RESPIRATORY TRACT RELATED INFECTIOUS SYNDROMES

Acute or Acute on Chronic Bronchitis

Antibiotics are NOT RECOMMENDED as >99% of acute bronchitis is caused by **viruses**.

Asthma Exacerbation

Supportive care. Antibiotics are NOT RECOMMENDED in the absence of pneumonia.

COPD Exacerbation (COPDE) **without** evidence of **pneumonia**

Per GOLD Guidelines, only the following patients presenting with COPDE may benefit from antibiotics

- **Increased sputum purulence** WITH increased dyspnea or sputum volume
- Severe exacerbation requiring invasive or non-invasive (e.g. BIPAP) mechanical ventilation
- Pneumonia as indicated by symptoms and imaging findings

Common causative pathogens: *S. pneumoniae, H. influenzae, M. catarrhalis,* viruses

Antibiotics, in order of preference	Comments
Doxycycline 100 mg PO/IV BID x 5 days	Has MRSA and atypical activity, some anti-inflammatory effects, may be protective against C. difficile
Azithromycin 500 mg PO/IV Q24 x 5 days	Has atypical activity Some anti-inflammatory effects
Levofloxacin* 750 mg PO/IV Q24 x 3-5 days	Increased risk of *C. difficile* and MRSA Black box warning for tendonitis, especially if >60 years old or concomitant steroids

*Routine use levofloxacin is discouraged. Levofloxacin may be considered in patients at high risk of adverse events from COPDE such as those with poor baseline functional status, >3 exacerbations/year, FEV1 <50%.

PNEUMONIA

Signs/symptoms: cough +/- purulent sputum, shortness of breath, hypoxia/hypoxemia, fever >38^{o}C, leukocytosis, wheezing, diminished breath sounds, pleuritic chest pain, rales/rhonchi, etc.
Diagnostic criteria: radiographic evidence of consolidation or infiltrates on x-ray and/or CT in immunocompetent patients

Community Acquired Pneumonia (CAP)	Healthcare-associated Pneumonia (HCAP)	Hospital Acquired Pneumonia (HAP)	Ventilator-associated Pneumonia (VAP)
Occurring in community patients with no recent extensive exposure to healthcare systems	Occurring in community patients with recent healthcare exposure defined as: -Nursing home / long-term care resident -Hospitalization ≥2 days within 90 days -Chronic dialysis patient -Home wound care within 30 days -Broad spectrum abx within 90 days	Occurring in patients in the hospital ≥48 hrs	Occurring in patients on invasive mechanical ventilation >48 hrs

Aspiration pneumonia: aspiration of bacteria from oropharynx or GI tract leading to pneumonia, and is distinct from aspiration pneumonitis, chemical pneumonitis, or aseptic pneumonitis

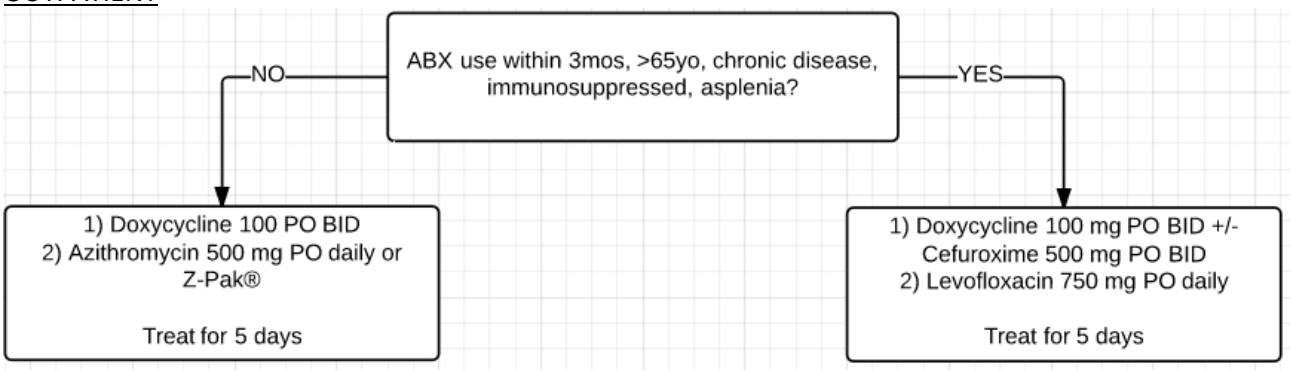
General principles: Recommendations are based on Sharp Healthcare antibiogram data as recommended by national guidelines. Initial broad-spectrum empiric antibiotic therapy must be accompanied by appropriate diagnostics and a commitment to choose culture-driven and pathogen-specific therapy to limit adverse drug effects, resistance development, and *C. difficile* infections. Clinical improvement may take 48-72 hours to become apparent. These recommendations apply to immunocompetent adult patients. For moderate to severely immunocompromised patients, consultation with Infectious Disease is recommended.

