Health PEI: Provincial Antibiotic Advisory Team Empiric Antibiotic Treatment Guidelines for Sepsis Syndromes in Adults

- COMMUNITY-ACQUIRED PNEUMONIA
- HEALTHCARE-ASSOCIATED PNEUMONIA
- INTRA-ABDOMINAL INFECTION
- URINARY TRACT INFECTION (WITH AND WITHOUT A FOLEY CATHETER)
- CELLULITIS, ERYSIPELAS, AND NECROTIZING FASCIITIS
- DIABETIC FOOT INFECTION
- MENINGITIS AND ENCEPHALITIS
- FEBRILE NEUTROPENIA
- *CLOSTRIDIUM DIFFICILE* INFECTION
- UNKNOWN SOURCE OF INFECTION

General notes for this document:

1) These guidelines recommend antimicrobial therapy for empiric treatment. Antibiotics are to be adjusted based on cultures and clinical response.
2) Severe penicillin allergy: Avoid piperacillin/tazobactam and cephalosporins, but meropenem is reasonable to give in severe sepsis or greater even with history of penicillin/ampicillin anaphylaxis but with close observation. References since 2006 suggest cross reaction ~1% or less. Consult Infectious Disease if in doubt for clarification or alternatives.
3) Renal impairment: Doses of antibiotics are for patients with normal renal function. Dose adjustment of some of the antibiotics may be required for patients with renal impairment.
4) For pregnancy: These guidelines do not specifically address contraindicated antimicrobials (including fluoroquinolones).
5) XDRO = eXtensively drug resistant organisms: typically Gram negative bacteria resistant to all but 2 classes of routinely used antibiotics.
6) References can be found in the provincially approved treatment guidelines for the specific infectious syndrome or available upon request.

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Community-Acquired Pneumonia	(Amoxicillin 1000 mg PO TID OR Ampicillin 2 g IV q6h) + (Azithromycin 500 mg PO/IV q24h OR Clarithromycin 500 mg PO BID) Severe PCN allergy and no previous fluoroquinolone in 90 Days: Levofloxacin 750 mg PO/IV q24h If macroaspiration: ADD Metronidazole 500 mg PO/IV q12h OR USE Amoxicillin/Clavulanate 500/125 mg PO TID (higher risk of Cdiff). Depending on season or travel history: Consider ADDING Oseltamivir 75 mg PO BID	Ceftriaxone 2 g IV q24h + (Azithromycin 500 mg IV q24h OR Levofloxacin 750 mg IV q24h) If macroaspiration, antibiotics in past 3 months, preceding URTI or influenza: Piperacillin/Tazobactam 4.5 g IV q6h + (Azithromycin 500 mg IV q24h OR Levofloxacin 750 mg IV q24h) Severe PCN allergy: Meropenem 1 g IV q8h + (Azithromycin 500 mg IV q24h OR Levofloxacin 750 mg IV q24h) OR Levofloxacin 750 mg IV q24h + Tobramycin 7 mg/kg IV q24h + Metronidazole 500 mg IV q12h (if macroaspiration) MRSA confirmed or suspected: ADD Linezolid 600 mg PO/IV q12h OR Vancomycin 25 mg/kg IV load, then 15 mg/kg IV q12h Depending on season or travel history: Consider ADDING Oseltamivir 75 mg PO BID	Meropenem 1g IV q8h + Levofloxacin 750 mg IV q24h + (Linezolid 600 mg PO/IV q12h OR Vancomycin 25 mg/kg IV load, then 15 mg/kg IV q12h) If fluoroquinolone contraindicated or previous resistance noted: Meropenem 1 g IV q8h + Tobramycin 7 mg/kg IV q24h + Azithromycin 500 mg IV q24h + (Linezolid 600 mg PO/IV q12h OR Vancomycin 25 mg/kg load, then 15 mg/kg IV q12h) Depending on season or travel history: Consider ADDING Oseltamivir 75 mg PO BID

