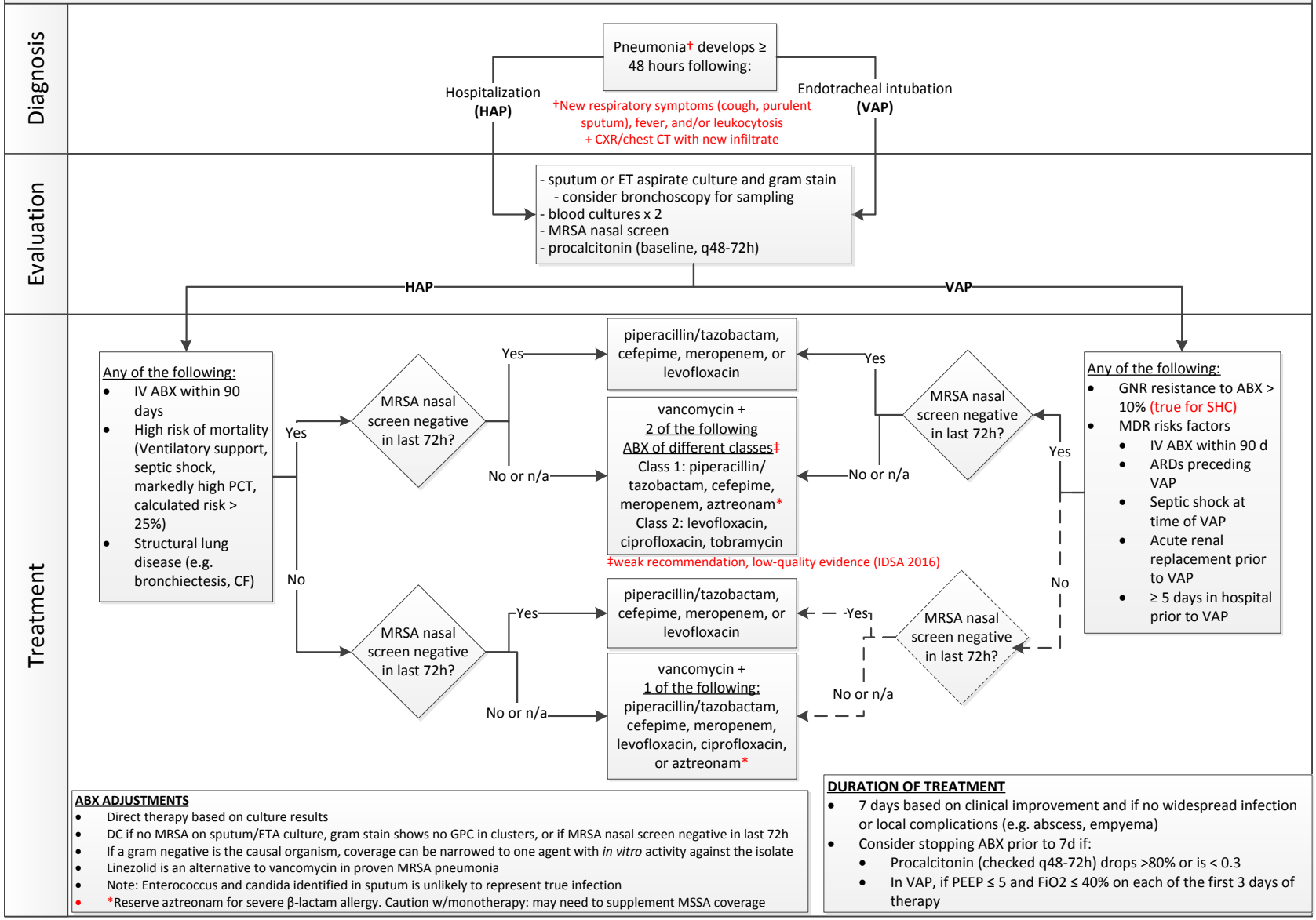
SHC Clinical Pathway: Hospital-Acquired and Ventilator-Associated Pneumonia

