Health PEI: Provincial Antibiotic Advisory Team Skin & Soft Tissue Infection Empiric Treatment Guidelines

Syndrome	Prevention Foot Care. Treatment of tinea pedis. Control of eczema. MRSA decolonization (selective) Major Hurdles Need for systemic vs topical vs just abscess drainage. Travel outside Canada, IV drug use, hobbies (fish tank), surgery, previous (90 days) or current antibiotic use, vasculopathy or diabetes, controlling dependent edema. MRSA risk factors. Insect bite precautions Considerations Underlying osteomyelitis, foreign body, insect bite, bacteremia, necrotizing fasciitis. Non-infectious: DVT, venous stasis, drug reactions, inflammatory or neoplastic conditions.	Non-SIRS / Pre-SIRS	SIRS / Sepsis (2 of 4) >38.3<36.0; HR>90; RR>20 or PaCO2<32; WBC <4 >12 or Bands	Severe Sepsis (1 of 7+) Mottled, anuria, Lactate>2, Plt<100, DIC, ARDS, fastΔLOC…	Septic Shock (Pressors) Refractory Septic Sh. (More Pressors)
Cellulitis / Erysipelas/ Necrotizing Fasciitis If **Fournier's gangrene** (pelvic / genital area gangrene) suspected: same treatment as severe sepsis. **PLEASE NOTE:** Redness and edema increase for 1-2 days after appropriate antibiotic use due to toxin release (yet pain, systemic symptoms, if present, will have improved).		One of the following three: Cephalexin 500 mg PO QID Cloxacillin 500 mg PO QID Cefadroxil 500-1000 mg PO BID (if drug coverage available) If in ER, going home, and poor tissue penetration is a concern: load with either Cefazolin 2g IV x1 + Probenecid 2g PO x 1 (avoid if CrCl <40) OR Ceftriaxone 1-2g IV x 1 If concern for MRSA: Add TMP/SMX 1-2 DS tablets PO BID If severe PCN allergy: Clindamycin 300 mg PO QID + (TMP/SMX 1-2 DS tablets PO BID OR Doxycycline 200 mg PO x 1 then 100 mg PO BID)	Cefazolin 2g IV x 1 dose then 1g (<70kg) or 2g (≥70kg) IV q8h If outpatient: Cefazolin 2g IV + Probenecid 1-2g PO q24h (avoid if CrCl <40) OR Ceftriaxone 2g IV x 1 dose then 1g (<70kg) or 2g (≥70kg) IV q24h If severe PCN allergy or MRSA suspected: Vancomycin 25 mg/kg IV load, then 15 mg/kg IV q12h or consult ID for outpatient options. If 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) If severe PCN allergy: see septic shock column. If MRSA confirmed or suspected: ADD Vancomycin 25 mg/kg IV load then 15 mg/kg IV q12h	Source control critical. Consider STAT consults to Surgery and Infectious Disease. Clindamycin 900 mg IV q8h + Meropenem 1g IV q8h (Administer Clindamycin rapidly first or at the same time) If Infectious Disease opinion not readily available: ADD Vancomycin 25 mg/kg IV load, then 15 mg/kg IV q12h
		Human or animal Bites: Amox/Clav 500/125 mg PO TID Salt water: Doxycycline 200 mg PO x 1 then 100 mg PO BID Fresh water: Ciprofloxacin 500 mg PO BID Sneaker associated: consider Ciprofloxacin 500 mg PO BID		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	

RE: Penicillin allergy: Avoid Piperacillin/Tazobactam, but Meropenem is reasonable to give in severe sepsis or greater even with history of anaphylaxis. Consult ID if in doubt.

