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ASP Antimicrobial Stewardship Program
Making every antibiotic count

Niagara Health Antimicrobial Handbook 2022-2023

Last updated February 2024

Compassion in Action Driven by Optimism Achieving Ambitious Results

Acknowledgements
The Niagara Health Antimicrobial Handbook for Adults has been produced by the Antimicrobial Stewardship Program.

Preamble

1. The antimicrobial selections represent empiric treatment options for adults only. Treatments should be modified when culture results are available.
2. Antimicrobial choices are listed in the order of preference, where the first alternative listed is considered first-line and the rest are second or third options.
3. It is important to determine the patient's antibiotic history in the last three months. If the patient has been exposed to antibiotics within this timeframe, consider selecting an antibiotic from a different class to avoid treatment failure secondary to antibiotic resistance.

Disclaimer

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Allergic Reactions

β-lactam and more specifically penicillin allergy is the most commonly reported allergy in hospitalised patients. **However, 90-95% of these allergy labels are inaccurate.** There are several reasons for this. Many patients have intolerances such as nausea which would not usually be a reason to avoid a β-lactam. Many are mis-labelled in childhood – e.g. viral rash that was thought to be antibiotic related. Even patients with a genuine allergy, may lose this allergy over time (80% will resolve after 10 years). The label of penicillin allergy is detrimental to patients and our system. **Penicillin allergy is associated with increased risk of *C. difficile* and MRSA infection.** These patients get more expensive, more toxic antibiotics.

A penicillin allergy label should be re-evaluated when possible and removed if appropriate.

Definitions

- *Drug allergy*: adverse drug reaction that results from a specific immunologic response to a medication.
- *Anaphylaxis*: acute, life-threatening allergic reaction which may involve skin, gastrointestinal, respiratory and cardiovascular symptoms.
- *Dermatologic reaction*: most common adverse drug events (often morbiliform or maculopapular rashes).
- *Pseudoallergic reaction*: idiosyncratic adverse drug reactions with signs and symptoms that mimic immunologic drug allergies, but in which immunologic mechanisms have not been demonstrated.
- *Adverse reactions*: any undesirable, or unintended affect caused by a medication. Often described as a drug allergy, but of non-immunologic etiology. Includes pseudoallergic and "allergic type" reactions and can include itching, nausea, diarrhea, constipation, headache, and hypotension.

β-lactam Allergic Reactions

Reaction	Pathophysiology	Onset	Recommendation
Non-allergic adverse reactions • Nausea or vomiting, diarrhea, headache)	Idiopathic	Variable	May use a β-lactam antibiotic
"Allergic type" delayed mild rash • Mild-to-moderate rash without fever or involvement of internal organs or mucous membranes	Idiopathic	Variable	May use β-lactam antibiotic from a different class
"Allergic" with immediate hypersensitivity reaction • Anaphylaxis (bronchospasm, hypotension, angioedema) • Hives (urticaria), pruritus	Type I or IgE-mediated	Minutes to hours	Avoid all β-lactam antibiotics Consider Infectious Diseases consult and referral to outpatient Allergist
Cytotoxic or cytolytic reaction • Hemolytic anemia • Cytopenia • Nephritis	Type II with antibody (usually IgG) mediated cell destruction	Days to weeks High doses	Avoid all β-lactam antibiotics
Immune complex-mediated • Serum-sickness-like reaction	Type III reaction with immune complex deposition and complement activation	7-21 days after initiation of drug	Avoid all β-lactam antibiotics
Delayed hypersensitivity reaction • Drug-induced hypersensitivity syndrome • Drug reaction with eosinophilia and systemic symptoms (DRESS)	Type IV reaction mediated by T cells	Days to weeks Upon re-challenge	Avoid all β-lactam antibiotics

Reaction	Pathophysiology	Onset	Recommendation
• Rash with fever and/or with involvement of internal organs or mucous membranes • Stevens-Johnson syndrome, toxic epidermal necrolysis • Morbilliform eruptions		symptoms usually within 24 hours	Consider Infectious Diseases consult
Pseudoallergic reactions • Includes urticaria, hypotension, wheezing, flushing	Idiosyncratic	Variable, usually within hours	Depends on reaction

Note: amoxicillin or ampicillin can cause mild delayed skin rashes that are often caused by an interaction between the amino-penicillin and a viral infection (e.g. infectious mononucleosis caused by Epstein-Barr Virus or cytomegalovirus). These are not true allergic reactions and therefore it is not necessary to avoid use of other β-lactam antibiotics.

β-lactam Antibiotics

Penicillins, cephalosporins, and carbapenems are chemically related β-lactam antibiotics with varying potential for cross-reactivity. The cross reactivity of penicillin to cephalosporins is >8% and penicillin to carbapenems is >1%.

Penicillins	Cephalosporins	Carbapenems
penicillin G	ce**FAZ**olin	ertapenem
penicillin VK	cephalexin	meropenem
amoxicillin	cef**TRIAX**one	imipenem
ampicillin	cefaclor	
cloxacillin	cefepime	
piperacillin	cefixime	
ticarcillin	cefuroxime	
	cef**OX**itin	
	cef**TAZ**idime	

Consider ID/Allergist consult if patient would benefit from beta-lactam allergy assessment.

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1. Johansson SG et al. Revised nomenclature for allergy for global use: Report of the Nomenclature Review Committee of the World Allergy Organization, October 2003. *J Allergy Clin Immunol*. 2004;113:832.
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3. Weiss ME and Adkinson NF. Immediate hypersensitivity reactions to penicillin and related antibiotics. *Clin Allergy*. 1988;18:515.
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Aminoglycoside (AMG) Dosing Guidelines

DISCLAIMER: Consider consulting ID or ASP before ordering aminoglycosides.

Background

Aminoglycosides are indicated in the treatment of infections due to Gram-negative aerobic bacilli, bacterial endocarditis in combination with other agents and surgical prophylaxis in combination with other agents. Tobramycin is the NH aminoglycoside of choice as levels are done in-house allowing for rapid availability of results for appropriate monitoring and dosage adjustments.

Toxicity associated with aminoglycosides includes nephrotoxicity and ototoxicity. Nephrotoxicity may be associated with elevated trough levels and is thought to be reduced by extended interval dosing. Aminoglycoside therapy may affect cochlear and/or vestibular function. Ototoxicity is not associated with either peak or trough aminoglycoside levels.

Note: Neonatal and pediatric patients are excluded from these guidelines. Physicians are encouraged to order aminoglycosides based on published Hospital for Sick Children's guidelines.

Dosing Recommendations

Extended interval aminoglycoside dosing (EIAD) is preferred over conventional dosing in patients that meet EIAD criteria. (See algorithm for aminoglycoside dosing.) The use of EIAD produces higher serum peak concentrations which optimizes bacterial killing. Drug related toxicity may also be decreased as EIAD results in an "aminoglycoside-free" period where accumulation of the aminoglycoside in tissues such as the kidney or inner ear may be reduced. Other advantages include convenience and reduced costs for monitoring, drug administration and preparation.

Conventional aminoglycoside dosing uses reduced doses at more frequent intervals to achieve target peak and trough levels.

Aminoglycoside synergy dosing involves the use of low dose gentamicin in combination with an antimicrobial agent that has activity against the cell wall of Gram-positive bacteria (such as β-lactams or vancomycin) in the treatment of Gram-positive infections.

Initial aminoglycoside dosing is determined based on ideal body weight (IBW) and creatinine clearance (CrCl).

Estimating IBW and CrCl using Cockcroft-Gault Equation

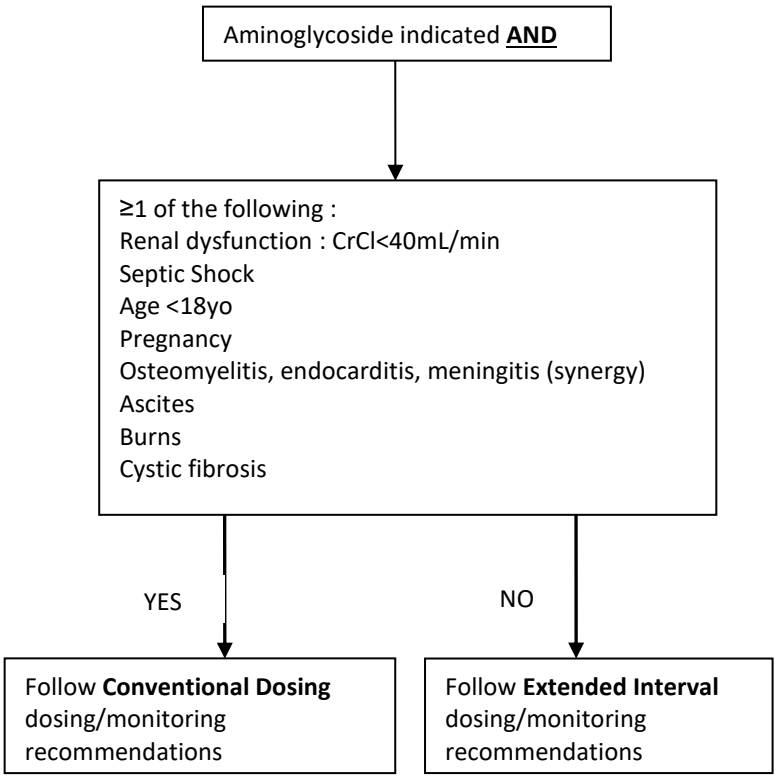
$$\boldsymbol{CrCl_{male}} = \frac{(\mathbf{140} - \boldsymbol{age}) \times \boldsymbol{weight}\ [\boldsymbol{kg}] \times \mathbf{1.2}}{\boldsymbol{serum\ creatinine}\ [\boldsymbol{\mu mol/L}]}$$

$$\boldsymbol{CrCl_{female}} = \mathbf{0.85} \times \boldsymbol{CrCl_{male}}$$

$$IBW_{male} = 50\ kg + 2.3 \times (inches\ over\ 5\ feet)$$
$$IBW_{female} = 45\ kg + 2.3 \times (inches\ over\ 5\ feet)$$

- If actual body weight (ABW) is less than IBW, use ABW
- If ABW > IBW + 30%, use adjusted body weight (AdjBW)
- AdjBW = [(actual body weight - IBW) x 0.4] + IBW

Aminoglycoside Dosing Algorithm



EIAD and Monitoring

Dosing for EIAD

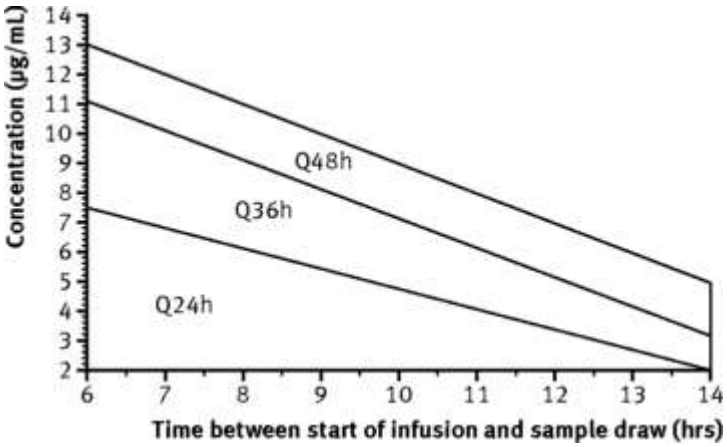
- Dosing can be determined by using CrCl to determine the dosing interval (see table 1) or the Hartford nomogram
- Use IBW to determine dose
- Use actual body weight if less than IBW
- Use adjusted body weight if actual body weight is greater than IBW + 30%
- Round dose to nearest 20mg increment for tobramycin or gentamicin and to the nearest 50mg increment for amikacin

EIAD using CrCl to Determine Interval

CrCl (mL/min)	Tobramycin and Gentamicin Dose[1,2]	Amikacin Dose[1,2]
≥60	4-7 mg/kg q24h	15m/kg q24h
40-59	4-7 mg/kg q36h	15mg/kg q36h