SHC Clinical Pathway: HAP/VAP Flowchart

v.08-29-2017



ABX ADJUSTMENTS

- Direct therapy based on culture results
- DC if no MRSA on sputum/ETA culture, gram stain shows no GPC in clusters, or if MRSA nasal screen negative in last 72h
- If a gram negative is the causal organism, coverage can be narrowed to one agent with *in vitro* activity against the isolate
- Linezolid is an alternative to vancomycin in proven MRSA pneumonia
- Note: Enterococcus and candida identified in sputum is unlikely to represent true infection
- *Reserve aztreonam for severe β-lactam allergy. Caution w/monotherapy: may need to supplement MSSA coverage

DURATION OF TREATMENT

- 7 days based on clinical improvement and if no widespread infection or local complications (e.g. abscess, empyema)
- Consider stopping ABX prior to 7d if:
  - Procalcitonin (checked q48-72h) drops >80% or is < 0.3
  - In VAP, if PEEP ≤ 5 and FiO2 ≤ 40% on each of the first 3 days of therapy

SHC Clinical Pathway: Hospital-Acquired and Ventilator-Associated Pneumonia

I. **Purpose:** to provide guideline-based recommendations for treatment of patients with hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP) within Stanford Health Care.

II. **Background**

The most recent guidelines for the treatment of HAP and VAP were released jointly in 2016 by the Infectious Diseases Society of America (IDSA) and the American Thoracic Society (ATS). These guidelines contained strong recommendations to tailor empiric antimicrobial coverage for HAP and VAP based on local microbiology and resistance patterns. This necessitated synthesis of data from the Stanford microbiology lab with the IDSA/ATS guidelines to produce recommendations for treatment of HAP and VAP in the specific context of Stanford Health Care. These treatment recommendations have been supplemented with the use of additional testing in order to ensure both adequate empiric antimicrobial coverage and appropriate, rapid de-escalation of therapy.

III. **Procedures/Guidelines**

1. Definitions

   Hospital-Acquired Pneumonia:
   a. new respiratory symptoms (e.g. cough, dyspnea, purulent sputum production), fever, and/or leukocytosis in a patient admitted >48 hours.
   b. Chest X-ray or CT scan with new pulmonary infiltrate.

   Ventilator-Associated Pneumonia:
   a. Purulent sputum production, worsened ventilator settings, fever, and/or leukocytosis in a patient on mechanical ventilation for >48 hours. The symptoms may not be the cause of requirement for mechanical ventilation.
   b. Chest X-ray or CT scan with a new pulmonary infiltrate.

2. Evaluation/Diagnosis

   Hospital-Acquired Pneumonia
   a. Sputum culture and gram stain
   b. Blood cultures x 2
   c. MRSA nasal screen if not done within the past 72 hours
      i. Do not repeat if previously positive during the current hospitalization
   d. Procalcitonin
      i. Obtain for baseline and trending only, value should not affect the clinical diagnosis of HAP

   Ventilator-Associated Pneumonia
   a. Endotracheal aspirate for gram stain and culture
      i. Consider bronchoscopy with bronchoalveolar lavage for pulmonary sampling
   b. Blood cultures x 2
   c. MRSA nasal screen if not done within the past 72 hours
      i. Do not repeat if previously positive during the current hospitalization
   d. Procalcitonin
      i. Obtain for baseline and trending only, value should not affect the clinical diagnosis of VAP

3. Treatment

Hospital-Acquired Pneumonia:

a. With Elevated Risk of Resistance
    i. If IV antibiotics within last 90 days, structural lung disease (bronchiectasis or cystic fibrosis) or elevated risk of mortality (septic shock, need for mechanical ventilation, calculated risk >25%)
        1. MRSA coverage: vancomycin or linezolid
        2. Broad-spectrum, anti-Pseudomonal coverage (2 agents from different classes)
            a. class 1: piperacillin/tazobactam, cefepime, meropenem, aztreonam (only for beta lactam allergy)
            b. class 2: levofloxacin, ciprofloxacin, tobramycin
    ii. For patients known to be colonized with resistant organisms, antibiotic choice should be guided by previous microbiology results
b. With Lower Risk of Resistance
    i. If no IV antibiotics within 90 days, no structural lung disease, not at high risk for mortality
        1. MRSA coverage (MRSA prevalence >20% at SHC): vancomycin or linezolid
        2. Broad-spectrum, anti-Pseudomonal coverage (1 drug): piperacillin/tazobactam, cefepime, meropenem, levofloxacin, ciprofloxacin, aztreonam (only for beta lactam allergy)