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Healthcare-Associated Pneumonia (hospitalization in an acute care hospital for ≥2 days within the prior 90 days; IV therapy, wound care of IV chemo within the prior 30 days; residence in nursing home or other LTC facility; attendance at a hospital or hemodialysis clinic within the prior 30 days)	Treatment dependent on previous exposure to antibiotics in 90 days (avoid using an antibiotic from the same class) Ceftriaxone 2 g IV q24h (if macroaspiration ADD Metronidazole 500 mg PO/IV q12h) OR Levofloxacin 750 mg PO/IV q24h (if macroaspiration ADD Metronidazole 500 mg PO/IV q12h) OR Amoxicillin/Clavulanate 500/125 mg PO TID If previous XDRO[5]: Ertapenem 1 g IV q24h (doesn't cover *Pseudomonas spp.)* Depending on season or travel history: Consider ADDING Oseltamivir 75 mg PO BID Swab for MRSA (nasal/rectal/throat) as necessary	[Piperacillin/Tazobactam 4.5 g IV q6h OR Meropenem 1 g IV q8h (if severe PCN allergy or previous XDRO[5])] + (Levofloxacin 750mg IV q24h OR Ciprofloxacin 400mg IV q8h if > 70kg, q12h otherwise) MRSA confirmed or suspected: ADD Linezolid 600 mg PO/IV q12h OR Vancomycin 25 mg/kg IV load, then 15 mg/kg IV q12h If fluroquinolone contraindicated or previous resistance noted: Substitute Levofloxacin or Ciprofloxacin with Tobramycin 7 mg/kg IV q24h unless *Legionella* suspected. Depending on season or travel history: Consider ADDING Oseltamivir 75 mg PO BID Swab for MRSA (nasal/rectal/throat) as necessary	Meropenem 1 g IV q8h + Ciprofloxacin 400 mg IV q8h + (Linezolid 600 mg PO/IV q12h OR Vancomycin 25 mg/kg IV load, then 15 mg/kg IV q12h) If Ciprofloxacin contraindicated or previous resistance noted: Substitute Ciprofloxacin with Tobramycin 7 mg/kg IV q24h unless *Legionella* suspected. Depending on season or travel history: Consider ADDING Oseltamivir 75 mg PO BID Swab for MRSA (nasal/rectal/throat) as necessary

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Intra-Abdominal (Source control critical for almost all infections)	Antibiotic Naïve: Cefoxitin 2 g IV q6h + Metronidazole 500 mg PO/IV q12h Non-severe PCN allergy: Ceftriaxone 2 g IV q24h + Metronidazole 500 mg PO/IV q12h Failed previous antibiotics or acquired after 7 days in hospital: Ertapenem 1 g IV q24h (as long as no history of *Pseudomonas spp.*) OR Piperacillin/Tazobactam 4.5 g IV q6h (as long as no history of XDRO[5] / ESBL) Severe PCN allergy: Levofloxacin 750 mg PO/IV q24h + Metronidazole 500 mg PO/IV q12h + Tobramycin 7 mg/kg IV x 1 dose MRSA confirmed or suspected: ADD Vancomycin 25 mg/kg IV load, then 15 mg/kg IV q12h	Piperacillin/Tazobactam 4.5 g IV q6h + Tobramycin 7 mg/kg IV x 1 dose Severe PCN allergy: Meropenem 1 g IV q8h OR Levofloxacin 750mg IV q24h + Vancomycin 25 mg/kg IV load, then 15 mg/kg IV q12h + Tobramycin 7 mg/kg IV q24h + Metronidazole 500 mg IV q12h Ascending cholangitis or *Enterococcus spp.* in blood or MRSA: ADD Vancomycin 25 mg/kg IV load, then 15 mg/kg IV q12h	Piperacillin/Tazobactam 4.5 g IV q6h + Tobramycin 7 mg/kg IV q24h + Vancomycin 25 mg/kg IV load, then 15 mg/kg IV q12h Severe PCN allergy: Meropenem 1 g IV q8h + Tobramycin 7 mg/kg IV q24h + Vancomycin 25 mg/kg IV load, then 15 mg/kg IV q12h Ascending cholangitis or perforation: Consider ADDING Caspofungin 70 mg IV first dose then 50 mg IV q24h