- EIAD dosing is based on the Hartford Nomogram
- ***Only applicable for **7 mg/kg** of tobramycin or gentamicin, or **15 mg/kg** of amikacin – plotting doses lower or higher than 7 mg/kg or 15 mg/kg respectively, may under or overestimate clearance
- **Initial level testing:** Single aminoglycoside serum level drawn 8 to 12 hours after the first dose
- The appropriateness of the EIAD frequency will be assessed by plotting the exact time and value of the 8 to 12 hour post-dose level on the nomogram below.
    - Tobramycin/gentamicin (7 mg/kg/dose): Plot level on graph
    - Amikacin (15 mg/kg/dose): Divide level in half, then plot on graph
- Adjust based on nomogram
    - **Below nomogram (< 2 mg/L**) → give dose once daily
    - **Q24H, Q36H, or Q48H region** → give dose at indicated interval

- **Above nomogram** → discontinue EIAD and switch to conventional dosing



Monitoring

- Serum creatinine should be drawn at baseline and every 3 days while on AMG.
- Monitor urine output q24h while on AMG.
- Baseline auditory testing should be done for patients with baseline auditory deficiencies and any patients expected to be on greater than 7 days of therapy.
- Serum AMG levels are NOT to be routinely drawn. Criteria for AMG levels are:
  - Expected duration of treatment > 3-5 days (i.e. documented infection). Obtain a trough level by day 7 of therapy and then weekly for duration of therapy. Troughs are drawn immediately prior to the dose.
  - Use of Hartford nomogram to assess appropriateness of EIAD frequency. Level should be drawn 8 to 12 hours after the first dose.
  - Renal function borderline (i.e. CrCl = 40-60 mL/min or in elderly patients) or fluctuating
  - Concurrent use of nephrotoxic drugs.
- If trough level is greater than 1.0 mg/L, re-assess need for AMG. Converting to conventional dosing may be required.

Target Trough levels for EIAD

Aminoglycoside	Desired Trough (mg/mL)
tobramycin	less than 0.5
gentamicin	less than 0.5
amikacin	less than 1

Conventional (Multiple Daily Dosing) Aminoglycoside Dosing and Monitoring

Dosing

- Use IBW to determine dose
- Use actual body weight if less than IBW
- Use adjusted body weight if actual body weight is greater than IBW + 30%
- Round dose to nearest 20mg increment for tobramycin or gentamicin and the nearest 50mg increment for amikacin

Recommended Dose for Conventional Dosing

CrCl (mL/min)	Tobramycin & Gentamicin in Severe Infections	Tobramycin & Gentamicin in Mild-to-Moderate Infections	Gentamicin for Synergy in Gram-Positive Infections	Amikacin
> 70	2 mg/kg Q8H	1.5 mg/kg Q8H	1 mg/kg Q8H	7.5 mg/kg Q12H
40 - 69	2 mg/kg Q12H	1.5 mg/kg Q12H	1 mg/kg Q12H	7.5 mg/kg Q12H
20 - 39	2 mg/kg Q24H	1.5 mg/kg Q24H	1 mg/kg Q24H	7.5 mg/kg Q24H

CrCl (mL/min)	Tobramycin & Gentamicin in Severe Infections	Tobramycin & Gentamicin in Mild-to-Moderate Infections	Gentamicin for Synergy in Gram-Positive Infections	Amikacin
< 20	2 mg/kg, then draw level in 24h to determine interval	1.5 mg/kg, then draw level in 24h to determine interval	1 mg/kg, then draw level in 24h to determine interval	7.5 mg/kg Q24H**,** then draw level in 24 h to determine interval
Hemodialysis	2 mg/kg Q48-72H, re-dose when pre-HD level less than 3-5mg/L	1.5 mg/kg Q48-72H, re-dose when pre-HD level less than 2-3 mg/L	1 mg/kg Q48-72H, re-dose when pre-HD level less than 1mg/L	7.5 mg/kg Q24-72H, re-dose when pre HD level less than 10mg/L
CRRT	2 mg/kg Q24-48H	1.5 mg/kg Q24-48H	1 mg/kg Q24-48H	10 mg/kg, then 7.5 mg/kg Q24-48H

Monitoring

- Serum creatinine should be drawn at baseline and every 3 days while on AMG.
- Serum AMG levels may be drawn as pre and post after the third or fourth regular dose, as long as a steady state is reached.
- Troughs are drawn immediately prior to the dose and peaks are drawn 30 minutes after completion of the infusion.
- Obtain a set of peak and trough levels every 7 days during therapy or if renal function changed.

Guidelines for desired serum concentrations in conventional dosing

Infection	Tobramycin and Gentamicin		Amikacin	
	Trough (mg/L)	Peak (mg/L)	Trough (mg/L)	Peak (mg/L)
Urinary tract infections	less than 2	4 - 6	Less than 5	15 - 20
Serious infections (bacteremia, pneumonia, sepsis, cellulitis, wound)	less than 2	6 – 10	less than 10	20 - 25
Life-threatening infections (e.g. *P. aeruginosa* pneumonia)	less than 2	8-10	less than 10	25 - 30
Synergy in gram positive infections	less than 1	3 - 5	NA	NA

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3. Nicolau D et al. Experience with a once-daily aminoglycoside program administered to 2 184 adult patients. *Antimicrob Agents Chemother*. 1995;39(3):650-55.
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6. Lexicomp. Gentamicin (systemic), Tobramycin (systemic), Amikacin: Drug Information. (accessed via UpToDate Sep 2022).
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8. Stanford Health Care Aminoglycoside Dosing Guide (accessed Jan 2023).

Antibiotic Dosing Guidelines for Adults with Renal Dysfunction

Note: The dosing recommendations are not intended for treatment of endocarditis or central nervous system infections.

Drug	CrCL >50	CrCL 30-49	CrCL 10-29	CrCL <10
acyclovir (IV)*	5-10 mg/kg IV q8h	5-10 mg/kg IV q12h	5-10 mg/kg IV q24h	2.5-5 mg/kg IV q24h
acyclovir (PO) (genital herpes)	400 mg PO q8h	NO CHANGE NEEDED		200 mg PO q12h
acyclovir (PO) (varicella zoster)	800 mg PO 5 times per day	NO CHANGE NEEDED	800 mg PO q8h	800 mg PO q12h
aminoglycosides	Refer to aminoglycoside dosing guidelines for conventional & extended interval dosage regimens			
amoxicillin	500-1000 mg PO q8h	NO CHANGE NEEDED	500-1000 mg PO q12h	500-1000 mg PO daily
amoxicillin/clavulanic acid	875/125 mg PO q12h	NO CHANGE NEEDED	Not recommended	
	500/125 mg PO q8h	NO CHANGE NEEDED	500/125 mg PO q12h	500/125 mg PO daily
amphotericin B (non-lipid formulation)	0.25-1.5 mg/kg IV q24h	NO CHANGE NEEDED		Not recommended†
amphotericin B (liposomal)	3-6 mg/kg IV q24h	NO CHANGE NEEDED		3-6 mg/kg IV q24-36h
ampicillin (dose dependent on indication)	1-2 g IV q4-6h	1-2 g IV q6-8h	1-2 g IV q8-12h	1-2 g IV q12-24h
azithromycin	250-500 mg IV/PO q24h	NO CHANGE NEEDED		
caspofungin	70 mg IV on Day 1, then 50 mg IV q24h	NO CHANGE NEEDED		
cefazolin (dose dependent on indication)	1-2 g IV q8h	**>35 mL/min:** NO CHANGE NEEDED	**10-34 mL/min:** 1-2 g IV q12h	1-2 g IV q24h
cefotaxime	1-2 g IV q8h	1-2 g IV q8-12h	1-2 g IV q8-12h	1-2 g IV q24h
cef**OX**itin	1-2 g IV q6-8h	1-2 g IV q8-12h	1-2 g IV q12-24h	1-2 g IV q24h
cef**TAZ**idime	1-2 g IV q8h	1-2 g IV q12h	1-2 g IV q24h	1-2 g IV q24-48h
cef**TRIAX**one	1-2 g IV q24h	NO CHANGE NEEDED		
cefuroxime axetil (PO)	500 mg PO q12h	NO CHANGE NEEDED		500 mg PO q24h
cephalexin	500-1000 mg PO q6h	500-1000 mg PO q8h	500-1000 mg PO q12h	500-1000 mg PO q12-24h
ciprofloxacin (IV)	400 mg IV q12h	NO CHANGE NEEDED	400 mg IV q24h	
ciprofloxacin (PO)	500-750 mg PO q12h	NO CHANGE NEEDED	500-750 mg PO daily	
clarithromycin	250-500 mg PO q12h	250-500 mg PO q12h	250-500 mg PO daily	
clindamycin (IV)	600-900 mg IV q8h	NO CHANGE NEEDED		
clindamycin (PO)	300-450 mg PO q6h	NO CHANGE NEEDED		
cloxacillin (IV)	1-2 g IV q4-6h	NO CHANGE NEEDED		
cloxacillin (PO)	500-1000 mg PO q6h	NO CHANGE NEEDED		
co-trimoxazole (IV) (trimethoprim [TMP]/ sulfamethoxazole [SMX]) (not for PCP treatment)	8-10 mg of TMP component/kg/day IV in 2-4 divided doses	50% of daily dose IV in 2-4 divided doses	50% of daily dose IV in 2-4 divided doses	Not recommended†

Drug	CrCL >50	CrCL 30-49	CrCL 10-29	CrCL <10
Double strength (DS) = (Trimethoprim [TMP] 160 mg/ Sulfamethoxazole [SMX] 800 mg) **Single strength (SS)** = TMP 80 mg/ SMX 400 mg)				
co-trimoxazole (PO) (not for PCP treatment)	1 DS (160/800 mg) PO q12h	NO CHANGE NEEDED	50% of dose (1 SS) PO q12h	Not recommended[†]
co-trimoxazole for *Pneumocystis jirovecii* (*carinii*) treatment	15-20 mg TMP/kg/day PO/IV divided q6-8h	NO CHANGE NEEDED	50% of daily dose IV/PO in 2-4 divided doses	5-10 mg TMP/kg IV/PO in 1-2 divided doses
DAPTOmycin	4-10 mg/kg IV q24h	NO CHANGE NEEDED	4-10 mg/kg IV q48h	
doxycycline	100 mg PO q12-24h	NO CHANGE NEEDED		
ertapenem	1 g IV q24h	NO CHANGE NEEDED	500 mg IV q24h	
ethambutol	15-25 mg/kg PO q24h (max 2g/day)	NO CHANGE NEEDED	15-25 mg/kg PO three times per week	
fluconazole	200-800 mg IV/PO q24h	50% of dose IV/PO q24h		25% of dose IV/PO q24h
flucytosine	25 mg/kg PO q6h	25 mg/kg PO q12-24h		25 mg/kg PO q24-48h
isoniazid	5 mg/kg PO q24h (max 300 mg)	NO CHANGE NEEDED		
itraconazole	100-200 mg PO q12-24h	NO CHANGE NEEDED		
levo**FLOX**acin[‡]	750 mg IV/PO q24h	**20-49 mL/min:** 750 mg IV/PO q48h	**<20 mL/min:** 750 mg IV/PO initially, then 500 mg IV/PO q48h	
	500 mg IV/PO q24h	**20-49 mL/min:** 500 mg IV/PO initially, then 250 mg IV/PO q24h	**<20 mL/min:** 500 mg IV/PO initially, then 250 mg IV/PO q48h	
linezolid	600 mg IV/PO q12h	NO CHANGE NEEDED		
meropenem	1-2 g IV q8h	1-2 g IV q12h	500 mg IV q12h	500 mg IV q24h
	500 mg IV q6h	500 mg IV q8h		
metronidazole	500 mg IV/PO q12h *C. difficile*: 500 mg IV/PO q8h	NO CHANGE NEEDED		
moxifloxacin[‡]	400 mg IV/PO q24h	NO CHANGE NEEDED		
nitrofurantoin macrocrystals (Macrobid®)	100 mg PO q12h	<50 mL/min: avoid		
nitrofurantoin	50 - 100 mg PO q6h (for feeding tube administration)	<50 mL/min: avoid		
oseltamivir (treatment dose)	**>60 mL/min:** 75 mg PO q12h x 5 days	**30-60 mL/min:** 75mg PO q24h x5 days 30mg PO q12h x 5 days	**10-30 mL/min:** 30 mg PO q24h x 5 days	Use with caution: Single 75mg PO once only
oseltamivir (prophylaxis dose)	**>60 mL/min:** 75 mg PO q24h until outbreak is over	**30-60 mL/min:** 30mg PO q24h until outbreak is over	**10-30 mL/min:** 30 mg PO q48h until outbreak is over	Use with caution: single 30mg PO once only

