2018

Guidance for the Empiric Selection of Antimicrobial Therapy for Inpatient Infections in Adults

2018 REVIEW AND UPDATES; IHS ANTIBIOTIC STEWARDSHIP WORKGROUP

Contents:

Guidance for Empiric Treatment of Inpatient Infections

General Clinical Considerations - Pneumonia[1]

- Local antibiograms should be developed and utilized by clinicians to better understand local HAP/VAP organisms and susceptibilities
- Clinical criteria should be used to determine empiric therapy
- Narrow-spectrum agents and monotherapy are preferred in the absence of clear risk factors
- PK/PD dosing is recommended over standard, manufacturer recommended dosing
- De-escalation to the narrowest antimicrobial as soon as microbiology and susceptibility data are available, even if there is clinical improvement on initial regimen; Lab should perform purulence grading on sputum specimens submitted for culture and rejected if minimum requirements not met
- Consider aspiration pneumonitis vs. true aspiration pneumonia. Anaerobic coverage is only indicated in classic aspiration pleuropulmonary syndrome with hx of LOC in the setting of etoh/drug overdose/seizure in patients with gingival disease or esophageal motility disorders
- Use of "ventilator bundle" in ventilated patients decreases risk of VAP (Elevation of HOB to 30-45 degrees, Daily SAT/SBT, oral care with chlorhexidine, Stress ulcer prophylaxis, DVT/PE prophylaxis)
- Consider procalcitonin protocol for guidance on treating lower respiratory infections when infectious etiology is unclear
- Fluoroquinolone monotherapy not recommended in regions where TB is prevalent

Options for Empiric Treatment[1]

Duration - 5 days for patients without immunosuppression or structural lung disease
7 days for moderate immunosuppression and/or structural lung disease
14 days for poor clinical response, improper initial antibiotic selection, severe Immunosuppression
Pt should be afebrile for 48 to 72 hours and clinically stable before discontinuing treatment

Suspected Infection	Common Pathogens	Therapy
Community Acquired (CAP) General Admission. If Risk Factors, treat as HAP below[2,5]	• *St. pneumo* • *H. flu* • *M. cat* • *Cl. pneumoniae* • *M. pneumoniae* • *Legionella sp.* • Anaerobes	Choose one from each section **OR** respiratory fluoroquinolone monotherapy **Section 1** [+] Ceftriaxone 1g IV Daily **OR** Ampicillin/Sulbactam 3g IV q6h **Section 2** Azithromycin 500mg IV/PO Daily **OR**

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	(see comment above)	Doxy/Minocycline 100mg IV/PO q12h **Monotherapy** Levofloxacin 750mg IV/PO Daily **OR** Moxifloxacin 400mg IV/PO Daily
Hospital Acquired Pneumonia (HAP) NOT at high risk of mortality and NO risk factors for MRSA[5]	• Gram (-) rods • +/- Anaerobes • Routine CAP organisms, atypicial organisms unlikely	Cefepime 2gm IV q8h (1st line) **OR** Cefepime 1gm IV q8h E.I. **OR** Piperacillin/tazobactam 4.5g IV q8h (2nd line) **OR** Piperacillin/tazobactam 3.375gm IV E.I. **OR** Levofloxacin 750mg IV daily (3rd line)
HAP – high risk of mortality and/or pseudomonal[2]/MDR[3] /MRSA[5] Risk Factors	• Pseudomonas • Other resistant Gram (-) rods • MRSA	Choose one from each section +/- MRSA coverage **Section 1** Cefepime 2gm IV q8h **OR** Cefepime 1gm IV q8h E.I. **OR** Ceftazidime 2g IV q8h **OR** Carbapenem **OR** Beta Lactam Allergic - Aztreonam 2g IV q8hr + Vancomycin **Section 2** Ciprofloxacin 400mg IV q8h x 7 days **OR** Levofloxacin 750mg IV Daily x 7days **OR** Tobramycin/Gentamicin 7mg/kg IV Daily EIAD[6] x 7 days

