

SETON Network Notes

A Publication of the Pharmacy and Therapeutics Committee

New Inpatient Adult Urinary Tract Infection/Pyelonephritis Treatment Pathway

Monica Dorobisz, PharmD, PGY1 Pharmacy Resident
Kate Shea, Infectious Diseases PharmD

A new clinical pathway for treatment of urinary tract infections (UTIs)/pyelonephritis was recently approved by the Anti-Infective Monitoring Subcommittee (AIMS) for use throughout the Seton Family of Hospitals (SFH). This pathway will soon be available on the SFH intranet under "Antimicrobial Management" in the "Clinical Practice" section. Clinical pathways are institution-specific evidence-based guidelines that incorporate local microbiology and resistance patterns which help guide prescribers through the diagnosis and treatment of the infection as well as proper streamlining once an organism is identified with susceptibilities reported. The recommendations found within the SFH pathways are based on current literature as well as local susceptibility patterns; therefore, may differ slightly from published or other institutions' guidelines. The use of clinical pathways has been shown to improve antimicrobial utilization in various institutions. Decreased mortality and possibly decreased emergence of resistant pathogens has been associated with use of clinical pathways in treatment of patients with infection. As the antimicrobial stewardship program at SFH expands, more clinical pathways will be developed and approved for use by AIMS. It is important to note that these pathways are not policies or protocols; they are made as a guide to help with making appropriate treatment choices and clinical judgment should always play a significant role.

UTI/pyelonephritis was chosen as the first pathway to be developed to help decrease key players in antimicrobial resistance: the third-generation cephalosporins (e.g., ceftriaxone) and fluoroquinolones (e.g., ciprofloxacin). Ceftriaxone and ciprofloxacin are currently the most commonly prescribed antibiotics for UTIs throughout the SFH network; however, their use should be discouraged due to their substantial potential in causing "collateral damage," as well as the enhanced activity and/or higher urine concentrations achieved with the use of the SFH-preferred agents. "Collateral Damage" is a term used in infectious diseases literature and is defined as an increase in the colonization or infection with more resistant organisms resulting from the use of specific antimicrobial agents. Prior use of third-generation cephalosporins and fluoroquinolones is linked to the prevalence of multi-drug resistant organisms including vancomycin-resistant enterococcus (VRE), methicillin-resistant *Staphylococcus aureus* (MRSA) and extended-spectrum β -lactamase-producing organisms (ESBLs). The third-generation cephalosporins in particular are capable of inducing or increasing the selection high-level AmpC β -lactamase production; therefore, should be avoided in the treatment of these organisms. AmpC β -lactamase-producing organisms including *Serratia spp.*, *Pseudomonas spp.*, *Acinetobacter spp.*, *Citrobacter spp.*, *Enterobacter spp.* and *Morganella spp.* (SPACEM organisms) typically produce this β -lactamase intrinsically at low levels and may be induced to high-level production by exposure to certain antimicrobial agents (e.g., ceftriaxone). *Pseudomonas spp.* and *Acinetobacter spp.* are much less likely to be induced to produce this high-level β -lactamase; however, typically can possess many other mechanisms of resistance.

The beginning of the UTI/pyelonephritis pathway focuses on diagnosis and appropriate indications for antimicrobial treatment. Diagnosis of patients with a UTI should only be made based on the presence or absence of symptoms and not simply on the presence of bacteria in the urine. Most patients with asymptomatic bacteriuria do not have an indication for antibiotics, even with the presence of pyuria. For example, most patients with a urine catheter will have bacteria cultured in their urine at some point, and just the insertion and presence of the catheter itself can cause WBC's, or pyuria, to be present in the urine due to inflammation. These patients will typically not require treatment with antibiotics if they do not present with symptoms of infection and should simply have their urine catheter removed or changed. A small subset of patients with asymptomatic bacteriuria will require treatment with antibiotics regardless of the presence or absence of symptoms. Antibiotic treatment is required in pregnant women, patients undergoing urologic procedures or transurethral resection, post-transplant or immunosuppressed patients, and may be considered in women with catheter-associated bacteriuria persisting 48 hours after catheter removal. Patients with asymptomatic bacteriuria or those presenting with symptoms should have their urine catheter removed or

changed if one is present, followed by a urinalysis and urine culture. Blood cultures should be drawn in patients who present with systemic symptoms.

