

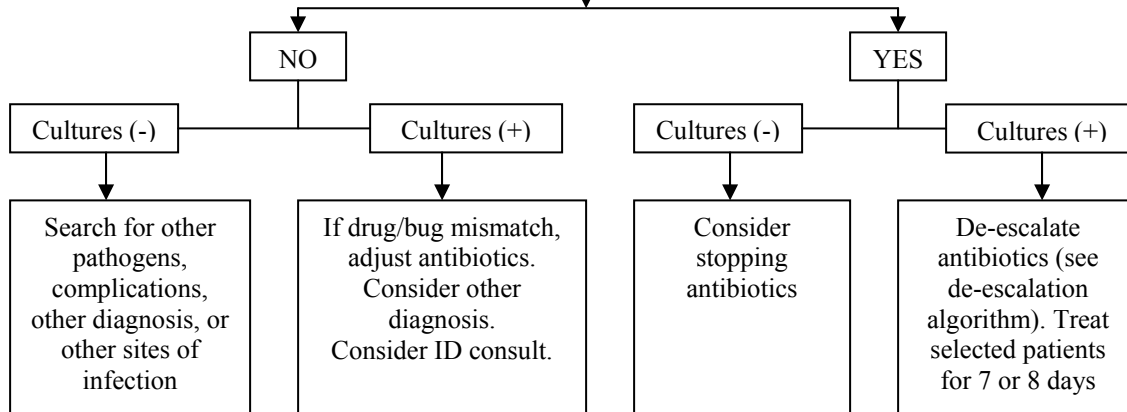
Wake Forest University Baptist Medical Center

Treatment of Hospital Acquired Pneumonia in Adults

Obtain lower respiratory tract sample for quantitative culture and microscopy prior to start of therapy
(Obtaining cultures should not delay initiation of treatment)

Assess risk factors ¹ and initiate treatment ²		
Hospital stay < 5 days & no risk of MDR pathogens ¹	Hospital stay 5 - 9 days OR Risk for MDR pathogens ^{1,3}	Hospital stay ≥ 10 days
Ceftriaxone 1 or 2 gm daily OR Moxifloxacin 400mg daily OR Amp/sulbactam 1.5 – 3 gm q6h	Vancomycin ⁴ PLUS EITHER ⁵ Cefepime 2 gm q12h OR Pip/tazo 4.5 gm q6h	Vancomycin ⁴ PLUS Amikacin - see aminoglycoside dosing guide PLUS EITHER ⁵ Cefepime 2 gm q12h OR Pip/tazo 4.5 gm q6h

Days 2 & 3: Check cultures and clinical response
Clinical Response at 48-72 hours?



¹Risk factors for multi-drug resistant (MDR) pathogens

- Antibiotics in previous 90 days
- Hospitalization for ≥ 2 days in the 90 days prior to current admission
- Residence in nursing home or extended care facility
- Home infusion therapy
- Chronic dialysis within 30 days
- Home wound care
- Family member with MDR pathogen
- Immunosuppressive disease or therapy

²Doses assume normal renal function

³Some of these patients may be at risk for MDR gram negative pathogens and therefore empiric systemic or inhaled amikacin may be warranted

⁴Vancomycin loading dose of 20mg/kg (rounded to nearest 250mg), then:

CrCl (mL/min)	Weight (kg)			
	≤ 60	61 - 79	80 - 99	≥ 100
≤ 10	Draw level (re-dose when level < 20mcg/mL)			
11 – 29	1.25g q48h	1.5g q48h	1.75g q48h	1g q24h
30 – 49	1g q24h	1.25g q24h	1.5g q24h	1.5g q24h
50 – 69	1.5g q24h	1g q12h	1g q12h	1.25g q12h
≥ 70	1g q12h	1.25g q12h	1.5g q12h	1.75g q12h

Keep trough serum level 15-20 mcg/mL

⁵For severe penicillin or cephalosporin allergy (anaphylaxis; immediate hives): aztreonam 2gm q8h