Ventilator-Associated Pneumonia:

a. As the rate of gram negative resistance (specifically among *Pseudomonas aeruginosa* isolates) to potential monotherapy agents is >10% and MRSA prevalence is >20% at SHC, all patients should receive MRSA and dual-agent, broad-spectrum, anti-Pseudomonal coverage. Patient-level risk factors that increase the risk of resistant organisms include: IV antibiotics within the last 90 days, structural lung disease (bronchiectasis or cystic fibrosis), septic shock at time of diagnosis, ARDS preceding VAP, 5 or more days of hospitalization prior to VAP diagnosis, or acute renal replacement prior to VAP
    i. MRSA coverage: vancomycin or linezolid
    ii. Broad-spectrum, anti-Pseudomonal coverage (2 agents from different classes):
        1. Class 1: piperacillin/tazobactam, cefepime, meropenem, aztreonam (only with beta lactam allergy)
        2. Class 2: levofloxacin, ciprofloxacin, tobramycin
b. For patients known to be colonized with resistant organisms, antibiotic choice should be guided by previous microbiology results

4. Adjustment

Hospital-Acquired Pneumonia:

a. Direct therapy based on culture results
b. Consider stopping MRSA coverage if nasal screen is negative
    i. If no screen is done, MRSA coverage can be stopped if sputum culture is negative for MRSA
c. If a gram negative is the causal organism and is susceptible to a suitable single agent, then coverage can be narrowed to one with *in vitro* activity against the isolate
d. Aztreonam monotherapy should be avoided in the absence of clear evidence of infection with a susceptible organism as this agent provides no gram-positive coverage
e. Duration of therapy should be 7 days based on clinical improvement and in the absence of more widespread infection or local complications such as abscess or empyema
f. Send procalcitonin q48-72 hours, antibiotics can be stopped prior to 7 days if value has decreased by >80% or is <0.3 and the patient is clinically improved

Ventilator-Associated Pneumonia:

a. Direct therapy based on culture results
b. Consider stopping MRSA coverage if nasal screen is negative

   i. If no screen is done, MRSA coverage can be stopped if ET aspirate culture is negative for MRSA
c. If a gram negative is the causal organism and is susceptible to a suitable single agent, then coverage can be narrowed to one with *in vitro* activity against the isolate
d. Aztreonam monotherapy should be avoided in the absence of clear evidence of infection with a susceptible organism as this agent provides no gram-positive coverage
e. Duration of therapy should be 7 days based on clinical improvement and in the absence of more widespread infection
f. Send procalcitonin q48-72 hours, antibiotics can be stopped prior to 7 days if value has decreased by >80% or is <0.3 and the patient is clinically improved
g. If PEEP ≤5 and FiO2 ≤40% on each of the first 3 days of therapy, consider stopping antibiotics

IV. References

1. De Jong E, van Oers JA, Beishuizen A, et al. Efficacy and safety of procalcitonin guidance in reducing the duration of antibiotic treatment in critically ill patients: a randomised, controlled, open-label trial. Lancet Infectious Diseases. 2016; 16: 819-27.
2. Kalil AC, Metersky ML, Klompas M, et al. Management of adults with hospital-acquired and ventilator-associated pneumonia: 2016 clinical practice guidelines by the Infectious Diseases Society of America and the American Thoracic Society. Clinical Infectious Diseases. 2016; 63(5): e61-e111.
3. Klompas M, Li L, Menchaca JT, Gruber S, Centers for Disease Control and Prevention Epicenters Program. Ultra-short-course antibiotics for patients with suspected ventilator-associated pneumonia but minimal and stable ventilator settings. Clinical Infectious Diseases. 2017; 64(7): 870-6.
4. Langsjoen J, Brady C, Obenauf E, Kellie S. Nasal screening is useful in excluding methicillin-resistant Staphylococcus aureus in ventilator-associated pneumonia. American Journal of Infection Control. 2014; 42: 1014-
5. Robicsek A, Suseno M, Beaumont JL, Thomson RB Jr, Peterson LR. Prediction of methicillin-resistant Staphylococcus aureus involvement in disease sites by concomitant nasal sampling. Journal of Clinical Microbiology. 2008; 46(2): 588-92.
6. Stolz D, Smyrnios N, Eggimann P, et al. Procalcitonin for reduced antibiotic exposure in ventilator-associated pneumonia: a randomised study. European Respiratory Journal. 2009; 34(6): 1364-75.