Symptomatic patients, as well as those falling into the category requiring treatment for asymptomatic bacteriuria, should be treated with antibiotics. To choose an appropriate empiric therapy, it is imperative to first assess whether patients are at risk for multi-drug resistant organisms (MDRs), as the antibiotic choice will differ depending on the presence of risk factors. Assessing for these risk factors holds true for any infection, not solely for the treatment of UTIs and pyelonephritis. Risk factors include: 1) broad spectrum antibiotic therapy in the last 90 days (including third-generation cephalosporins or fluoroquinolones), 2) family member with infection involving MDR pathogen, 3) current hospitalization of at least five days, 4) nursing home or long-term care residence 5) hospitalized for two days within the last 90 days, 6) long-term dialysis within 30 days and 7) home infusion treatment. Patients who do not possess any of these risk factors will likely have a UTI caused by a less-resistant *E. coli* (most frequently isolated organism), *Proteus spp.* or *Klebsiella spp.* The empiric treatment recommendation for these patients is cefazolin, which achieves such high urine concentrations that even strains reported as *intermediate* to cefazolin should be considered appropriate treatment for a UTI. Ampicillin/sulbactam +/- gentamicin should be used if a Gram-positive organism is suspected, such as *Enterococcus spp.* in pregnant patients. Ampicillin is the drug of choice for *Enterococcus spp.* when susceptible, while gentamicin covers Gram-negative organisms. Patients who are critically ill or possess any of the risk factors for MDRs will not only be at risk for infection with organisms such as *Citrobacter*, *Enterobacter* and *Pseudomonas spp.*, but also more resistant strains of the same organisms as those not at risk. The recommendation for these patients is to receive empiric treatment with either cefepime or piperacillin/tazobactam. Both of these drugs are appropriate empiric treatment options; however, cefepime may have a slight advantage because it is nearly 100% renally eliminated, provides enhanced stability against AmpC-producing organisms and lacks the unnecessary anaerobic coverage possessed by piperacillin/tazobactam. In the treatment of UTIs/pyelonephritis in patients with a true β -lactam allergy, defined as anaphylaxis (typically occurs in less than 0.015% of the population), empiric options include aztreonam, gentamicin or tobramycin, or ciprofloxacin. The cross-reactivity of a penicillin allergy with cephalosporins is so low (approximately 5%) that typically cephalosporins can still be used for treatment in patients whose reaction is non-anaphylactic (e.g., rash).

Once an organism is identified on culture, it is very important to streamline therapy to the most narrow spectrum agent possible. The SFH treatment pathway provides both IV and PO options with the most narrow-spectrum agents typically listed first. To choose an antibiotic, the susceptibility report should be reviewed and the list within the pathway typically can be followed in descending order until a susceptible drug is found. For example, if a pan-sensitive *E. coli* is reported, the narrowest spectrum agent would be ampicillin IV/amoxicillin PO, if resistant to ampicillin, the next agent to evaluate is cefazolin IV/cephalexin PO. Oral antimicrobials are also available on the pathway as options for the treatment of UTIs caused by ESBL-producing organisms once susceptibility is verified; however, these agents should be limited to treatment of infections within the urinary tract due to the high urinary concentrations achieved as opposed to non-urinary sites. For all other sites, meropenem should be considered first-line therapy in the treatment of infections caused by ESBLs.

Finally, the duration of antibiotic therapy is determined based on classifications of uncomplicated UTI, complicated UTI or pyelonephritis. Uncomplicated UTIs are defined as cystitis in non-pregnant women of child-bearing age. These patients can be treated for three days (quinolones and tmp/smx) to five days (β -lactams and nitrofurantoin). However, if these women possess any risk factors that would classify a UTI as complicated, including diabetes mellitus, pregnancy, elderly, indwelling catheter, immunosuppression, voiding dysfunctions or anatomic abnormalities/obstructions, recurrent infection, renal insufficiency, nosocomial UTI or a UTI caused by a resistant organism, a longer-duration of treatment (seven to 14 days) is recommended. In addition, all male patients with a UTI are considered complicated and should receive at least seven days of antimicrobial therapy. Treatment of patients with pyelonephritis should be 10-14 days.

In conclusion, the SFH UTI/pyelonephritis pathway can be used as a guide for appropriate antibiotic treatment indications, empiric antimicrobial choices, streamlining to the most narrow spectrum agent and appropriate duration of treatment. When alternative therapies are available, third-generation cephalosporins and fluoroquinolones should be avoided as treatment options due to their ability to cause "collateral damage."