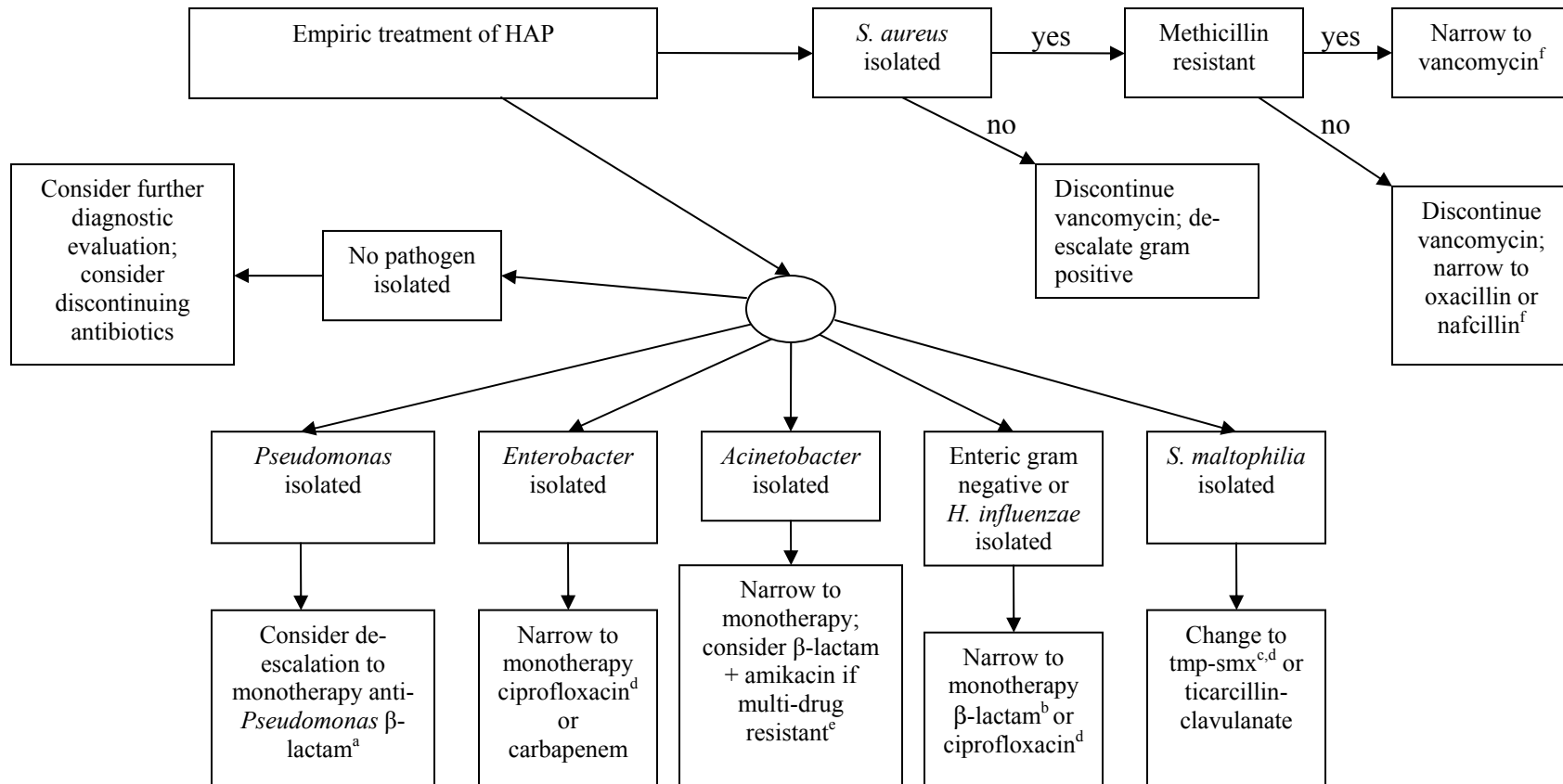
Principles on Which Guidelines are Based

