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TREATMENT PATHWAY FOR ADULT PATIENTS WITH PNEUMONIA

The purpose of this document is to guide the appropriate treatment of adult patients presenting with pneumonia. Three pathways with different empiric treatment regimens based on risk of infection with multidrug-resistant (MDR) pathogens (including MRSA, Pseudomonas spp., Acinetobacter spp., organisms not susceptible to beta-lactams (ceftriaxone or ampicillin-sulbactam) and/or fluoroquinolones (ciprofloxacin, levofloxacin)) are shown below.

Pathway A: Community-Onset
(No Risk Factors listed in Pathway B)

Patients presenting from the community without an risk factors for drug-resistant pathogens (includes patients admitted to the ICU for respiratory failure who do not meet Pathway B criteria)

For dosing, alternative treatment options, duration, and important comments
Click here for Pathway A Recommendations

Empiric Treatment

Ampicillin-sulbactam
+
Azithromycin

*see treatment guidelines for appropriate use of ceftriaxone as an alternative agent

Pathway B: Community-Onset, Risk Factors

Patients presenting with any of the following risk factors for drug-resistant pathogens OR unknown etiology of septic shock:

- History of infection or colonization with Pseudomonas spp., MRSA, or pathogens resistant to standard CAP therapy (ampicillin-sulbactam or ceftriaxone) within previous 12 months
- Severe community-acquired pneumonia (septic shock **OR** requiring mechanical ventilation **OR** high clinical concern for needing ICU care[α]), AND meeting 1 of the following criteria:
  - Hospitalization for at least 48 hours AND use of any intravenous antibiotic, fluoroquinolone, or linezolid within previous 90 days

  OR
  - Immunocompromised, defined as:
    - AIDS (CD4 <200)
    - Neutropenia (ANC <1000)
    - Kidney or liver or heart transplant recipient within previous 1 year
    - Solid organ transplant recipient treated for rejection within previous 6 months
    - Lung transplant recipient
    - Allogeneic stem cell transplant within previous 1 year or those with chronic GVHD
    - Autoimmune disorders on biologic agents (TNFα inhibitors, rituximab, etc.)

For dosing, alternative treatment options, duration, and important comments
Click here for Pathway B Recommendations

Empiric Treatment

Cefepime
(+ tobramycin if admitted to ICU)
+
Vancomycin

Pathway C: Hospital-Onset

- Hospital-acquired pneumonia (current hospitalization for ≥72 hours)
- Ventilator-associated pneumonia

For dosing, alternative treatment options, duration, and important comments
Click here for Pathway C Recommendations

Empiric Treatment

Cefepime
(+ tobramycin if admitted to ICU)
+
Vancomycin

Utilization of procalcitonin (PCT) levels

- Consider diagnosis of a viral respiratory tract infection in patients with a low [#] PCT level (<0.25 mcg/L). **Antibiotics are discouraged in these patients and should be discontinued.**[^]
- Patients with AKI/CKD, massive trauma, major surgery, post-partum, acute GVHD, and cytokine stimulants may have false elevations in PCT levels [^]

[#]Repeat 6-12 hours after 1st level if no antibiotics started and clinical suspicion for bacterial pneumonia persists
[^]See UMHS Procalcitonin Usage Guidelines for more information

