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

<table>
<thead>
<tr>
<th>Antibiotics, in order of preference</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doxycycline 100 mg PO/IV BID x 5 days</td>
<td>Has MRSA and atypical activity, some anti-inflammatory effects, may be protective against C. difficile</td>
</tr>
<tr>
<td>Azithromycin 500 mg PO/IV Q24 x 5 days</td>
<td>Has atypical activity</td>
</tr>
<tr>
<td>Levofloxacin* 750 mg PO/IV Q24 x 3-5 days</td>
<td>Increased risk of C. difficile and MRSA</td>
</tr>
</tbody>
</table>

*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°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

<table>
<thead>
<tr>
<th>Community Acquired Pneumonia (CAP)</th>
<th>Healthcare-associated Pneumonia (HCAP)</th>
<th>Hospital Acquired Pneumonia (HAP)</th>
<th>Ventilator-associated Pneumonia (VAP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Occurring in community patients with no recent extensive exposure to healthcare systems</td>
<td>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</td>
<td>Occurring in patients in the hospital ≥48 hrs</td>
<td>Occurring in patients on invasive mechanical ventilation ≥48 hrs</td>
</tr>
</tbody>
</table>

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.
Community-Acquired Pneumonia (CAP)

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

**OUTPATIENT**

- **ABX use within 3mos, >65yo, chronic disease, immunosuppressed, asplenia?**
  - **NO**
  - 1) Doxycycline 100 PO BID
  - 2) Azithromycin 500 mg PO daily or Z-Pak®
  - Treat for 5 days
  - **YES**
  - 1) Doxycycline 100 mg PO BID +/- Cefuroxime 500 mg PO BID
  - 2) Levofloxacin 750 mg PO daily
  - Treat for 5 days

**INPATIENT**

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

- **Empirc Therapy:** ICU and non-ICU patients

  - **Presence of Pseudomonas risk factors?**
    - structural lung disease (e.g. CF, pulmonary fibrosis, bronchiectasis),
    - recurrent COPDE requiring steroids/ABX
  - **NO**
  - 1) Ceftriaxone 2 g IV Q24 + Doxycycline 100 mg IV/PO BID
  - 2) Levofloxacin 750 mg IV/PO Q24
  - **YES**
  - **Subset of HCAP patients (see HCAP algorithm)**
    - 1) Piperacillin-Tazobactam 3.375 g IV Q8 (over 4 hours) + Doxycycline 100 mg IV/PO BID
    - 2) Levofloxacin 750 mg IV/PO Q24
    - Consider adding tobramycin x 24 hours to the above regimen, especially for ICU patients, and re-evaluate respiratory culture gram stain and/or blood culture for “presumptive Pseudomonas”

  - **Post-influenza with severe or necrotizing pneumonia?**
    - If so, start empiric vancomycin IV for MRSA pneumonia and consider ID consultation
  - **De-escalate based on cultures and/or urinary tests, if positive. Narrow therapy if no Pseudomonas isolated.**

  - **Clinically stable at 48-72 hours?**
    - Afebrile x 48 hours and vitals at baseline, eating
    - **NO**
      - Continue therapy x 7-14 days and/or consider alternative diagnoses
    - **YES**
      - Change to PO antibiotics. Treat for 5 days.
      - Treat for 7 days if immunocompromised and/or structural lung disease

**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

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Recommendation (listed in order of preference)</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. pneumoniae, PCN susceptible or urinary antigen positive (93.5% at SHC susceptible to PCN)</td>
<td>Penicillin G 2 million units IV Q4 Amoxicillin 500 mg PO TID Levofloxacin 750 mg IV/PO Q24 (if intolerable to others)</td>
</tr>
<tr>
<td>S. pneumoniae, PCN-resistant, cephalosporin-susceptible (97% at SHC susceptible to CTX)</td>
<td>Ceftriaxone 2 g IV Q24 Cefdinir 300 mg PO BID Levofloxacin 750 mg IV/PO Q24 (if intolerable to others)</td>
</tr>
<tr>
<td>H. influenzae, non-beta-lactamase producing</td>
<td>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)</td>
</tr>
<tr>
<td>H. influenzae, beta-lactamase producing</td>
<td>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)</td>
</tr>
<tr>
<td>Legionella pneumophilia</td>
<td>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</td>
</tr>
<tr>
<td>S. aureus (MSSA)</td>
<td>Cefazolin 2 g IV Q8 Nafcillin 2g IV Q4 Cephalexin 500 mg PO QID</td>
</tr>
<tr>
<td>S. aureus (MRSA)</td>
<td>Vancomycin per pharmacy Doxycycline 100 mg IV/PO Q12 Linezolid* 600 mg IV/PO Q12 (if resistant/intolerable to others)</td>
</tr>
<tr>
<td>CAP, cultures negative or not available</td>
<td>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)</td>
</tr>
</tbody>
</table>

