

Assessment and Management of Hospital-Acquired and Ventilator-Associated Pneumonia in Children

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INTRODUCTION

Hospital-acquired pneumonia (HAP) and Ventilator-associated pneumonia (VAP) are healthcare-acquired conditions with significant risk of morbidity and mortality. Hospitalized patients may have multiple risk factors for pneumonia, such as recumbent position, impaired cough reflex, procedural sedation, immunocompromised status, and/or artificial airways. Prompt recognition of pneumonia in hospitalized patients can prevent serious complications. However, cultures of respiratory secretions are difficult to obtain in patients without an artificial airway or have limited specificity in patients with an endotracheal tube or tracheostomy tube.

This guideline document will address the diagnosis and treatment of HAP and VAP in pediatric patients at UNC Children's. Guidelines for HAP and VAP prevention are maintained separately.

Inclusion Criteria

- Current admission at UNC Children's other than Newborn Critical Care Center
- Age ≤ 21 years
- Hospitalized (including at other hospitals) >48 hours at the time of evaluation

Exclusion Criteria

- Patients outside the PICU with a tracheostomy

DIAGNOSIS OF HAP AND VAP

Definition of HAP and VAP

HAP is pneumonia that develops at least 48 hours after hospital admission. VAP is HAP that develops at least 48 hours following endotracheal intubation.

When to suspect HAP

Patient with new lung infiltrate PLUS clinical evidence that infiltrate is infectious, with at least one of:

- New onset of fever
- Purulent (may be unusually thick, colors other than white/tan) and/or significantly increased sputum
- Leukocytosis or leukopenia (new)
- Increasing FiO₂/supplemental oxygen requirement

When to suspect VAP

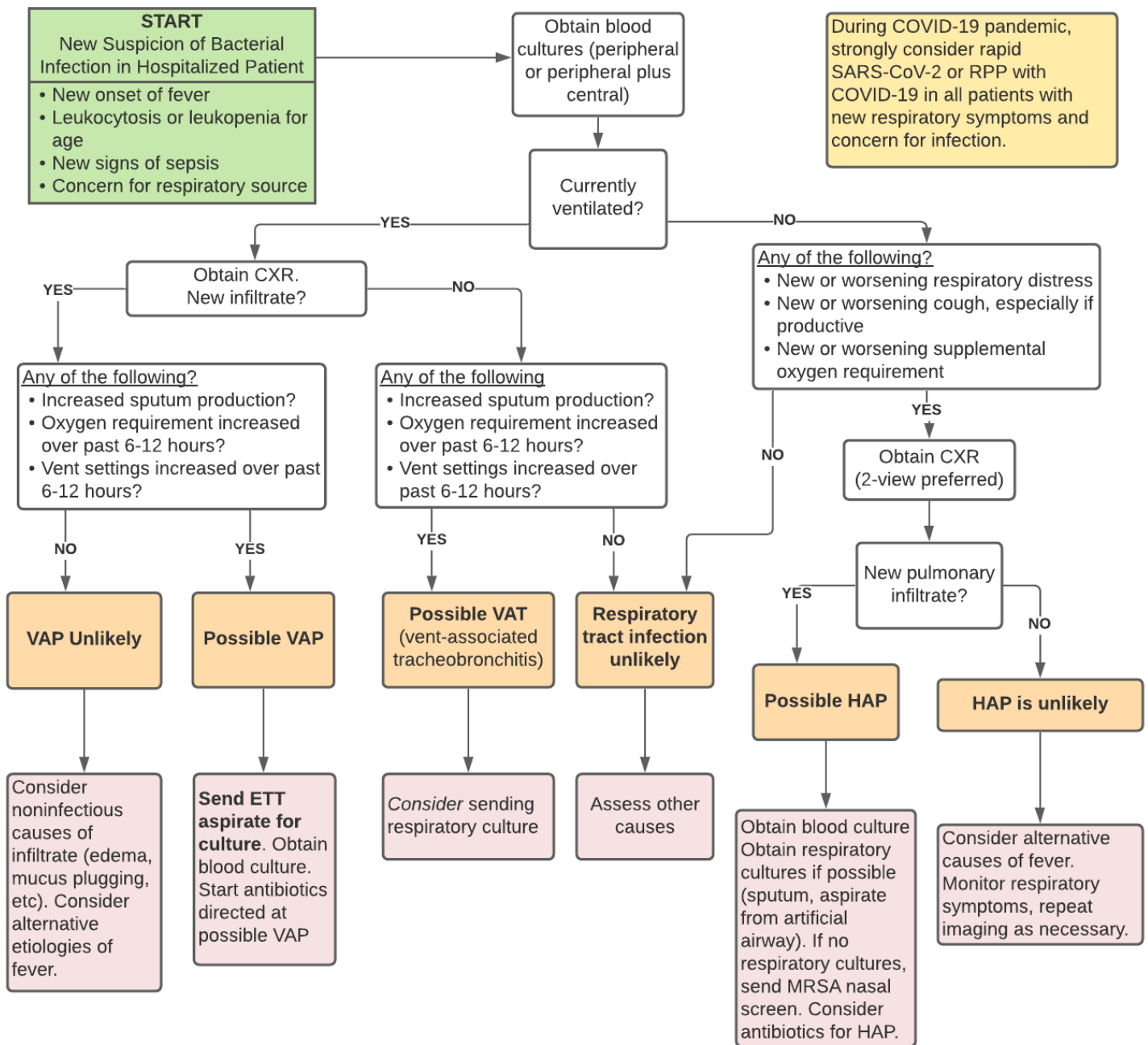
Patient meeting HAP criteria after >48 hours of endotracheal intubation.

