PROTOCOL

Ventilator Associated Pneumonia Diagnosis and Treatment Protocol

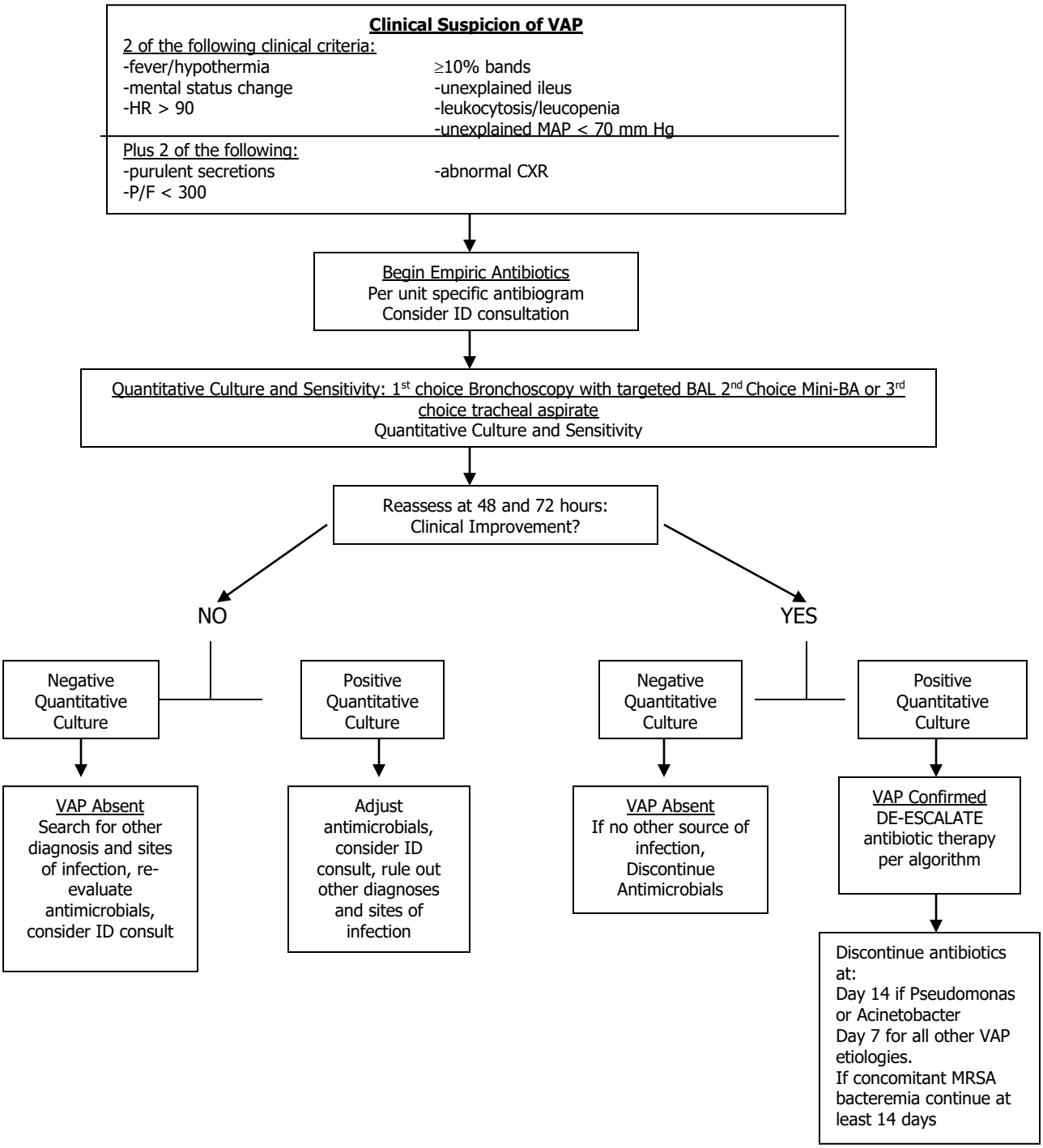
Scope: Prescribers and Pharmacists

Population: The antimicrobial guidelines apply only to immunocompetent patients in the ICU based on specific surveillance data from these units and the types of patients treated in them. **Your Unit may have different antibiograms and may need to adjust the antibiotics below!** For the purposes of this protocol Ventilator Associated Pneumonia (VAP) will be defined as a new pneumonia not incubating at the time of intubation.