Drug	CrCL >50	CrCL 30-49	CrCL 10-29	CrCL <10
penicillin G (IV)	2-4 Million Units (MU) IV q4-6h	2-4 MU IV q6-8h		2-4 MU IV q8-12h
penicillin V (PO)	250-500 mg PO q6h	NO CHANGE NEEDED		250-500 mg PO q8h
piperacillin/tazobactam	3.375 g IV q6h	**41-50 mL/min:** NO CHANGE NEEDED **20-40 mL/min:** 2.25 g q6h **<20 mL/min:** 2.25 g q8h		
piperacillin/tazobactam (for nosocomial pneumonia treatment)	4.5 g IV q6h	**41-50 mL/min:** NO CHANGE NEEDED **20-40 mL/min:** 3.375 g q6h **<20 mL/min:** 2.25 g q6h		
pyrazinamide	15-30 mg/kg PO q24h (max 2.5 g)		15-30 mg/kg three times per week (max 2.5 g)	
rif**AMP**in (tuberculosis dosing)	10 mg/kg PO q24h (max 600 mg q24h)	NO CHANGE NEEDED		5 mg/kg PO q24h
tigecycline	100 mg IV load, then 50 mg IV q12h	NO CHANGE NEEDED		
vancomycin (IV)	Refer to vancomycin dosing guidelines			
vancomycin (PO) (for *C.difficile* treatment)	125-500 mg PO q6h	NO CHANGE NEEDED		
voriconazole (IV)	6 mg/kg IV q12h x 2 doses, then 4 mg/kg IV q12h	Not recommended due to accumulation of vehicle		
voriconazole (PO)	200-300 mg PO q12h	NO CHANGE NEEDED		

* In obese patients, consider dosing acyclovir IV with knowledge of both ideal body weight and adjusted body weight, to avoid overdosing and subsequent toxicity, as well as underdosing and lower systemic exposure.
† Please consult Infectious Diseases to discuss therapeutic alternatives.
‡ Moxifloxacin is the respiratory fluoroquinolone on formulary at Niagara Health

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5. Sunnybrook Antimicrobial Handbook (accessed via Metrodis Jan 2023)

Antibiotic Dosing Guidelines for Adults Requiring Renal Replacement Therapy (CRRT and IHD)

Note: The dosing recommendations are not intended for treatment of endocarditis or central nervous system infections.

Drug	Recommended Dose for IHD	Dose After IHD?*	Loading Dose?†	Recommended Dose for CRRT
acyclovir (IV)	2.5-5 mg/kg IV q24h	Yes	None Required	5-10 mg/kg IV q12-24h
aminoglycosides	Refer to aminoglycoside dosing guidelines	Yes	Yes	Refer to aminoglycoside dosing guidelines
amoxicillin	500 mg PO q24h	Yes	None Required	500 mg PO q8-12h
amoxicillin/clavulanic acid	500/125 mg PO q24h	Yes	None Required	Limited data
ampicillin	1-2 g IV q12-24h (dose dependent on indication)	Yes	2 g	1-2 g IV q6-8h (dose dependent on indication)
azithromycin	250-500 mg IV/PO q24h (No adjustment needed)	No	None Required	250-500 mg IV/PO q24h (No adjustment needed)
caspofungin	70 mg IV x 1 dose, then 50 mg IV q24h (no adjustment needed)	No	70 mg (if load not given previously)	70 mg IV x 1 dose, then 50 mg IV q24h (no adjustment needed)
ce**FAZ**olin	1 g IV q24h ***or*** 2 g IV post hemodialysis‡	Yes	2 g	2 g IV q12h
cef**TAZ**idime	1 g IV q24h ***or*** 1-2 g IV post-hemodialysis	Yes	2 g	2 g IV q8-12h
cef**TRIAX**one	1-2 g IV q24h (No adjustment needed)	No	2 g	1-2 g IV q12-24h (No adjustment needed)
cefuroxime	500 mg PO q12h	Yes	None Required	Limited data
ciprofloxacin	400 mg IV q24h 500 mg PO q24h	Yes	None Required	400 mg IV q8-12h 500-750mg PO q12h (dose dependent on indication)
clindamycin (IV)	600-900 mg IV q8h (No adjustment needed)	No	None Required	600-900 mg IV q8h (No adjustment needed)
co-trimoxazole (PO)	Dose dependent on indication: consult Infectious Disease/pharmacy			
DAPTOmycin	4-10 mg/kg IV q48h	Yes	None Required	4-10 mg/kg IV q24h
ertapenem	500 mg IV q24h	Yes	None Required	1000 mg IV q24h
fluconazole	400-800 mg IV/PO loading dose, then 100-400 mg IV/PO q24h (dose dependent on indication)	Yes	400-800 mg (if load not given previously)	Loading dose: 800 mg IV/PO Maintenance dose: 600-800 mg/day IV/PO in 1 to 2 divided doses (dose dependent on indication)
levofloxacin§	750 mg IV/PO initial dose, then 500 mg q48h	Yes	750 mg	500-750 mg IV/PO q24h
Linezolid	600 mg IV/PO q12h (No adjustment needed)	Yes	None Required	600 mg IV/PO q12h (No adjustment needed)

Drug	Recommended Dose for IHD	Dose After IHD?*	Loading Dose?†	Recommended Dose for CRRT
meropenem	500-1000 mg IV q24h (dose dependent on indication)	Yes	1 g	1-2 g IV q8h (dose dependent on indication)
metroNIDAZOLE	500 mg IV/PO q12h *C. difficile*: 500 mg IV/PO q8h (No adjustment needed)	Yes	None Required	500 mg IV/PO q12h *C. difficile*: 500 mg IV/PO q8h (No adjustment needed)
moxifloxacin§	400 mg IV/PO q24h (No adjustment needed)	No	None Required	400 mg IV/PO q24h (No adjustment needed)
oseltamivir (treatment dose)	Limited data 30 mg PO post-IHD over the course of 5 days	Yes	None Required	Limited data 75 mg PO q24h
oseltamivir (prophylaxis dose)	Limited data 30 mg post every other-IHD until outbreak is over	Yes	None Required	Limited data
penicillin G	1-2 Million Units (MU) IV q4-6h (dose dependent on indication)	Yes	None Required	2-4 Million Units (MU) IV q4-6h (dose dependent on indication)
piperacillin/tazobactam	2.25 g IV q8h	Yes	None Required	3.375-4.5 g IV q6h
tigecycline	100 mg IV x 1 dose, then 50 mg IV q12h (No adjustment needed)	No	100 mg (if load not given previously)	100 mg IV x 1 dose, then 50 mg IV q12h (No adjustment needed)
vancomycin	Refer to vancomycin HD dosage guidelines	Yes	Yes	Refer to vancomycin HD dosage guidelines

* Dosing after IHD means space dosing so that one dose is given after hemodialysis (NOT a supplemental dose). For example, for a drug dosed q12h: on hemodialysis days, if patient is dialyzed in the morning, give dose at noon after dialysis and next dose at midnight.
† Loading dose not generally required if antimicrobial initiated prior to starting CVVHDF.
‡ Only given on hemodialysis days.
§ Moxifloxacin is the respiratory fluoroquinolone on formulary at Niagara Health.

References

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2. Aronoff GR et al. *Drug Prescribing in Renal Failure: Dosing Guidelines for Adults, Fourth Edition*. Philadelphia, PA: American College of Physicians. 2002.
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6. Sunnybrook Antimicrobial Handbook (accessed via Metrodis Jan 2023).

Antibiotic Prophylaxis in Surgery

Timing

To achieve adequate drug concentrations at the onset and throughout the operative procedure the initial dose must be given intravenously in the immediate pre-operative period (within 60 minutes for most antibiotics; 120 minutes for vancomycin and fluoroquinolones).

If surgery is longer than 4-6 hours a second intra-operative dose is advisable for some antibiotic regimens. (ce**FAZ**olin: re-dose at 4 hours intra-op; clindamycin: re-dose at 6 hours intra-op; metro**NIDAZOLE**: re-dose at 8 hours intra-op; vancomycin: re-dose at 12 hours intra-op).

Duration

A single dose of preoperative antibiotics is sufficient for most surgical procedures. **In general, post-operative doses should not exceed 24 hours**.

Choice of Antibiotics

Surgical Specialty	Patient Selection	Antibiotic Regimens		
		Recommended Regimen	**Anaphylaxis to β-lactams**	**MRSA Positive**
General Surgery	Laparoscopic cholecystectomy • For high risk only: o >70 years o Obstructive jaundice o Diabetes o Acute inflammation	ce**FAZ**olin* 2 g IV pre-op	vancomycin† 15 mg/kg IV + tobramycin‡ 5 mg/kg IV pre-op	vancomycin† 15 mg/kg IV + tobramycin‡ 5 mg/kg IV pre-op
	Biliary, pancreas, liver	ce**FAZ**olin* 2 g IV pre-op	vancomycin† 15 mg/kg IV + tobramycin‡ 5 mg/kg IV pre-op	vancomycin† 15 mg/kg IV + tobramycin‡ 5 mg/kg IV pre-op
	Colorectal surgery	ce**FAZ**olin* 2 g IV + metro**NIDAZOLE** 500 mg IV pre-op	vancomycin† 15 mg/kg IV + tobramycin‡ 5 mg/kg IV + metro**NIDAZOLE** 500 mg IV pre-op	vancomycin† 15 mg/kg IV + tobramycin‡ 5 mg/kg IV + metro**NIDAZOLE** 500 mg IV pre-op
	Appendectomy	ce**FAZ**olin* 2 g IV + metro**NIDAZOLE** 500 mg IV pre-op	vancomycin† 15 mg/kg IV + tobramycin‡ 5 mg/kg IV + metro**NIDAZOLE** 500 mg IV pre-op	vancomycin† 15 mg/kg IV + tobramycin‡ 5 mg/kg IV + metro**NIDAZOLE** 500 mg IV pre-op