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		If MRSA Vancomycin[7] loading dose 1-2 g IV then maintenance to a target trough 15-20 mcg/mL **OR** Linezolid 600mg IV/PO q12h
Ventilator Associated Pneumonia (VAP)[3,4,5]	• Enterobacter sp. • Pseudomonas sp. • MRSA • Other Gram (-)	Choose one from each section **Section 1: Gram-Positive Antibiotics With MRSA Activity** Vancomycin[7] loading dose 1-2 g IV then maintenance to a target trough 15-20 mcg/mL **OR** Linezolid 600mg IV/PO q12h **Section 2: Gram-Negative Antibiotics With Antipseudomonal Activity: β-Lactam–Based Agents** Cefepime 2gm IV q8h **OR** Cefepime 1gm IV q8h E.I. **OR** Ceftazidime 2g IV q8h **OR** Piperacillin/tazobactam 4.5g IV q6h **OR** Piperacillin/tazobactam 3.375gm IV E.I. **OR** Carbapenem **OR** Aztreonam 2 g IV q8h **Section 3: Gram-Negative Antibiotics With Antipseudomonal Activity: Non β-Lactam–Based Agents** Ciprofloxacin 400mg IV q8h **OR** Levofloxacin 750mg IV Daily **OR** Tobramycin/Gentamicin 7mg/kg IV Daily EIAD[6] -

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References & Footnotes - Pneumonia

1. Adapted from Johns Hopkins Antibiotic Guidelines 2015-2016 http://www.hopkinsmedicine.org/amp/guidelines/antibiotic_guidelines.pdf

AND

Kalil AC, Metersky ML, Kompas M, et al. Management of adults with hospital-acquired Ventilator-associated pneumonia: 2016 clinical practice guidelines by the Infectious Diseases Society of America and the American Thoracic Society. CID. 2016. http://cid.oxfordjournals.org/

2. Pseudomonas Risk Factors in CAP – structural lung disease, COPD exacerbations with multiple courses of antibiotics and/or chronic steroid use may warrant coverage for pseudomonas
3. Risk factors for MDR HAP, MRSA VAP/HAP, or MDR Pseudomonas VAP/HAP: Prior intravenous antibiotic use within 90 days
4. Risk factors for MDR VAP: Prior intravenous antibiotic use within 90 days, Septic shock at time of VAP, ARDS preceding VAP, 5 or more days of hospitalization prior to the occurrence of VAP, acute renal replacement therapy prior to VAP onset
5. MRSA risk factors-intravenous antibiotic treatment during the prior 90 days, and treatment in a unit where the prevalence of MRSA among S. aureus isolates is not known or is >20%. Prior detection of MRSA by culture or non-culture screening may also increase the risk of MRSA. If MRSA coverage is omitted, the antibiotic regimen should include coverage for MSSA.
6. Extended Interval Aminoglycoside Dosing (EIAD) – consult the pharmacist. One of the above regimens may be considered appropriate in regions with high FQ or cefepime resistant GNRs. De-escalate based upon available culture/susceptibility data and modify duration based upon clinical response.
7. Example of wt-based vancomycin loading protocol:
   - <50 kg: Vancomycin 1gm IV x 1 (then RPh to dose)
   - 50-70 kg: Vancomycin 1.5gm IV x 1 (then RPh to dose)
   - >70 kg: Vancomycin 2gm IV x 1 (then RPh to dose)

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General Clinical Considerations – Urinary Tract[1]

Asymptomatic bacteriuria is defined as isolation of bacteria in an appropriately collected urine specimen from an individual **WITHOUT** signs or symptoms of infection.

- Incidental findings on a urine analysis or culture in an asymptomatic patient should be ignored **UNLESS** identified purposely for screening in pregnancy or urologic procedure with anticipated mucosal bleeding where antibiotics are always indicated.
- Treatment of asymptomatic bacteriuria is **NOT** appropriate for non-pregnant, premenopausal women, diabetics, elderly, nursing home residents, spinal cord injury or indwelling catheters.
- Presence of pyuria, nitrites or leukocyte esterase on urine analysis **WITHOUT** signs & symptoms of infection is not an indication for antibiotics.

Urinary Tract Infection

- Use carbapenems ONLY if history of ESBL producing organisms
- Consider local antibiogram; Patient history and risk for MDROs
- Conversion to oral therapy as soon as possible is recommended
- De-escalation to the narrowest antibiotic to cover microbiology and susceptibility data should be done as soon as data is available, even if there is clinical improvement on initial regimen
- Do not obtain urine analysis or culture from a urinary catheter that has been in place longer than 3 days. Collect urine analysis and culture from clean catch midstream, straight catheterization or **newly** placed indwelling catheter per protocol.
- *E. coli* is the most common pathogen (75-95%) of urinary tract infections.
- *Base empiric treatment on local E. coli* susceptibilities
- *Enterococcus sp.* are rarely pathogenic organisms when isolated from non-sterile sites like the urinary tract and do not warrant empiric treatment.
- If *Staphylococcus aureus* is identified in urine culture, further work-up for possible *Staphylococcus aureus* bacteremia is recommended; obtain blood cultures x 2
- A positive urine culture is defined as:
  - Clean catch specimen with $>10^5$ cfu/ml of ≥1 bacterial species
  - Catheterized specimen with $>10^3$ cfu/ml of ≥1 bacterial species
  - <20 squamous cells /hpf for any specimen
- Start empiric antibiotics after urine culture obtained
- Antibiotic selection and dosing is based on adults with normal renal/hepatic function and may need to be adjusted for renal/hepatic impairment