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Urinary Tract Infection (for complete treatment recommendations refer to PAAT UTI Empiric Treatment Guidelines)	In absence of Indwelling Foley Catheter or Urinary Stent		
	Ampicillin 1 g IV q6h + Tobramycin 5 mg/kg IV q24h OR Ceftazidime 1 g IV q8h OR Ciprofloxacin 400 mg IV q12h or 500 mg PO BID + (Tobramycin 5 mg/kg IV x 1 dose OR Ceftriaxone 1 g IV x 1 dose)	Piperacillin/Tazobactam 4.5 g IV q6h + Ciprofloxacin 400 mg IV q12h Severe PCN allergy: Meropenem 1 g IV q8h + Ciprofloxacin 400 mg IV q12h	Meropenem 1 g IV q8h + [Tobramycin 7 mg/kg IV q24h OR Ciprofloxacin 400 mg IV q12h (renal sparing)]
	In presence of Indwelling Foley Catheter or Urinary Stent (Catheter should be removed or changed)		
	Piperacillin/Tazobactam 4.5 g IV q6h OR Meropenem 1 g IV q8h If previous culture (90d) or stat Gram points to yeast, *Enterococcus spp.* or MRSA: ADD appropriate therapy.	Meropenem 1 g IV q8h + Vancomycin 25 mg/kg IV load, then 15 mg/kg IV q12h + Fluconazole 400 mg IV first dose then 200 mg IV q24h If previous growth of *P. aeruginosa* in the last 90 days: ADD Ciprofloxacin 400 mg IV q12h (renal sparing) OR Tobramycin 7 mg/kg IV q24h	Meropenem 1 g IV q8h + [Tobramycin 7 mg/kg IV q24h OR Ciprofloxacin 400 mg IV q12h (renal sparing)] + [Vancomycin 25 mg/kg IV load, then 15 mg/kg IV q12h OR Linezolid 600 mg PO/IV q12h (if VRE is a concern)] + (Fluconazole 400 mg IV first dose then 200 mg IV q24h OR Amphotericin B (Fungizone®) 0.5 – 0.7 mg/kg IV q24h (if significant renal impairment consult Infectious Disease)

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Cellulitis, Erysipelas and Necrotizing Fasciitis (for complete treatment recommendations refer to PAAT SSTI Empiric Treatment Guidelines) **Fournier's gangrene** (pelvic/genital area gangrene) suspected: same treatment as Severe Sepsis	**Exceptions:** Human and animal bites, fresh water, salt water contact, or concern for *Pseudomonas spp.* "Sneakers" ARE NOT covered below. Cefazolin 2 g IV x 1 dose then 1 g (<70kg) or 2 g (≥70kg) IV q8h If severe PCN allergy or MRSA suspected: Vancomycin 25 mg/kg IV load, then 15 mg/kg IV q12h If wound foul smelling: ADD Metronidazole 500 mg PO/IV q12h for anaerobic coverage	Clindamycin 900 mg IV q8h + Piperacillin/Tazobactam 4.5 g IV q6h (administer Clindamycin rapidly first or at the same time) Severe PCN allergy: Clindamycin 900 mg IV q8h + Meropenem 1 g IV q8h (administer Clindamycin rapidly first or at the same time) MRSA confirmed or suspected: ADD Vancomycin 25 mg/kg IV load, then 15 mg/kg IV q12h Consider IVIG for necrotizing fasciitis (1 g/kg day 1 and 0.5 g/kg days 2 and 3) if suspected or known *Staphylococcus aureus* or Group A Streptococcus infection.	Clindamycin 900 mg IV q8h + Meropenem 1 g IV q8h (administer Clindamycin rapidly first or at the same time) Source control critical. Consider STAT consults to Surgery and Infectious Disease. If Infectious Disease opinion not readily available: ADD Vancomycin 25 mg/kg IV load, then 15 mg/kg IV q12h Consider IVIG for necrotizing fasciitis (1 g/kg day 1 and 0.5 g/kg days 2 and 3) if suspected or known *Staphylococcus aureus* or Group A Streptococcus infection.