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Logic for guidelines:

1. Pathogens in typical cellulitis can include β-hemolytic Streptococcus (Group A, B, C, and G) with Group B more common with diabetics, PVD, recurrent infections, trauma/excoriation, and lymphedema. *Staphylococcus aureus* in non-immunocompromised patients typically presents with folliculitis or trauma leading to an abscess. Community acquired MRSA can occasionally present as streptococcal disease above. Outside of water exposure, bites, burns, or trauma (including through footwear), Gram-negatives do not have a significant role in an immunocompetent host. Ceftriaxone was previously thought to be a poor choice, but has reasonable *Staphylococcus aureus* coverage (except if MRSA or if bacteremia, endocarditis, or osteomyelitis is a concern). Dosage for ceftriaxone may need to be modified (increased frequency and or dose).
2. Macrolides (e.g. clarithromycin, azithromycin) are listed as a treatment option in penicillin allergic patients with mild cellulitis/erysipelas in a number of other references (Johns Hopkins, Sanford, Capital Health NS). However, **due to significant resistance in PEI, macrolides are not included as an option in these empiric treatment guidelines**.
3. In non-immunocompromised cases and patients without systemic toxicity, an abscess with less than 2 cm of surrounding erythema can be treated conservatively with drainage, soaks, and topical Bactroban® (mupirocin) and close follow-up.
4. Clindamycin has very good Group A Streptococcus coverage (91%) yet for *Staphylococcus aureus* infections the susceptibility rate is 68% (Health PEI Antibiogram 2012). Therefore in severe penicillin allergic patients with minor disease, Clindamycin plus additional anti-Staphylococcal treatment (TMP/SMX or doxycycline) is recommended. However, clindamycin is one of the antibiotics associated with the highest risk of *Clostridium difficile* infection (CDI). Buffie et al. demonstrated that a single dose of clindamycin markedly reduces the diversity of the intestinal microbiota of mice for at least 28 days, with an enduring loss of ~90% of normal microbial taxa from the cecum which resulted in sustained susceptibility to Cdiff-induced colitis. Caution is recommended when using clindamycin, especially if the patient has a history of a previous CDI.
5. A once daily cefazolin/probenecid combination is convenient to administer as outpatient antimicrobial therapy for empiric treatment of moderate SSTI. Pharmacokinetic data and available clinical information suggests that a cefazolin/probenecid regimen is effective for treatment of SSTI. Probenecid has been shown to inhibit the tubular secretion of cefazolin, thereby prolonging the half-life and serum concentration of cefazolin. Cefazolin/probenecid provides narrow-spectrum antimicrobial coverage, theoretically limiting the development of antimicrobial resistance.[12]
6. In severe sepsis or septic shock, clindamycin is given rapidly first (followed by other recommended therapy) to deactivate toxin production and more readily kill organisms that are in stationary phase. Unless there is an absence of source control, clindamycin as add on therapy should be given for no longer than 3 days.

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Health PEI Physician Reviewers: Dr. Katherine Burleigh, Dr. Scott Cameron, Dr. Greg German, Dr. Ayodeji Harris-Eze, Dr. Edmund Harrison, Dr. Michael Irvine, Dr. Ronald Whalen, Dr. Scott Wotherspoon.

Syndrome:

Diabetic Foot Infection

(Grading using modified IDSA Criteria)

X-ray of ulcer important for management

Confirm swab of ulcer
(Improve sample collection by only targeting infected appearing wounds and after gentle clearing of superficial exudate.)

Prevention: Wound care including debridement, off-loading and appropriate foot wear, and glucose control. Vascular considerations.

Major Hurdles:
Rule out foreign body, fasciitis, septic arthritis, peripheral arterial disease, necrosis or osteomyelitis.
Osteomyelitis suspected if one of:
1. Probe to bone or hard endpoint,
2. ESR >60,
3. Delayed healing of wound,
4. New abnormal bony changes on X-ray.
If suspected then obtain a rapid Infectious Disease opinion.

Non-SIRS / Pre-SIRS

Grade 1: No signs of infection: No systemic therapy needed. Consider topical therapy in borderline cases (see topical therapy box).

Grade 2: Mild local infection (2 or more of): 1. Erythema (>0.5cm but ≤2cm around the ulcer), 2. Local warmth, 3. Local pain/tenderness, 4. Local induration/swelling, 5. Purulent discharge grossly or microbiologically (>1+ WBC on Gram stain).

Topical therapy (see topical therapy box)
AND one of the following five PO antibiotics:
-Cephalexin 500 mg PO QID (if >70kg give 1g for first dose)
-Cloxacillin 500 mg PO QID (if >70kg give 1g for first dose)
-Cefadroxil 500-1000 mg PO BID (if drug coverage available)
-Clindamycin 300 mg PO QID (for severe PCN allergy)
-Amoxicillin/Clavulanate 500/125 mg PO TID [if Gram-negatives or anaerobes (foul smell) a concern]
If MRSA suspected: screen, start therapy above, and monitor closely.
If MRSA colonized or wound positive: ADD TMP/SMX 1-2 DS tablets PO BID

Grade 3: Moderate Infection, Uncomplicated: Grade 2 criteria but erythema ≥ 2 cm or lymphangitis.