Tracheitis and Tracheobronchitis

Potentially pathogenic bacteria frequently colonize respiratory devices. Occasionally they may cause infection of proximal airways *without* frank pneumonia – the absence of alveolar infiltrates and usually the absence of a new oxygenation defect.

Note: Consider respiratory viral infections in the differential diagnosis of suspected HAP/VAP.

FIGURE 1. Diagnostic algorithm for VAP and HAP.



EMPIRIC ANTIBIOTIC SELECTION FOR SUSPECTED HAP AND VAP

Overview of Antibiotic Selection

Review prior cultures; strongly consider coverage of any pathogens isolated from respiratory cultures during current or recent admissions.

Most patients should receive cefepime alone, but there are many exceptions as listed below. Cefepime has good activity against Gram-negative and most Gram-positive pathogens (excluding MRSA), including many oral anaerobes.

Severe Beta-Lactam Allergy

Includes any of the following (consult ID or ASP if uncertain):

- Urticaria or anaphylaxis (IgE-mediated)
- Angioedema
- Respiratory or cardiovascular compromise
- Stevens-Johnson syndrome or Toxic Epidermal Necrolysis (TEN)
- DRESS syndrome (Drug Reaction with Eosinophilia and Systemic Symptoms)
- Acute Generalized Exanthematous Pustulosis (AGEP)

Indications for vancomycin

- Sepsis/septic shock (follow Code Sepsis protocols)
- History of MRSA colonization or infection in the last 2 years
- Necrotizing pneumonia
- Use of aztreonam (limited Gram-positive coverage)
- Significant immune compromise

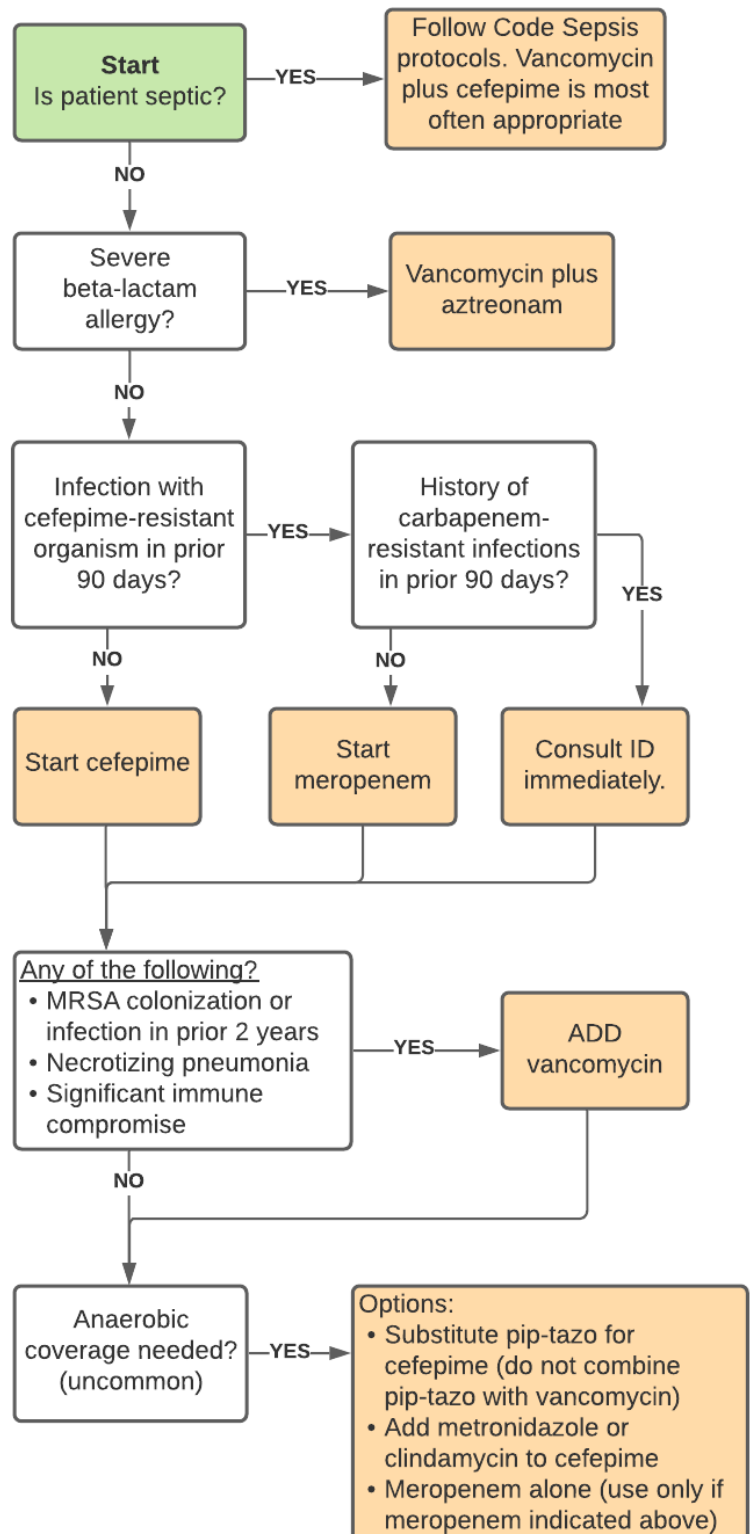
Alternatives to vancomycin in patients with renal impairment or true allergy

