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Review of Treatment Options for Pneumonia in the Inpatient Setting

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7/16/2020

Pneumonia

- Community acquired pneumonia (CAP)
- ~~Healthcare associated pneumonia (HCAP)~~
- Hospital-acquired pneumonia (HAP)
- Ventilator associated pneumonia (VAP)
- Aspiration pneumonia

AMERICAN THORACIC SOCIETY DOCUMENTS

Diagnosis and Treatment of Adults with Community-acquired Pneumonia

An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America

Joshua P. Metlay*, Grant W. Waterer*, Ann C. Long, Antonio Anzueto, Jan Brozek, Kristina Crothers, Laura A. Cooley, Nathan C. Dean, Michael J. Fine, Scott A. Flanders, Marie R. Griffin, Mark L. Metersky, Daniel M. Musher, Marcos I. Restrepo, and Cynthia G. Whitney; on behalf of the American Thoracic Society and Infectious Diseases Society of America

THIS OFFICIAL CLINICAL PRACTICE GUIDELINE WAS APPROVED BY THE AMERICAN THORACIC SOCIETY MAY 2019 AND THE INFECTIOUS DISEASES SOCIETY OF AMERICA AUGUST 2019

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

Table 2. Differences between the 2019 and 2007 American Thoracic Society/Infectious Diseases Society of America Community-acquired Pneumonia Guidelines

Recommendation	2007 ATS/IDSA Guideline	2019 ATS/IDSA Guideline
Sputum culture	Primarily recommended in patients with severe disease	Now recommended in patients with severe disease as well as in all inpatients empirically treated for MRSA or *Pseudomonas aeruginosa*
Blood culture	Primarily recommended in patients with severe disease	Now recommended in patients with severe disease as well as in all inpatients empirically treated for MRSA or *P. aeruginosa*
Macrolide monotherapy	Strong recommendation for outpatients	Conditional recommendation for outpatients based on resistance levels
Use of procalcitonin	Not covered	Not recommended to determine need for initial antibacterial therapy
Use of corticosteroids	Not covered	Recommended not to use. May be considered in patients with refractory septic shock
Use of healthcare-associated pneumonia category	Accepted as introduced in the 2005 ATS/IDSA hospital-acquired and ventilator-associated pneumonia guidelines	Recommend abandoning this categorization. Emphasis on local epidemiology and validated risk factors to determine need for MRSA or *P. aeruginosa* coverage. Increased emphasis on deescalation of treatment if cultures are negative
Standard empiric therapy for severe CAP	β-Lactam/macrolide and β-lactam/fluoroquinolone combinations given equal weighting	Both accepted but stronger evidence in favor of β-lactam/macrolide combination
Routine use of follow-up chest imaging	Not addressed	Recommended not to obtain. Patients may be eligible for lung cancer screening, which should be performed as clinically indicated

Definition of abbreviations: ATS = American Thoracic Society; CAP = community-acquired pneumonia; IDSA = Infectious Diseases Society of America; MRSA = methicillin-resistant *Staphylococcus aureus*.

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TJUH Antimicrobial Guidelines

- Confluence
  - https://confluence.jefferson.edu/
  - Antimicrobial Stewardship

Community Acquired Pneumonia (CAP)

- Occurs within 48 hours of hospital admission
- Severe CAP
  - Patients with 1 major or ≥3 minor criteria

Major Criteria	Minor Criteria
• Septic shock with need for vasopressors • Respiratory failure requiring mechanical ventilation	• Respiratory rate ≥ 30 breaths/min • PaO_2/FiO_2 ratio ≤ 250 • Multilobar infiltrates • Confusion/disorientation • Uremia (BUN ≥20mg/dl) • Leukopenia (WBC <4,000 cells/µl • Thrombocytopenia (plt <100,000/µl) • Hypothermia (<36°C or <96.8°F) • Hypotension requiring aggressive fluid resuscitation

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

Community Acquired Pneumonia

Major bacterial causes	CAP
	Streptococcus pneumoniae
	Haemophilus influenza
	Mycoplasma pneumoniae
	Staphylococcus aureus
	Legionella spp
	Chlamydia pneumonia
	Moraxella catarrhalis

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Routine Diagnostic Work-up

- History and Physical Exam
- Vital signs
- Pulse oximetry and/or ABG
- Chest x-ray (PA and lateral)
- CBC with differential
- Basic metabolic panel
- Sputum and blood cultures
- Procalcitonin is not recommended in adults with clinically suspected and radiographically confirmed pneumonia
- Other diagnostics may be required in the appropriate clinical setting (travelers, immunocompromised patients, HIV infection, etc.)