Which cephalosporins are safe in patients with penicillin allergy? Historical rates of cross-reactivity were likely inflated. Penicillin allergies may also be falsely reported. Based on more recent literature, cephalosporins, especially higher generation cephalosporins such as ceftriaxone and cefepime, are typically considered safe in patients with penicillin allergy.

Community-Acquired Pneumonia (CAP)

Common Pathogens: *Streptococcus pneumoniae, Mycoplasma pneumoniae, Haemophilus influenzae, Chlamydophila pneumoniae*, *Legionella*, respiratory viruses, *Staphylococcus aureus* (post-viral infections)

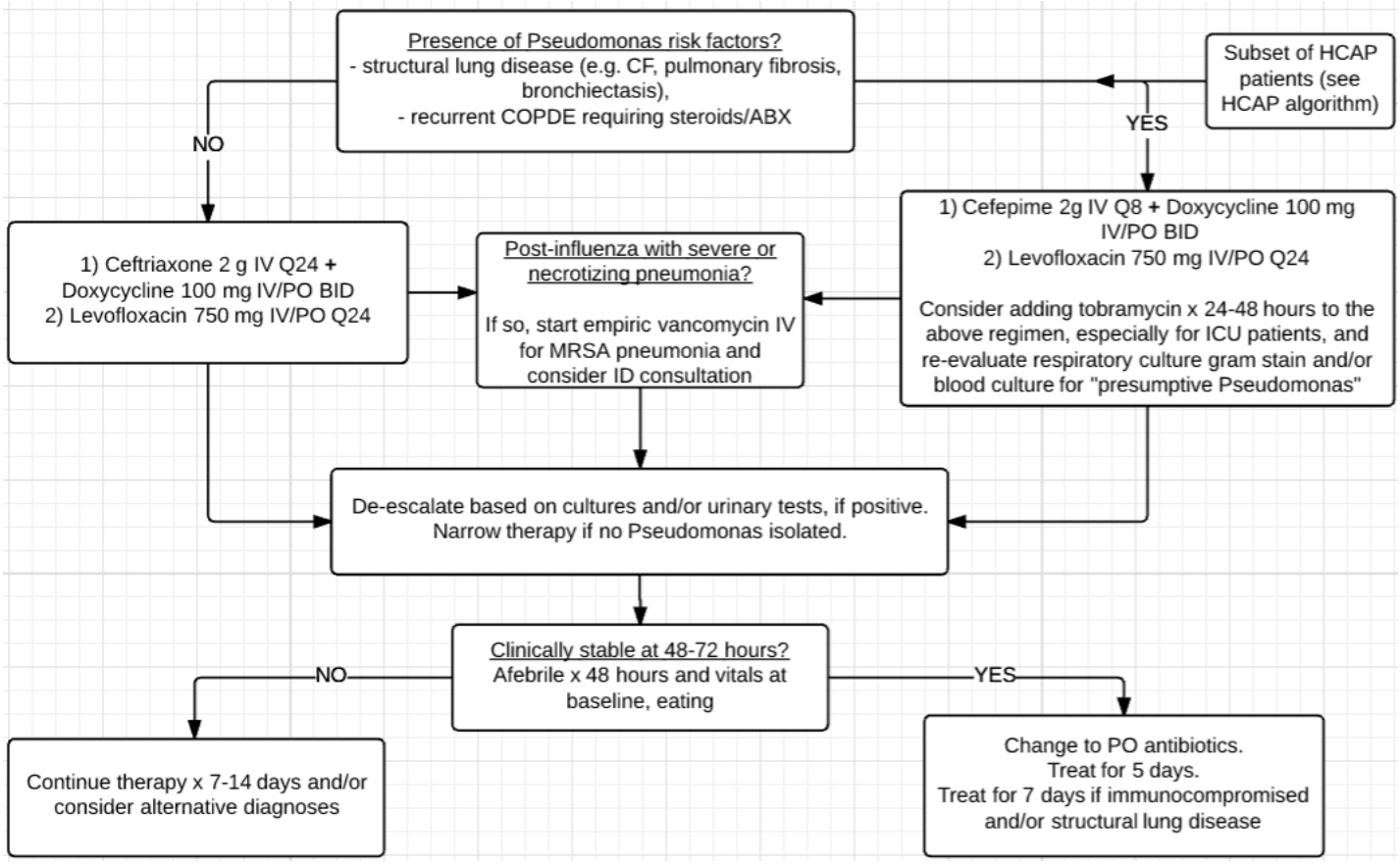
OUTPATIENT



INPATIENT

Diagnostics: Blood culture, respiratory culture, S. pneumoniae urinary antigen, Legionella urinary antigen, influenza screening (during flu season), MRSA nares screen, +/- Procalcitonin

Empiric Therapy: ICU and non-ICU patients



Fluoroquinolones are not preferred first line agents for CAP given availability of alternative agents and increased risk of adverse effects associated with fluoroquinolones: increased risk of *C. difficile*, central nervous system side effects, tendon rupture particularly in elderly and patients receiving steroids

Culture-directed therapy: Select narrowest spectrum agent based on susceptibilities

Pathogen	**Recommendation (listed in order of preference)** Doses for normal renal/hepatic function
S. pneumoniae, PCN susceptible or urinary antigen positive (93.5% at SHC susceptible to PCN)	Penicillin G 2 million units IV Q4 Amoxicillin 500 mg PO TID Levofloxacin 750 mg IV/PO Q24 (if intolerable to others)