Surgical Specialty	Patient Selection	Antibiotic Regimens		
		Recommended Regimen	**Anaphylaxis to β-lactams**	**MRSA Positive**
	Gastroduodenal/esophageal (including bariatric)	ce**FAZ**olin* 2 g IV pre-op	vancomycin† 15 mg/kg IV + tobramycin‡ 5 mg/kg IV pre-op	vancomycin† 15 mg/kg IV + tobramycin‡ 5 mg/kg IV pre-op
	Anorectal procedures • Hemorrhoidectomy • Fistulotomy • Sphincterotomy for fissure	None required	None required	None required
Gynecological and Obstetric	Emergency or elective C-section	ce**FAZ**olin* 2 g IV pre-op	clindamycin 900 mg IV + tobramycin‡ 5 mg/kg IV pre-op	vancomycin† 15 mg/kg IV + tobramycin‡ 5 mg/kg IV pre-op
	Hysterectomy or surgery for pelvic organ prolapse/stress urinary incontinence surgery	ce**FAZ**olin* 2 g IV pre-op	clindamycin 900 mg IV pre-op + tobramycin‡ 5 mg/kg IV pre-op	vancomycin† 15 mg/kg IV pre-op + tobramycin‡ 5 mg/kg IV pre-op
Head and Neck Surgery, Plastic Surgery	Breast, thyroid, parathyroid	ce**FAZ**olin* 2 g IV pre-op	vancomycin 15 mg/kg IV pre-op	vancomycin† 15 mg/kg IV pre-op
	Head and neck surgery involving incision of oral, pharyngeal or nasal mucosa	ce**FAZ**olin* 2 g IV pre-op	clindamycin 900 mg IV pre-op	vancomycin 15 mg/kg IV + metro**NIDAZOLE** 500 mg IV pre-op
	Minor plastic surgery or no incision of mucosa	None required	None required	None required
	Ocular surgery	Eye drops pre-op as per protocol	Eyedrops pre-op as per protocol	Eyedrops pre-op as per protocol
Orthopedic	Total joint replacement, hip fracture	ce**FAZ**olin* 2 g IV pre-op and then 1g IV q8h x 24h post-op	vancomycin† 15 mg/kg IV pre-op and then q12h x 24 h post-op§	vancomycin† 15 mg/kg IV pre-op and then q12h x 24 h post-op§
Thoracic/ Vascular/ Pacemaker¶	All except carotid or brachial	ce**FAZ**olin* 2 g IV pre-op	vancomycin† 15 mg/kg IV pre-op	vancomycin† 15 mg/kg IV pre-op
Urology#	Lower Tract			
	Cystoscopy with manipulation	ce**FAZ**olin* 2 g IV pre-op	ciprofloxacin 400 mg IV or 500 mg PO pre-op	N/A as no skin breach
	Transrectal ultrasound (TRUS) with prostate biopsy	ciprofloxacin 400 mg IV or 500 mg PO pre-op	ciprofloxacin 400 mg IV or 500 mg PO pre-op	N/A as no skin breach

Surgical Specialty	Patient Selection	Antibiotic Regimens		
		Recommended Regimen	Anaphylaxis to β-lactams	MRSA Positive
	Upper Tract			
	Shock wave lithotripsy or ureteroscopy[¥]	ce**FAZ**olin[*] 2 g IV pre-op	ciprofloxacin 400 mg IV or ciprofloxacin 500 mg PO pre-op	N/A as no skin breach
	Open or Laparoscopic			
	Not entering GU or GI tract (e.g. radical nephrectomy, laparoscopic nephrectomy)	ce**FAZ**olin[*] 2 g IV pre-op	vancomycin[†] 15 mg/kg IV pre-op	vancomycin[†] 15 mg/kg IV pre-op
	Entering GU tract (e.g. radical prostatectomy)	ce**FAZ**olin[*] 2 g IV pre-op	vancomycin[†] 15 mg/kg IV + tobramycin[‡] 5 mg/kg IV pre-op	vancomycin[†] 15 mg/kg IV + tobramycin[‡] 5 mg/kg IV pre-op
	Entering GU and GI tract (e.g. radical cystectomy with ileoconduit, ileoconduit construction)	ce**FAZ**olin[*] 2 g IV pre-op + metro**NIDAZOLE** 500 mg IV pre-op	vancomycin[†] 15 mg/kg IV + tobramycin[‡] 5 mg/kg IV + metro**NIDAZOLE** 500 mg IV pre-op	vancomycin[†] 15 mg/kg IV + tobramycin[‡] 5 mg/kg IV + metro**NIDAZOLE** 500 mg IV pre-op

[*] If patient weight ≥120kg, use ceFAZolin 3 IV pre-op.
[†] Vancomycin dosing is based on actual body weight.
[‡] Tobramycin dosing based on Ideal Body Weight (IBW) or Adjusted Body Weight (AdjBW) if weight is greater than 20% of IBW [AdjBW = IBW + 0.4 × (actual body weight - IBW)].
[§] Dosing depends on renal function.
[¶] Prophylaxis should be provided for all pacemaker insertions.
[#] Prophylaxis should be targeted to preoperative urinary cultures. For assistance with prophylaxis for resistant organisms, consult Infectious Diseases.
[¥] If high risk features: immunosuppression, > 70 years of age, diabetes mellitus, active infection/infected stone/obstructive pyelonephritis.

References

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Bacterial Meningitis

An ID consult is strongly recommended for all cases of bacterial meningitis.

Choice of Antibiotics

Patient Population	Usual Organisms	Empiric Antimicrobial Regimens*
Age 18-50 years and immunocompetent	*S. pneumoniae*, *N. meningitides*, *H. influenzae*	cef**TRIAX**one 2 g IV q12h† + vancomycin 20 mg/kg IV x 1 dose, then 15 mg/kg IV q12h
		β-lactam allergy (non-anaphylaxis): meropenem 2g IV q8h + vancomycin 20 mg/kg IV x 1 dose, then 15 mg/kg IV q12h
		β-lactam allergy (anaphylaxis): Consult ID + vancomycin 20 mg/kg IV x 1 dose, then 15 mg/kg IV q12h + moxifloxacin 400 mg IV q24h
Age > 50 years, or presence of risk factors: • Alcoholism • Immunocompromised • Pregnancy	*S. pneumoniae*, *L. monocytogenes*, *N. meningitides*, Enterobacterales (e.g. *Klebsiella* or *E. coli*)	cef**TRIAX**one 2 g IV q12h† + vancomycin 20 mg/kg IV x 1 dose, then 15 mg/kg IV q12h + ampicillin 2 g IV q4h
		β-lactam allergy (non-anaphylaxis): meropenem 2g IV q8h + vancomycin 20 mg/kg IV x 1 dose, then 15 mg/kg IV q12h
		β-lactam allergy (anaphylaxis): Consult ID + vancomycin 20 mg/kg IV x 1 dose, then 15 mg/kg IV q12h + moxifloxacin 400 mg IV q24h

* Once cultures are available, therapy can be tailored.

† Change cefTRIAXone to cefTAZidime 2 g IV q8h for patient with a history of neurosurgery or head trauma in last 30 days, a neurosurgical device, or a CSF leak due to high risk of *P. aeruginosa* and *Acinetobacter* infections.

Consider **dexamethasone** 0.15 mg/kg IV q6h x 4 days. Initiate dose 15-20 min before, or with first antibiotic dose but do NOT give if first dose of antibiotics has already been given. Consider discontinuing dexamethasone if meningitis is not caused by *S. pneumoniae*.

Duration of Therapy

Causative Organism	Duration
N. meningitides	7 days
H. influenzae	7-10 days
S. pneumoniae	10-14 days
Group B *Streptococcus*	14-21 days
L. monocytogenes	21 days
Enterobacterales (e.g. *Klebsiella* or *E.coli*)	21 days

References

1. Van de Beek D et al. Community-Acquired Bacterial Meningitis in Adults. *NEJM.* 2006; 352: 44-53.
2. Tunkel AR et al. IDSA Guidelines Practice Guidelines for the Management of Bacterial Meningitis. *Clin Infect Dis.* 2004:39:1267-84,

Candidemia/Invasive Candidiasis

Clinical Considerations

1. ID consultation is mandatory.
2. We particularly recommend patients with ocular symptoms, prolonged candidemia, and those who are intubated to undergo an ophthalmologic examination by an ophthalmologist to look for evidence of endophthalmitis.
3. Central intravenous catheters should be removed in patients with candidemia.

Choice of Antifungals

Indication for Therapy	Causative Organisms	Antimicrobial Regimens
Non-neutropenic adult while awaiting speciation	*C. albicans*, *C. tropicalis*, and *C. glabrata*	caspofungin 70 mg IV load, followed by 50 mg IV q24h
		amphotericin B liposomal 3-5 mg/kg IV q24h
Initial therapy when *Candida* species has been identified (**Note**: therapy can be further tailored once sensitivities are available)	*C. albicans*, *C. tropicalis*, and *C. parapsilosis*	fluconazole 800 mg IV/PO load, followed by fluconazole 400 mg IV/PO q24h
	C. glabrata	caspofungin 70 mg IV load, then 50 mg IV q24h
	C. krusei, which is intrinsically resistant to fluconazole	caspofungin 70 mg IV load, then 50 mg IV q24h
	C. lusitaniae, which is commonly resistant to amphotericin B	fluconazole 800 mg IV/PO load, followed by fluconazole 400 mg IV/PO q24h

Duration of Therapy

Typical duration is 14 days after the first negative blood culture, as the patient has no metastatic complications and resolution of signs and symptoms of infection.

References

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3. Pappas PG, Kauffman CA, Andes DR et al. Clinical Practice Guidelines for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America. *Clin Infect Dis.* 2016;62:e1-e50.

Clostridioides difficile-Associated Diarrhea (CDAD)

Clinical Considerations

Management of all cases should include:

- Discontinue inciting antibiotics, when possible.
- Do not start new exacerbating antibiotics, when possible.
- Avoid motility and antimotility agents, opioids, stool softeners, laxatives, and proton pump inhibitors.
- Review hydration status.
- For severe complicated disease consider Infectious Disease consultation.

Antibiotic Regimens

Indication for Therapy	Clinical Criteria	Antibiotic Regimens
Mild-to-moderate	○ WBC ≤15 ○ SrCr <1.5 times baseline	vancomycin 125 mg PO* q6h x 10-14 days
		fidaxomicin‡ 200 mg PO q12h x 10 days
Severe, uncomplicated disease	○ WBC > 15 ○ SrCr > 1.5 times baseline	vancomycin 125 mg PO* q6h x 10-14 days
		fidaxomicin‡ 200 mg PO q12h x 10 days
Severe, complicated disease	○ WBC > 15 ○ SrCr > 1.5 times baseline ○ Hypotension or shock ○ Ileus ○ Toxic megacolon or perforation	vancomycin 125-500 mg PO/NG* q6h +/- metro**NIDAZOLE** 500 mg IV q8h x 14 days, then reassess **Note**: if complete ileus, PR administration of vancomycin should be considered†
		fidaxomicin‡ 200 mg PO q12h x 10 days +/- metro**NIDAZOLE** 500 mg IV q8h x 14 days, then reassess

* Intravenous vancomycin is not effective for CDAD treatment.
† PR dosing: Vancomycin 500 mg in 50 mL catheter tipped syringe, may add 50 mL NS PR after provision of vancomycin, clamp rectal tube for 3 hr (caution with toxic megacolon). Consider consulting general surgery.
‡ fidaxomicin is restricted to ID

Treatment of Recurrent Disease

- Consider Infectious Diseases consultation.
- Prevent recurrent antimicrobial exposures.
- Consider vancomycin pulse/taper regimen.
- Consider referral for fecal microbiota transplantation (FMT). The closest centres are in Hamilton and Toronto.

References

1. Loo VG et al. Association of Medical Microbiology and Infectious Disease Canada treatment practice guidelines for *Clostridium difficile* infection. *J Assoc Med Microbiol Infect Dis Canada*. 2018;3(2):71-92.
2. Van Prehn J et al. European Society of Clinical Microbiology and Infectious Diseases: 2021 update on the treatment guidance document for *Clostridioides difficile* infection in adults. *Clin Microbiol Infect*. 2021;27 Suppl 2:S1-S21.
3. Cohen et al. Clinical Practice Guidelines for *Clostridium difficile* Infection in Adults: 2010 Update by the Society for Healthcare Epidemiology of America (SHEA) and the Infectious Diseases Society of America (IDSA). *Infect Control Hosp Epidemiol*. 2010:31:431-455.