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Additional Considerations

	Nonsevere CAP	Severe CAP	HAP	VAP
Sputum for Gram's stain and culture	Optional but recommended if: • Empirically treating MRSA or *Pseudomonas* • Prior respiratory isolation of MRSA or *Pseudomonas* • Recent hospitalization and IV antibiotics within the last 90 days	Yes	Yes	Yes
Blood cultures x 2	Optional but recommended if: • Empirically treating MRSA or *Pseudomonas* • Prior respiratory isolation of MRSA or *Pseudomonas* • Recent hospitalization and IV antibiotics within the last 90 days	Yes	Yes	Yes
MRSA nasal screen	Optional but recommended if: • Empirically treating MRSA • Prior respiratory isolation of MRSA • Recent hospitalization and IV antibiotics within the last 90 days	Optional but recommended if: • Empirically treating MRSA • Prior respiratory isolation of MRSA • Recent hospitalization and IV antibiotics within the last 90 days	Yes	Yes
Streptococcus pneumonia urinary antigen	No	• Select patients admitted to an ICU	No	No
***Legionella* urinary antigen and *Legionella* culture**	Only suggested if: Significant clinical concern OR concern for *Legionella* outbreak	• Yes	Only suggested if: Significant clinical concern OR concern for *Legionella* outbreak	Only suggested if: Significant clinical concern OR concern for *Legionella* outbreak
Flu A/B and RSV PCR	During flu season or significant clinical concern			
Respiratory pathogen panel	Concern for viral etiology in patients who are immunocompromised or critically ill			
HIV screen	If clinically indicated			
EKG	If treating with QTc prolonging antibiotic (ie. azithromycin, levofloxacin)			

Community Acquired Pneumonia

- Assess risk factors for community acquired *MRSA (ca-MRSA):*
  - Recent hospitalization and IV antibiotics within the last 90 days
  - Preceding or concurrent influenza like illness
  - CAP requiring ICU admission
  - Necrotizing or cavitary infiltrates
  - Empyema
  - Previous colonization or infection with MRSA
  - Intravenous drug abuse
  - Immunocompromised patients

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Community Acquired Pneumonia

- Assess risk factors for *Pseudomonas aeruginosa*
  - Recent hospitalization AND IV antibiotic use within the past 90 days
  - Immunocompromised patients
  - Structural lung disease (CF, bronchiectasis)
  - Hospitalization for ≥2 days within 90 days
  - Residence in a nursing home or extended care facility
  - Home infusion therapy (including antibiotics)
  - Home wound care
  - Family member with multidrug-resistant organisms (MDRO)
  - Chronic hemodialysis (HD) within 30 days