V. Document Information

A. Original Author/Date: Matthew Hitchcock, MD, 8/15/2017
B. Gatekeeper: Antimicrobial Stewardship Program
C. Review and Renewal Requirement
   This document will be reviewed every three years and as required by change of law or practice
D. Revision/Review History:
   SASS team 8/15/2017
E. Approvals
   1. Antimicrobial Subcommittee: 8/17/2017
   2. P&T: 9/15/2017

Appendix A. ICU specific antibiograms 2/2015-1/2017

ICU All Specimens

	Isolates	Aztreonam	Ceftazidime	Ciprofloxacin	Ertapenem	Cefepime	Levofloxacin	Meropenem	Moxifloxacin	Tobramycin	Pip/Tazo
Citrobacter freundii	11	37.5%	54.5%	72.7%	100%	90.9%	90.9%	100%	62.5%	90.9%	70%
Enterobacter aerogenes	31	85.7%	83.9%	96.8%	96.8%	100%	96.8%	100%	96.4%	96.8%	83.9%
Enterobacter cloacae	59	69.8%	69.5%	93.2%	84.2%	96.5%	96.6%	100%	94.3%	96.6%	74.6%
Escherichia coli	133	75.8%	81.2%	64.7%	97.7%	84.5%	63.9%	99.2%	64.4%	81.2%	83.5%
Klebsiella oxytoca	18	80%	94.4%	100%	100%	100%	100%	100%	100%	88.9%	77.8%
Klebsiella pneumoniae	83	92.6%	92.8%	94%	100%	95.2%	96.4%	100%	98.1%	97.6%	91.6%
Pseudomonas aeruginosa	94	67.1%	74.5%	86.2%	-	80.9%	92%	81.9%	-	95.7%	79.8%
Serratia marcescens	27	96.3%	96.3%	88.9%	100%	100%	96.3%	100%	88.9%	96.3%	100%
Stenotrophomonas maltophila	34						91.20%				

MRSA represents 34.6% of all ICU *Staphylococcus aureus* isolates from all sources and 33% of isolates in sputum

ICU Respiratory Specimens

	Isolates	Aztreonam	Ceftazidime	Ciprofloxacin	Ertapenem	Cefepime	Levofloxacin	Meropenem	Moxifloxacin	Tobramycin	Pip/Tazo
Citrobacter freundii	5	20%	20%	40%	100%	100%	80%	100%	40%	80%	60%
Enterobacter aerogenes	27	85.2%	81.5%	96.3%	96.3%	100%	96.3%	100%	96.3%	96.3%	81.5%
Enterobacter cloacae	40	70%	67.5%	92.5%	84.6%	97.4%	97.5%	100%	95%	95%	72.5%
Escherichia coli	41	75.6%	78%	65.9%	97.6%	75.6%	65.9%	100%	65.9%	87.8%	80.5%
Klebsiella oxytoca	22	90.9%	100%	100%	100%	100%	100%	100%	100%	100%	90.9%
Klebsiella pneumoniae	37	94.6%	89.2%	97.3%	100%	94.6%	100%	100%	100%	97.3%	91.9%
Pseudomonas aeruginosa	61	72.1%	80.3%	86.9%	-	78.7%	91.2%	80.3%	-	96.7%	80%
Serratia marcescens	25	96%	96%	88%	100%	100%	96%	100%	88%	96%	100%
Stenotrophomonas maltophila	28						92.9%				

MRSA represents 34.6% of all ICU *Staphylococcus aureus* isolates from all sources and 33% of isolates in sputum

Conditional Antibiograms for ICU Pathogens (All Specimens)

