

## Health PEI: Antimicrobial Stewardship Subcommittee Urinary Tract Infection Empiric Treatment Guidelines

Urinary Tract Infection	Non-SIRS / Pre-SIRS		SIRS / Sepsis (2 of 4) >38.3<36.0; HR>90; RR>20 or PaCO <sub>2</sub> <32; WBC <4 >12 or Bands	Severe Sepsis(1 of 7+) Mottled, anuria, Lactate>2, Plt<100, DIC, ARDS, fast Δ LOC	Septic Shock (Pressors) Refractory Septic Sh. (More Pressors)
<p>- Antibiotics are listed in the numerical order of preference.</p> <p>- Tailoring of treatment after susceptibilities are known is highly recommended.</p> <p><b>Major Hurdles</b></p> <ul style="list-style-type: none"> <li>• True symptoms?</li> <li>• Previous antibiotics past 90 days (esp. same class)</li> <li>• Pregnancy</li> <li>• Travel outside of Canada</li> </ul> <p><b>Considerations</b></p> <ul style="list-style-type: none"> <li>• Prostatitis</li> <li>• Vaginitis</li> <li>• PID</li> <li>• Urethritis</li> <li>• Diverticulitis</li> <li>• Appendicitis</li> <li>• GU tuberculosis</li> </ul>	FEMALE CYSTITIS (<6d Symptoms)	EARLY FEMALE PYELONEPHRITIS	In Absence of Indwelling Foley Catheter or Urinary Stent		
	<ol style="list-style-type: none"> <li>1. Nitrofurantoin 100mg BID x 5d (if CrCl &gt; 30 mL/min)</li> <li>2. TMP/SMX 160/800mg BID x 3d**</li> <li>3. Fosfomycin 3g x 1 dose~</li> </ol>	<ol style="list-style-type: none"> <li>1. Levo 750mg x 5d</li> <li>2. Cipro<sup>∞</sup> 500mg BID x 7d</li> <li>3. TMP/SMX 160/800mg BID x 10d</li> <li>4. Cefixime 400mg x 10d^ ( 14 days if SIRS/Sepsis outpatient)</li> </ol>	<ol style="list-style-type: none"> <li>1. Cipro/Levo as per Early Pyelo</li> <li><b>ADD</b> Ceftriaxone 1g x 1 dose</li> <li><b>OR</b> Tobra 5mg/kg x 1 dose</li> </ol> <p>IF previous Cipro resistance or use in past 6 mths</p> <ol style="list-style-type: none"> <li>2. Ampicillin &amp; Ceftazidime</li> <li>3. Pip/Tazo</li> </ol>	Pip/Tazo & Cipro	Mero & Cipro (Renal Sparing) OR Mero & Tobra
	MALE CYSTITIS (<6d Symptoms)	MALE RECURRENT CYSTITIS or EARLY MALE PYELONEPHRITIS	In Presence of Indwelling Foley Catheter or Urinary Stent (Catheter should be removed or changed)		
	<ol style="list-style-type: none"> <li>1. Nitrofurantoin 100mg BID x 5-7d (if CrCl &gt; 30 mL/min) – reassess after treatment</li> <li>2. TMP/SMX 160/800mg BID x 7d**</li> <li>3. Fosfomycin 3g x 2 doses~ (give 2<sup>nd</sup> dose 3 days after 1<sup>st</sup> dose)</li> </ol>	<ol style="list-style-type: none"> <li>1. Levo 750mg x 5d</li> <li>2. Cipro<sup>∞</sup> 500mg BID x 7d</li> <li>3. TMP/SMX 160/800mg BID x 14d</li> <li>4. Cefixime 400mg x 10d^ ( 14 days if SIRS/Sepsis outpatient)</li> </ol>	<ol style="list-style-type: none"> <li>1. Pip/Tazo</li> <li>2. Meropenem</li> </ol> <p>If <i>previous culture (in past 90d) or stat gram points to yeast, Enterococcus or MRSA: add appropriate therapy.</i></p>	Mero, Vanco & Fluconazole	As above, PLUS:  ADD Vanco (or Linezolid if VRE is a concern)  ADD Fluconazole, or Voriconazole, or Amphotericin-B

\*\*In sulfa allergic patients (no hx of Stevens-Johnson Syndrome) consider using trimethoprim alone, with monitoring.

~ Currently an open benefit on the PEI Formulary for all nursing home patients. Special authorization required for all others.

^ Currently not a benefit on the PEI Formulary      ∞ Not to suggest an endorsement of a particular brand

**Allergies:** A patient with a reported penicillin/cephalosporin allergy may still be able to receive a beta-lactam antimicrobial. Cross-reactivity between penicillin and cephalosporins is due to similarities in the side chains and not similarities in the beta-lactam ring structure as previously suspected. Please see the Beta-Lactam Allergy Management Guidelines and Beta-Lactam Cross Allergy Matrix for further information. <http://www.healthpei.ca/src/microbiology>.