Community-Acquired Pneumonia (CAP)

Choice of Antimicrobials

Indication for Therapy	Usual Causative Organisms	Antimicrobials Regimens
Outpatient treatment • Individual with comorbidities (chronic heart, lung, liver or renal disease, diabetes, alcoholism, malignancies, asplenia) • Individuals with immunosuppressive disease or on immunosuppressant therapy • Use of antibiotics in last 3 months (consider selecting an antibiotic from a different class as previous exposure to antibiotics within this timeframe is a risk factor for developing drug-resistant *Streptococcus pneumoniae*)	*S. pneumoniae*, *M. pneumoniae*, *C. pneumoniae*, *H. influenzae*, *M. catarrhalis* *Legionella* spp., Enterobacterales	amoxicillin/clavulanate 875/125 mg PO q12h +/- azithromycin 500 mg PO day 1, then 250 mg PO daily x 4 days* OR amoxicillin/clavulanate 875/125 mg PO q12h +/- doxycycline 100 mg PO q12h x 7 days*
		β-lactam allergy (anaphylaxis): moxifloxacin 400 mg PO q24h
Inpatient admission (non-ICU)	*S. pneumoniae*, *M. pneumoniae*, *C. pneumoniae*, *H. influenzae*, *Legionella* spp.	cef**TRIAX**one 1 g IV q24h +/- azithromycin 500 mg IV/PO day 1, then 250-500 mg IV/PO q24h x 4 days* OR cef**TRIAX**one 1 g IV q24h +/- doxycycline 100 mg PO q12h x 7 days*
		β-lactam allergy (anaphylaxis): moxifloxacin 400 mg IV/PO q24h
		Options for oral step-down therapy from cefTRIAXone includes one of: amoxicillin/clavulanate 875/125 mg PO q12h OR cefuroxime 500 mg PO q12h
Inpatient ICU admission • Always provide atypical coverage	S*. pneumoniae*, *S. aureus*, *Legionella* spp., Gram-negative bacilli, *H. influenzae*	cef**TRIAX**one 1 g IV q24h + azithromycin 500 mg IV q24h
		β-lactam allergy (anaphylaxis): moxifloxacin 400 mg IV q24h
Influenza suspected	Influenza A or B	**Add** oseltamavir 75 mg PO q12h x 5 days
Macroaspiration suspected	Oral anaerobes	cef**TRIAX**one 1g IV q24h (CTX has adequate oral anaerobic coverage and may be used alone). In the setting of severe anaerobic pulmonary infection (e.g. lung abscess, empyema):

Indication for Therapy	Usual Causative Organisms	Antimicrobials Regimens
		metroNIDAZOLE 500 mg IV/PO q12h may be added.
		amoxicillin/clavulanate 875/125 mg PO q12h
MRSA suspected	Methicillin-resistant *Staphylococcus aureus*	**Add** vancomycin 15 mg/kg IV q12h (Dose as per hospital guidelines)
Pseudomonas suspected	*Pseudomonas aeruginosa*	Refer to Hospital Acquired Pneumonia Guidelines

* Consider adding atypical coverage when "enhanced surveillance directive" from Public Health has been issued or when patients have not responded to drug therapy after 48 hours.

If the patient has received antibiotics within the last 3 months, consideration should be given to prescribing an agent from a different class.

Duration of Therapy

Minimum of 3 days. Patients should be afebrile for 48h and clinically stable before discontinuation of therapy.

References

1. Mandell LA et al. Infectious Diseases Society of America/American Thoracic Society Consensus Guidelines on the Management of Community-Acquired Pneumonia in Adults. *Clin Infect Dis*. 2007;44:S27-72.
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Hospital Acquired Pneumonia (HAP) & Ventilator Associated Pneumonia (VAP)

Definitions

- Hospital Acquired Pneumonia (HAP): pneumonia that occurs >48 after hospital admission, which was not incubating at the time of admission.
- Ventilator Associated Pneumonia (VAP): pneumonia that arises greater than 48-72 hour after endotracheal intubation.

Choice of Antimicrobials

Indication for Therapy	Usual Causative Organisms	Antibiotic Regimens
Early or Late onset HAP or VAP • No previous antibiotics in last 3 months • No immunosuppressive disease • No bronchiectasis • Not intubated • Hemodynamically stable	*Streptococcus pneumonia* *Haemophilus influenza* Methicillin-sensitive *Staphylococcus aureus* (MSSA) Enteric gram-negative bacilli (*E. coli*, *K. pneumoniae*, *Enterobacter* spp., *Proteus* spp., *Serratia marcescens*, *Pseudomonas*) **Note:** Pseudomonas is an infrequent cause of pneumonia in non-critical care areas at NH	cef**TRIAX**one 1g IV q24h
		β-lactam allergy (anaphylaxis): moxifloxacin 400 mg IV q24h
HAP or VAP • Prolonged hospital stay • Immunosuppressive disease or therapy • Hemodynamically unstable • Previous antibiotics in last 3 months • Bronchiectasis • Intubated	Pathogens listed above *plus* the following pathogens that have the potential for multi-drug resistance: *Pseudomonas aeruginosa* *Klebsiella pneumoniae* *Acinetobacter* spp.	piperacillin-tazobactam 3.375 g IV q6h
		β-lactam allergy (non-anaphylaxis): meropenem 1 g IV q8h
		β-lactam allergy (anaphylaxis): Consider ID consult + vancomycin 15 mg/kg IV q12h + ciprofloxacin 400 mg IV q12h +/- tobramycin (see dosing guidelines)
HAP or VAP with MRSA suspected	Methicillin-resistant *Staphylococcus aureus* (MRSA) Risk factors include: • MRSA colonization • Head trauma • Diabetes • Hospitalization in ICU	**Add** vancomycin 20 mg/kg IV x 1 dose, then 15 mg/kg IV q12h

Duration of Therapy

Patients initially treated with appropriate antibiotics typically require only 7-8 days of total therapy, except for *P. aeruginosa* and *S. aureus* pneumonia which may require a longer duration of treatment.

Combination regimens of a β-lactam and aminoglycoside to treat *P. aeruginosa* infections are not routinely recommended due to the lack of documented clear benefit. Combination therapy should be considered in specific patient circumstances such as previous infection with multi-drug resistant *P. aeruginosa*, febrile neutropenia, etc.

References

1. American Thoracic Society/Infectious Diseases Society of America. Guidelines for the Management of Adults with Hospital-Acquired, Ventilator-Associated and Healthcare-Associated Pneumonia. *Am J Respir Crit Care Med*. 2005;171:388-416.
2. Chastre J, Wolff M, Fagon JY et al. Comparison of 8 vs. 15 Days of Antibiotic Therapy for Ventilator-Associated Pneumonia in Adults. *JAMA*. 2003;90:2588-98.
3. Hilf M, Yu VL, Sharp J et al. Antibiotic therapy for Pseudomonas aeruginosa bacteremia: outcome correlations in a prospective study of 200 patients. *Am J Med*. 1989;87:540-6.
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Infective Endocarditis (IE)

Clinical Considerations

Empiric treatment of IE is not recommended. A microbiologic diagnosis should be aggressively sought before therapy is started. **Please consult with Infectious Diseases service if empiric therapy is being considered.**

Choice of Antimicrobials

Indication for Therapy	Usual Causative Organisms	Antimicrobial Regimens
Streptococcal endocarditis (penicillin-susceptible strains)	Viridans group streptococci (*S. sanguis, S. mitis, S. salivarius, S. mutans*), *Streptococcus bovis*	**Native Valve**
		penicillin G sodium 12-18 MU IV divided q4-6h x 4-6 weeks
		cef**TRIAX**one 2 g IV/IM q24h x 4-6 weeks
		Shorter treatment duration (only with ID consultation): penicillin G sodium 12-18 MU IV divided q4-6h x 2 weeks OR cef**TRIAX**one 2 g IV/IM q24h x 2 weeks + gentamicin* 1 mg/kg IV q8h x 2 weeks
		β-lactam allergy (anaphylaxis): vancomycin† IV x 4 weeks
		Prosthetic Valve
		penicillin G sodium 24 MU IV divided q4-6h x 6 weeks +/- gentamicin* 1 mg/kg IV q8h x 2 weeks
		cef**TRIAX**one 2 g IV/IM q24h x 6 weeks +/- gentamicin* 1 mg/kg IV q8h x 2 weeks
		β-lactam allergy (anaphylaxis): vancomycin† IV x 6 weeks
Staphylococcal endocarditis	*Staphylococcus aureus* (MSSA)	**Native Valve**
		cloxacillin 2 g IV q4h x 6 weeks
		ce**FAZ**olin 2 g IV q8h x 6 weeks
		β-lactam allergy (anaphylaxis): vancomycin† IV x 6 weeks
		Prosthetic Valve
		cloxacillin 2 g IV q4h x 6 weeks OR ceFAZolin 2 g IV q8h x 6 weeks + rif**AMP**in 300 mg PO q8h x 6 weeks + gentamicin* 1 mg/kg IV q8h x 2 weeks
		β-lactam allergy (anaphylaxis): vancomycin† IV x 6 weeks + rif**AMP**in 300 mg PO q8h x 6 weeks + gentamicin* 1 mg/kg IV q8h x 2 weeks
	Enterococcus spp.	**Native Valve**

Indication for Therapy	Usual Causative Organisms	Antimicrobial Regimens
Enterococcal endocarditis (penicillin, gentamicin and vancomycin susceptible strains)		ampicillin 2 g IV q4h x 6 weeks + cefTRIAXone 2g IV q12h x 6 weeks
		ampicillin 2 g IV q4h x 4-6 weeks[‡] + gentamicin[*] 1 mg/kg IV q8h x 4-6 weeks
		β-lactam anaphylaxis or resistant organism: vancomycin[†] IV x 6 weeks + gentamicin[*] 1 mg/kg IV q8h x 6 weeks
		Prosthetic Valve
		ampicillin 2 g IV q4h x 6 weeks + cefTRIAXone 2g iv q12h x 6 weeks
		ampicillin 2 g IV q4h x 6 weeks + gentamicin* 1 mg/kg IV q8h x 6 weeks
		β-lactam anaphylaxis or resistant organism: vancomycin[†] IV x 6 weeks + gentamicin[*] 1 mg/kg IV q8h x 6 weeks
Endocarditis caused by other pathogens	Coagulase-negative staphylococci, MRSA, *Enterococcus* (drug-resistant), HACEK species, fungi, culture-negative	Consult Infectious Diseases.

[*] There is insufficient data for the use of high dose (once-daily) aminoglycosides in the treatment of IE. Target peak 3-4 mg/L, trough < 1 mg/L. Addition of gentamicin in IE caused by staphylococci in absence of prosthetic material is optional as clinical benefit of this practice has not been established.
[†] Vancomycin - dose as per hospital guidelines. Target trough 13-20 mg/L.
[‡] Treat x 6 weeks if patient has had symptoms of illness for greater than 3 months.

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3. Fernandez-Hidalgo N, Almirante B, Gavalda J et al. Ampicillin plus ceftriaxone is as effective as ampicillin plus gentamicin for treating enterococcus faecalis infective endocarditis. *Clin Infect Dis*. 2013;56(9):1261-8.