No antibiotics in past 90 days and not MRSA:
Cefazolin 2g IV x 1 dose then Cephalexin 500mg PO QID.
If previous antibiotics in past 90 days (but not a fluoroquinolone) then consider ADDING Ciprofloxacin 500 mg PO BID or 400 mg IV q12h.
If foul smell: ADD Metronidazole 500 mg PO/IV q12h.
If severe PCN allergy: Levofloxacin 750 mg PO/IV q24h +/- Metronidazole 500 mg PO/IV q12h

Grade 3: Moderate Infection, Complicated: (septic arthritis, abscess, fasciitis, or osteomyelitis). Obtain culture(s), treat as SIRS/Sepsis (or if fasciitis see Cellulitis chart), obtain specialist opinion.

Grade 4: Severe Infection/Systemic Illness

SIRS / Sepsis (2 of 4) >38.3<36.0; HR>90; RR>20 or PaCO2<32; WBC <4 >12 or Bands	Severe Sepsis (1 of 7+) Mottled, anuria, Lactate>2, Plt<100, DIC, ARDS, fastΔLOC…	Septic Shock (Pressors) Refractory Septic Sh. (More Pressors)
Cefazolin 1g (<70kg) or 2g (≥70kg) IV q8h OR Ceftriaxone 1g (<70kg) or 2g(≥70kg) IV q24h If MRSA suspected: ADD TMP/SMX 1-2 DS tablets PO BID MRSA confirmed or severe PCN allergy: Vancomycin IV (see dosing box). STAT Gram stain of ulcer to exclude significant Gram-negatives.	Piperacillin/ Tazobactam 4.5 g IV q6h + Vancomycin IV (see dosing box) Severe PCN allergy, known ESBL, foreign travel in the past year or antibiotic failure: Meropenem 1 g IV q8h + Vancomycin IV (see dosing box)	Meropenem 1 g IV q8h + [Tobramycin 7 mg/kg IV q24h OR Ciprofloxacin 400 mg IV q12h (renal sparing)] + [Vancomycin IV (see dosing box) OR Daptomycin* 8 – 10 mg/kg IV q24h]. Source control critical. Consider STAT consults to Orthopedics and Infectious Disease.
If antibiotics in past 3 months or foul smell and NOT *Pseudomonas spp.*: (Ceftriaxone 1g (<70kg) or 2g (≥70kg) IV q24h + Metronidazole 500 mg PO/IV q12h) OR Ertapenem 1g IV q24h MRSA confirmed or suspected: ADD Vancomycin IV Severe PCN allergy: consult ID		
If *Pseudomonas spp.* a concern (e.g. previous *Pseudomonas*, green exudate, severe immune def.) Piperacillin/Tazobactam 4.5 g IV q6h MRSA confirmed or suspected: ADD Vancomycin IV Severe PCN allergy: consult ID		

*Daptomycin use is limited to patients having a true allergy to Vancomycin IV or upon the opinion of an Infectious Disease consultant.

Vancomycin dosing:
Vancomycin 25 mg/kg IV load, then 15 mg/kg IV q12h

Selected topical therapy options: Iodosorb®, Bactroban®, dilute vinegar soaks, Dakin's solution (¼ strength). See Logic for indications and recipes.

RE: Penicillin allergy: Avoid Piperacillin/Tazobactam, but Meropenem is reasonable to give in severe sepsis or greater even with history of anaphylaxis. Consult ID if in doubt.