S. pneumoniae, PCN- resistant, cephalosporin-susceptible (97% at SHC susceptible to CTX)	Ceftriaxone 2 g IV Q24 Cefdinir 300 mg PO BID Levofloxacin 750 mg IV/PO Q24 (if intolerable to others)
H. influenzae, non-beta-lactamase producing	Ampicillin 1 g IV Q6 Amoxicillin 500 mg PO TID Cefazolin 2 g IV Q8 Cephalexin 500 mg PO QID Levofloxacin 750 mg IV/PO Q24 (if intolerable to others)
H. influenzae, beta-lactamase producing	Ampicillin/sulbactam 3 g IV Q6 Amoxicillin/clavulanate 875 mg PO BID Cefuroxime 750 mg IV Q8 Cefuroxime 500 mg PO BID Levofloxacin 750 mg/PO Q24 (if resistant/intolerable to others)
Legionella pneumophilia	Azithromycin 500 mg IV/PO Q24 x 7-10 days Levofloxacin 750 mg IV/PO Q24 x 7-10 days Consider ID consultation and adjunctive rifampin for severely ill
S. aureus (MSSA)	Cefazolin 2 g IV Q8 Nafcillin 2g IV Q4 Cephalexin 500 mg PO QID
S. aureus (MRSA)	Vancomycin per pharmacy Doxycycline 100 mg IV/PO Q12 Linezolid* 600 mg IV/PO Q12 (if resistant/intolerable to others)
CAP, cultures negative or not available Unless strong suspicion for Legionella, 3 days of atypical coverage is usually adequate	Cefdinir 300 mg PO BID Amoxicillin/clavulanate 2g PO BID (high dose to target any potential drug-resistant S. pneumoniae) Levofloxacin 750 mg IV/PO Q24 (if intolerable to others)

Which CAP patients need MRSA coverage? Doxycycline provides excellent S. aureus coverage at SHC, including MRSA. Community-acquired MRSA pneumonia may present as a secondary bacterial pneumonia after influenza/viral infection. For suspected necrotizing pneumonia secondary to MRSA or severe pneumonia status post influenza, coverage with vancomycin IV (or linezolid if allergy) along with ID Consultation is recommended.

