Sepsis: Empiric Antibiotic Selection Pathway

Early initiation of appropriate therapy is associated with improved outcomes in severe sepsis and septic shock and these guidelines are intended for use in patients with these syndromes only. All patients with suspected sepsis should have appropriate cultures obtained, although antimicrobial therapy should not be unduly delayed for this. Delays in initiating active therapy have been associated with worsened clinical outcomes and so antimicrobials should be initiated as rapidly as possible. The addition of a second antimicrobial agent can expand the empiric coverage for resistant Gram-negative pathogens. This combination therapy has been advocated by international consensus guidelines (Surviving Sepsis Campaign) in critically ill patients in severe sepsis or septic shock given delays to active therapy in this population has been associated with an increased mortality. Despite the clear mortality benefit of initially active therapy in critically ill patients, combination therapy remains controversial. The addition of a second agent has not been definitively associated with improved outcomes and depending on the severity of illness and patient population may be associated with worsened outcomes. Therefore, the addition of a second agent (e.g. tobramycin added to anti-pseudomonal beta-lactam) should be based on patient severity of illness, the likelihood of isolating resistant Gram-negative pathogens, and the potential adverse effects of additional therapy. Antibiotic therapy should be narrowed to target the isolated pathogen when culture results become available. Patients who have milder forms of infection may be more appropriately treated with narrow spectrum agents and antibiotic choices in these patients should be based upon current guidelines and clinical judgment. De-escalation to a single active agent is strongly recommended when culture and susceptibility results return.

EIAD: extended interval aminoglycoside dosing panel
+- denotes that the drug is optional and use should be based on assessment of severity of infection and likelihood of resistance or isolation of the pathogen the agent targets

<table>
<thead>
<tr>
<th>Suspected Source of Infection</th>
<th>Suggested Antibiotics</th>
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<tbody>
<tr>
<td>Unknown (includes catheter related blood stream infection)</td>
<td>Vancomycin IV per pharmacy consult (initial 25mg/kg loading dose) PLUS EITHER Piperacillin/tazobactam 4.5g IV q8h, infused over 4 hours OR Cefepime 1 gm IV q6hr +/- Tobramycin 7 mg/kg IV EIAD</td>
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<tr>
<td>Severe beta-lactam allergy (anaphylaxis, hives):</td>
<td>Vancomycin IV per pharmacy consult (initial 25mg/kg loading dose) PLUS Aztreonam 2 gm IV q8h +/- Tobramycin 7 mg/kg IV EIAD</td>
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<tr>
<td>Intra-abdominal Source</td>
<td>Piperacillin/tazobactam 4.5g IV q8h, infused over 4 hours OR Cefepime 1g q6h hours PLUS Metronidazole 500 mg IV q8h +/- Gentamicin OR Tobramycin 7 mg/kg IV EIAD +/- Vancomycin per pharmacy consult (initial 25mg/kg loading dose)</td>
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‡Consider Micafungin 100mg IV qday in patients at high risk for invasive candidiasis. Major risk factors predicting candidemia at TNMC include: 1) Broad-spectrum antibiotics, 2) Central venous catheter, 3) Receipt of TPN, 4) Abdominal surgery, and 5) Steroid use. Presence of 2 or fewer of the risk factors suggests a 99.4% chance of not developing candidemia, while patients with >2 risk factors have a 4.7% risk of developing candidemia. See Institutional Guidelines for the Treatment of Invasive Candidiasis for further information.
| Urinary Tract | Severe beta-lactam allergy (anaphylaxis, hives):  
Vancomycin per pharmacy consult (initial 25mg/kg loading dose)  
PLUS  
Aztreonam 2gm IV q8h PLUS Metronidazole 500 mg IV q8h  
+-/  
Gentamicin OR Tobramycin 7 mg/kg IV EIAD |
| --- | --- |
| Patients should be assessed for risk of multi-drug resistant pathogens. | Not at risk for multi-drug resistant organisms  
Ceftriaxone 1g IV q24h (2 grams if >80kg)  
+-/  
Gentamicin 7 mg/kg EIAD |
| Suggested risk factors for resistant pathogens:  
1) Residence in long-term care facility (LTCF)  
2) Recent receipt of broad spectrum antibiotics  
3) History of MDR urinary pathogen  
4) History of recurrent UTI  
5) Nosocomial UTI | Severe beta-lactam allergy (anaphylaxis, hives):  
Aztreonam 2 gm IV q8hr  
+-/  
Gentamicin 7 mg/kg IV EIAD |
| | At risk for multi-drug resistant organisms  
Cefepime 1 gm IV q6hr OR  
Piperacillin/tazobactam 4.5g IV q8h, infused over 4 hours  
+-/  
Gentamicin 7 mg/kg IV EIAD  
+-/  
Vancomycin per pharmacy consult (initial 25mg/kg loading dose)  
Severe beta-lactam allergy (anaphylaxis, hives):  
Aztreonam 2 gm IV q8h  
PLUS  
Gentamicin 7 mg/kg IV EIAD  
PLUS  
Vancomycin per pharmacy consult (initial 25mg/kg loading dose) |
| Community Acquired Pneumonia – No Pseudomonas Risk Factors Excludes nursing home patients. | Ceftriaxone 1 gram (2 grams if > 80 kg) IV q24h  
PLUS EITHER  
Levofloxacin 750 mg IV q24h OR  
Azithromycin 500 mg IV q24h |
| See clinical pathways for pneumonia at www.nebraskamed.com/asp | Severe beta-lactam allergy (anaphylaxis, hives):  
Levofloxacin 750 mg IV q24h  
+-/  
Vancomycin IV per pharmacy consult (initial 25mg/kg loading dose)  
+-/  
Aztreonam 2 gm IV q8h |
| Community Acquired Pneumonia – Pseudomonas Risk Factors (structural lung disease, >10mg prednisone/day, malnutrition) Excludes nursing home patients. | Cefepime 1 gm IV q6hr OR  
Piperacillin/tazobactam 4.5g IV q8h, infused over 4 hours  
PLUS  
Azithromycin 500 mg IV q24h  
+-/  
Tobramycin 7 mg/kg IV EIAD |
**See clinical pathways for pneumonia at**
www.nebraskamed.com/asp