Intra-Abdominal Infections

Choice of Antimicrobials

Indication for Therapy	Usual Causative Organisms	Antimicrobial Regimens
Community-acquired, uncomplicated (non-perforated appendicitis, perforations without established infection)	Enterobacterales, anaerobes, +/- Gram-positive cocci (stomach/duodenum)	cef**TRIAX**one 1g IV q24h + metro**NIDAZOLE** 500 mg IV/PO q12h
		β-lactam allergy (anaphylaxis): ciprofloxacin 400/500 mg IV/PO q12h + metro**NIDAZOLE** 500 mg IV/PO q12h
Community-acquired, complicated, mild-to-moderate (perforated appendicitis, diverticulitis)	Enterobacterales, anaerobes (including *B. fragilis*)	cef**TRIAX**one 1g IV q24h + metro**NIDAZOLE** 500 mg IV/PO q12h
		β-lactam allergy (anaphylaxis): ciprofloxacin 400/500 mg IV/PO q12h + metro**NIDAZOLE** 500 mg IV/PO q12h
Community-acquired complicated, severe (shock, new organ failure, ICU patient)	Enterobacterales, anaerobes (including *B. fragilis*)	cef**TRIAX**one 1g IV q24h + metro**NIDAZOLE** 500 mg IV/PO q12h
		piperacillin-tazobactam 3.375 g IV q6h
		β-lactam allergy (anaphylaxis): ciprofloxacin 400/500 mg IV/PO q12h + metro**NIDAZOLE** 500 mg IV/PO q12h
Healthcare-associated, mild-to-moderate (hospitalized ≥ 5 days, anastomotic leak, post-operative abscess, recent antibiotics, recent hospitalization)	Enterobacterales, anaerobes, *Enterococcus* spp., +/- drug-resistant gram-negative bacilli	cef**TRIAX**one 1 g IV q24h + metro**NIDAZOLE** 500 mg IV/PO q12h
		piperacillin-tazobactam 3.375 g IV q6h
		β-lactam allergy (anaphylaxis): vancomycin[β] 20 mg/kg IV x1 dose, then 15 mg/kg IV q12h + ciprofloxacin 400/500 mg IV/PO q12h + metro**NIDAZOLE** 500 mg IV/PO q12h
Healthcare-associated, severe (hospitalized ≥ 5 days, anastomotic leak, shock, ICU, recent antibiotics, recent hospitalization)	Enterobacterales, anaerobes, *Enterococcus* spp., +/- drug-resistant gram- negative bacilli	piperacillin-tazobactam 3.375 g IV q6h
		β-lactam allergy (anaphylaxis): vancomycin[β] 20 mg/kg IV x1 dose, then 15 mg/kg IV q12h + ciprofloxacin 400/500 mg IV/PO q12h + metro**NIDAZOLE** 500 mg IV/PO q12h
		β-lactam allergy (non-anaphylaxis): meropenem 1 g IV q8h

Indication for Therapy	Usual Causative Organisms	Antimicrobial Regimens
Biliary tract (e.g. acute cholangitis), mild-to-moderate	Enterobacterales, anaerobes, *Streptococcus* spp., and *Enterococcus* spp.[*†]	cef**TRIAX**one 1 g IV q24h +/- metro**NIDAZOLE** 500 mg IV/PO q12h
		β-lactam allergy (anaphylaxis): ciprofloxacin 400/500 mg IV/PO q12h +/- metro**NIDAZOLE** 500 mg IV/PO q12h
Biliary tract, severe (severe physiological disturbance, advanced age, immunocompromised state, or bilio-enteric anastomosis)	Enterobacterales, anaerobes, *Streptococcus* spp., *Enterococcus* spp.[*]	piperacillin-tazobactam 3.375 g IV q6h
		β-lactam allergy (anaphylaxis): vancomycin[‡] 20 mg/kg IV x1 dose, then 15 mg/kg IV q12h + ciprofloxacin 400/500 mg IV/PO q12h + metro**NIDAZOLE** 500 mg IV/PO q12h
Prophylaxis for spontaneous bacterial peritonitis	Enterobacterales, *S. pneumoniae*, *Streptococcus* spp.	**Short term** (e.g. GI bleed): cef**TRIAX**one 1 g IV q24h x 7 days
		Long term (e.g. previous episode of SBP or ascitic fluid protein <10 g/L): co-trimoxazole 1 DS (trimethoprim [TMP] 160 mg/sulfamethoxazole [SMX] 800 mg) PO daily OR ciprofloxacin 500 mg PO daily

[*] Cephalosporins alone are not active against *Enterococcus* species.

[†] Community-acquired biliary infection, activity against enterococci is not required, because the pathogenicity of enterococci has not been demonstrated. For selected health care associated infections or immunosuppressed patients, particularly those with hepatic transplantation, enterococcal infection may be significant and require treatment.

[‡] vancomycin dosing based on actual body weight.

Duration of Therapy

After source control is complete and there is resolution of clinical signs of infection (normalization of WBC count and absence of fever), antimicrobials can be discontinued. This can be as short as 24 hours after uncomplicated intra-abdominal infections or 4-7 days for complicated intra-abdominal infections. If source control is achieved, longer durations of therapy have not been associated with improved outcomes.

Patients undergoing cholecystectomy for acute cholecystitis should have antimicrobial therapy discontinued within 24 hours unless there is evidence of infection outside the wall of the gallbladder.

References

1. Solomkin J et al. Diagnosis and management of complicated intra-abdominal infections in adults and children: guidelines by the Surgical Infection Society and the Infectious Diseases Society of America. *Clin Infect Dis*. 2010; 50:133-64.
2. Antibiotics for complicated intra-abdominal infections. *Pharmacist's Letter/Prescriber's Letter*. 2010; 26(3):260321.
3. Toronto Antimicrobial Stewardship Corridor (TASC). Best Practice in General Surgery: Management of Intra-Abdominal Infections, Dec 2011.

Intravenous to Oral Antimicrobial Conversion

Clinical Considerations

1. Consider spectrum of coverage required per indication and choose the appropriate PO regimen to ensure similar coverage of specific organisms.
2. Stay within the same antimicrobial class, if possible, to prevent drug/bug mismatch as a result of switching.
3. Oral step-down may not be appropriate in some infectious indications (i.e. endocarditis, meningitis, certain prosthetic joint infections, etc.) or patient populations (i.e. intractable vomiting, short gut syndrome, intractable diarrhea).
4. As always, culture results and patient factors should be considered.

The chart below contains suggested options for IV to PO step-down of empiric antimicrobials or when microbiology is not available in patients with normal renal function.

Choice of Antimicrobials

IV Antimicrobial Regimen	Suggested PO Equivalent Regimen
ampicillin 1 g IV q4-6h	Urinary source: amoxicillin 500 mg PO q8h Other sources: amoxicillin 1 g PO q8h
piperacillin/tazobactam 3.375 g IV q6h	No pseudomonal coverage required: amoxicillin/clavulanic acid 875/125 mg PO q12h Pseudomonal coverage required: Consider Infectious Diseases consultation Febrile neutropenia: ciprofloxacin 500 mg PO q12h + amoxicillin/clavulanic acid 875/125 mg PO q12h
ce**FAZ**olin 1 g IV q8h	cephalexin 500 mg PO q6h
ce**FAZ**olin 1 g IV q8h + metro**NIDAZOLE** 500 mg IV q12h	amoxicillin/clavulanic acid 875/125 mg PO q12h OR cephalexin 500 mg PO q6h + metro**NIDAZOLE** 500 mg PO q12h
cef**TRIAX**one 1 g IV q24h	Urinary source: amoxicillin/clavulanic acid 875/125 mg PO q12h Respiratory source: amoxicillin/clavulanic acid 875/125mg PO q12h OR cefuroxime 500 mg PO q12h Intra-abdominal source: amoxicillin/clavulanic acid 875/125 mg PO q12h
cef**TRIAX**one 1 g IV q24h + azithromycin 250 mg IV q24h	azithromycin 250 mg PO daily + either: amoxicillin/clavulanic acid 875/125 mg PO q12h OR cefuroxime 500 mg PO q12h

IV Antimicrobial Regimen	Suggested PO Equivalent Regimen
cef**TRIAX**one 1 g IV q24h + metro**NIDAZOLE** 500 mg IV q12h	cephalexin 500 mg PO q6h **+** metro**NIDAZOLE** 500 mg PO q12h OR amoxicillin/clavulanic acid 875/125 mg PO q12h
ertapenem OR meropenem	No PO step-down recommended. Consider Infectious Diseases consultation
ciprofloxacin 400 mg IV q12h	ciprofloxacin 500 mg PO q12h
ciprofloxacin 400 mg IV q12h + metro**NIDAZOLE** 500 mg IV q12h	ciprofloxacin 500 mg PO q12h + metro**NIDAZOLE** 500 mg PO q12h
levofloxacin* 500-750 mg IV q24h	levofloxacin* 500-750 mg PO q24h
moxifloxacin 400 mg IV q24h	moxifloxacin 400 mg PO q24h
clindamycin 600 mg IV q8h	clindamycin 300 mg PO q6h

* Moxifloxacin is the respiratory fluoroquinolone on formulary at Niagara Health.

Ophthalmic Infections

Clinical Considerations

Red flag symptoms requiring Ophthalmology consultation include:

- Reduction of visual acuity
- Ciliary flush: A pattern of injection in which the redness is most pronounced in a ring at the limbus (the limbus is the transition zone between the cornea and the sclera)
- Photophobia
- Severe foreign body sensation that prevents the patient from keeping the eye open
- Cornea opacity
- Fixed pupil
- Severe headache with nausea
- Contact lens wearers

Choice of Antimicrobials

Indication for Therapy	Usual Causative Organisms	Antimicrobial Regimens
Bacterial Conjunctivitis	*Staphylococcus aureus*, *Streptococcus pneumoniae*, *Haemophilus* spp., *Moraxella catarrhalis*	Polysporin 1-2 drops to affected eye(s) QID
		tobramycin 0.3% 1-2 drops to affected eye(2) QID
		moxifloxacin 0.5% 1 drop to affected eye(s) TID

References

1. *Guideline for the treatment and management of acute bacterial conjunctivitis in children and adults*. University of Texas, School of Nursing, Family Nurse Practitioner Program. Austin (TX): University of Texas, School of Nursing; 2005. Available at: http://www.guideline.gov/browse/archive.aspx?type=2
2. Sheikh A, Hurwitz A. Antibiotics versus placebo for acute bacterial conjunctivitis. *Cochrane Database of Systematic Reviews*. 2006. Available at: http://www.cochrane.org/reviews/en/ab001211.html.
3. Anti-infective Guidelines for Community-acquired Infections. Anti-infective Review Panel. 2013 Edition.

Pelvic Inflammatory Disease (PID)

Choice of Antimicrobials

Indication for Therapy	Usual Causative Organisms	Antimicrobial Regimens
Ambulatory (outpatient)	*Chlamydia trachomatis*, *Neisseria gonorrhoeae*, anaerobes, Enterobacterales	cef**TRIAX**one 250 mg IM x 1 dose + doxycycline‡ 100 mg PO q12h x 14 days +/- metro**NIDAZOLE*** 500 mg PO q12h x 14 days
Severe, requiring hospitalization	*Chlamydia trachomatis*, *Neisseria gonorrhoeae*, anaerobes, Enterobacterales	cef**TRIAX**one† 1 g IV q24h + metro**NIDAZOLE**† 500 mg IV/PO q12h + doxycycline‡ 100 mg PO q12h
		β-lactam allergy (anaphylaxis): clindamycin† 900 mg IV q8h + tobramycin (as per hospital guidelines)†

* metro**NIDAZOLE** should be added if a tuboovarian abscess is suspected.
† When patient clinically improved, step down to oral antibiotic therapy with doxycycline 100 mg PO q12h *or* clindamycin 450 mg PO q6h or amoxicillin/clavulanic acid 875/125 mg PO q12h (clindamycin or amoxicillin/clavulanic acid preferred if tuboovarian abscess suspected) x 14 days total.
‡ Doxycycline should not be used in pregnant woman >15 weeks gestational age.