What's the treatment duration for CAP patients with uncomplicated *S. pneumoniae* bacteremia? Prolonged antibiotic treatment is NOT necessary if good early clinical response. Treat based on recommended durations above.

How long does it take for cough and imaging abnormalities (e.g. infiltrate on chest x-ray) to resolve? May take 4-6 weeks to improve/resolve, even with appropriate management. Duration of treatment should be based on clinical response as noted above. Repeat imaging may not be appropriate for test of cure.

What is the role of oseltamivir? Oseltamivir is indicated for the alleviation of flu symptoms when initiated within 48 hours of symptom onset. However, the CDC recommends treatment with oseltamivir in patients hospitalized for influenza, regardless of time from symptom onset. The **sensitivity/specificity of SHC's influenza molecular influenza test is >99%** for appropriately collected nasopharyngeal specimens. For hospitalized patients diagnosed with influenza, including influenza pneumonia, start oseltamivir and consider discontinuing all antibiotics unless strong suspicion for secondary bacterial pneumonia. Treatment duration for influenza is 5 days, although prolonged courses should be considered in critically ill patients with poor early clinical response. Use of **Peramivir IV** for hospitalized influenza patients is not supported by studies. Peramivir IV is restricted at SHC to ID and ICU for patients with contraindications to oral or enteral administration of oseltamivir.

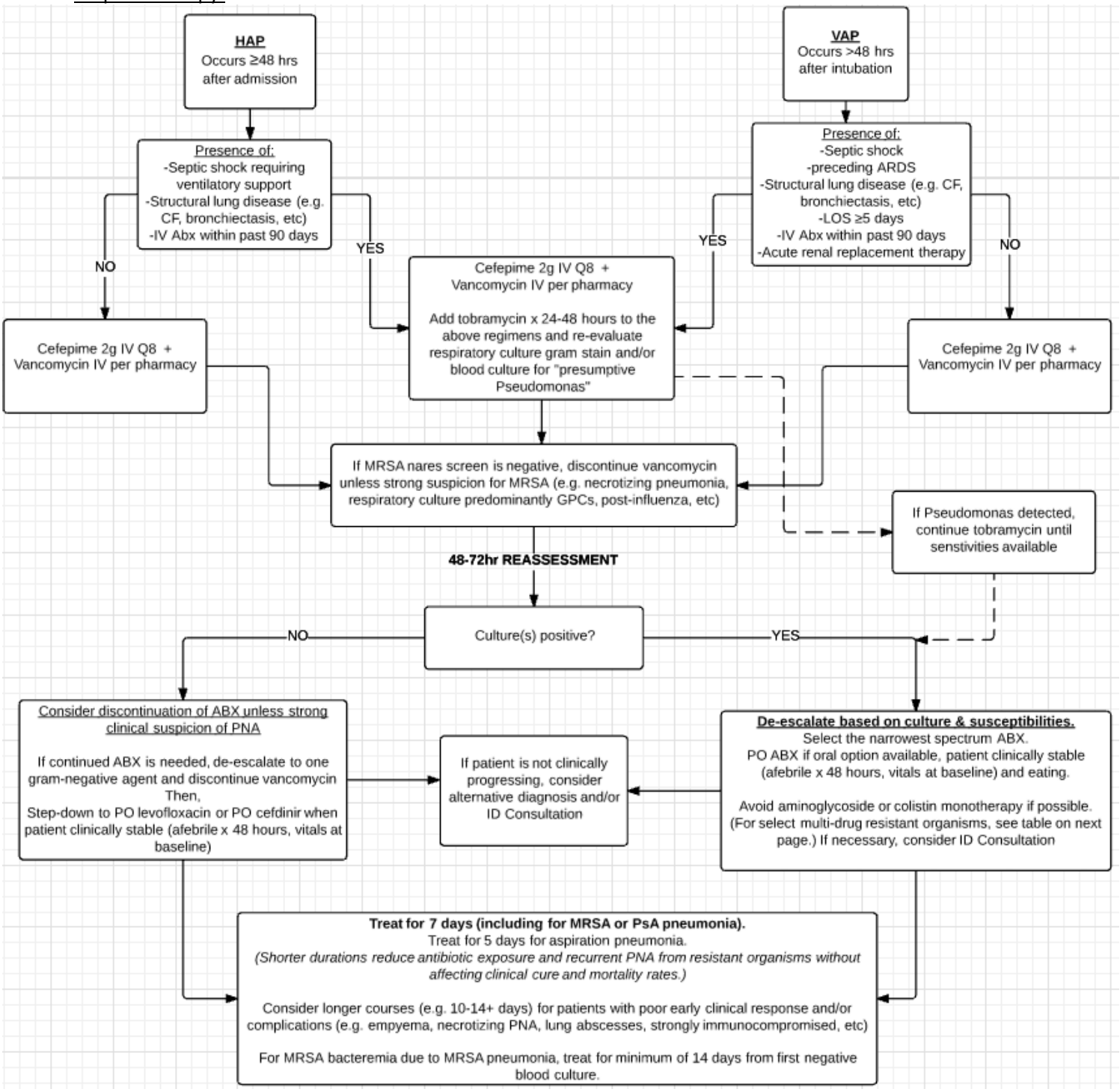
Hospital-Acquired and Ventilator-Associated Pneumonia (HAP / VAP)