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Options for Empiric Treatment

Suspected infection	Common Organisms	Therapy
Pyelonephritis	• *E. coli* • *Kl. pneumoniae* • Other enterics • Enterococcus sp. (See note above)	Ceftriaxone 1 gm IV q 24 hours **OR** Ciprofloxacin 400 mg IV q 12 hours

Treatment Notes

- Duration typically 14 days for beta-lactam based therapies; 5 days if using levofloxacin 750mg daily or 7 days for ciprofloxacin (avoid FQ in pregnancy). Cephalosporins not active vs. enterococcus sp, consider if no improvement on initial regimen or enterococcus isolated in blood culture.
- Consider cefepime or piperacillin/tazobactam for hx of pseudomonas/other resistant GNR

Complicated Cystitis/Catheter-Associated Cystitis	• E. coli • Other Enterics • Enterococcus sp. (see note above) • Staph sp. • Assess for MDRO*	Ceftriaxone 1gm IV q24h(no risk for MDRO)[2] **OR** Cefepime 1gm IV q8hr EI **OR** Cefepime 2gm IV q12h **OR** 1gm IV q8h **OR** Piperacillin/Tazobactam 3.375gm IV q8h EI[3] **OR** Piperacillin/Tazobactam 3.375gm IV q6h **OR** 4.5gm IV q8h **+/-** Aminoglycoside

Treatment Notes*

- Risk factors for MDRO: Residence long-term care facility and presence of invasive devices; long term catherization; broad-spectrum ABX exposure in previous 90 days; Hx of MDRO; Recurrent UTI; Nosocomial UTI; CONSIDER LOCAL ANTIBIOGRAM. Carbapenem is the preferred empiric treatment choice if hx of ESBL producing organism in previous 60 days.
- Duration of 3 days may be considered for young, healthy women ≤ 65 years of age with no S&Sx of upper tract infection and catheter removal.
- Duration of 7 days is reasonable with prompt resolution of symptoms
- Duration of 10-14 days if delayed response, regardless if catheterized or not
- After either defervescence or elimination of complicating factor (ex. Stent, catheter, stone), antibiotics can be stopped in 3-5 days

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References & Footnotes – Urinary Tract

1. Adapted from Johns Hopkins Antibiotic Guidelines 2015-2016 http://www.hopkinsmedicine.org/amp/guidelines/antibiotic_guidelines.pdf
2. Risk Factors for MRSA: Central venous catheter; indwelling hardware; known colonization/history; recent (within 3mo) or current prolonged hospitalization > 2wks; transfer from nursing home or subacute facility; Injection drug use.
3. High Dose Extended Interval recommended; consult pharmacy for dosing

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General Clinical Considerations – Skin & Skin Structure

- Incision and drainage with breakup of cavities and probing loculations is essential in the treatment o abscesses, furuncles, and carbuncles
- Gram stain and culture of pus is recommended for impetigo and treatment of purulent cellulitis and abscesses; epidermoid cysts should not be cultured
- Non-purulent cellulitis can often be adequately treated with 5 days of antibiotics
- Patients should also receive therapy for predisposing conditions such as tinea pedis, trauma, and venous eczema.
- Local antibiograms should be reviewed for empiric MRSA treatment of purulent skin and soft tissue infections.
- When there are multiple drugs of choice, consider frequency of dosing and nursing time (i.e. cefazol q8h vs. nafcillin q4h for MSSA); Pip/Tazo 3.375g IV q6h = Pip/Tazo 4.5g IV q8h
- Concurrent use of Vancomycin and Pip/tazo associated with increased risk of nephrotoxicity.