Outcome: The goal of the Clinical VAP Diagnosis and Treatment Protocol is to provide a standard approach to the diagnosis and treatment of VAP

Protocol:

VAP Diagnostic and Treatment Algorithm



A negative quantitative culture is < 10,000 CFUs on a BAL or mini-BAL or <100,000 by quantitative tracheal aspirate.
A positive culture is greater than the above listed CFU counts.

Figure 1

Unit Specific Antimicrobial Algorithms

A. Medical Intensive Care Unit Algorithm

1st Line Regimen	Dosage (Normal Renal Function: CrCl ≥ 50 mL/min)	Adjustment for failure (CrCl in mL/min):		
		30 – 49	< 30	CRRT
Vancomycin	☐ Refer to Hospital Vancomycin Protocol			
Plus:				
Doripenem	1 g q8h (4 hour infusion)	500 mg q8h (4 hour infusion)	500 mg q12h (4 hour infusion)	Max dose
Plus:				
Tobramycin	7 mg/kg once daily	Refer to Hospital Once Daily Aminoglycoside Protocol		

For those patients who have recently received doripenem (previous 2 weeks) or are currently on it when VAP is diagnosed, a 2nd Line regimen should be initiated, as follows:

2nd Line Regimen	Dosage (Normal Renal Function: CrCl ≥ 50 mL/min)	Adjustment for failure (CrCl in mL/min):		
		30 – 49	< 30	CRRT
Vancomycin	Refer to Hospital Vancomycin Protocol			
Plus:				
Cefepime **OR**	2 g q8h (3 hour infusion)	2 g q12h (0.5hr)	1 g q12h (0.5hr)	Max dose
Piperacillin/tazobactam	2.25 g IV load, then 18 g (continuous infusion)	13.5 g CI	9 g CI	Max dose
Plus:				
Tobramycin	7 mg/kg once daily	Refer to Hospital Once Daily Aminoglycoside Protocol		

B. Surgical Intensive Care Unit Algorithm

1st Line Regimen	**Dosage (Normal Renal Function: CrCl ≥ 50 mL/min)**	**Adjustment for failure (CrCl in mL/min):**		
		30 – 49	< 30	CRRT
Vancomycin	Refer to Hospital Vancomycin Protocol			
Plus:				
Cefepime	2 g q8h (3 hour infusion)	2 g q12h (0.5hr)	1 g q12h (0.5hr)	Max dose
Plus:				
Tobramycin	7 mg/kg once daily	Refer to Hospital Once Daily Aminoglycoside Protocol		

For those patients who have recently received cefepime (recent 2 weeks) or are currently on it when VAP is diagnosed, a 2nd Line regimen should be initiated, as follows:

2nd Line Regimen	**Dosage (Normal Renal Function: CrCl ≥ 50 mL/min)**	**Adjustment for failure (CrCl in mL/min):**		
		30 – 49	< 30	CRRT
Vancomycin	Refer to Hospital Vancomycin Protocol			
Plus:				
Doripenem	1 g q8h (4 hour infusion)	500 mg q8h (4 hour infusion)	500 mg q12h (4 hour infusion)	Max dose
Plus:				
Tobramycin	7 mg/kg once daily	Refer to Hospital Once Daily Aminoglycoside Protocol		

C. Neurosurgical Intensive Care Unit Algorithm

1st Line Regimen	Dosage (Normal Renal Function: CrCl ≥ 50 mL/min)	Adjustment for failure (CrCl in mL/min):		
		30 – 49	< 30	CRRT
Vancomycin	Refer to Hospital Vancomycin Protocol			
Plus:				
Cefepime **OR**	2 g q8h (3 hour infusion)	2 g q12h (0.5hr)	1 g q12h (0.5hr)	Max dose
Piperacillin/tazobactam	2.25 g IV load, then 18 g (continuous infusion)	13.5 g CI	9 g CI	Max dose
Plus:				
Tobramycin	7 mg/kg once daily	Refer to Hospital Once Daily Aminoglycoside Protocol		

For those patients who have recently received cefepime or piperacillin/tazobactam or are currently on one of these agents when VAP is diagnosed, the alternative regimen should be initiated as 2nd Line therapy.

The following provisions apply to all units:

I. For patients who can not receive aminoglycosides, ciprofloxacin 400 mg IV q8hours or levofloxacin 750 mg IV q24hours can be substituted.
II. ALL patients with suspected VAP should have 2 blood cultures ordered on VAP DAY 1.
III. Patients with documented β-lactam allergies should have aztreonam 2 g q 8 hours with 3 hour infusions.
IV. Patients with a recent history of resistant pathogen(s) colonization or infection to the principal beta-lactam agent should have antibiotics individualized preferably with a high dose extended infusion beta-lactam.