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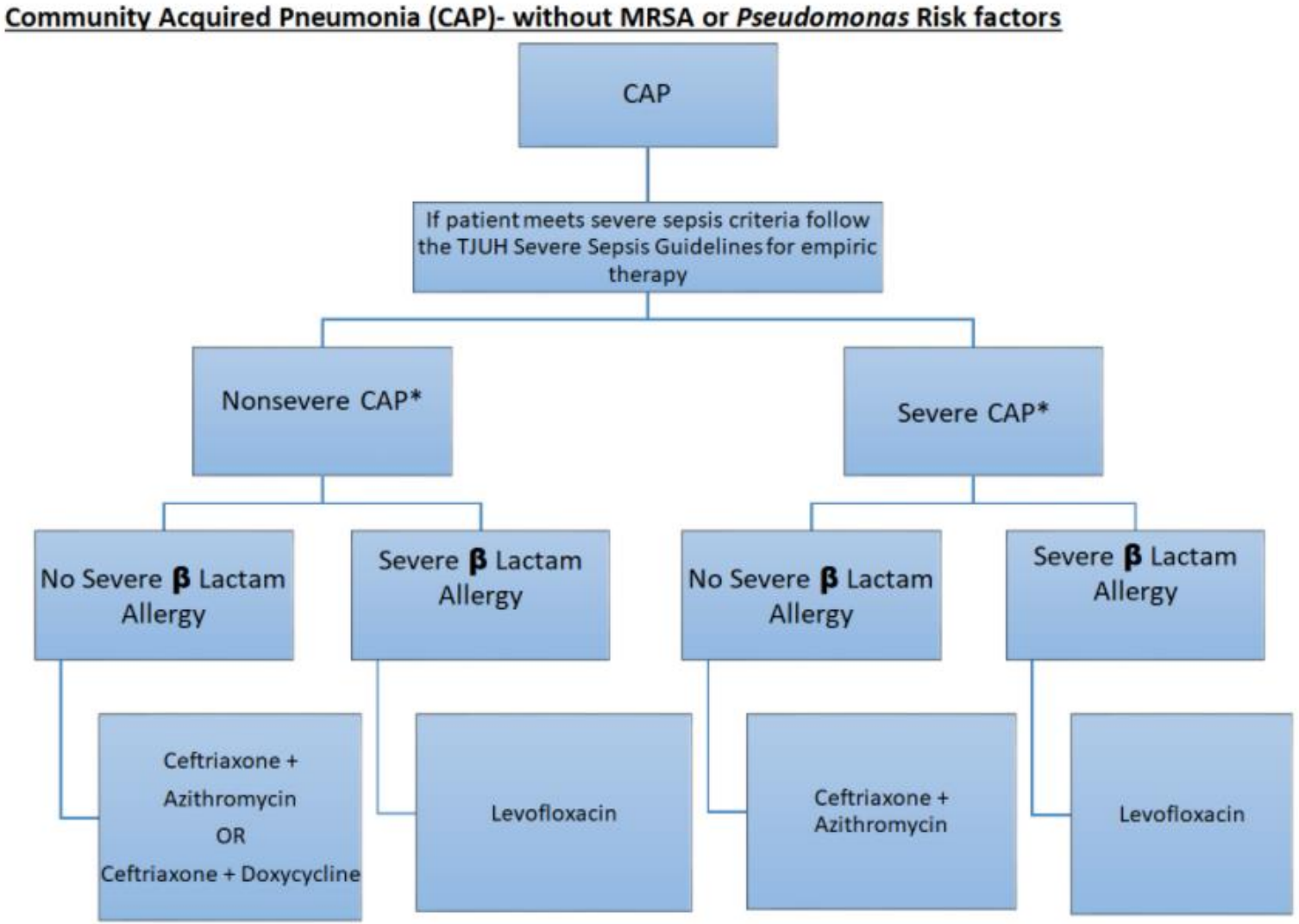
CAP Treatment Algorithm



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CAP Treatment Algorithm

*Additional Treatment to Consider		
	Nonsevere CAP	**Severe CAP**
Prior respiratory isolation of MRSA	• Add vancomycin • Deescalate based on MRSA nasal screen and sputum culture	• Add vancomycin • Deescalate based on MRSA nasal screen and sputum culture
Prior respiratory isolation of *Pseudomonas aeruginosa*	• Add cefepime in place of ceftriaxone • Deescalate based on sputum culture	• Add cefepime in place of ceftriaxone • If severe β Lactam allergy add aztreonam • Deescalate based on sputum culture
Recent hospitalization or IV antibiotics within the past 90 days	• Withhold MRSA and Pseudomonas coverage • Obtain MRSA nasal screen and sputum culture • If results are positive, initiate MRSA or *Pseudomonas* coverage	• Add vancomycin • Add cefepime in place of ceftriaxone • Deescalate based on MRSA nasal screen and sputum culture
Flu A/B positive	• Add oseltamivir	• Add oseltamivir

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Community Acquired Pneumonia

- Which antimicrobial regimen would you select for a non-ICU pt suspected to have non-severe CAP?
  - A. Vancomycin and Cefepime
  - B. Meropenem
  - C. Ceftriaxone and Azithromycin
  - D. I order what Shirley tells me to

CAP De-escalation of Therapy

- De-escalation of therapy
  - Based on clinical improvement and culture results
  - For non critically ill patients, transition to oral therapy as soon as possible
  - Pts initially treated with ceftriaxone + azithromycin:
    - Cefuroxime 500 mg po q12hr* **+/-** azithromycin 500 mg po q24hr
  - Pts initially treated with levofloxacin or PCN allergic:
    - Levofloxacin 750 mg po daily*