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## Prevention of Recurrent UTI

Best Available Evidence (start here)	Some Evidence	Weak or No Evidence
<b>1. Remove indwelling Foley catheter</b> <ul style="list-style-type: none"> <li>only catheterize when absolutely necessary</li> <li>some studies show benefit using bladder scanners to detect the need for catheters<sup>16</sup></li> </ul>	<b>1. Probiotics</b> <ul style="list-style-type: none"> <li><b>PO:</b> mixed study results for prevention</li> <li><b>PV:</b> vaginal delivery of <i>Lactobacillus</i> shows promise<sup>17</sup> (dosed on off days of vaginal estrogen tx)</li> </ul>	<b>1. Cranberry juice/pineapple juice/D-Mannose</b> <ul style="list-style-type: none"> <li>mixed study results, no definitive efficacy shown</li> <li>Juices likely have little harmful effect in <u>non-diabetic</u> patients</li> </ul>
<b>2. Estrogenized vaginal mucosa</b> (Vagifem®, Premarin®) <ul style="list-style-type: none"> <li>used for post-menopausal women only</li> <li>doses used in studies were same as for vaginal atrophy</li> <li>if not effective, consider swabbing vaginal mucosa for lactobacilli/yeast*</li> </ul>	<b>2. Controlled diabetes</b> <ul style="list-style-type: none"> <li>some studies suggest tighter glucose control may help prevent recurrences</li> </ul>	<b>2. Postcoital voiding</b> (see below for prophylaxis) <ul style="list-style-type: none"> <li>no reduced risk shown</li> <li>unlikely to be harmful</li> </ul>
	<b>3. Renal stone investigation &amp; extraction</b> <ul style="list-style-type: none"> <li>has been shown to help prevent recurrent infections in approx 50% of patients with asymptomatic renal stones<sup>18</sup></li> </ul>	<b>3. Liberal fluid intake</b> <ul style="list-style-type: none"> <li>no reduced risk shown</li> <li>unlikely to be harmful</li> </ul>

\*If negative, may consider a trial of three times weekly vaginal estrogen (off-label use)

**Expert opinion:** Timed voiding and/or double voiding can be helpful as they promote complete emptying and a reduction in urine stasis/dwell time.

### Prophylactic antibiotics

- Should only be used for **3-6 months without Infectious Disease or Urology involvement**
- For patients experiencing 4 or more symptomatic UTIs within a 12 month period, **and only after non-antimicrobial measures have been unsuccessful**. Urological referral for consideration of cystoscopy is also recommended (GP may order an ultrasound on referral).
- Studies have only assessed benefit for 1-2 years
- Choice of abx should be based upon susceptibility patterns from previous UTIs
  - Ciprofloxacin, moxifloxacin and amoxicillin-clavulanic acid should NOT be used for chronic prophylaxis

Three different approaches exist (all have shown to be effective in managing recurrences):

- Self-initiated treatment** – self-diagnosis and treatment with a short course of an antimicrobial. Instruct patient to call their medical provider if symptoms do not resolve within 48 hours of starting therapy.
- Postcoital prophylaxis** (women) – a single postcoital antimicrobial dose (for women whose UTIs appear related to sexual intercourse)
- Continuous prophylaxis** – regimens include:
  - TMP/SMX 40/200mg po daily
  - Fosfomycin 3g po every 10 days (typical frequency)
  - Nitrofurantoin 50 - 100mg po daily (NOT MacroBID) - not recommended for long-term use in those > 65 due to pulmonary fibrosis
  - Cephalexin 125 - 250mg po daily
  - Trimethoprim 100mg daily (sulfa allergic patients)

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### Logic for guidelines:

1. The oral antibiotic that urinary isolates of *E. coli* in PEI have the highest susceptibility to is nitrofurantoin. As per the Health PEI Antibigram 2016, the local susceptibilities of urine isolates of *E. coli* to select antibiotics are as follows: nitrofurantoin 94%, TMP/SMX 82%, cefixime 94%, amox/clav 86%, ciprofloxacin 85%. Cephalexin data (59%) is difficult to interpret due to changes in internationally set breakpoints for susceptibility. Yet cephalexin does concentrate in the urine, which would increase its effectiveness beyond 59%.
2. Avoid collateral damage: nitrofurantoin does not have a serious effect on other bacteria outside the urinary tract, TMP/SMX has lower *C. difficile* risk than levofloxacin, ciprofloxacin, or amox/clav.
3. Resistance to levofloxacin and ciprofloxacin is greater than 10% which necessitates conservation (limit use in non-serious infections or prophylaxis) and supplementation (addition of a second agent is recommended for the treatment of serious infections). IDSA guidelines recommend, for treatment of pyelonephritis, when there is >10% fluoroquinolone resistance, an initial one-time IV/IM dose of a long-acting antimicrobial (such as ceftriaxone or an aminoglycoside) be given. Furthermore, fluoroquinolone toxicity is an increasing concern such as retinal detachment, ligament tears in the elderly or on steroids, and QT-interval prolongation (especially in patients with other risk factors). Moxifloxacin should never be used to treat a UTI because it does not concentrate in the urine.
4. Gentamicin vs tobramycin: gentamicin is considered more nephrotoxic than tobramycin and tobramycin has a greater spectrum of activity for empiric treatment of UTIs
5. Shorter durations (ex: TMP/SMX x 3d) can be used even in those >65 years of age (including Nursing Home patients) as long as there is close monitoring and the patient has had less than or equal to 6 days of symptoms. Shorter durations have been shown to decrease resistance and the risk of *C. difficile*.

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