### Severe beta-lactam allergy (anaphylaxis, hives):
- Levofloxacin 750 mg IV q24h
  - **PLUS**
  - Aztreonam 2 g IV q8h
  - +/-
  - Tobramycin 7 mg/kg IV EIAD

### Nosocomial Pneumonia:
- **healthcare-associated pneumonia (HCAP),**
- **hospital-acquired pneumonia (HAP),**
- **ventilator-associated pneumonia (VAP)**

**Classification as healthcare-associated pneumonia:**
- Antimicrobial therapy in preceding 90 d
- Hospitalization for >2d in preceding 90 d
- Residence in a nursing home or extended care facility
- Home wound care
- Home infusion therapy (including antibiotics)
- Chronic dialysis within 30 d
- Immunosuppressive disease and/or therapy

See clinical pathways at
www.nebraskamed.com/asp

Add azithromycin if requiring coverage of atypical pathogens (e.g. *Legionella sp.*) Do not combine with levofloxacin.

In patients with beta-lactam allergy add levofloxacin if suspicion for *S. pneumoniae* infection and/or clindamycin if concern for aspiration pneumonia/anaerobes

Vancomycin IV per pharmacy consult (initial 25mg/kg loading dose)
(Linezolid is also an option)
  - **PLUS**
  - Piperacillin/tazobactam 4.5g IV q8h, infused over 4 hours OR
  - Cefepime 1 gm IV q6hr
  - +/-
  - Tobramycin 7 mg/kg IV EIAD
  - +/-
  - Azithromycin 500 mg IV q24h

Severe beta-lactam allergy (anaphylaxis, hives):
Vancomycin IV per pharmacy consult (initial 25mg/kg loading dose)
  - **PLUS**
  - Aztreonam 2 gm IV q8h
  - **PLUS**
  - Tobramycin 7 mg/kg IV EIAD
  - +/-
  - Levofloxacin 750mg IV q24h
  - +/-
  - Azithromycin 500 mg IV q24h
  - +/-
  - Clindamycin 600 mg IV q8h

### Skin/Soft Tissue:

**Vancomycin IV - Preferred (initial loading dose of 25mg/kg)**
  - **OR**
  - Daptomycin 6 mg/kg IV
  - **OR**
  - Oxacillin 2g IV Q4H if MRSA not suspected or ruled out

### Necrotizing Skin/Soft Tissue:
- **Gas Gangrene or Necrotizing Fasciitis**
  - (Add Clindamycin if Streptococci suspected or evidence of toxic shock syndrome present)

Vancomycin (preferred) or Daptomycin as above
  - **PLUS**
  - Piperacillin/tazobactam 4.5g IV q8h, infused over 4 hours
  - +/-
  - Clindamycin 900mg IV Q8H