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Diabetic Foot Infection (for complete treatment recommendations refer to PAAT SSTI Empiric Treatment Guidelines)	Cefazolin 1 g (<70kg) or 2 g (≥70kg) IV q8h OR Ceftriaxone 1 g (<70kg) or 2 g (≥70kg) IV q24h MRSA suspected: ADD TMP/SMX 1-2 DS tablets PO BID MRSA confirmed or severe PCN allergy: Vancomycin 25 mg/kg IV load, then 15 mg/kg IV q12h. STAT Gram stain of ulcer to exclude significant Gram negatives. If antibiotics in past 3 months or foul smell and NOT *Pseudomonas spp*.: (Ceftriaxone 1 g (<70kg) or 2 g (≥70kg) IV q24h + Metronidazole 500 mg PO/IV q12h) OR Ertapenem 1 g IV q24h MRSA confirmed or suspected: ADD Vancomycin 25 mg/kg IV load, then 15 mg/kg IV q12h Severe PCN allergy: consult ID If *Pseudomonas spp.* a concern (e.g. previous *Pseudomonas*, green exudate, severe immune deficiency) : Piperacillin/Tazobactam 4.5 g IV q6h MRSA confirmed or suspected: ADD Vancomycin 25 mg/kg IV load, then 15 mg/kg IV q12h Severe PCN allergy: consult ID	Piperacillin/Tazobactam 4.5 g IV q6h + Vancomycin 25 mg/kg IV load, then 15 mg/kg IV q12h Severe PCN allergy, known ESBL, foreign travel in past year or antibiotic failure: Meropenem 1 g IV q8h + Vancomycin 25 mg/kg IV load, then 15 mg/kg IV q12h	Meropenem 1 g IV q8h + [Tobramycin 7 mg/kg IV q24h OR Ciprofloxacin 400 mg IV q12h (renal sparing)] + (Vancomycin 25 mg/kg IV load, then 15 mg/kg IV q12h OR Daptomycin* 8-10 mg/kg IV q24h) Source control critical. Consider STAT consults to Orthopedics and Infectious Disease. *Daptomycin use is limited to patients having a true allergy to Vancomycin IV or upon the opinion of an Infectious Disease consultant.

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Meningitis and Encephalitis	For Meningitis: Dexamethasone 10 mg IV q6h x 4 days Give Dexamethasone 15-20 minutes before, or with, the first dose of antibiotics. Do not give Dexamethasone if: unable to meet the above timing recommendations OR recent neurosurgery. Stop Dexamethasone if no evidence of *Streptococcus pneumoniae* Ceftriaxone 2 g IV q12h + Vancomycin 25 mg/kg IV load, then 15 mg/kg IV q12h ADD Ampicillin 2 g IV q4h if septic shock or refractory septic shock, immunocompromised, alcoholic, pregnant, or > 50 years of age Recent neurosurgery: Ceftazidime 2 g IV q8h + Vancomycin 25 mg/kg IV load, then 15 mg/kg IV q12h ADD Metronidazole 500 mg IV q8h if Septic shock. Consider infectious disease consultation. Severe PCN allergy: Meropenem 2 g IV q8h + Vancomycin 25 mg/kg IV load, then 15 mg/kg IV q12h Encephalitis (including new onset seizures): see above and ADD Acyclovir 10 mg/kg IV q8h		