Common Pathogens: Gram-negative rods (Enterobacteriaceae e.g. *E.coli, Klebsiella*, etc), *S. aureus* (MRSA, MSSA), *Pseudomonas*

Enterococcus, Candida, +/- Acinetobacter, +/- Stenotrophomonas isolated from respiratory tracts frequently represents colonization and should not be treated with antimicrobials routinely

Diagnostics: Blood culture, respiratory culture (if intubated, semi-quantitative endotracheal aspirate), MRSA nares screen, Procalcitonin, influenza screening (during flu season)

Empiric Therapy:



Culture-directed therapy for select organisms: Select narrowest spectrum agent based on susceptibilities

Pathogen	Recommendation
Pseudomonas	Monotherapy, based on susceptibilities (avoid aminoglycoside monotherapy)
Acinetobacter	Combination therapy preferred for severe disease Options include: ampicillin-sulbactam, imipenem, colistin, minocycline Tigecycline is not routinely recommended
ESBL-Producing GNRs	Meropenem for critically ill patients. Ertapenem if no Pseudomonas May consider fluoroquinolones based on susceptibilities and clinical progress Consider ID Consultation
Carbapenem-resistant GNRs	ID Consultation given high associated mortality and may require combination therapy Options include ceftazidime-avibactam, colistin, tigecycline, etc

What are the treatment recommendations for Ventilator-associated Tracheobronchitis (VAT)? Defined as "fever with no other recognizable cause, with new or increased sputum production, positive endotracheal aspirate with heavy growth yielding a new bacteria and no radiographic evidence of pneumonia." **Antibiotics are not routinely recommended** given the benefits of antimicrobial therapy is not clear and may not outweigh risks. Antibiotics may be considered if VAT is believed to be contributing to mucus plugging and/or ventilator weaning difficulty. If suspect HSV-induced VAT, consider antiviral therapy and ID consultation.

What is the role of "double coverage"? "Double coverage" often refers to using antibiotics from 2 different classes to **empirically** cover for potentially resistant organisms, particularly *Pseudomonas*. Studies have demonstrated double coverage did not result in improved clinical outcomes such as mortality, but was associated with higher risks of adverse effects compared to monotherapy. Therefore, **for most infections, monotherapy treatment is recommended**. EMPIRIC double coverage for 24-48 hours can be considered in patients presenting with septic shock and/or at risk for multi-drug resistant organisms (see HAP/VAP algorithm). When susceptibilities are available, monotherapy with an active agent is typically recommended. For patients failing monotherapy with known activity against the organism, please consider ID consultation.

What is the role of aminoglycosides (e.g. gentamicin/tobramycin/amikacin) in HAP/VAP? Aminoglycoside monotherapy is NOT recommended for treatment of pneumonia given poor lung tissue penetration and associated higher morality/morbidity. Aminoglycosides are preferred for double coverage of gram-negatives given relatively higher rates of gram-negative resistance to fluoroquinolones.