Type of Infection	Suspected Organism	Recommended Treatments
Impetigo Gram stain and culture of pus is recommended, but treatment without culture is reasonable	*Staphylococcus aureus* and *Streptococcus pyogenes* most common	**Limited lesions** Mupirocin topically BID x 5 D **Numerous lesions or outbreaks** Cephalexin 250mg PO QID x 7D *True Penicillin Allergy* Clindamycin 300mg PO QID x 7D **MRSA Suspected or confirmed** TMP/SMX 1-2 DS tabs PO BID x 7D

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Non-purulent Cellulitis[4] and Erysipelas	*Streptococcus pyogenes*, Other causes may be other β-hemolytic streptococci, and gram-negative organisms SIRS Criteria • Temperature > 38°C or < 36°C • Tachypnea > 24 breaths/min • Tachycardia > 90/min • WBC > 12,000 or < 4000 cells/μL **Moderate Infection** • 1 SIRS criteria, may treat orally • 2 SIRS criteria or treatment failure, IV recommended **Severe Infection** – 2 or more SIRS criteria, or >2 SIRS criteria with hypotension, immune compromise, or rapid disease progression	**Mild – Moderate (Oral Treatment)** *****Note – Likely would not be admitted***** Penicillin VK 250-500mg PO QID x 5D[1], **OR** Cephalexin 250mg PO QID x 5D[1], PLUS Ibuprofen 400-600mg PO TID, if no contraindications exist *True Penicillin Allergy* Clindamycin 300mg PO QID x 5D[1] **Moderate (Intravenous)** Cefazolin 1g IV q8h PLUS Ibuprofen 400-600mg PO TID, if no contraindications exist *True Penicillin Allergy* Clindamycin 600mg IV q8h **Cellulitis associated with penetrating trauma, MRSA IV drug use** Vancomycin 15mg/kg/dose IV q12h **OR** Amp/Sulbactam 3g IV q6h PLUS Ibuprofen 400-600mg PO TID, if no contraindications exist **Severe (Intravenous therapy & surgical evaluation)** *Empiric Broad-Coverage for Polymicrobial* Vancomycin LD 1-2g then maintenance 15mg/kg/dose IV q12h + Piperacillin-Tazobactam 4.5g IV q8h or Piperacillin-Tazobactam 3.375g infused over 4 hours IV q8h *Streptococcus pyogenes* or *Clostridial* species See Necrotizing Fasciitis dosing ***Vibrio vulnificus*** Doxycycline 100mg IV/PO q12h + Ceftriaxone 2g IV q24h ***Aeromonas hydrophila*** Doxycycline 100mg IV/PO q12h + Ciprofloxacin 400mg IV q12h
Purulent Cellulitis[4] (furuncle/carbuncle/abscess) Carbuncles and Abscesses: Gram stain and culture of pus is recommended, but treatment without culture is reasonable Epidermoid Cysts: Culture of pus not recommended	*Staphylococcal aureus* (MSSA or MRSA) most common Cutaneous abscesses are often polymicrobial with skin and adjacent mucous membrane flora Epidermoid cysts: often skin flora and inflammation due to rupture of cyst SIRS Criteria • Temperature > 38°C or < 36°C • Tachypnea > 24 breaths/min	**Mild** *****Note – Likely would not be admitted***** Incision and drainage, break up cavity and probe loculations **Moderate (1 SIRS Criteria)** Incision and drainage with culture and sensitivity PLUS ***Empiric Tx should cover MRSA*** TMP/SMX 1 -2 DS tabs PO BID x 5-10D[1], **OR** Doxycycline 100mg PO BID x 5-10D[1] PLUS Ibuprofen 400-600mg PO TID, if no contraindications exist ***Known MSSA*** Cephalexin 1g TID x 5-10D[1], **OR** Amoxicillin-Clavulanate 875mg PO BID x 5-10D[1] PLUS Ibuprofen 400-600mg PO TID, if no contraindications exist *True Penicillin Allergy* Clindamycin 300mg PO TID x 5-10D[1]