- Linezolid - usually preferred, monitor for drug-drug interactions
- Trimethoprim-sulfamethoxazole
- Ceftaroline - only if contraindications to above (requires ID or ASP approval)
- Clindamycin recommended only when isolate is known to be susceptible

Dedicated Anaerobic Coverage

Rarely necessary in VAP. Cefepime has good coverage of oral anaerobes. Exceptions include: very high risk of aspiration due to underlying neurologic conditions, witnessed aspiration preceding pneumonia, poor dentition. Anaerobic coverage is also warranted for lung abscesses.

FIGURE 2. Antibiotic selection for suspected HAP or VAP



Expanded Gram-negative coverage

Generally indicated only when patients have known prior cefepime-resistant infections OR if patient is worsening on empiric coverage. In most cases, the recommended approach is to use meropenem OR add an aminoglycoside.

Prior colonization with multi-drug resistant organisms

Many patients with suspected VAP/VAT have had recent positive respiratory cultures (within the prior 90 days). Empiric coverage of recently identified organisms is usually reasonable, especially in patients with a tracheostomy or who have remained intubated since the prior culture. When a new infection is suspected, coverage *should not be limited* to prior organisms. Certain organisms, such as *Acinetobacter*, *Stenotrophomonas*, *Achromobacter*, etc., have idiosyncratic susceptibility patterns. Prior susceptibilities should be reviewed and may change empiric antibiotic coverage.

Aerosolized Antibiotics

Rarely recommended. Occasional exceptions may be made for highly drug-resistant organisms.

TABLE 1. Antibiotic selection for suspected HAP/VAP in common scenarios.

Scenario	Empiric Regimen
Most cases	Cefepime alone
Sepsis or septic shock	Vancomycin plus cefepime
Severe allergy to penicillins and cephalosporins	Vancomycin plus aztreonam
MRSA colonization or prior MRSA infection	Vancomycin plus cefepime
Anaerobic coverage needed	Piperacillin-tazobactam OR cefepime plus metronidazole. Do not add vancomycin to piperacillin-tazobactam
Recent infection with multi-drug resistant organism (MDRO) within prior 30-60 days	Use prior susceptibilities as appropriate. Consider ID consultation. Generally do not use a narrower-spectrum regimen than otherwise recommended for the scenario. <ul style="list-style-type: none">• ESBL producer: meropenem• Carbapenem-resistant: consult ID

DEFINITIVE TREATMENT OF HAP AND VAP

Determining if the patient truly has pneumonia

Definitions of HAP and VAP *require* a positive respiratory culture for definitive diagnosis (not always possible in HAP). Respiratory cultures have poor specificity, and positive results often represent colonization of an airway device or respiratory tract epithelium. Consider the following factors in assessing whether the patient has pneumonia.

TABLE 2. Clinical factors that are more or less suggestive of pneumonia.