Meropenem-Resistant								
	Isolates	Amikacin	Tobramycin	Ceftazidime	Cefepime	Levofloxacin	Ciprofloxacin	Pip/Tazo
Pseudomonas	16	44%	77%	35%	65%	41%	47%	63%
Cefepime-Resistant								
	Isolates	Amikacin	Tobramycin	Ertapenem	Meropenem	Levofloxacin	Ciprofloxacin	Pip/Tazo
E coli	27	100%	4%	92%	100%	9%	9%	65%
Klebsiella pneumoniae	8	100%	25%	88%	88%	63%	38%	50%
Pseudomonas	15	53%	64%	-	41%	75%	71%	0%
Pip/Tazo-Resistant								
	Isolates	Amikacin	Tobramycin	Meropenem	Ceftazidime	Cefepime	Levofloxacin	Ciprofloxacin
Pseudomonas	39	69%	82%	50%	0%	4%	38%	71%

MRSA represents 34.6% of all ICU *Staphylococcus aureus* isolates from all sources and 33% of isolates in sputum

Appendix B. All inpatient antibiogram 2/2015-1/2017

All In-Patient, All Specimens

	Isolates	Aztreonam	Ceftazidime	Ciprofloxacin	Ertapenem	Cefepime	Levofloxacin	Meropenem	Moxifloxacin	Tobramycin	Pip/Tazo
Citrobacter freundii	39	62.5%	82.1%	89.7%	100%	94.4%	94.9%	100%	81.3%	97.4%	89.5%
Enterobacter aerogenes	65	83.3%	80%	100%	100%	98.3%	100%	100%	100%	98.5%	86.2%
Enterobacter cloacae	123	74.4%	71.9%	93.4%	83.1%	97.3%	95.9%	98.4%	96.3%	95.9%	70.8%
Escherichia coli	800	77.6%	86.4%	66.2%	99.1%	91.6%	66.2%	100%	59.7%	83.2%	90.3%
Klebsiella oxytoca	57	78.8%	96.5%	93%	100%	98.2%	93.0%	100%	93.8%	91.2%	78.9%
Klebsiella pneumoniae	305	87.4%	92.1%	89.8%	99.3%	93.5%	92.8%	99.3%	91.5%	91.1%	92.4%
Morganella morganii	20	100%	75%	90%	100%	100%	90%	1005%	60%	95%	100%
Proteus mirabilis	69	95.2%	95.7%	81.2%	100%	100%	85.5%	100%	81%	92.8%	100%
Pseudomonas aeruginosa	261	69.7%	80.8%	83.5%	-	80.1%	82.9%	83.9%	-	96.9%	85.5%
Serratia marcescens	55	98.1%	98.2%	89.1%	98.2%	100%	96.4%	98.2%	90.6%	96.4%	98.1%
Stenotrophomonas maltophila	58						87.90%				

MRSA represents 36% of all *Staphylococcus aureus* isolates no matter the source

All In-Patient Sputa

	Isolates	Aztreonam	Ceftazidime	Ciprofloxacin	Ertapenem	Cefepime	Levofloxacin	Meropenem	Moxifloxacin	Tobramycin	Pip/Tazo
Citrobacter freundii	7	42.9%	42.9%	57.1%	100%	100%	85.7%	100%	57.1%	85.7%	71.4%
Enterobacter aerogenes	30	83.3%	73.3%	100%	96.7%	100%	100%	100%	100%	96.7%	83.3%
Enterobacter cloacae	48	72.3%	70.2%	93.6%	83%	97.8%	97.9%	97.9%	95.7%	95.7%	74.5%
Escherichia coli	58	75.9%	75.9%	60.3%	98.3%	75.9%	60.3%	100%	60.3%	81%	82.8%
Klebsiella oxytoca	15	86.7%	100%	93.3%	100%	100%	93.3%	100%	93.3%	100%	86.7%
Klebsiella pneumoniae	57	93%	91.2%	96.5%	100%	93%	98.2%	100%	98.2%	94.7%	93%
Pseudomonas aeruginosa	99	62.6%	75.8%	82.8%	-	71.7%	81.6%	80.8%	-	96%	78.1%
Serratia marcescens	33	97%	97%	84.8%	100%	100%	93.9%	100%	84.8%	97%	100%
Stenotrophomonas maltophila	47						87.2%				

MRSA represents 36% of all *Staphylococcus aureus* isolates no matter the source