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Indication	Common Pathogens	Empiric Therapy	Duration of Therapy	Comments
Pathway A (Part I, non-ICU)				
Inpatient community-acquired pneumonia, no risk factors **(Non-ICU patient)**	*Streptococcus pneumonia* *Haemophilus influenzae* *Moraxella catarrhalis* *Mycoplasma pneumoniae* *Chlamydia pnemoniae* *Legionella* species	Preferred: **Ampicillin-sulbactam*** 3 g IV q6h **+ Azithromycin** 500 mg IV/PO x1 day, then 250 mg q24h x4 days Low/medium risk PCN allergy: **Ceftriaxone** 2 g IV q24h **+ Azithromycin** 500 mg IV/PO x1 day, then 250mg q24h x4 days Consider the addition of anaerobic coverage with **metronidazole** 500 mg PO q8h if empyema or lung abscess present High risk PCN and cephalosporin allergy: **Levofloxacin*** 750 mg IV/PO q24h Consider the addition of anaerobic coverage with metronidazole 500 mg PO q8h *if* empyema or lung abscess present Addition of vancomycin Consider if high clinical suspicion for CA-MRSA (prior isolation of MRSA from respiratory culture in past 12 months or post-influenza pneumonia)	Uncomplicated/Aspiration Pneumonia: • **5 days** for patients who defervesce within 72 hours and have *no more than 1* sign of CAP instability at the time of antibiotic discontinuation† • Patients with delayed response should discontinue therapy 48-72 hours after defervesce and have no more than 1 sign of CAP instability† at time antibiotic discontinuation. Complicated Pneumonia: • Patients with empyema, infected pleural effusions, and bacteremia secondary to pneumonia may require longer durations of therapy. Bacteremic pneumococcal pneumonia should be treated for a minimum of 7-14 days. ID consult is recommended for patients with bacteremia. Pathogen-Specific Considerations: • Uncomplicated pneumonia with non- fermenting GNRs (e.g., Pseudomonas, Achromobacter, Acinetobacter, Stenotrophomonas) or *Staphylococcus aureus* should receive 7 days of therapy if defervescensce within 72 hours and have *no more than 1* sign of CAP instability at the time of antibiotic discontinuation†. Delayed response will likely require longer durations. †**CAP clinical signs of instability (if different than patient baseline status)** • HR ≥ 100 bpm • RR ≥ 24 breaths/min • SBP ≤ 90 mmHg • Arterial O_2 sat ≤ 90% or pO_2 ≤ 60 mmHg on room air • Altered mental status	• Appropriately tailor therapy based on respiratory culture results. • Anaerobic coverage is not necessary for patients with pneumonia following an aspiration event. Only those with empyema or lung abscess should receive empiric anaerobic coverage. • For culture negative pneumonia, transition to oral therapy when patient is afebrile with clinical improvement and hemodynamically stable for 48 hours: • 1st line: **Amoxicillin-clavulanate*** 875 mg BID **+ Azithromycin** (complete 5-day course of azithromycin) • Low/medium risk PCN allergy: **Cefuroxime*** 500 mg BID plus azithromycin (complete 5-day course of azithromycin) • High risk PCN or cephalosporin allergy: **Levofloxacin*** 750 mg PO q24h • Adjust levofloxacin and ampicillin-sulbactam for renal dysfunction. Always give levofloxacin loading dose of 750 mg x1 dose • Use **azithromycin** 500 mg q24 h *if documented or high clinical suspicion for Legionella* (can pursue further diagnostic testing → respiratory legionella PCR) • In setting of macrolide allergy can use **doxycycline** for atypical coverage in absence of *Legionella* concern. • In patients with documented Mycoplasma, use of doxycycline should be preferred for treatment due to concern for macrolide resistance. • Antibiotic coverage of atypical organisms can be discontinued if the respiratory panel (RPAN) and urine antigens are negative. • See front page for tips on *utilization of procalcitonin (PCT) levels*

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Indication	Common Pathogens	Empiric Therapy	Duration of Therapy	Comments
Pathway A (Part II, ICU)				

Inpatient community-acquired pneumonia, no risk factors
 	
(ICU patient)
	Streptococcus pneumonia
	
	Haemophilus influenzae
	
	Moraxella catarrhalis
	
	Mycoplasma pneumoniae
	
	Chlamydia pnemoniae
	
	Legionella species
		Preferred:
		Ampicillin-sulbactam* 3 g IV q6h
		+ Azithromycin 500 mg IV q24h x5 days
		
		Low/medium risk PCN allergy:
		Ceftriaxone 2 g IV q24h
		+ Azithromycin 500 mg IV q24h x5 days
		
		Consider the addition of anaerobic coverage with **metronidazole** 500 mg IV q8h if empyema or lung abscess present
		
		High risk PCN and cephalosporin allergy:
		Vancomycin** IV (see nomogram)
		+ **Aztreonam** 2 g IV q8h
		+ **Azithromycin** 500 mg IV q24h x5 days
		
		Consider the addition of anaerobic coverage with metronidazole 500 mg IV q8h if empyema or lung abscess present
		
		Addition of vancomycin
		Consider if high clinical suspicion for CA-MRSA (prior isolation of MRSA from respiratory culture in past 12 months or post-influenza pneumonia)
			Uncomplicated/Aspiration Pneumonia:
			• **5 days** for patients who defervesce within 72 hours and have *no more than 1* sign of CAP instability at the time of antibiotic discontinuation†
			• Patients with delayed response should discontinue therapy 48-72 hours after defervesce and have no more than 1 sign of CAP instability† at time antibiotic discontinuation.
			