Renal Dose Adjustments for levofloxacin and ciprofloxacin

Drug	CrCl	Dose
Ciprofloxacin	>50 mL/min	400 mg IV q8h
	30-50 mL/min	400 mg IV q12h
	<30 mL/min and HD patients	400 mg IV q24h
	CRRT	400 mg IV q12h
Levofloxacin	> 50 mL/min	750 mg IV q24h
	20-49 mL/min	750 mg IV q48h
	< 20 mL/min and HD	750 mg IV once and then 500 mg q48h
	CRRT	750 mg IV once and then 500 mg q24h

Pharmacist Responsibilities and De-escalation algorithm:

1. Provide renal dose adjustments for empiric antibiotics as listed above per protocol.
2. Day 3-4: In consultation with the providers assist with de-escalation based on the patients' clinical conditions and cultures.
    a. Assess the clinical status of the patient including if pneumonia (VAP) is still a working diagnosis and if the patient has another active bacterial infection.
    b. If pneumonia is no longer part of the differential diagnosis discontinue antimicrobials as warranted.
    c. If pneumonia is the only active bacterial infection de-escalate as follows in patients without any antimicrobial allergy contra-indications for patients infected by
        i. MSSA: begin nafcillin 2 g IV q 4 h or cefazolin 1 g q 8 h; discontinue other antimicrobials.
        ii. MRSA: continue vancomycin, discontinue other antimicrobials. For patients not responding to vancomycin after 72 hours, the prescriber may switch to linezolid.
        iii. Streptococcus pneumoniae: begin penicillin 4 MU IV q 4 h (if MIC is less than 1 mcg/mL may use 2 MU q 4 h) or ceftriaxone 1 g q 24 h, discontinue other antimicrobials.
        iv. *Haemophilus influenzae or Moraxella catarrhalis*: begin ceftriaxone 1 g q 24 h, discontinue other antimicrobials including beta-lactamase positive strains.
        v. E. coli*, Klebsiella*, or Proteus*: use one of the following as warranted based on susceptibilities; 1st choice-cefazolin 1 g q 8

h, 2nd choice ceftriaxone 1 g q 24 h, 3rd choice ampicillin/sulbactam 3 g q 6 h, 4th choice ciprofloxacin 750 mg PO q 12 h or levofloxacin 750 mg IV q 24 h, 5th choice cefepime 1 g q 8 h. discontinue other antimicrobials.

vi. ESBL producing organisms (Some E. coli and Klebsiella): begin ertapenem 1 g q 24 h, discontinue other antimicrobials.
vii. Pseudomonas: use one of the following as warranted based on susceptibilities: 1st choice cefepime 2 g q 8 h, 2nd choice piperacillin/tazobactam 18 g continuous infusion, 3rd choice ceftazidime 2 g q 8 h, 4th choice doripenem 500 mg q 8 h (4 hour infusion), discontinue other antimicrobials.
viii. Acinetobacter: use one of the following as warranted based on susceptibilities: 1st choice ampicillin/sulbactam 3 g q 6 h, 2nd choice doripenem 500 mg q 8 h (4 hour infusion), discontinue other antimicrobials.
ix. Serratia*, Providencia*, Morganella*, Citrobacter*, or Enterobacter*: Do not use 1st-3rd generation cephalosporins even if susceptible. Use one of the following as warranted based on susceptibilities: 1st choice cefepime 1 g q 8 h or ertapenem 1 g q 24 h, 3rd choice ciprofloxacin PO 750 mg q 12 h or ciprofloxacin 400 mg q 8 h. For patients without fluid restrictions or tolerating oral medications use Bactrim 5-6 mg/kg q 12 h (typically 2 Bactrim DS tabs twice a day).
x. *Stenotrophomonas maltophilia:* Use Bactrim 5-6 mg/kg q 12 h (typically 2 Bactrim DS tabs twice a day).
xi. Enterococcus is an extremely rare cause of pneumonia; consider other sources of infection if clinically indicated.
xii. Candida does not cause pneumonia-do not treat without infectious diseases approval.
xiii. Mixed normal flora: 1st choice ampicillin/sulbactam 3 grams IV q 6 h, 2nd choice ceftriaxone 1 gram IV q 24 h, consider ID consult before initiating therapy as this result may not indicate pneumonia. Discontinue all other antimicrobials.

*Bactrim is an appropriate 1st choice option when susceptible in patients without fluid restriction or tolerating oral medications. Bactrim 5-6 mcg/kg q 12 h (typically 2 Bactrim DS tabs twice a day).