*requires renal dosing

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CAP Duration of Therapy

Organism	Duration of therapy
Gram-positive	
MSSA	7 days
MRSA	7 days
S. pneumoniae	5 days
Gram-negative	
Enterobactericeae (E. coli, Enterobacter, Serratia, Klebsiella, etc)	7 days
Pseudomonas	7 days
Acinetobacter	7 days
Atypicals	
Legionella, Mycoplasma	7-14 days
Chlamydia pneumoniae	10-14 days

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CAP Therapy Discontinuation

- Discontinue abx if:
  - Afebrile for 48-72 hrs **AND** has no more than 1 of the following:
    - HR > 100 beats/min
    - RR > 24 breaths/min
    - BP < 90 mm Hg
    - O2 sat < 90%
    - Altered mental status
  - Cough and CXR abnormalities can take several weeks to improve
    - No need to extend duration if clinically well

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CAUTION
A WORD OF
WARNING

Fluoroquinolone (FQ) Safety

- FDA warnings and precautions
  - Increased risk of tendonitis and tendon rupture
  - Risk of worsening symptoms for those with myasthenia gravis
  - Potential for irreversible peripheral neuropathy
  - Increase in mental health adverse effects and blood glucose disturbances
  - Increased risk of aneurysm and dissection
  - *C.difficile*

https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/020634s070lbl.pdf#page=52

Hospital-Acquired Pneumonia (HAP)

- Pneumonia that occurs ≥ 48 hours after admission
- Not incubating at the time of admission
- Also referred to as nosocomial pneumonia

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HAP Suspected Organisms

Nosocomial Pneumonia*
Escherichia coli
Klebsiella pneumoniae
Enterobacter spp
Pseudomonas aeruginosa
Acinetobacter spp
Staphylococcus aureus including MRSA
Streptococcus spp

*HAP and VAP may be caused by a wide variety of pathogens, can be polymicrobial, and depends in large part upon whether the patient has risk factors for MDR pathogens. Differences in patient factors and the hospital flora also influence the patterns of pathogens seen.

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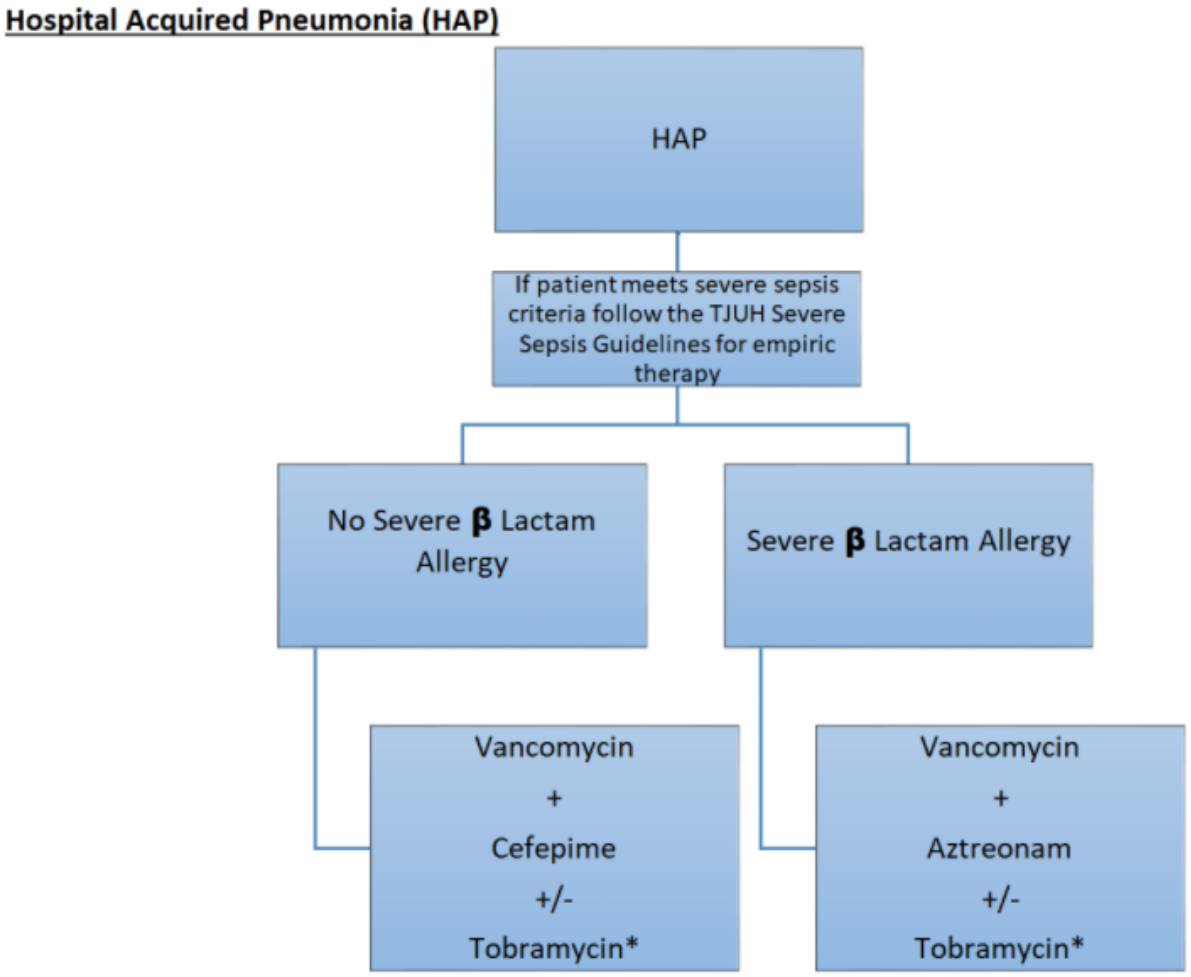
HAP Treatment Algorithm