			Complicated Pneumonia:
			• Patients with empyema, infected pleural effusions, and bacteremia secondary to pneumonia may require longer durations of therapy. Bacteremic pneumococcal pneumonia should be treated for a minimum of 7-14 days. ID consult is recommended for patients with bacteremia.
			
			Pathogen-Specific Considerations:
			• Uncomplicated pneumonia with non- fermenting GNRs (e.g., Pseudomonas, Achromobacter, Acinetobacter, Stenotrophomonas) or *Staphylococcus aureus* should receive 7 days of therapy if defervescensce within 72 hours and have *no more than 1* sign of CAP instability at the time of antibiotic discontinuation†. Delayed response will likely require longer durations.
			
			†**CAP clinical signs of instability (if different than patient baseline status)**
			• HR ≥ 100 bpm
			• RR ≥ 24 breaths/min
			• SBP ≤ 90 mmHg
			• Arterial O_2 sat ≤ 90% or pO_2 ≤ 60 mmHg on room air
			• Altered mental status
				• Appropriately tailor therapy based on respiratory culture results.
				
				• Anaerobic coverage is not necessary for patients with pneumonia following an aspiration event. Only those with empyema or lung abscess should receive empiric anaerobic coverage.
				
				• IV therapy for first 24 hours for ICU patients
				
				• For culture negative pneumonia, transition to oral therapy when patient is afebrile with clinical improvement and hemodynamically stable for 48 hours:
				  • 1st line:
				  Amoxicillin-clavulanate* 875 mg BID
				  + Azithromycin (complete 5-day course of azithromycin)
				  • Low/medium risk PCN allergy:
				  Cefuroxime* 500 mg BID plus azithromycin (complete 5-day course of azithromycin)
				  • High risk PCN or cephalosporin allergy:
				  Levofloxacin* 750 mg PO q24h
				
				• Adjust levofloxacin, ampicillin-sulbactam, aztreonam, and piperacillin-tazobactam for renal dysfunction. Always give levofloxacin loading dose of 750 mg x1 dose
				
				• Use **azithromycin** 500 mg q24 h *if documented or high clinical suspicion for Legionella* (can pursue further diagnostic testing → respiratory legionella PCR)
				
				• In setting of macrolide allergy can use **doxycycline** for atypical coverage in absence of *Legionella* concern.
				
				• In patients with documented Mycoplasma, use of doxycycline should be preferred for treatment due to concern for macrolide resistance.
				
				• Antibiotic coverage of atypical organisms can be discontinued if the respiratory panel (RPAN) and urine antigens are negative.
				
				• See front page for tips on *utilization of procalcitonin (PCT) levels*

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Pathway B
(Previous culture data should be used to guide empiric therapy)