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	• Tachycardia > 90/min • WBC > 12,000 or < 4000 cells/μL **Moderate Infection** • 1 or 2 SIRS Criteria • Multiple abscesses • Extremes of age • Lack of response to I&D **Severe** • >2 SIRS criteria + hypotension, • Immune compromise • Severe disease progression	**Moderate (2 SIRS Criteria)** ***Empiric Tx should cover MRSA[3]*** Vancomycin Loading dose 1-2g then 15mg/kg/dose IV q12h, **OR** Linezolid 600mg IV/PO q12h PLUS Ibuprofen 400-600mg PO TID, if no contraindications exist **Severe** Incision and drainage with culture and sensitivity PLUS ***Empiric Therapy[3]*** See "Sepsis with SSSI as Source" PLUS Ibuprofen 400-600mg PO TID, if no contraindications exist ***Known MSSA*** Cefazolin 2g IV q8h PLUS Ibuprofen 400-600mg PO TID, if no contraindications exist *True Penicillin or cephalosporin Allergy* Clindamycin 600mg IV q8h
Surgical Site Infections	*Staphylococcus aureus* (MSSA and MRSA) and Gram negative bacteria *Streptococcus pyogenes* or *Clostridial* sp in the first 48 hours after surgery Antibiotics usually not needed, but may be beneficial if: • Erythema and induration > 5cm from the wound edge • Temperature >38.5°C • Heart rate > 100/min • WBC > 12,000/μL	Suture removal + incision and drainage **Operations of trunk, head, neck, and extremities** Cefazolin 2g IV q8h, **OR** Vancomycin 15mg/kg IV q12h **Operations of GI tract** Ceftriaxone 1g IV q24h + Metronidazole 500mg IV/PO q8h, **OR** Piperacillin-tazobactam 4.5g IV q 8H **OR** Piperacillin-Tazobactam 3.375g infuse over 4 hours IV q 8H **Operations of Axilla, Perineum, Female genital tract** Metronidazole 500mg IV/PO q8h + Ceftriaxone 1g IV q24h, **OR** Metronidazole 500mg IV/PO q8h + Ciprofloxacin 400mg IV q12h
Necrotizing Fasciitis	Polymicrobial (mixed anaerobe and aerobe) Group A *Streptococcus* CA- MRSA	Prompt Surgical consultation, if suspected **Polymicrobial** Vancomycin Loading dose 1-2g then 15mg/kg IV q12h + + Ceftriaxone 1-2 g IV q24h + Clindamycin 600mg IV q 8H **OR** Linezolid 600mg IV/PO q12h (sub for Vancomycin) + Piperacillin/tazobactam 4.5g IV q8h **OR** 3.375g EI q8h **Group A Streptococcus** Penicillin G 4 million Units IV q4h + Clindamycin 600mg IV q8h Duration of treatment is based upon clinical improvement. Usually, clindamycin is administered for a minimum of 72 hours or until patient is hemodynamically stable for 24 hours. Penicillin is continued for a total of 10-14 days or longer based upon extent of surgical debridement.

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		Staphylococcus aureus Vancomycin Loading dose 1-2g then 15mg/kg IV q12h, **OR** Linezolid 600mg IV/PO q12h
Clostridial myonecrosis (gas gangrene)	*C. perfringens, rarely C. septicum*	Immediate surgical debridement Aqueous PCN G 4 MU IV q4h PLUS Clindamycin 600mg IV q8H
Diabetic Foot Infections		Piperacillin-tazobactam 4.5g IV q8h, **OR** Ampicillin-sulbactam 3g IV q6h **PLUS** Vancomycin 15mg/kg q12h
Animal Bites		**Human/Dog/Cat Bites – Oral therapy** Amoxicillin-clavulanate 875mg PO BID, **OR** Doxycycline 100mg PO BID **Human/Dog/Cat Bites – Intravenous therapy** Ampicillin-sulbactam 3g IV q6h, **OR** Doxycycline 100mg IV q12h

References & Footnotes – Skin & Skin Structure

[1] 5 days is often adequate, even if inflammation still persists. Immunocompromised patient may require 7 – 14 days. Treatment may be extended if there is no improvement.

[2] Clindamycin may be used if resistance less than 10% in your institution

[3] Other empiric therapy options are daptomycin and linezolid

[4] "Patients should also receive therapy for predisposing conditions such as tinea pedis, trauma, and venous eczema." Stevens et al, Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections: 2014 Update by the Infectious Diseases Society of America, pg 16

[5] Patel N, Scheetz MH, Drusano, GL, Lodise TP. Identification of optimal renal dosage adjustments for traditional and extended-infucion piperacillin-tazobactam dosing regimens in hospitalized patients. Antimicrob. Agents Chemother. 2010;54: 460-465.

Lodise TP, Lomaestro BM, Drusano GL. Application of antimicrobial pharmacodynamic concepts into clinical practice: focus on B-lactam antibiotics. Pharmacotherapy. 2006;26: 1320-1332.

Kim A, Sutherland CA, Kuti JL, Nicolau DP. Optimal dosing of piperacillin-tazobactam for the treatment of pseudomonas aeruginosa infections: prolonged or continuous infusion? Pharmacotherapy. 2007;27: 1490-1497.

Kaufman SE, Donell RW, Hickey WS. Rationale and evidence for extended infusion of piperacillin-tazobactam. Am J Health Syst Pharm. 2011;68: 1521-1526.