1. **Cultures.** Obtaining quantitative or semi-quantitative cultures of lower respiratory tract (LRT) secretions is essential to providing optimal care to patients with VAP. Acceptable methods to obtain culture specimens include protected specimen brush, bronchial alveolar lavage, and tracheal aspirate.
2. **Adequate empiric therapy.** Giving initial empiric therapy that covers the causative pathogen (“adequate” therapy) yields improved outcomes when compared with treating patients with “inadequate” initial therapy. Therefore it is important that the initial empiric antibiotic regimen covers the most likely pathogens. Studies to date have shown linezolid and vancomycin to be equivalent in the treatment of pneumonia. The decision to prefer vancomycin over linezolid is based on linezolid’s expense and risk of resistance.
3. **Double gram-negative therapy.** The purpose of using double gram-negative therapy is to expand the likelihood of covering the causative pathogen with an empiric regimen. In most cases using two antibiotics to cover a single gram-negative organism offers no advantage over using a single drug.
4. **Local microbiologic data.** Current national treatment guidelines recommend using local microbiologic data to determine treatment algorithms. Our guidelines are based on an analysis of pathogens causing nosocomial pneumonia at WFUBMC. Key points from this analysis include:
 - a. MRSA needs to be empirically covered for all late pneumonias (onset > day 4 of hospitalization).
 - b. Ciprofloxacin does not significantly expand the empiric coverage offered by piperacillin-tazobactam or cefepime and therefore there is no advantage to adding ciprofloxacin to these beta-lactams as empiric coverage of HAP.
 - c. Resistance to piperacillin-tazobactam and cefepime is more likely after the patient has been in the hospital for more than 10 days. Amikacin is the only antibiotic that reliably covers gram-negative pathogens that are resistant to these beta-lactams.
5. **De-escalation.** Narrowing antibiotic treatment in response to culture results is necessary to limit antibiotic resistance and is not detrimental to patient care. If there is a significant growth of a pathogen from a LRT culture, antibiotic therapy can be narrowed to target that pathogen (aminoglycoside monotherapy is generally not recommended for treatment of pneumonia). If a particular organism does not grow from a LRT culture (and there has been no antibiotic change in the 72 hours prior to obtaining the culture), it is very unlikely that that organism is the cause of the pneumonia. (ie, in most cases, if the cultures don’t grow MRSA, the vancomycin can be stopped).
6. **Duration.** A multi-center trial demonstrated that eight days of therapy for HAP was just as effective as 15 days, although there was trend toward greater relapse rates in patients infected with *Pseudomonas aeruginosa*. Shorter courses of therapy have been associated with less antimicrobial resistance and superinfections. Efforts should be made to limit the duration of therapy for patients initially treated with appropriate antibiotics to 7 or 8 eight days, provided that the patient does not have a pneumonia due to *Pseudomonas aeruginosa* or a necrotizing pneumonia due to *S. aureus* and that the patient has demonstrated a good clinical response.

Algorithm for De-escalation of HAP Antibiotics When Culture and Susceptibility Results are Available

Assumptions: 1) Cultured bacteria is causative pathogen, 2) Isolate is susceptible to recommended antibiotic(s).

Further interpretation is needed if multiple organisms are isolated.



- Anti-*Pseudomonas* β-lactams include cefepime, piperacillin, meropenem, or aztreonam. Consensus guidelines do not make preference to combination therapy over monotherapy for *Pseudomonas**
- Options include: ampicillin-sulbactam, piperacillin-tazobactam, cefazolin, ceftriaxone, or cefepime, depending on susceptibilities. Carbapenems or aztreonam not recommended unless susceptibilities and/or patient allergies dictate.
- tmp-smx = trimethoprim-sulfamethoxazole
- Consider IV to PO switch when appropriate
- Cases of HAP due to MDR *Acinetobacter* are complicated. Consider requesting infectious diseases consult.
- If *S. aureus* is the only pathogen isolated

* American Thoracic Society and the Infectious Diseases Society of America. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. *Am J Respir Crit Care Med* 2005;171:388-416.

Amikacin Dosing² – HAP Guidelines

Table 1: Dosing Weight

Is patient obese? If **NO**, dosing weight = total body weight. If **YES**, calculate dosing weight below.
 Dosing weight calculation:
 1. Calculate lean body weight (LBW):
 $LBW = 2.3 (\text{inches over } 5 \text{ feet tall}) + [45 (\text{female}) \text{ or } 50 (\text{male})]$
 2. If total body weight (TBW) is >40% above lean body weight (LBW), dosing weight = $LBW + 0.4(TBW - LBW)$