Indication	Empiric Therapy	Duration	Comments
Patients presenting with any of the following risk factors for drug-resistant pathogens OR unknown etiology of septic shock: • History of infection or colonization with Pseudomonas spp., MRSA, or other MDR gram-negative pathogens (resistant to ampicillin-sulbactam or ceftriaxone) within previous 12 months • In patients with severe community-acquired pneumonia (septic shock **OR** requiring mechanical ventilation **OR** high clinical concern for needing ICU level care[α]), **AND:** 1. Hospitalization for at least 48 hours AND use of any intravenous antibiotic, fluoroquinolone, or linezolid within previous 90 days **OR** 2. Immunocompromised, defined as: ○ AIDS (CD4 <200) ○ Neutropenia (ANC <1000) ○ Kidney or liver or heart transplant recipient within previous 1 year ○ Solid organ transplant recipient treated for rejection within previous 6 months ○ Lung transplant recipient ○ Allogeneic stem cell transplant within previous 1 year or those with chronic GVHD ○ Autoimmune disorders on biologic agents (TNFα inhibitors, rituximab, etc.)	Preferred: **Cefepime*** 2 g IV q8h (+ **Tobramycin*** IV if admitted to ICU) + **Vancomycin**** IV (see nomogram) NOTE: If patient has a history of Pseudomonas or MDR gram-negative pathogen ONLY, empiric vancomycin use is not necessary. If MRSA history ONLY, use of cefepime is not necessary (preferred regimen would be ampicillin-sulbactam + vancomycin). Low/medium risk cephalosporin allergy: **Meropenem*** 2 g IV q8h (+ **Tobramycin*** IV if admitted to ICU) + **Vancomycin**** IV (see nomogram) Consider the addition of anaerobic coverage with **metronidazole** 500 mg IV q8h *if* empyema or lung abscess present High risk PCN and cephalosporin allergy: **Aztreonam*** 2 g IV q8h (+ **Tobramycin*** IV if admitted to ICU) + **Vancomycin**** IV (see nomogram) Consider the addition of anaerobic coverage with metronidazole 500 mg IV q8h *if* empyema or lung abscess present ***Linezolid*** *may be used in patients with vancomycin allergy (not vancomycin infusion reaction). See restriction criteria for appropriate empiric and definitive use of linezolid.*	Uncomplicated/Aspiration Pneumonia: • **5 days** for patients who defervesce within 72 hours and have *no more than 1* sign of CAP instability at the time of antibiotic discontinuation┼ • Patients with delayed response should discontinue therapy 48-72 hours after defervesce and have no more than 1 sign of CAP instability┼ at time antibiotic discontinuation. Complicated Pneumonia: • Patients with empyema, infected pleural effusions, and bacteremia secondary to pneumonia should receive longer durations of therapy. Bacteremic pneumococcal pneumonia should be treated for a minimum of 7-14 days. ID consult is recommended for patients with bacteremia. Pathogen-Specific Considerations: • Uncomplicated pneumonia with non- fermenting GNRs (e.g., Pseudomonas, Achromobacter, Acinetobacter, Stenotrophomonas) or *Staphylococcus aureus* should receive 7 days of therapy if defervescensce within 72 hours and have *no more than 1* sign of CAP instability at the time of antibiotic discontinuation┼. Delayed response will likely require longer durations. ┼CAP clinical signs of instability (if different than patient baseline status) • HR ≥ 100 bpm • RR ≥ 24 breaths/min • SBP ≤ 90 mmHg • Arterial O2 sat ≤ 90% or pO2 ≤ 60 mmHg on room air	If atypical pathogens are suspected, start **azithromycin** 500 mg IV x1 day, followed by 250 mg IV/PO daily x4 days. Use **azithromycin** 500 mg q24h if high clinical suspicion for *Legionella*. Treatment duration may be longer for confirmed *Legionella*. In setting of macrolide allergy can use **doxycycline** for atypical coverage in non-ICU patients and in the absence of *Legionella* concern In patients with documented or high clinical suspicion for *Mycoplasma*, use of **levofloxacin*** should be preferred for treatment due to concern for macrolide resistance. Discontinue vancomycin if no evidence of MRSA colonization (negative MRSA nasal swab) if clinically appropriate. In patients with evidence of colonization (positive MRSA nasal swab) or if unknown, discontinue vancomycin after 48-72 hours if no positive respiratory cultures for MRSA and clinically appropriate. Vancomycin can be continued for gram-positive coverage in patients with no microbiological diagnosis who are receiving aztreonam due to allergies. Antibiotic therapy is not generally recommended for patients with ventilator-associated tracheobronchitis (defined as fever with no other recognizable cause, with new or increased sputum production, positive endotracheal aspirate culture, and no radiographic evidence of pneumonia). *Definitive therapy should be tailored to culture results.* In patients with negative respiratory cultures who are clinically stable after 48 hours, deescalate antibiotic therapy to CAP treatment. Oral antibiotics should be considered in clinically stable patients. • Preferred: **Amoxicillin-clavulanate*** 875 mg BID • Low/medium risk PCN allergy: **Cefuroxime*** 500 mg BID • High risk PCN allergy: **Levofloxacin*** 750 mg PO q24h • In patients with VAP or in those with inadequate cultures, physician discretion is advised. See front page for tips on *utilization of procalcitonin (PCT) levels*