GIMC Adult Antibiotic Guidelines, Jonathan V. Iralu, MD, FACP, NAIHS Chief Clinical Consultant for Infectious Disease, from August 3, 2016

Other recommendations from:
Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections: 2014 Update by the Infectious Diseases Society of America, Stevens et al, Clinical Infectious Diseases Advance Access published June 18, 2014
And
Cellulits, A Review, Raff and Kroshinsky; JAMA, July 19, 2016, Volume 316, Number 3, pages 325-335

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Sepsis-General Clinical Considerations[1]

- Prior to initiating antibiotics, collect blood cultures x 2 and cultures from other possible sources of infection (1C)
- Obtain a lactic acid level at baseline and q6hr and maintain hemodynamic stability with 30ml/kg total fluid resuscitation and vasopressors as needed.
- Initiate broad-spectrum antibiotic therapy within 1 hour of identification of sepsis. Mortality increases if there are gaps in empiric coverage (1B) and even modest delays in therapy (1B)
- Initial choice of therapy should consider patients history, gram-stain data, local antibiogram, and formulary
- De-escalation to the narrowest spectrum antibiotic regimen should be done as soon as culture and sensitivity data is available even when clinical improvement on initial regimen (1B)
- Consider procalcitonin for sepsis without a source.
- See table for common dosing
- Concurrent use of Vancomycin and Pip/tazo associated with increased risk of nephrotoxicity

Options for Empiric Treatment

Suspected Source	Common Pathogens	Therapy
No Clear Source	• Gram (+) • Gram (-) • Anaerobes	Piperacillin/Tazobactam[3,4] **OR** Cefepime **PLUS** Vancomycin **+/-** Aminoglycoside*

*Treatment Notes:

- Use meropenem if history of ESBL or recent extended use of pip/tazo or cefepime.
- Add Aminoglycoside if local antibiogram requires empiric gram(-) double coverage
- Vancomycin should be discontinued if no resistant gram (+) organisms found in cultures

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Intra-Abdominal	• Gram (-) rods • Anaerobes • Enterococcus sp.	Piperacillin/Tazobactam[3,4] **OR** Cefepime **AND** Metronidazole Consider adding Vancomycin for recent GI surgery
Urinary Tract	• Screen for MDRO* • E. coli • Other Enterics • Enterococcus sp.	Ceftriaxone - if no risk for MDRO **If MDRO risks are present:** Cefepime **OR** Piperacilliin/Tazobactam[3,4] **+/-** Aminoglycoside*

Treatment Notes*

Risk factors for MDRO: Infection related to indwelling or supra-pubic catheter, residence long-term care facility; broad-spectrum antibiotics within past 90 days; Hx of MDRO; Recurrent UTI; Nosocomial UTI; CONSIDER LOCAL ANTIBIOGRAM
Add Aminoglycoside if local antibiogram requires empiric gram(-) double coverage

Skin/Soft Tissue*	• Staph sp. • Group A Strep	Vancomycin **+** Ampicillin/sulbactam

Treatment Notes*

- SSTI alone will seldom result in sepsis
- Consider monotherapy withVancomycin for purulent infections or Cefazolin for non-purulent infections if not in septic shock
- Vancomycin + Ampicillin/Sulbactam for SSTI associated with IVDU to address oral flora from needle licking

Necrotizing Fasciitis/Gas Gangrene	• Staph *sp.* • Group A Strep • C. perfringens • Polymicrobial	Vancomycin **AND** Clindamycin **PLUS** Cefepime **OR** Piperacillin/Tazobactam[3,4]
Community Acquired Pneumonia (CAP)	• S. pneumo • H. Influenza • M. cat. • Mycoplasma pneumonia	Ceftriaxone **PLUS** Azithromycin **OR** Levofloxacin*

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	• Chlamydia pneumoniae • Legionella	

Treatment Notes*

- Use Levofloxacin for type I PCN hypersensitivity

CAP w/risk for pseudomonas*	• As above • Pseudomonas aeruginosa	Cefepime **OR** Piperacillin/Tazobactam[3,4] **PLUS** Azithromycin **+/-** Aminoglycoside*

Treatment Notes*

- History of pseudomonas, structural lung disease, chronic steroid use (>10mg prednisone/day) CONSIDER LOCAL ANTIBIOGRAM
- Add Aminoglycoside if local antibiogram requires empiric gram(-) double coverage

Nosocomial Pneumonia*	• MRSA • Resistant gram (-) rods • CAP organisms • Anaerobes (if aspiration)	Vancomycin **PLUS** Cefepime **OR** Piperacillin/Tazobactam[3,4]