Pneumonia Less Likely	Pneumonia More Likely
Recent positive culture for same organism	Absence of prior positive culture for colonizing organism
Gram stain with >25 PMNs/LPF	Gram stain with 2+ PMNs or greater
Gram stain without organisms (usually rejected by lab; it is rarely helpful to request culture)	Gram stain with 2+ or greater organisms
Light growth of organisms on culture	Moderate or heavy (2+ or greater) growth of organisms
Culture obtained from tracheal aspirate or ETT aspirate	Culture obtained by sputum or bronchoalveolar lavage (BAL)
Low pre-test probability (low suspicion for pneumonia when cultures sent)	High pre-test probability (syndrome highly consistent with pneumonia)

Adjusting empiric therapy in response to species identification

In most cases, the species will be known before susceptibilities are available. Antibiotics may need to be adjusted depending on the identification. This table is meant to address the most common and clinically significant results.

TABLE 3. Targeting therapy before and after susceptibilities are available

Organism	Before Susceptibilities	After Susceptibilities
<i>Staphylococcus aureus</i>	Vancomycin (preferred) or linezolid. If patient is doing well on cefepime alone, it may not be necessary to add vancomycin.	MSSA: nafcillin or cefazolin MRSA: vancomycin or linezolid
<i>Pseudomonas aeruginosa</i>	Continue empiric antipseudomonal beta-lactam (most often cefepime). If patient is declining, consider addition of IV tobramycin.	Use most targeted therapy possible.
Gram-negative enterics (<i>E. coli</i> , <i>K. pneumoniae</i> , etc)	Most are susceptible to 3 rd and 4 th generation cephalosporins and piperacillin-tazobactam.	Most targeted therapy possible. Ampicillin, ampicillin-sulbactam, and cefazolin are all acceptable if organism is susceptible.
Potential AmpC producers (<i>Enterobacter</i> , <i>Citrobacter</i> , <i>Serratia</i>)	Cefepime is preferred. Very severe illness: meropenem	Cefepime or meropenem. Other cephalosporins and pip-tazo should usually not be used.
<i>Acinetobacter baumannii</i>	Consult ID. Meropenem and ampicillin-sulbactam are most likely to be active. If patient is declining, consider addition of levofloxacin or IV amikacin.	Use most targeted therapy possible. Often this is ampicillin-sulbactam. Cefepime, ceftazidime, and meropenem are often used.
<i>Stenotrophomonas maltophilia</i>	Trimethoprim-sulfamethoxazole is preferred. When contraindicated, levofloxacin or minocycline are options.	TMP-SMX if active. Levofloxacin is second-line, then minocycline.

Duration of treatment for nosocomial respiratory infections

The generally accepted duration for HAP and VAP is **7 days**. Note that these may need to be extended when purulent complications develop, such as necrotizing pneumonia or empyema.

Treatment of ventilator-associated tracheobronchitis is controversial, but some experts believe it is warranted as treatment may decrease the risk of later VAP and decrease time on ventilator. When treating this condition, the maximum recommended duration is 5 days.

TABLE 4. Duration of Therapy for HAP, VAP, and VAT

Diagnosis	Definition	Duration	Comment
HAP or VAP	Systemic signs of infection <i>plus</i> pulmonary infiltrate <i>plus</i> increased sputum and/or increased ventilatory/oxygen needs	7 days	May be complicated by necrotizing pneumonia or pleural empyema. In these cases, longer durations are warranted. Consult ID.
Ventilator-associated tracheobronchitis	Systemic signs of infection <i>plus</i> purulent sputum and positive culture <i>without</i> pneumonia on CXR	0-5 days	Treatment <i>may</i> reduce risk of later VAP and <i>may</i> reduce time to extubation. If treatment, no more than 3-5 days.

Dosing recommendations for commonly used antibiotics

TABLE 5: Antibiotic Dosing Recommendations for Patients >1 Month of Age without Renal Dysfunction

Antibiotic	Dosing Information	Max Dose	Renal Adjustment Needed?
Aztreonam	40 mg/kg/dose IV q8h	2000mg	YES
Cefepime	50 mg/kg/dose IV q8h	2000mg	YES
Ceftaroline	<2 yo: 8 mg/kg/dose IV q8h 2-<18 yo & ≤33kg: 12 mg/kg/dose IV q8h ≥2 yo & >33kg: 600 mg IV q12h	600mg	YES
Clindamycin	13 mg/kg/dose IV/PO q8h	600mg	NO
Linezolid	<12 yo: 10 mg/kg/dose IV/PO q8h ≥12 yo: 600mg IV/PO q12h	600mg	YES (only HD/PD)
Meropenem	20 mg/kg/dose IV q8h	1000mg	YES
Metronidazole	10 mg/kg/dose IV/PO q8h	500mg	NO
Piperacillin/tazobactam	<9 mo: 80 mg piperacillin/kg/dose IV q6h ≥9 mo: 100 mg piperacillin/kg/dose IV q6h	4000mg piperacillin	YES
Trimethoprim/sulfamethoxazole	5 mg TMP/kg/dose IV/PO q8h	320mg TMP	YES
Vancomycin	Dose per pharmacy	2000mg	YES

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