3. Day 7: Request physician discontinue antimicrobials for pneumonias caused by all pathogens except Pseudomonas and Acinetobacter. If the pathogen is MRSA and the patient had a concomitant bacteremia, continue MRSA therapy for at least 14 days.

4. Day 14: Request physician discontinue antimicrobials for pneumonias caused by Pseudomonas and Acinetobacter.

BAL and Mini-BAL:

Bronchoalveolar Lavage (BAL)

Notes:

- There is no absolute contraindication to the performance of a BAL though careful consideration of the necessity of the procedure should be taken in the following cases:
  - Platelet count < 50,000
  - Uncorrected coagulopathy
  - Refractory Hypoxemia
  - Pulmonary Hypertension
  - Recent Myocardial Infarction or Active Coronary Ischemia

- The choosing of the optimal site should be based on the chest X-ray. Multiple sites can be sampled if there is more than one area of infiltrate with suspected pneumonic infection.
- If multiple sites are sampled, the aspirate may be pooled or sent separately at the discretion of the performing clinician
- All samples should be sent for quantitative culture
- Recovered instillate increases with larger volumes instilled
- Small instilled volumes increase the likelihood of contamination with mucous and upper airway cells
- History of smoking or COPD decreases fluid recovery rate
- Fluid recovery decreases with increasing age
- Room air or warmed Normal Saline should be used as the instillate
- Whenever possible, the patient should be repositioned such that the area to be sampled is not dependent; this will increase yield considerably
- If samples are being sent for AFB, viral culture and/or cytology, larger volumes of aspirate will be necessary and the amount of instillate may require adjustment

Procedure for BAL

1) Increase FiO2 to 100%
2) Set a Rate on the ventilator
3) Pass bronchoscope through endotracheal tube and into a subsegmental bronchus until the lumen is occluded
4) 20 cc of saline should be instilled, suctioned and discarded (or suctioned through the channel without a trap in place) in order to cleanse the bronchoscope channel and clear the airway of mucous and upper airway cells that have been tracked into the area by wedging the bronchoscope

5) Attach Leuken's trap to the suction channel; the location of where this is attached within the suction system should be left to the discretion of the performing clinician

6) At least two and preferably three sequential 30 cc aliquots of normal saline should be instilled into the area and suctioned into the Leuken's trap with the scope wedged in place. A "dwell" time of approximately 3-7 seconds should occur between instillation and suctioning of each 30 cc aliquot of saline.
   - If there is significant airway collapse, discontinuous suction should be utilized **OR** the instillate can be withdrawn slowly using a 30 cc syringe through the working channel of the scope and the aspirate can be transferred to a Leuken's trap directly from the syringe

Mini-Bronchoalveolar Lavage

Notes:
- Contraindications same as traditional BAL
- Sensitivity and Specificity similar to bronchoscopic BAL and are better than tracheal aspirate in the case of Ventilator Associated Pneumonia
- Narrow diameter of the mini-BAL catheter allows sampling through smaller endotracheal tubes than can be obtained with bronchoscopic BAL
- The procedure is "blind" so that area of lung sampled is not under control of the operator (the side can be controlled)

Procedure for mini-BAL

1) Obtain order from the ICU attending or attending of record
2) Gather and prepare necessary equipment
    - Mini-BAL catheter
    - Printed lab slip with labeled Leuken's trap
    - Sterile saline-room temp or warmed
    - Sterile drape
    - Sterile gloves
3) Increase FiO2 to 100%
4) Set a rate on the ventilator
5) Don mask and sterile gloves
6) Place sterile drape over patient
7) Open mini-BAL catheter package and place on sterile field
8) Fill 30 cc syringe with 30 cc of sterile saline
9) Pass catheter through access port elbow extending to 1 ½ inches (see figure 2). Attach access port elbow between the endotracheal tube and the ventilator circuit (see figure 3). Once the adapter is secured onto the ET tube, extend the BAL catheter to the end of the ET tube. Align the numbers on the ET tube with the numbers on the BAL catheter to show when this has been achieved.