What is the role of inhaled/nebulized antibiotics in HAP/VAP? May be considered in patients with VAP caused by GNRs only susceptible to aminoglycosides or colistin. May be considered as adjunctive therapy in CF patients or as last resort measures in patients not responding to IV antibiotics alone. Inhaled or nebulized antibiotics should not be used for suppressive therapy in patients with endotracheal colonization.

Drug Class	Drug	**Recommended Dose* for Pneumonia** (for normal renal/hepatic function)
Beta-Lactams		
Penicillins	Ampicillin-sulbactam	3 g IV Q6
	Piperacillin-tazobactam	3.375 - 4.5 g IV Q8 over 4 hours
Cephalosporins	Ceftriaxone	2 g IV Q24
	Cefepime	2 g IV Q8 (can decrease to 1 g Q8 if no PsA)
Monobactams	Aztreonam	2 g IV Q8
Carbapenems	Meropenem	1 g IV Q8 over 3 hours
	Ertapenem	1 g IV Q24
	Imipenem-cilastatin	1 g IV Q8
Fluoroquinolones	Levofloxacin	750 mg IV/PO Q24
	Ciprofloxacin	400 mg IV Q8 (can decrease to Q12 if no PsA)
Aminoglycosides	Tobramycin	Per pharmacy, target peak/trough dependent on dosing
	Gentamicin	Per pharmacy, target peak/trough dependent on dosing
Glycopeptides	Vancomycin	per pharmacy, to target trough 15-20 mcg/mL
Oxazolidinones	Linezolid	600 mg IV/PO Q12

*Doses may be adjusted to target to specific MICs to optimize pharmacokinetics/pharmacodynamics.
For doses of other antimicrobial agents, please refer to SHC's Antimicrobial Dosing Guidelines and/or contact pharmacy.

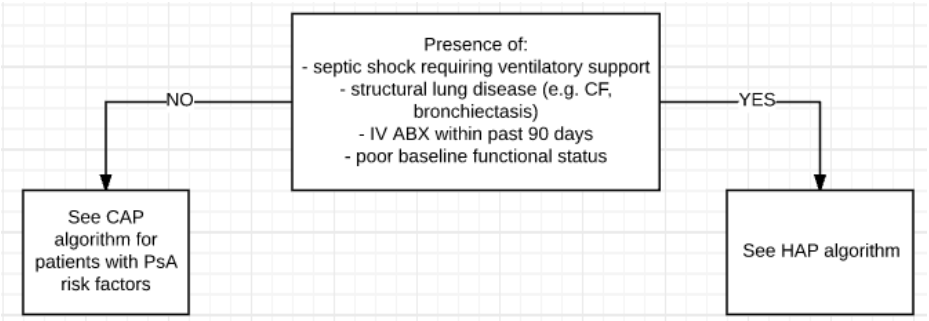
Healthcare-Associated Pneumonia (HCAP)

NOTE: Previous recommendations for HCAP set forth in 2005 grouped these patients with HAP/VAP patients. Subsequent studies have demonstrated that many HCAP patients are at low risk for drug-resistant organisms and are unnecessarily exposed to broad-spectrum antimicrobials as recommended. The following recommendations are based on studies, international guidelines, and local ID expert experience, and may evolve as national guidelines are updated.

Common Pathogens: *Streptococcus pneumoniae*, gram-negative rods, *S. aureus* (MRSA, MSSA), and other organisms implicated in CAP and HAP/VAP

Diagnostics for inpatient management: Blood culture, respiratory culture (if intubated, semi-quantitative endotracheal aspirate or quantitative invasive cultures), MRSA nares screen, PCT-Pneumonia, influenza screening (during flu season)