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HAP Treatment Algorithm

- Double coverage for gram-negative organisms
  - Patients who have received prior intravenous antibiotics within the preceding 90 days
  - Structural lung disease (ie. bronchiectasis, CF)
- At risk for multidrug-resistant (MDR) gram-negative pathogens, including *pseudomonas*, should receive 2 different agents with gram-negative activity

Additional Considerations

	Nonsevere CAP	Severe CAP	HAP	VAP
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Respiratory pathogen panel	Concern for viral etiology in patients who are immunocompromised or critically ill			
HIV screen	If clinically indicated			
EKG	If treating with QTc prolonging antibiotic (ie. azithromycin, levofloxacin)			

HAP De-escalation of Therapy

- Deescalate based on clinical improvement and culture results.
  - For non-critically ill patients, transition to oral therapy as soon as possible.
- Culture–negative step down therapy:
  - Obtain MRSA nasal swab upon admission.
  - If no MRSA isolated and nasal screen negative, consider discontinuation of vancomycin after 48hrs
- If no culture data available and the patient is improving, you can deescalate to levofloxacin 750mg PO q24h

HAP Duration of Therapy

- 7 days!

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HAP Therapy Discontinuation

- Discontinue antibiotics if:
  - Patient is afebrile for 48-72hours AND has no more than 1 of the following:
    - HR >100 beats/min
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    - BP < 90mmg Hg
    - O2 Sat < 90%
    - Altered Mental Status
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MRSA Nasal Screen

Active surveillance cultures of methicillin-resistant *Staphylococcus aureus* as a tool to predict methicillin-resistant *S. aureus* ventilator-associated pneumonia*

Jeannie D. Chan, PharmD, MPH; Timothy H. Dellit, MD; Julie A. Choudhuri, RN, MSPH; Elizabeth McNamara, RN, MN; Elizabeth J. Melius, RN, MN, MPH; Heather L. Evans, MD, MS; Joseph Cuschieri, MD; Saman Arbabi, MD, MPH; John B. Lynch, MD, MPH

Chan JD, Dellit TH, Choudhuri JA, et al. Active surveillance cultures of methicillin-resistant Staphylococcus aureus as a tool to predict methicillin-resistant S. aureus ventilator-associated pneumonia. *Crit Care Med*. 2012;40(5):1437-1442. doi:10.1097/CCM.0b013e318243168e

MRSA Nasal Screen

- Prospective observational study conducted at a university-affiliated urban teaching hospital
- VAP patients ≥ 16 years old
  - 924 episodes of suspected VAP evaluated with bronchoscopy
  - 393 pts had microbiologically confirmed VAP
    - 5 excluded due to <16 yrs or screen not performed
  - 54 patients were colonized with MRSA by ASC
    - Common sites: nares, posterior oropharynx, trachea

Chan JD, Dellit TH, Choudhuri JA, et al. Active surveillance cultures of methicillin-resistant Staphylococcus aureus as a tool to predict methicillin-resistant S. aureus ventilator-associated pneumonia. *Crit Care Med*. 2012;40(5):1437-1442. doi:10.1097/CCM.0b013e318243168e