References

1. *Canadian Guidelines on Sexually Transmitted Infections, January 2010 Edition*. Ottawa, ON: Public Health Agency of Canada, 2010. Available at: http://www.phac-aspc.gc.ca/std-mts/sti-its/pdf/sti-its-eng.pdf
2. Public Health Agency of Canada update on the Treatment of Gonococcal Infections. Available at: http://www.phac-aspc.gc.ca/std-mts/sti-its/alert/2011/alert-gono-eng.php
3. Supplementary statement for recommendations related to the diagnosis, management, and follow-up of pelvic inflammatory disease. Available at: http://www.phac-aspc.gc.ca/std-mts/sti-its/cgsti-ldcits/assets/pdf/pid-aip-eng.pdf

Prevention of Bacterial Endocarditis

Choice of Antibiotics

Indication for Therapy	Usual Causative Organisms	Antimicrobial Regimens
Patients with high risk cardiac conditions[*] undergoing the following interventions: • Dental procedures involving manipulation of gingival tissue/periapical region of teeth or perforation of the oral mucosa • Respiratory tract procedures involving excision of the mucosa (i.e. tonsillectomy, andenoidectomy and bronchoscopy with biopsy) • Procedures involving infected skin, skin structure or musculoskeletal tissue	Viridans group streptococci, other *Streptococcus* spp., *Staphylococcus* spp.	**Standard General Prophylaxis[†]**
		amoxicillin 2 g PO x 1 dose 1 hour prior to procedure
		β-lactam allergy (non-anaphylaxis): cephalexin 2 g PO x 1 dose 1 hour prior to procedure
		β-lactam allergy (anaphylaxis): clindamycin 600 mg PO x 1 dose 1 hour prior to procedure OR clarithromycin 500 mg PO x 1 dose 1 hour prior to procedure
		Unable to take Oral Medications
		ampicillin 2 g IV/IM x 1 dose within 30 min before procedure
		β-lactam allergy (non-anaphylaxis): ce**FAZ**olin 1 g IV x 1 dose 1 hour prior to procedure
		β-lactam allergy (anaphylaxis): vancomycin 15 mg/kg IV once (not to exceed 2 grams) within 120 minutes prior to procedure
Gastrointestinal and genitourinary procedures	*Enterococcus* spp.	Routine prophylaxis no longer recommended[‡]

[*] Cardiac conditions associated with highest risk of adverse outcomes from endocarditis:

- Prosthetic cardiac valve
- Previous infective endocarditis
- Congenital heart disease (CHD) with non-repaired cyanotic CHD (including palliative shunts & conduits) **or** completely repaired congenital heart defect with prosthetic material or device during first 6 months after procedure **or** repaired CHD with residual defects at the site or adjacent to the site of a prosthetic patch or device
- Cardiac transplant recipients who develop cardiac valvulopathy (i.e. documented substantial leaflet pathology and regurgitation)

[†] In the event that an antibiotic is inadvertently not given prior to the procedure the dosage may be given up to 2 hours afterwards.

[‡] Patients with an established GI/GU infection or enterococcal colonization should receive prophylaxis with amoxicillin/ampicillin or vancomycin (if patient has a penicillin allergy).

References:

1. Prevention of Infective Endocarditis – Guidelines from the American Heart Association Rheumatic Fever, Endocarditis and Kawasaki Disease Committee. *Circulation*. 2007; 116:1736-1754.

Skin & Soft Tissue Infections (SSTI)

Choice of Antimicrobials

Indication for Therapy	Usual Causative Organisms	Antimicrobial Regimens
Purulent SSTI (ie. skin abscesses, carbuncles and furuncles)	*Staphylococcus aureus*	Antimicrobials not routinely recommended for management of uncomplicated purulent SSTIs Incision and drainage most effective management Recurrent infection (x5-7 days of): co-trimoxazole 1 DS (trimethoprim [TMP] 160 mg/sulfamethoxazole [SMX] 800 mg) PO q12h OR doxycycline 100mg PO q12h
Non-purulent SSTI Uncomplicated cellulitis, impetigo, erysipelas OR Superficial ulcers with cellulitis in non-diabetic patients	Group A, C, and G , *Streptococcus* *Staphylococcus aureus*	cephalexin 500 mg PO q6h x 5-7 days
		ce**FAZ**olin 1 g IV q8h[†] x 5-7 days
		β-lactam allergy (anaphylaxis): moxifloxacin 400 mg PO q24h OR clindamycin 300 mg PO q6h or 600 mg IV q8h
	Methicillin-resistant *Staphylococcus aureus* (MRSA) suspected	co-trimoxazole 1 DS (trimethoprim [TMP] 160 mg/sulfamethoxazole [SMX] 800 mg) PO q12h + cephalexin 500 mg PO q6h
		doxycycline 100 mg PO q12h + cephalexin 500 mg PO q6h
		vancomycin (dosing as per hospital guidelines)
Necrotizing fasciitis[*] **Note:** If MRSA suspected, add vancomycin	Invasive Group A *Streptococcus*	penicillin G 4 MU IV q4h + clindamycin 900 mg IV q8h +/- IVIG 1 g/kg x 1, then 0.5 g/kg at days 2 and 3 (if signs of streptococcal toxic shock syndrome) + Consider ID consult
		β-lactam allergy (anaphylaxis): vancomycin (dose as per hospital guidelines) + clindamycin 900 mg IV q8h +/- IVIG 1 g/kg x 1, then 0.5 g/kg on days 2 and 3 (if signs of streptococcal Toxic Shock Syndrome) + Consider ID consult
	Mixed aerobic Gram-negative bacilli and anaerobes	piperacillin/tazobactam 3.375 g IV q6h
		cef**TRIAX**one 1-2 g IV q24h + metro**NIDAZOLE** 500 mg IV q12h

Indication for Therapy	Usual Causative Organisms	Antimicrobial Regimens
Diabetic foot infection OR Decubitus ulcer (infected) **Note:** If MRSA suspected, add vancomycin	Most **mild** superficial infections are *S. aureus* and *Streptococcus* spp. More **complicated** infections may include *S. aureus*, *Streptococcus* spp., Enterobacterales, and anaerobes	**Mild infection:** superficial, localized with no systemic involvement
		cephalexin 500 mg PO q6h
		amoxicillin/clavulanic acid 875 mg/125 mg PO q12h
		co-trimoxazole 1 DS (trimethoprim [TMP] 160 mg/sulfamethoxazole [SMX] 800 mg) PO q12h + metro**NIDAZOLE** 500 mg PO q12h
		ce**FAZ**olin 1 g IV q8h[†]
		Moderate infection: full thickness ulcer with deep tissue involvement; **NO** systemic illness
		cef**TRIAX**one 1 g IV q24h + metro**NIDAZOLE** 500 mg PO/IV q12h
		amoxicillin/clavulanic acid 875 mg/125 mg PO q12h
		metro**NIDAZOLE** 500 mg PO/IV q12h + moxifloxacin 400 mg PO q24h
		Severe infection: systemic or bone involvement[*]
		piperacillin/tazobactam 3.375 g IV q6h
		cef**TRIAX**one 1 g IV q24h + metro**NIDAZOLE** 500 mg PO/IV q12h
		β-lactam allergy (anaphylaxis): metro**NIDAZOLE** 500 mg PO/IV q12h + moxifloxacin 400 mg PO q24h
Cellulitis/phlebitis secondary to IV line **Note:** Majority of cases can be treated with catheter removal and warm compress TID alone.	*S. aureus*, coagulase-negative staphylococci (including *S. epidermidis*)	**If antibiotics required:** ce**FAZ**olin 1 g IV q8h[†]
		β-lactam anaphylaxis or MRSA suspected: vancomycin (dose as per hospital guidelines)
Human bites[‡] **Note:** Give tetanus booster (Td) if none in the past 5 years.	*S. aureus*, *Streptococcus* spp., oral anaerobes, *Haemophilus* spp., *Eikenella corrodens*	Non-severe infections:
		amoxicillin/clavulanic acid 875 mg/125 mg PO q12h
		Severe infections:
		cef**TRIAX**one 1 g IV q24h + metro**NIDAZOLE** 500 mg PO/IV q12h
		piperacillin/tazobactam 3.375 g IV q6h
		β-lactam allergy (anaphylaxis): metro**NIDAZOLE** 500 mg PO/IV q12h + one of: moxifloxacin 400 mg PO/IV q24h **OR** doxycycline 100 mg PO q12h **OR** co-trimoxazole DS (trimethoprim [TMP] 160 mg/sulfamethoxazole [SMX] 800 mg) 2 tabs PO q12h

Indication for Therapy	Usual Causative Organisms	Antimicrobial Regimens
Animal bites (dogs and cats) **Note:** Give tetanus booster (Td) if none in the past 5 years, and consider rabies (Public Health Ontario – rabies)	*S. aureus*, *Streptococcus* spp., oral anaerobes, *Pasteurella multocida*[¶], *Captnocytophaga canimorsus*	**Prophylaxis[§] (x3-5 days)**
		amoxicillin/clavulanic acid 875 mg/125 mg PO q12h OR amoxicillin/clavulanic acid 500 mg/125 mg PO q8h
		Treatment (non-severe):
		amoxicillin/clavulanic acid 875 mg/125 mg PO q12h
		Treatment (severe):
		cef**TRIAX**one 1 g IV q24h + metro**NIDAZOLE** 500 mg PO/IV q12h
		piperacillin/tazobactam 3.375 g IV q6h
		β-lactam allergy (anaphylaxis): metro**NIDAZOLE** 500 mg PO/IV q12h + one of: moxifloxacin 400 mg PO/IV q24h **OR** doxycycline 100 mg PO q12h **OR** co-trimoxazole DS (trimethoprim [TMP] 160 mg/sulfamethoxazole [SMX] 800 mg) 2 tabs PO q12h

[*] Severe soft tissue infections may require a combined medical and surgical approach. Consultation with Infectious Diseases and Surgical Services is recommended.

[†] Consider ceFAZolin 2 g IV q8h for patients greater than 100 kg.

[‡] Human bites do not generally require prophylaxis, but can be considered if the wound is through the dermis, especially on the hand.

[§] Consider prophylaxis for animal bites if:

- moderate to severe injury <8 hours old, especially if edema or crush injury
- deep puncture wounds (especially due to cat bites)
- hand wounds or in close proximity to a bone or joint (particularly prosthetic joints)
- immunocompromised patients (including those with splenectomy, liver disease, or steroid therapy)
- wounds requiring closure
- wound is in the genital area.

[¶] Clinical failures have been noted in patients treated with first-generation cephalosporins (eg. cephalexin), and clindamycin. These agents have poor in vitro activity against *P. multocida* and should be avoided.

Duration of Therapy

Most cases of uncomplicated cellulitis can be managed using oral therapy alone. If intravenous therapy is needed initially (inability to take oral medications or early concern regarding aggressive infection), step-down to oral antibiotics should be considered within 48-72 hours. **A total duration of therapy of 5-7 days is sufficient for most uncomplicated skin and soft tissue infections**.

References

1. Stevens DL et al. Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections: 2014 Update by the Infectious Diseases Society of America Clinical Infectious Diseases. *Clin Infect Dis*. 2014:1-43.
2. Stevens DL, Bisno AL, Chambers HF et al. Guidelines for Skin and Soft-Tissue Infections. *Clin Infect Dis*. 2005;41:1373-80.
3. Mermel LA, Farr BM, Sherertz RJ et al. Guidelines for the Management of Intravascular Catheter-Related Infections. *Clin Infect Dis*. 2001;32:1249-72.
4. Lipsky BA, Berendt AR, Cornia PB, Pile JC et al. Diagnosis and Treatment of Diabetic Foot Infections. *Clin Infect Dis*. 2012;54:132-173.
5. UpToDate. Wolters Kluwer Health. http://www.uptodate.com/contents/search (accessed July 22, 2017).

Splenectomy Vaccination Guidelines

Recommended Vaccines

Vaccine	Brand on Formulary	Dose & Timing	Notes
Pneumococcal conjugate 13-valent (Pneu-C-13) vaccine	Prevnar-13	0.5 mL deep IM (deltoid) x 1 dose	Must wait at least 1 year after any dose of Pneu-P-23 before giving Pneu-C-13.*
Pneumococcal polysaccharide 23-valent (Pneu-P-23) vaccine	Pneumovax-23	0.5 mL SC/IM x 1 dose Booster after 5 years	Must wait at least 8 weeks after any dose of Pneu-C-13 before giving Pneu-P-23.
Meningococcal quadrivalent conjugate (Men-C-ACYW) vaccine	Menactra	0.5 mL IM (deltoid preferred) x 2 doses at least 8 weeks apart Booster every 5 years	
Multicomponent meningococcus serogroup B (4CMenB) vaccine	Bexsero	0.5 mL IM given x2 doses at least 4 weeks apart	Not part of the routine immunization schedule, but recommended for high-risk individuals.
Haemophilus b (Hib) conjugate vaccine	Act-HIB	0.5 mL IM x 1 dose	
Influenza vaccine	varies	given annually	

* NACI recommends administration of Pneu-C-13 (Prevnar-13) at least one year after any previous dose of Pneu-P-23 (Penumovax-23) vaccine, due to the theoretical potential for decrease in antibody titers following immunization with Pneu-P-23 vaccine.