Treatment Notes*

- Includes HAP and VAP ("HCAP" is no longer used)

Common Dosing in Sepsis (Before Renal Adjustment)		
Drug	**Indication**	**Dose**
Vancomycin	**Loading Dose** **MRSA bacteremia, osteomyelitis, septic joint, pneumonia, Necrotizing fasciitis.** **SSTI**	**25 - 30 mg/kg IV** **goal trough 15-20 mcg/mL** **goal trough 10-15 mcg/mL**

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Cefepime	**Sepsis** **UTI**	**2gm IV q8h or 1gm IV q8h EI (each dose over 4 hours)** **1gm IV q8h EI (each dose over 4 hours)** **2gm IV q12h**
Piperacillin/Tazobactam	**Sepsis**	**4.5gm IV q6h** **3.375gm IV q8h EI (each dose over 4 hrs)** [3,4]
Ceftriaxone	**Sepsis/UTI/CAP**	**2gm IV q24h**
Clindamycin	**Sepsis/SSTI**	**900mg IV q8h**
Levofloxacin	**Sepsis/CAP**	**750mg IV q24h**
Azithromycin	**Sepsis/CAP**	**500mg IV q24h**

References & Footnotes - Sepsis

1. Dellinger RP, Levy MM, Rhodes A, et al. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock: 2012. Crit Care Med 2013; 41:580.

   Strength of evidence: High (A) to Very Low (D)

   Strength of recommendation: Strong (1); Weak (2)

   Adapted from Johns Hopkins Antibiotic Guidelines 2015-2016
   http://www.hopkinsmedicine.org/amp/guidelines/antibiotic_guidelines.pdf

AND

   The Nebraska Medical Center: empiric antibiotic selection pathway for sepsis
   http://www.nebraskamed.com/app_files/pdf/careers/education-programs/asp/sepsis-antibiotics-2012.pdf

2. Risk Factors for MRSA: Central venous catheter; indwelling hardware; known colonization/history; recent (within 3mo) or current prolonged hospitalization > 2wks; transfer from nursing home or subacute facility; Injection drug use. CONSIDER LOCAL ANTIBIOGRAM
3. Extended Infusion over 4hrs; if very high risk of MDR gram(-) rods, consider 4.5gm q8h EI CONSIDER LOCAL ANTIBIOGRAM
4. High Dose Extended Interval recommended; consult pharmacy for dosing

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Clostridioides difficile Infection (CDI)

Treatment and Prevention Recommendations

Testing Considerations:	
Only test patients who have ≥ 3 loose stools in a 24 hour period and not on laxatives. Test of cure should not be performed.	Children <2 years old should not be tested for *C.difficile* when presenting with diarrhea due to high carriage rates and high risk of false positive results
Supporting Management Strategies:	
Discontinue proton pump inhibitors, histamine-2 blockers and antacids if no ongoing indication: gastrointestinal bleed, H. pylori infection, gastric/duodenal ulcer, erosive esophagitis, chronic NSAID use or steroids (>20 mg/day prednisone equivalent)	
Do not use antiperistalsis agents such as loperamide, atropine/diphenoxylate, bismuth subsalicylate if a definitive diagnosis of *C.difficile* exits	
Antibiotic therapy indicated for treatment of other infections should be narrowed in spectrum of activity and the shortest duration established based upon clinical response.	
If antibiotics are continued or started for other infections and duration of *C.difficile* treatment of 10-14 days of QID dosing has completed, continue enteral vancomycin BID until other antibiotics have been stopped.	
High Risk and Prophylaxis Considerations:	
Recent hospitalization or known contact in the community Immunocompromised Female gender Age > 65 yo	Prior abx in previous 90 days Risk of causing *C.difficile*: PPI>H2 Blockers>Antacids Antineoplastic use in the past 8 weeks Loss of intestinal function or Ileus/obstruction Recent procedures: Enema/NG Tube/Surgical Procedure
High Risk Antibiotics:	3rd/4th generation cephalosporins Clindamycin Beta-lactam/Beta-Lactamase Inhibitors Fluoroquinolones Carbapenems
Consider prophylaxis with a probiotic in high risk patients who are placed on high risk antibiotics and in area with increased rates of C. difficile. Continue for 7 days after cessation of antibiotic therapy (ex. Lactobacillus GG 1 capsule PO daily). ***Note: Avoid probiotics in patients with neutropenia, uncontrolled HIV infection, immunosuppressant therapy for transplants, active malignancy undergoing chemotherapy or radiation, pancreatitis with sepsis, prosthetic heart valves or have ileus/gastrointestinal obstruction*	
Consider prophylaxis with a probiotic and Vancomycin 125mg PO BID in patients who have had a *C.difficile* infection diagnosis within the last 6 months and placed on high risk antibiotics. Continue vancomycin for duration of concomitant antibiotic therapy and probiotic for an additional 7 days.	
Transmission Prevention Considerations	
Shedding Time 1-4 weeks after conclusion of CDI treatment with vancomycin the frequencies of skin and environmental shedding increased to 58% and 50%, respectively (Figure 1). These percentages were greater than they were at the end of CDI treatment (32% and 14%, respectively).	