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Logic for guidelines:

1. A multi-disciplinary approach for the treatment of ulcers has been proven to improve outcomes. The team may include: Wound Care Nurses, Vascular Surgery, Orthopedic Surgery, Plastic Surgery, Infectious Disease consultants, Physiatry, Internal Medicine, Orthotists, and Diabetes Educators. Future multidisciplinary guidelines forthcoming.
2. Most diabetic foot infections (DFI) are polymicrobial; however, if patient hasn't recently received antibiotic therapy, they are often monomicrobial and due to either staphylococcal or streptococcal infection. Superficial infections (cellulitis, cellulitis involving blisters and shallow ulcers) are typically caused by *Staphylococcus aureus* or β-hemolytic *Streptococcus* (Group A, B, C, and G). Infections of ulcers that are chronic or previously treated with antibiotics may be caused by aerobic Gram-negative bacilli as well as *S. aureus* or streptococci. Deep tissue infections, osteomyelitis, and gangrene are more often polymicrobial, including aerobic Gram-negative bacilli and anaerobes, but *Staphylococcus aureus* is also common as a single pathogen.[7]
3. Ertapenem has very good *Streptococcus* (except *Enterococcus*), MSSA, anaerobic, and Gram negative coverage except for *Pseudomonas* and *Acinetobacter*. Allowing for once daily therapy as well as preserving some portions of the normal microbiota.
4. Topical therapy options:
    - Iodosorb® (cadexomer iodine) for polymicrobial infections or before culture results known. Apply every 1 to 3 days depending on local effect.
    - Bactroban® (mupirocin) for *Staphylococcus aureus* and/or *Streptococcus spp*.
    - With guidance from infectious disease or enterostomal therapy nurse or other experts consider:
        - Dilute vinegar soaks for *Pseudomonas spp.* infection or colonization [1 tablespoon (15 mL) diluted white vinegar in 250 mL of Normal Saline, Sterile Water or well boiled water] - soak for 5-10 minutes.
        - Dakin's solution (1/4 strength) for highly exudative infected wounds with the need for further debridement as an adjunct to physical debridement. Obtain from local pharmacy. Dakin's solution is contraindicated if vascular insufficiency.

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Provincial Drugs & Therapeutics Committee

Memorandum Version 2

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From: Provincial Drugs & Therapeutics Committee

To: All Island Physicians, Nurse Practitioners, and Pharmacists

Date: April 29, 2014

RE: **Provincial Skin and Soft Tissue Infection Empiric Treatment Guidelines**

The Provincial Antibiotic Advisory Team (PAAT) has developed the attached **Provincial Skin and Soft Tissue Infection (SSTI) Empiric Treatment Guidelines** which were modified and approved by a number of PEI Physician reviewers. The guidelines were approved by the Provincial Drugs & Therapeutics Committee in February, 2014.

The SSTI Empiric Treatment Guidelines follow the same layout as the previously approved and distributed UTI and *Clostridium difficile* infection guidelines. These guidelines contain two tables separated into the following syndromes: 1) cellulitis, erysipelas, necrotizing fasciitis and Fournier's gangrene; 2) diabetic foot infection.

Highlights of cellulitis, erysipelas and necrotizing fasciitis include:

1) Cefazolin is the mainstay routine therapy for inpatients and outpatients when IV therapy is required. When probenecid PO is given 30 minutes before the infusion, q24h dosing is permitted for outpatients.
2) Weight based dosing for cefazolin and ceftriaxone to provide an effective loading dose and optimize efficacy.
3) Clindamycin as a short term adjunct for severe sepsis to synergize with beta-lactam therapy.

Highlights of diabetic foot infection include:

1) Applying international standardized grading of diabetic foot infections.
2) Using narrow therapy targeted to Gram positives for initial episodes in routine cases.
3) Relying on smell of the ulcer, antibiotic use in past 90 days, and microbiology results including screening patients for MRSA.
4) Acclimatizing clinicians to using topical therapies in addition to systemic therapies in collaboration with experts including enterostomal therapy nurses.

Introduced in the guidelines, cefadroxil is a first generation cephalosporin like cephalexin (Keflex®) with the added advantage of twice daily dosing to improve adherence. The approximate cost of a 10-day supply ranges from $30 - $55, depending on the dose. Cefadroxil is not covered under Provincial Pharmacare drug programs.

These guidelines can be found on the following website: www.healthpei.ca/micro

For questions on the Provincial SSTI Empiric Treatment Guidelines, please contact the PAAT co-chairs Greg German (Infectious Disease Consultant and Health PEI Medical Microbiologist; 894-2515; GJGerman@ihis.org) or Jennifer Boswell (Provincial Antimicrobial Stewardship Pharmacist; 894-2587; JLBoswell@ihis.org).