Timing of Vaccination

Date (Scheduled Surgery)	Date (Emergent Surgery)	Vaccines
10 weeks prior to surgery	2 weeks after splenectomy	Pneu-C-13 (Prevnar-13) Men-C-ACYW (Menactra) 4CMenB (Bexsero) Hib (Act-HIB)
2 weeks prior to surgery	10 weeks after splenectomy	Pneu-P-23 (Pneumovax-23) Men-C-ACYW (Menactra) 4CMenB (Bexsero)
Routine follow-up	Routine follow-up	Annual influenza immunization Pneu-P-23 (Pneumovax-23) booster at 5 years Men-C-ACYW (Menactra) booster every 5 years

References

1. Immunization of persons with chronic diseases. In: *Canadian Immunization Guide*. May 2022.
2. Canadian National Advisory Council on Immunization (NACI), Statement on conjugate meningococcal vaccine for serogroups A, C, Y and W135, May 2007.
3. Canadian National Advisory Council on Immunization (NACI), Update on meningococcal disease and meningococcal vaccine conjugate recommendations, April 2009.
4. Canadian National Advisory Council on Immunization (NACI), Update on the use of 13-valent pneumococcal conjugate vaccine (PNEU-C-13) in addition to 23-valent pneumococcal polysaccharide vaccine (PNEU-P-23) in immunocompetent adults 65 years of age and older – Interim Recommendation, October 2016.
5. Advisory Committee on Immunization Practices (ACIP) Recommended Immunization Schedule for Adults Aged 19 Years and Older — United States, 2013;62(01):9-19. Available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/su6201a3.htm.

Staphylococcus aureus Bacteremia

Clinical Considerations

Patients with *Staphylococcus aureus* bacteremia require a mandatory Infectious Diseases consult. Unless there are significant issues with IV access, do not place central venous access or PICC lines until blood cultures are sterile.

S. aureus should NEVER be treated as a contaminant.

Assessment and Management

- Clinical assessment to identify the source as well as the presence and extent of septic complications of the infection.
- Elimination and/or debridement of sites of infection (e.g. removal of intravenous and intra-arterial catheters that were in place while the patient was bacteremic).
- Follow-up blood cultures every 48 hours after start of treatment until clearance of *S. aureus* from blood.
- Echocardiography (TTE initially +/- TEE).
- PICC line for prolonged antibiotic treatment should only be placed once sterilization of blood cultures has been documented.

Choice of Antibiotics

- **Empiric:** vancomycin 20mg/kg IV x 1 load dose then 15mg/kg IV q12h (adjusted for renal function; refer to vancomycin dosing guidelines)
- **Targeted:**
    - Methicillin-sensitive S. aureus (MSSA): cloxacillin 2g IV q4h or ceFAZolin 2g IV q8h
    - Methicillin-resistant S. aureus (MRSA): continue vancomycin IV
        - Trough level prior to dose 4 dose to target level 13-20.
        - Consider pharmacy consultation for vancomycin IV monitoring and dosing.
- Intravenous therapy is recommended for the entire duration of treatment.

Duration of Therapy

- 2 weeks from last positive blood cultures with negative follow-up blood cultures after 48-96 hours of appropriate treatment, absence of endocarditis by TEE, no indwelling devices, patient defervesced within 72 hours after initiation of appropriate treatment, and no signs/symptoms of complications/metastatic focus.
- Minimum 4-6 weeks if these criteria are not met.

References

1. Liu C, Bayer A, Cosgrove SE, Daum RS, Fridkin SK, Gorwitz RJ, Kaplan SL, Karchmer AW, Levine DP, Murray BE, J Rybak M, Talan DA, Chambers HF. Clinical practice guidelines by the Infectious Diseases Society of America for the treatment of methicillin-resistant *Staphylococcus aureus* infections in adults and children. *Clin Infect Dis*. 2011;52(3):e18.
2. Lowy FD. *Staphylococcus aureus* infections. *NEJM*. 1998;339(8):520.

Urinary Tract Infections (UTIs)

These guidelines are for empiric treatment. Therapy should be tailored according to urine culture and susceptibility results once available. Once clinically stable, oral therapy is recommended for any patients originally started on IV therapy.

Indication for Therapy	Usual Causative Organisms	Antibiotic Regimens
Asymptomatic bacteriuria	Enterobacteriaceae, *Enterococcus* species, *Pseudomonas*	No treatment recommended, except in the cases of pregnancy or patients scheduled to undergo invasive urological procedures where mucosal bleeding is expected, such as TURP
Uncomplicated lower tract (Acute cystitis or urethritis) Uncomplicated UTIs are defined as symptomatic bacteriuria in adult non-pregnant women with apparently normal urinary tracts	Enterobacteriaceae (including *E. coli*, *Klebsiella*, and *Proteus*), *Staphylococcus saprophyticus*, *Enterococcus* species	Nitrofurantoin (MacroBID) 100 mg p.o. every 12 hours for 5 days
		Co-trimoxazole DS 1 tablet p.o. every 12 hours for 3 days
Uncomplicated lower urinary tract infection in pregnancy		First-line: amoxicillin/clavulanic acid 875 mg/125 mg p.o. every 12 hours for 5 to 7 days Alternative: cephalexin 500 mg p.o. every 6 hours for 5 to 7 days Alternative: nitrofurantoin (MacroBID) 100 mg p.o. every 12 horus for 7 days*
Complicated or catheter-associated Treat catheter-associated bacteriuria only if clinical symptoms of urinary tract infection are present.	Enterobacteriaceae (including *E. coli*, *Klebsiella*, and *Proteus*), *Staphylococcus saprophyticus*, *Enterococcus* species	Co-trimoxazole DS 1 tab p.o. every 12 hours for 7 days
		Amoxicillin/clavulanic acid 875 mg /125 mg p.o. every 12 hours for 7 days
	Pseudomonas	CefTAZidime 1 g IV every 8 hours for 7 days
		Ciprofloxacin 500 mg p.o. every 12 hours for 7 days**
Upper tract Mild-to-moderate pyelonephritis not requiring hospitalization in women	Enterobacteriaceae (including *Serratia*, *Enterobacter*, and *Citrobacter*), *S. saprophyticus*, and *Enterococcus* species	Co-trimoxazole DS 1 tab p.o. every 12 hours for 7 days
		Ciprofloxacin 500 mg p.o. every 12 hours for 7 days
Upper tract Moderate-to-severe acute pyelonephritis	Enterobacteriaceae (including *Serratia*, *Enterobacter*, and *Citrobacter*), *S. saprophyticus*, and *Enterococcus* species	CefTRIAXone 1 g IV every 24 hours for 7 days
		Ciprofloxacin 500 mg p.o. every 12 horus for 7 days
		In pregnancy: ceftriaxone 1 g IV every 24 hours for 7 days

* There is a theoretical risk of hemolytic anemia in the fetus or newborn, especially in those with G6PD deficiency, but case reports are rare. Numerous studies have shown the use of nitrofurantoin in pregnancy to be safe[1,3].

** Therapy can be stopped at 3 days in individuals less than 60 years if catheter is removed.

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Vancomycin (IV) Dosing and Therapeutic Monitoring Guidelines

Background

Vancomycin exerts its antibacterial activity by inhibiting bacterial cell wall synthesis, a process that is time-dependent (time>MIC). Protein binding is moderate (~50%) and penetration of the drug into the lung and CNS is poor.

Dosing Recommendations

The usual dose is 1000 mg (for a 70 kg patient) or 10-15 mg/kg Actual Body Weight rounded to the nearest 250 mg, including obese patients or patients < 50kg. For obese patients can consider adjusted body weight dosing based on height and weight. Maximum dose is 2 g.

A loading dose of 20 mg/kg Actual Body Weight maybe considered in patients who are critically ill and where serious MRSA infection is suspected.

Loading Dose

Actual Body Weight (kg)	Initial Dose (mg)	Infusion Time (min)
Less than 60	1000	60
60-70	1250	90
71-80	1500	120
81-90	1750	120
Greater than 90	2000	120

Maintenance Dose

Actual Body Weight (kg)	Initial Dose (mg)	Infusion Time (min)
Less than 60	750	60
60-70	1000	60
71-80	1250	90
81-90	1500	90
Greater than 90	1750	120

The ***initial*** dosing interval for all patients (empiric treatment and serious gram-positive infections) is based on estimated creatinine clearance using the Cockcroft-Gault equation:

$$eC_{Cr} = \frac{(140 - \text{Age}) \times \text{Mass (in kilograms)} \times \text{Constant}}{[\text{Serum Creatinine (in } \mu\text{mol/L})]}$$

Where *Constant* is 1.23 for men and 1.04 for women.

Dosing Interval

Creatinine Clearance (mL/min)	Dosing Interval*
≥50	q12h
10-49	q24-36h
<10	q48h
Hemodialysis (IHD/SLED)	Consult Pharmacy
CVVHD	q24h

These are initial recommendations only and assume relatively stable renal function. Use clinical judgement and account for patient's clinical status and severity of infection. Dose and dosing interval should be adjusted based on trough levels.

Monitoring Recommendations

Serum Creatinine

- Baseline and twice weekly while on vancomycin.

- The risk of nephrotoxicity during vancomycin monotherapy is < 10% when trough concentrations are maintained ≤ 15 mg/L. The incidence of nephrotoxicity is ~10-20% for patients with trough levels maintained between 15-20 mg/L.
- The risk of nephrotoxicity is further increased if any of the following apply:
    - duration of therapy exceeds 14 days
    - the dose per day exceeds 4 g
    - trough vancomycin levels are maintained above 20 mg/L
    - potentially nephrotoxic agents are being used concomitantly – aminoglycosides, amphotericin B, cisplatin, diuretics, NSAIDs, or radiocontrast dye

Vancomycin Levels

- Peak levels are no longer routinely performed due to lack of evidence correlating efficacy and toxicity.
- Trough level should normally be drawn at steady state and should be obtained 30 minutes prior to the next scheduled dose (i.e. pre-4th dose in patients with normal renal function).
- In patients receiving IHD/SLED levels are drawn pre-hemodialysis either before session or with AM labs on days of scheduled session.

Indication for Monitoring Vancomycin Trough Levels

- Duration of treatment expected to be a minimum of 5 days.
- If duration of treatment is greater than 7 days, recheck level weekly as vancomycin may accumulate.
- Treatment of serious or deep-seated infections that may require more aggressive dosing.
- For safety, in patients at risk of nephrotoxicity: concurrent nephrotoxic medications, pre-existing or unstable renal function, age greater than 60, or extremes of weight (under 50 or over 100 kg).

Target Trough Levels

There is no definitive evidence that supports a relationship between trough concentrations and organism eradication or overall patient outcome. The following recommendations are based on pharmacokinetic and pharmacodynamic properties of vancomycin.

Indications	**Target Trough (mg/L)**
Most indications	8-15
Serious or deep-seated Gram-positive infections: • Bacteremia • Meningitis • Pneumonia • Endocarditis • Osteomyelitis	12-18 (Note: more aggressive dosing with trough targets >15 must be balanced with the risk of acute kidney injury which is associated with higher trough concentrations)
IHD/SLED • Levels are drawn pre-hemodialysis (either before session or with AM labs on day of scheduled session)	15-20

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