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Pathway C (Previous culture data should be used to guide empiric therapy)			
Indication	**Empiric Therapy**	**Duration**	**Comments**
Hospital-acquired pneumonia (current hospitalization for ≥72 hours) **Ventilator-associated pneumonia**	Preferred: **Cefepime*** 2 g IV q8h (+ **Tobramycin*** IV if admitted to ICU) + **Vancomycin**** IV (see nomogram) Low/medium risk cephalosporin allergy: **Meropenem*** 2 g IV q8h (+ **Tobramycin*** IV if admitted to ICU) + **Vancomycin**** IV (see nomogram) Consider the addition of anaerobic coverage with **metronidazole** 500 mg IV q8h *if* empyema or lung abscess present High risk PCN and cephalosporin allergy: **Aztreonam*** 2 g IV q8h (+ **Tobramycin*** IV if admitted to ICU) + **Vancomycin**** IV (see nomogram) Consider the addition of anaerobic coverage with **metronidazole** 500 mg IV q8h *if* empyema or lung abscess present **Linezolid** may be used in patients with vancomycin allergy (not vancomycin infusion reaction). See restriction criteria for appropriate empiric and definitive use of linezolid.	7 days for uncomplicated pneumonia with rapid clinical response within 72 hours (including patients with Pseudomonas, Stenotrophomonas, Acinetobacter, or Burkholderia) Patients with empyema, infected pleural effusions, and bacteremia secondary to pneumonia may require longer durations of therapy.	If atypical pathogens are suspected, start **azithromycin** 500 mg IV x1 day, followed by 250 mg IV/PO daily x4 days. Use **azithromycin** 500 mg q24h if high clinical suspicion for *Legionella*. Treatment duration may be longer for confirmed *Legionella*. In setting of macrolide allergy can use **doxycycline** for atypical coverage in non-ICU patients and in the absence of *Legionella* concern In patients with documented or high clinical suspicion for *Mycoplasma*, use of **levofloxacin*** should be preferred for treatment due to concern for macrolide resistance. Discontinue vancomycin if no evidence of MRSA colonization (negative MRSA nasal swab) if clinically appropriate. In patients with evidence of colonization (positive MRSA nasal swab) or if unknown, discontinue vancomycin after 48-72 hours if no positive respiratory cultures for MRSA and clinically appropriate. Vancomycin can be continued for gram-positive coverage in patients with no microbiological diagnosis who are receiving aztreonam due to allergies. Antibiotic therapy is not generally recommended for patients with ventilator-associated tracheobronchitis (defined as fever with no other recognizable cause, with new or increased sputum production, positive endotracheal aspirate culture, and no radiographic evidence of pneumonia). *Definitive therapy should be tailored to culture results.* In patients with negative respiratory cultures who are clinically stable after 48 hours, deescalate antibiotic therapy to CAP treatment. Oral antibiotics should be considered in clinically stable patients. • Preferred: **Amoxicillin-clavulanate*** 875 mg BID • Low/medium risk PCN allergy: **Cefuroxime*** 500 mg BID • High risk PCN allergy: **Levofloxacin*** 750 mg PO q24h • In patients with VAP or in those with inadequate cultures, physician discretion is advised. See front page for tips on *utilization of procalcitonin (PCT) levels*

Footnotes:

* Dose may need to be adjusted for renal dysfunction

** For ADULTS: Dose per vancomycin nomogram with AUC goal 400-600 mcg*hr/mL

α High clinical concern for needing ICU level care can be defined as having at least 3 of the following: RR ≥30 breaths/min, SpO_2 <90% OR O_2 supplementation ≥7 L, multilobar infiltrates, confusion, hypothermia (<36°C), severe sepsis

NOTE: See Beta-lactam Allergy Evaluation and Empiric Therapy Guidance document for further allergy information. High-risk allergies are defined as: respiratory symptoms (chest tightness, bronchospasm, wheezing, cough), angioedema (swelling, throat tightness), cardiovascular symptoms (hypotension, dizzy/lightheadedness, syncope/passing out, arrhythmia), anaphylaxis. If a patient has a high-risk allergy to penicillins, cephalosporins, or carbapenems, the only beta-lactam antibiotic that can be safely used without Allergy consult is aztreonam (if the allergy is to ceftazidime or aztreonam, aztreonam should be avoided as well).

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Revision History:
- 8/20: Revised/added pathways B & C
- 10/20: Adjusted ceftriaxone dosing
- 03/21: Updated vancomycin dosing & hyperlinks
- 07/21: Updated pathway B & C empiric antibiotic selection
- 09/21: Updated vacomycin infusion reaction terminology