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Febrile Neutropenia (And not associated with another suspected source) Consider Medical Oncology Consult for all potential admissions.	<u>Admit:</u> Ceftazidime 2g IV q8h OR Piperacillin/Tazobactam 3.375 g IV q6h (< 70 kg) OR 4.5 g IV q6h (≥ 70 kg) ADD Vancomycin 25 mg/kg IV load, then 15 mg/kg IV q12h after blood cultures if: 1) severe mucositis; 2) MRSA colonized; 3) clinically apparent serious, catheter-related infection; 4) pneumonia; 5) No improvement in 3-4 days Severe PCN allergy: Obtain blood cultures x 2 START Ciprofloxacin 400 mg IV q12h and consult Med Onc. or Infectious Disease for other antibiotic suggestions <u>Rapid outpatient protocol:</u> (Page Medical Oncologist or covering Associate on-call to facilitate outpatient follow-up) 1) Defined as "low risk" 2) no previous fluoroquinolone in 90 days 3) no recent history of resistant organisms 4) no penicillin allergy (Consult if PCN allergy) Ciprofloxacin 750 mg PO BID + Amoxicillin/Clavulanate 500/125 mg PO TID	Piperacillin/Tazobactam 4.5 g IV q6h PCN allergy or ESBL: Meropenem 1 g IV q8h Recent history of resistant *Pseudomonas aeruginosa*: ADD Tobramycin 7 mg/kg IV x 1 dose ADD Vancomycin 25 mg/kg IV load, then 15 mg/kg IV q12h after blood cultures if: 1) severe mucositis; 2) MRSA colonized; 3) clinically apparent serious, catheter-related infection; 4) pneumonia; 5) No improvement in 3-4 days ADD Caspofungin 70 mg IV first dose then 50 mg IV q24h if no improvement in 4-5 days	Meropenem 1 g IV q8h + Tobramycin 7 mg/kg IV q24h + Vancomycin 25 mg/kg IV load, then 15 mg/kg IV q12h. ADD Caspofungin 70 mg IV first dose then 50 mg IV q24h if: 1) refractory septic shock; 2) septic shock for greater than 72 hours. (Consult Inf. Dis. or Med Onc before starting Amphotericin B liposomal.)

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Clostridium difficile (for complete treatment recommendations refer to PAAT Cdiff Empiric Treatment Guidelines) Revised Aug 2019 Next review 2024	**AND** **(specifically for C diff):** **WBC ≥ 15 <u>or</u> Albumin <30** Vanco 125 mg PO q6h x 14 days (once stabilized, can switch to QID dosing)	• Vancomycin 500 mg PO/NG q6h x 3 days, **<u>then</u>** Vancomycin 125 mg PO/NG q6h x 11 days (can continue to 2nd recurrence strategy if indicated. See PAAT Cdiff empiric treatment guidelines) **<u>AND</u>** • Metronidazole 500 mg IV q8h (administer until no longer critically ill) **<u>AND</u>** Consider surgical consult	Investigate alternative diagnosis and: • For toxic megacolon: consult surgery for possible subtotal colectomy or loop ileostomy. • Vancomycin 500 mg (PO/ NG) q6h **AND** • Metronidazole 500 mg IV Q8h **AND** Consult infectious disease and surgery ASAP
	Abd flat plate to rule out toxic megacolon, repeat in 3 days if no clinical improvement		
	<u>If presence of ileus</u>: add **Vancomycin 500 mg PR q6h** (500 mg in 500 mL N/S by retention enema via Foley catheter held for 3 hours)		
Unknown (excluding Central Nervous System infection)	Ceftriaxone 2 g IV q24h + Levofloxacin 750 mg PO/IV q24h + Metronidazole 500 mg PO/IV q12h OR Piperacillin/Tazobactam 4.5 g IV q6h	(Piperacillin/Tazobactam 4.5 g IV q6h OR Meropenem 1g IV q8h) + Vancomycin 25 mg/kg IV load, then 15 mg/kg IV q12h Recent antibiotic use or suspected XDRO[5]: ADD Tobramycin 7 mg/kg IV q24h Consider Infectious Disease opinion	Meropenem 1 g IV q8h + Ciprofloxacin 400 mg IV q12h + Tobramycin 7 mg/kg IV x 1 dose + [Vancomycin 25 mg/kg IV load, then 15 mg/kg IV q12h OR Linezolid 600 mg PO/IV q12h (if VRE is a concern)] Consider Infectious Disease opinion