Guidance for Empiric Treatment of Inpatient Infections

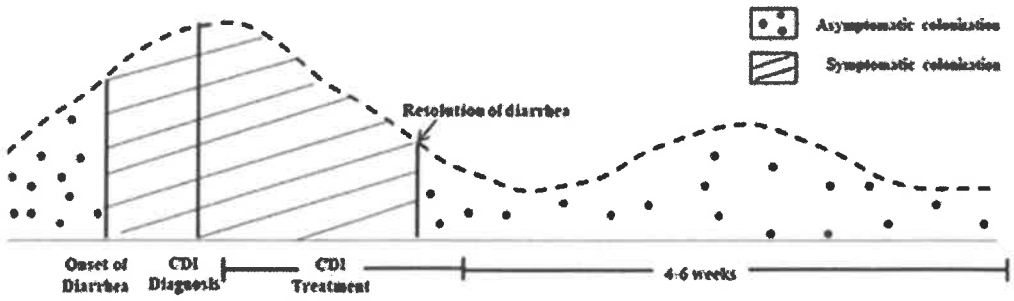

FIGURE 1. Frequency of Skin Contamination and Environmental Shedding[116]

Skin contamination and environmental surface shedding of *C. difficile* often persist at the time of resolution of diarrhea, and recurrent shedding is common 1–4 weeks after therapy.

Clostridioides difficile
Infection control contact precaution recommendations.
1. Patients with *C. difficile* infection (CDI) should stay in contact isolation for at least 48 hours after resolution of diarrhea.
2. Hospitals should consider extending contact precautions through the duration of hospitalization if elevated rates of CDI are present despite appropriate infection prevention and control measures.
3. At this time, insufficient evidence exists to make a formal recommendation as to whether patients with CDI should be placed in isolation on contact precautions if they are readmitted to the hospital.
4. Hand hygiene for patients, care givers and family members should include soap and water; alcohol based hand sanitizers are not effective.

***C. difficile* Infection Treatment Recommendations:**		
Severity of C diff	**Treatment of Choice**	**Duration**
Non-severe infection (patient presents with diarrhea ≥ 3 loose stools in 24 hrs with pain or cramping)	**Adult**: Vancomycin 125 mg PO QID* or Fidaxomicin 200mg PO BID	10 days
	Peds: Metronidazole 7.5mg /kg/dose PO TID or Vancomycin 10mg/kg/dose QID	10 days
	**Metronidazole 500mg PO TID may be considered if oral vancomycin or fidaxomicin is unavailable*	
Severe infection (fever, serum albumin <3g/dl, SCr > 1.5 x baseline, WBC ≥15,000 cells/mm3)	**Adult:** Vancomycin 125mg PO QID or Fidaxomicin 200mg PO BID	10 days
	Peds: Vancomycin 10mg/kg/dose QID	10 days
First recurrence	If metronidazole** was used as initial tx: Vancomycin or fidaxomicin standard dosing	10 days
	If vancomycin was used as initial tx: Fidaxomicin standard dosing.	10 days
	Consider vancomycin dosing strategy offered in second recurrence section below.	6 weeks
Second or greater recurrence	Vancomycin 125mg PO QID X 2 weeks then taper accordingly: 125mg PO BID X 7 days	6 weeks

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	125mg PO once daily X 7 days 125mg PO every other day X 7 days 125mg PO every 3 days X 7days Vancomycin standard dosing x 10 days followed by rifaximin 400mg PO TID x 20 days Consider gastroenterology consultation for Fecal microbiota transplantation.	30 days
	***Note: Metronidazole should not be used for recurrence or long-term due to potential for cumulative neurotoxicity.*	
Fulminant: Severe infection presentation with shock, ileus, or toxic megacolon	General Surgery Consultation required Vancomycin 500mg PO/NG QID **PLUS** Metronidazole 500mg IV TID If ileus **ADD** Vancomycin 500mg in 100mL SWNS rectally QID as retention enema	

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