MRSA Nasal Screen

- Sensitivity 70.3% (95% CI, 52.8-83.6)
- Specificity 92% (95% CI, 88.5-94.5)
- Positive predictive value 48.1% (95% CI, 34.5-62)
- Negative predictive value ***96.7%*** (95% CI, 94-98.3)

Chan JD, Dellit TH, Choudhuri JA, et al. Active surveillance cultures of methicillin-resistant Staphylococcus aureus as a tool to predict methicillin-resistant S. aureus ventilator-associated pneumonia. *Crit Care Med*. 2012;40(5):1437-1442. doi:10.1097/CCM.0b013e318243168e

MRSA Nasal Screen

- High negative predictive value
  - Indicates that negative screens are very accurate for excluding MRSA as a cause of pneumonia

Aspiration Pneumonia

- Aspiration – inhalation of oropharyngeal or gastric contents into larynx and lower respiratory tract
  - Contents may include:
    - Different substances (blood, vomitus, food particles)
    - Oropharyngeal secretions
    - Microbiological flora

Waybright, RA et al. Treatment of clinical aspiration: A reappraisal. Am J Health-Syst Pharm – Vol 70 Aug 1 2013; 1291-1300.

Aspiration Pneumonia

- Complications of aspiration:
  - Chemical pneumonitis
    - Damage of lung parenchyma after inhalation of sterile stomach or oropharyngeal contents into lower airway
      - Due to gastric acid and delayed inflammatory reaction
    - Non-infectious process
  - Aspiration pneumonia
    - Infectious process
    - Occurs after inhalation of colonized pathogenic bacteria into lower airway from oropharyngeal area or colonized gastric contents
    - Often occurs silently

Waybright, RA et al. Treatment of clinical aspiration: A reappraisal. Am J Health-Syst Pharm – Vol 70 Aug 1 2013; 1291-1300.

Aspiration Pneumonia

- Despite distinct physiological processes, clinical presentation can be difficult to distinguish
- Bacteriology
  - Associated microbial spectrum included gram positive (*S. aureus*, *S. pneumoniae*), gram negative (*H. influenzae*, enterobacteriaceae), and anaerobes (*bacteroides*, *peptostreptococcus*, *fusobacterium*)
  - From studies from the 1970s

Waybright, RA et al. Treatment of clinical aspiration: A reappraisal. Am J Health-Syst Pharm – Vol 70 Aug 1 2013; 1291-1300.

Aspiration Pneumonia

- Broader spectrum antibiotics not necessarily more effective
- Potential abx choice should target nonresistant gram positive (*Staphylococcus* and *Streptococcus* species) and gram negative (Enterobacteriaceae, *H. influenzae*)

Aspiration Pneumonia

- Pneumonia (fever, cough, infiltrate) that develops 48 – 72 hrs after suspected or witnessed aspiration event