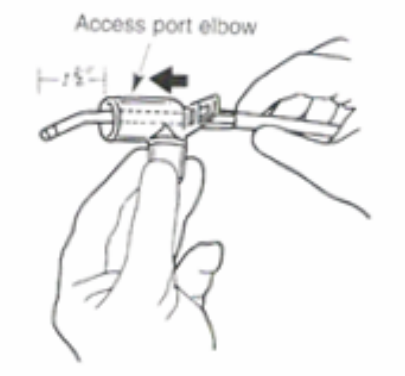


Figure 2

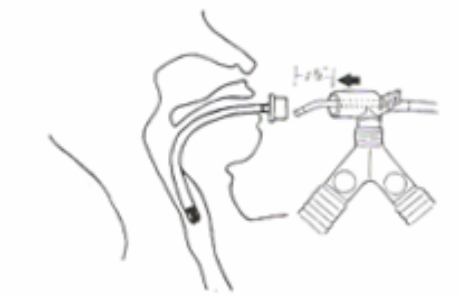


Figure 3

10) Extend the BA: catheter 2-4 cm (depending on ET tube position and patient size) beyond the end of the ET tube and flush the catheter with 2 cc sterile saline.
11) Direct the catheter tip into the chosen lung by orienting the O_2 port to the side of the chosen lung.
12) Advance the catheter until about 10 cm of BAL catheter protrudes beyond the access elbow, (see Figures 2 and 4) then advance the inner catheter from the outer catheter until resistance is met. The inner catheter should now be in a wedge position (see Figure 5).

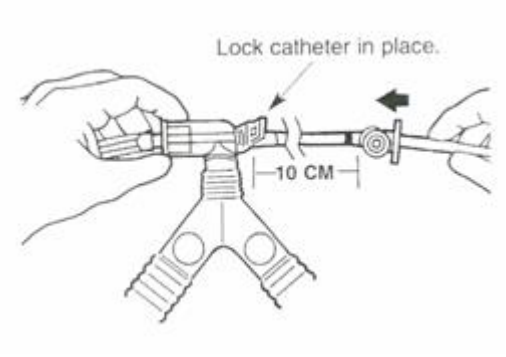


Figure 4

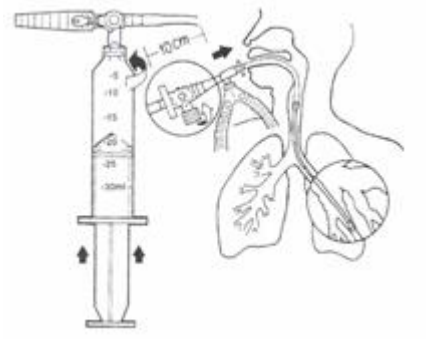


Figure 5

13) Lock the catheter in place. Note: the catheter should protrude no more than 15 cm from the patient's mouth

14) Attach a 30 cc syringe to the BAL catheter stop-cock and instill 30 cc of saline (see figure 6).

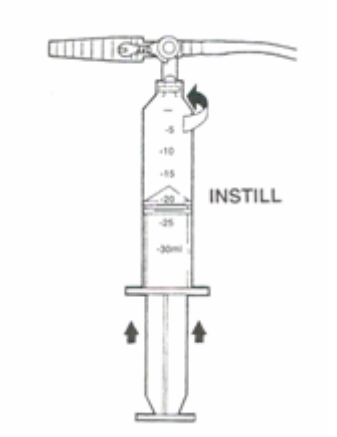


Figure 6

15) Aspirate the sample into a specimen trap by reversing stop-cock and setting the wall vacuum regulator to 40-50 mm Hg **or** pull the sample back into the syringe (see figure 7).

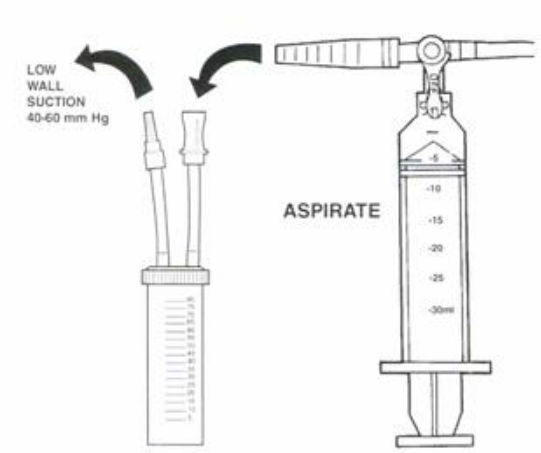


Figure 7

16) Repeat two to three times until adequate sample volume has been obtained (usually at least ~10-15 cc).
17) Disconnect the specimen trap, unlock the catheter and retract the inner catheter. Remove the BAL catheter and elbow access adapter from the endotracheal tube and ventilator circuit. Reconnect the ventilator tubing to the ET tube.
18) Be sure all specimen lab slips are present and that all specimen(s) are labeled.
19) Send the specimen to the lab for quantitative analysis.

Key Word Search: healthcare associated infection, healthcare associated pneumonia, nosocomial pneumonia, ventilator associated pneumonia, HAP, VAP