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 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.
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:**

- **HAP** Occurs <48 hrs after admission
  - Presence of:
    - Septic shock requiring ventilatory support
    - Structural lung disease (e.g. CF, bronchiectasis, etc)
    - IV Abx within past 90 days
  - 1) Piperacillin-Tazobactam + Vancomycin
  - 2) Ceftazidime + Vancomycin

- **VAP** Occurs >48 hrs after intubation
  - Presence of:
    - Septic shock -preceding ARDS
    - Structural lung disease (e.g. CF, bronchiectasis, etc)
    - LOS ≥5 days
    - IV Abx within past 90 days
    - Acute renal replacement therapy
  - 1) Piperacillin-Tazobactam + Vancomycin
  - 2) Ceftazidime + Vancomycin

1. Add tobramycin x 24 hours to the above regimens and re-evaluate respiratory culture gram stain and/or blood culture for "presumptive Pseudomonas" if MRSA nares screen is negative, discontinue vancomycin unless strong suspicion for MRSA (e.g. necrotizing pneumonia, respiratory culture predominantly GPCs, etc)

2. 48-72hr REASSESSMENT

- If MRSA nares screen is negative, discontinue vancomycin unless strong suspicion for MRSA (e.g. necrotizing pneumonia, respiratory culture predominantly GPCs, etc)
- If MRSA nares screen is positive, continue tobramycin until sensitivities available
- If Pseudomonas detected, continue tobramycin until sensitivities available

- Consider discontinuation of ABX unless strong clinical suspicion of PNA
  - If continued ABX is needed, de-escalate to one gram-negative agent and discontinue vancomycin
  - Step-down to PO levofloxacin or PO cefdinir when patient clinically stable (abstinence x 48 hours, vital at baseline)

- If patient is not clinically progressing, consider alternative diagnosis and/or ID Consultation

- De-escalate based on culture & susceptibilities,
  - Select the narrowest spectrum ABX
  - PO ABX if oral option available, patient clinically stable (abstinence x 48 hours, vital at baseline) and eating
  - Avoid aminoglycoside or colistin monotherapy if possible
  - (For select multi-drug resistant organisms, see table on next page) If necessary, consider ID Consultation

- Treat for 7 days (including for MRSA or PsA pneumonia)
  - Treat for 5 days for aspiration pneumonia.
  - (Shorter durations reduce antibiotic exposure and recurrent PNA due to resistant organisms without affecting clinical cure and mortality rates.)

- Consider longer courses (e.g. 10-14+ days) for patients with poor early clinical response and complications (e.g. empyema, necrotizing PNA, lung abscesses, strongly immunocompromised, etc)

- For MRSA bacteremia due to MRSA pneumonia, treat for minimum of 14 days from first negative blood culture.
Culture-directed therapy for select organisms: Select narrowest spectrum agent based on susceptibilities

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

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

*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:**

- **Presence of:**
  - septic shock requiring ventilatory support
  - structural lung disease (e.g., CF, bronchiectasis)
  - IV ABX within past 90 days
  - poor baseline functional status

  **See CAP algorithm for patients with PsA risk factors**

- **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

  **Radiographic evidence of pneumonia?**

  **(History of) Gastric content aspiration, definite or suspected?**

  **Aspiration event NO ABX**

  **Supportive care NO ABX**

  **Community: Ceftriaxone Nosocomial: Cefepime, Piperacillin-Tazobactam**

  **Duration: 5 days**

  **Aspiration occurring after seizures or overdoses in patients with gingival disease or esophageal motility disorders?**

  **Community: Amoxicillin-sulbactam**

  **Nosocomial, ICU: Piperacillin-Tazobactam**

  **Alternative: Cefepime + Metronidazole**

  **Duration: 5 days**
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

References:
2. Barlett JG. How important are anaerobic bacteria in aspiration pneumonia: when should they be treated and what is optimal therapy. Infect Dis Clin North Am, 2013;27(1):149-55