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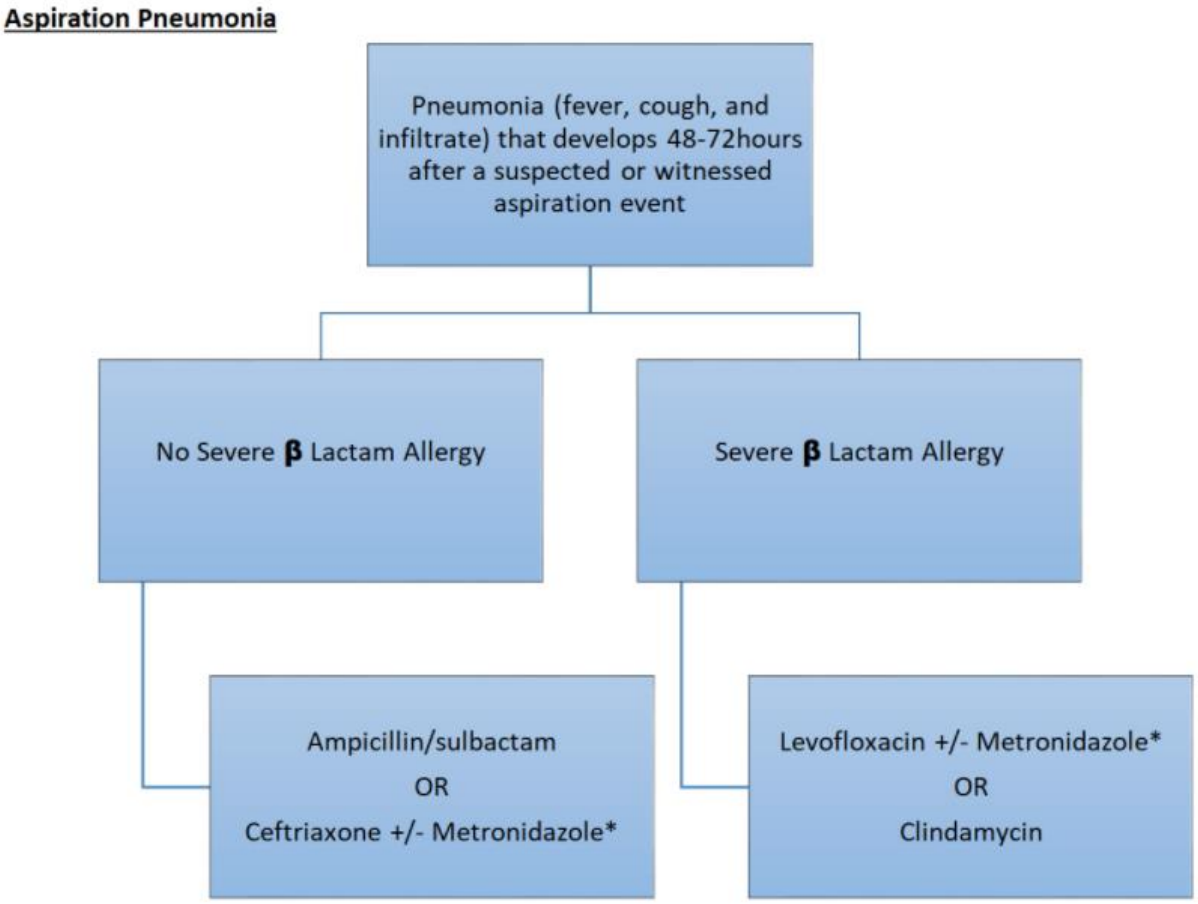
Question

- In aspiration pneumonia, should you cover for anaerobes?
  - Yes
  - No

Aspiration Pneumonia



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Aspiration Pneumonia

- Assess for risk factors for anaerobic infection:
  - Loss of consciousness due to alcoholism
  - Seizures
  - Gingival disease
  - Esophageal motility issues
  - Lung abscess
  - Empyema

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Aspiration Pneumonia

- De-escalation of therapy
  - Culture negative step down therapy:
    - Amoxicillin/clavulanate (Augmentin) 875 mg po q12hr
      OR
    - Levofloxacin 750 mg po q24hr +/- metronidazole
      OR
    - Cefuroxime 500 mg po q12hr (if anaerobic coverage not required)
- Reassess patients in 48-72 hrs, if no symptoms or confirmatory cx or imaging, likely chemical pneumonitis and can discontinue abx

https://confluence.jefferson.edu/display/AGS/TJUH+Guidelines+for+Inpatient+Treatment+of+Pneumonia

Antimicrobial Dosing

Antimicrobial	Recommended Dosing
Amoxicillin/ Clavulanate	875mg po q12h
Ampicillin/Sulbactam	1.5gm iv q6h
Azithromycin	500mg iv/po q24h
Aztreonam	1gm iv q8h
Amikacin	CrCl > 20ml/min: 15mg/kg iv (dosing interval based on renal function)
Cefepime	CrCl ≥ 60ml/min: 2000mg iv q8h given as a 3hr infusion
Ceftriaxone	1gm iv q24h
Cefuroxime	500mg po q12h
Clindamycin	600mg iv/po q8h
Doxycycline	100mg iv/po q12h
Levofloxacin	750 mg iv/po q24h
Linezolid	600mg iv/po q12h
Meropenem	CrCl > 50ml/min: 1-2gm iv q8h given as a 3hr infusion
Metronidazole	500mg iv/po q12h
Oseltamivir	75mg PO twice daily
Tobramycin	CrCl >20ml/min: 6 mg/kg iv (dosing interval based on renal function)
Vancomycin	Loading dose 25mg/kg rounded to nearest 500mg; consult pharmacy or intranet guidelines for maintenance dosing

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Wrap-up

- De-escalate when appropriate
  - Prolonged use of broad spectrum abx can lead to:
    - Resistance
    - C. diff infections
- Longer duration does not equal better outcomes!

Questions?