Table 2: Dosing Interval

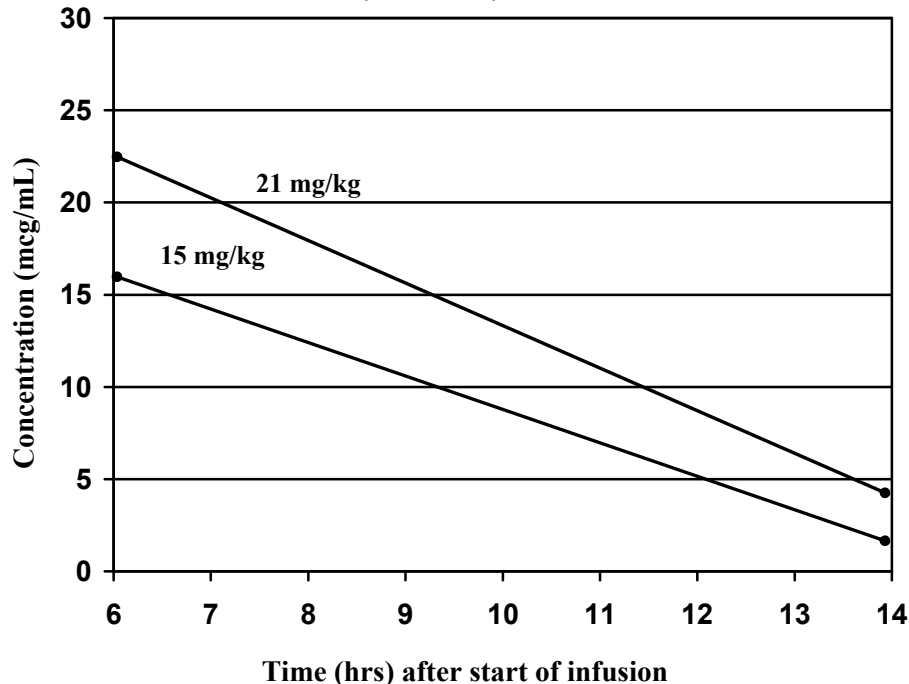
CrCl (mL/min)	Dosing Interval
≥ 90	Every 8 hours
60-89	Every 12 hours
25-59	Every 24 hours
10-24	Every 48 hours
<10	Per levels
CRRT	Per levels
Hemodialysis ²	After HD

Table 3: Monitoring

Key Points About Obtaining Levels

- If using **TRADITIONAL DOSING**, peak and trough concentrations should be obtained around the 4th dose (to ensure steady state).
 - ⇒ Peak concentrations should be obtained at least 30 minutes after a 1 hour infusion.
 - ⇒ Trough concentrations should be obtained just before the next scheduled dose.
 - ⇒ Adjust dose to **peak ≥ 27 mcg/mL** and **trough ≤ 4 mcg/mL**
- Peaks and troughs are not necessary if dosing by **ONCE DAILY** method (use nomogram)

Once Daily Amikacin Nomogram (ODAmik) - Adults



Dose Confirmation on Nomogram

- Confirmation should occur after first dose
- In place of peak & trough concentrations, follow the sequence below:
 1. Obtain random serum concentration
 2. Plot concentration on nomogram
 3. If below line for respective dose, continue dose
 4. If above line, use flow chart of traditional dosing shown above
 5. Repeat dose confirmation every 7 days and/or in the event of changes in renal function

ODAmik Nomogram Dosing

- Use total body weight unless patient is obese
- If obese, see **Table 1** above to calculate dosing weight
- Dose is **15 or 21 mg/kg q24 hours**
- Consider 15 mg/kg when pathogen MIC is known to be ≤ 4 mcg/mL

¹ Round dose to nearest **50 mg**
² Consultation with a clinical pharmacist for amikacin dosing is recommended

Calculate dosing weight (see **Table 1**)

Is CrCl >60mL/min?

Yes

Use **ONCE DAILY AMIKACIN (ODAmik) NOMOGRAM** (see dosing nomogram below)

No

Loading Dose¹ = **10 mg/kg**

Select dosing interval (see **Table 2**)

If patient fails **ONCE DAILY AMIKACIN NOMOGRAM**

Maintenance Dose¹ = **8 mg/kg** every dosing interval

Refer to algorithm for de-escalation of HAP antibiotics