP
  - 22 RCTs with > 8,000 patients
- Can you go even lower??

Li JZ et al. Am J Med 2007;120:783-90.
Dimopoulous G et al. Drugs 2008;68:1841-54.
Uranga A et al. JAMA Int Med 2016;176:1257-65.
Dunbar et al. Clin Infect Dis 2003;37:752-60.
File TM et al. J Antimicrob Chemother 2007;60:112-20
El Moussaoui R et al. BMJ 2006;332:1355

Discontinuing β-lactam treatment after 3 days for patients with community-acquired pneumonia in non-critical care wards (PTC): a double-blind, randomised, placebo-controlled, non-inferiority trial

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Risk class (Points)	Mortality (%)	Recommended site of care
I (<50)	0.1	Outpatient
II (51–70)	0.6	Outpatient
III (71–90)	2.8	Outpatient or brief inpatient
IV (91–130)	8.2	Inpatient
V (>130)	29.2	Inpatient

- Double-blind, placebo-controlled RCT at 16 centers in France 2013-2018 of hospitalized adults with moderately severe CAP not requiring an ICU
- If stable after 3 days of treatment with β-lactam therapy, randomized to receive β-lactam therapy (amox/clav 1 gram tid) or placebo for 5 more days
- Primary outcome: cure 15 days after first abx start (T ≤37.8°C, Sx improvement, no extra abx)
- 706 patients assessed for eligibility → 310 eligible patients → 153 8d and 157 3d
  - Median age 73.0 years, 41% female
  - Median PSI score 82 (IQR 58–104)
  - Micro: 2% bacteremic, micro diagnosis in 10%--*S. pneumo* and *H. flu*
- Cure at day 15: 68% 8d vs 77% 3d, NS
- LOS: six 8d vs five 3d
- AEs: 19% 8d vs 14% 3d

Dihn A et al. Lancet. 2021; 397: 1195–203

Duration of Therapy for CAP—Considerations

- Issues with study
  - Bias to null
    - Bacterial diagnosis in only 10% (and only 2% bacteremic), no legionella, no viral testing reported
    - Liberal definition of failure with failure in 27%: no resolution/improvement of respiratory Sx, and/or T ≥ 37.9°C and/or receipt of additional abx)
      - Purulent sputum (24%), dyspnea (22.6%), cough (21.0%), cough and purulent sputum (17.1%)
    - Europe does not use empiric atypical coverage
- There are many patients admitted to US hospitals for CAP that are like the patients in this study and who can receive 3 days of therapy
  - No CAP in the first place
  - No bacterial CAP in the first place
  - Mild disease

Durations

- Consider prolonging therapy to at least **7 days** if—
  - The patient is immunocompromised
  - The patient has underlying structural lung disease (not including asthma)
  - The patient did not have an adequate clinical response to therapy within 72 hours
- If the patient has a nontraditional CAP pathogen such as Legionella, *Pseudomonas aeruginosa*, or *S. aureus*, longer durations of therapy are usually required, particularly if there is associated bacteremia
- A lingering cough and chest X-ray abnormalities may take several weeks to improve

Summary of Guideline Changes - Diagnostics

Recommendation	2007 ATS/IDSA Guideline	2019 ATS/IDSA Guideline
Sputum Culture	Patients with severe disease	Patients with severe disease and all inpatients treated empirically for MRSA or *P. aeruginosa*
Blood Culture	Patients with severe disease	Patients with severe disease and all inpatients treated empirically for MRSA or *P. aeruginosa*
Procalcitonin	Not covered	Not recommended to determine need for initial antibiotic therapy
Routine use of follow-up chest imaging	Not covered	Not recommended

Metlay J, et al. Am J Respir Crit Care Med 2019;200:e45-67.

Summary of Guideline Changes - Treatment

Recommendation	2007 ATS/IDSA Guideline	2019 ATS/IDSA Guideline
Macrolide monotherapy	Strong recommendation for outpatients	Conditional recommendation for outpatients based on resistance
Empiric therapy for severe CAP	Beta-lactam/macrolide and beta-lactam/fluoroquinolone given equal weighting	Stronger evidence in favor of beta-lactam/macrolide combination
Use of HCAP Category	Accepted as per 2005 ATS/IDSA hospital-acquired and ventilator-associated pneumonia guidelines	Abandon the category and focus on local epidemiology and validated risk factors to determine need for MRSA or *P. aeruginosa* coverage
Use of corticosteroids	Not covered	Not universally recommended, consider in patients with septic shock

Metlay J, et al. Am J Respir Crit Care Med 2019;200:e45-67.

COPD Exacerbations

Distinguishing a COPD Exacerbation From CAP

- Distinguishing COPD and CAP in a patient with a known history of COPD can be challenging.
- If a chest x ray does not show evidence of a new infiltrate, the patient is more likely to have a COPD exacerbation.

- Although not all patients with a COPD exacerbation need antibiotics, patients requiring hospitalization for COPD are likely to have a moderate to severe COPD exacerbation for which antibiotic therapy is recommended.
- Antibiotics should be given when patients have three cardinal symptoms: increase in dyspnea, sputum volume, and sputum purulence or patients requiring mechanical ventilation (invasive or non-invasive)

Management of COPD Exacerbations

- Common bacteria associated with COPD exacerbations include *H. influenzae* and *S. pneumoniae*
- Sputum Gram-stain and culture are not needed in many cases of COPD exacerbation, but can be considered for patients with extensive prior antibiotic exposure or a severe COPD exacerbation
- Most patients can be treated with 3 days of azithromycin
- If a patient is already taking azithromycin, consider doxycycline, amoxicillin/clavulanate, or cefuroxime for a 5-day course
- Avoid use of fluoroquinolones unless prior or current microbiology indicates infection with organisms resistant to standard therapy

Bach PB et al. Ann Intern Med 2001;134:600-20.
El Moussaoui R et al. Thorax 2008;63:415-22.

Take Homes

- Treatment regimens for inpatient management of CAP have not changed substantially from 2007 guidelines
- HCAP has been retired and individualized risk factors for MRSA and *P. aeruginosa* should guide broader spectrum empiric therapy
- Corticosteroids should not be routinely used for most CAP patients based on current data
- 5 days of therapy in patients with clinical stability is adequate
- Multiple emerging treatment options are available

Best Practices in the Diagnosis and Treatment of Community-Associated Lower Respiratory Tract Infection

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