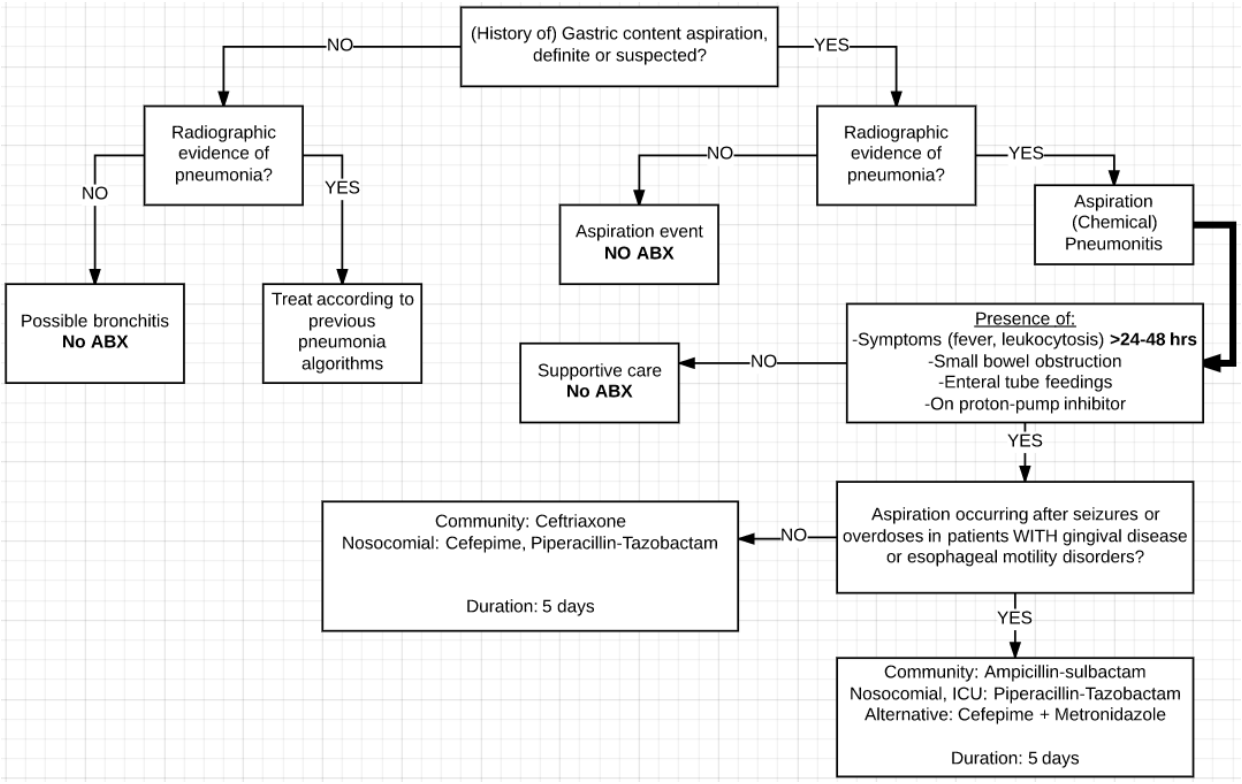
Empiric Therapy & Culture-directed therapy:



Aspiration Events: Aspiration Pneumonitis and Aspiration Pneumonia

Common Pathogens: oral pharyngeal aerobes and anaerobes, common pneumonia organisms

- risk of anaerobic infection in aspiration pneumonia is overstated and routine coverage of anaerobic pathogens is not supported by literature



What's the approach for suspected aspiration? Many aspiration events are aseptic and do not require antibiotic treatment, even in the setting of fever/leukocytosis, which may self-resolve. For aspiration pneumonia, **ceftriaxone and other cephalosporins cover oral anaerobes and should be sufficient for many patients.** Anaerobic coverage (e.g. against *B. fragilis*) should only be considered in patients with classic aspiration pleuropulmonary syndromes – after seizures or overdoses in patients WITH concomitant gingival disease or esophageal motility disorders AND with radiographic evidence of new infiltrates. Anaerobic coverage should also be considered in patients with lung abscesses, necrotizing pneumonia, and/or empyema. Aspiration pneumonitis SHOULD NOT be treated with antimicrobial agents.

- ➔ Antibiotics with good anaerobic activity (e.g. against *B. fragilis*, etc): ampicillin-sulbactam, amoxicillin-clavulanate, piperacillin-tazobactam, cefotetan, cefoxitin, clindamycin, metronidazole, ertapenem, meropenem, imipenem-cilastatin, tigecycline

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