

Cook Children's Medical Center
Clinical Excellence Committee and Antibiotic Stewardship Committee

Evidence based pathway for the diagnosis and management of pediatric urinary tract infections

Statement

This clinical pathway is based upon currently available medical evidence and/or a consensus of primary care and specialty care providers at Cook Children's Health Care System. These clinical pathways are intended to be a guide for practitioners and may need to be adapted for each specific patient based on the practitioner's professional judgement, consideration of any unique circumstances, the needs of each patient and their family, and/or the availability of various resources at the healthcare institution where the patient is located.

Definitions

- A. **Asymptomatic bacteriuria:** Presence of positive urine culture, regardless of urinalysis results, without signs or symptoms of UTI
- B. **Cystitis:** Dysuria, urgency, frequency, or suprapubic pain without fever or other symptoms with a urinalysis and culture consistent with UTI.
- C. **Pyelonephritis:** Fever or flank pain with urinalysis and culture consistent with UTI
- D. **Sterile pyuria:** White blood cells present in urine without bacteria. It may occur in association with infections such as partially treated UTI, appendicitis, tuberculosis, fungal, viral or parasitic infections. It can also occur with immunologic conditions, such as acute glomerulonephritis, systemic lupus erythematosus, and Kawasaki disease, or with foreign body, kidney stones, interstitial nephritis, analgesic nephropathy and papillary necrosis^[1]

Inclusion Criteria

- Patients ages 2 months to 18 years
- Patient with suspected or confirmed UTI

Exclusion Criteria

- Catheter-associated UTI
- Suspected or confirmed anatomic genitourinary abnormalities
- Immunocompromised host
- Pregnancy
- Recent history of sexual abuse
- Suspected sepsis

Background ^[2-4]

Acute urinary tract infection (UTI) is common in children. By the age of 7 years, 8.4% of girls and 1.7% of boys will have at least one UTI. The peak incidence of UTI is in infancy, with a second peak in the toddler years and an increased incidence again in adolescent years. The most common uropathogen is *Escherichia coli*, accounting for over 80% of cases in children. Other less common uropathogens include *Klebsiella*, *Proteus*, *Enterobacter*, *Citrobacter*, *Staphylococcus saprophyticus*, and *Enterococcus*.

Cystitis is an infection of the lower urinary tract and is the most common form of UTI. This refers to an infection isolated to the bladder. Pyelonephritis occurs when microbes ascend to the upper urinary tract and infect the renal parenchyma.

While many national guidelines and research studies for pediatric UTI use an age cut-off of 24 months, this was largely done as a means to separate those children who are not toilet trained from those children who are toilet trained. While this guideline does make different recommendations on treatment and management of pediatric UTI based on age, this was done to be consistent with the larger body of literature. That being said, it is appropriate for a provider to follow the less than 24 month guidelines for those children who are older than 24 months but not yet toilet trained.

Clinical Signs and Symptoms ^[5-7]

Clinical signs and symptoms depend on the age of the child. Symptoms are systemic rather than localized in early childhood.

Infants and Preschoolers	School Age Children to 18 years
Diarrhea	
Failure to Thrive	
Vomiting	Vomiting
Fever	Fever
Strong smelling urine	Strong smelling urine
Abdominal or flank pain	Abdominal or flank pain
New onset urinary incontinence	New onset urinary incontinence
Dysuria (preschoolers)	Dysuria
Urgency (preschoolers)	Urgency

Risk factors for UTI

- Male
 - Uncircumcised < 1 year
 - All < 6 months
- Female, in general
 - Particularly < 1 year

Diagnosis ^[4, 5, 8, 9]

- To help prevent overtreatment of asymptomatic bacteriuria, if patient is ≥ 6 months of age, a reflex urine culture will be performed by the lab.
- The reflex process:
 - If the Macroscopic UA is abnormal (positive blood, positive leukocyte esterase, protein ≥ 30 mg/dl), a Microscopic UA will be performed
 - If the Microscopic UA has ≥ 10 WBCs, a Urine Culture will be performed
 - A standalone Urine Culture will remain orderable in EPIC but should be limited to <6 months of age or immunocompromised

Criteria for establishing diagnosis include the following:

1. Fever (100.4 or higher)

In less common situations, a patient may have clinical evidence of cystitis or pyelonephritis, including history of dysuria, exam findings consistent with cystitis or pyelonephritis and lab evidence of a urinary tract infection, but lack fever. In those situations, it is acceptable to treat for a urinary tract infection, however treatment should not be given for a patient who is otherwise well and has asymptomatic bacteriuria.
2. Positive urinalysis (UA):
 - a. ≥ 10 WBC per HPF on microscopy demonstrate pyuria

- Positive urine culture of a single uropathogen with $\geq 50,000$ CFU/mL (applies to both urine samples obtained via catheterization, suprapubic aspiration and clean catch midstream)

Urine culture specimen source:

Age	Specimen type
≤ 2 years or if not toilet trained	catheterization or suprapubic aspiration
> 2 years or if toilet trained	clean catch midstream

Do NOT send urine collected in a bag for culture.

While it is reasonable to perform a screening UA from a bagged specimen in children under 2 years old or in those children who are not toilet trained, if that UA is concerning for a UTI, then a urine sample obtained via catheterization or suprapubic aspiration should be obtained BEFORE starting antibiotics because antibiotics administered prior to culture collection will obscure the diagnosis of UTI.

Admission Criteria

- Less than 2 months of age
- Ill appearance
- Poor oral intake
- Unable to take oral antibiotics
- Vomiting
- Immunosuppression
- Urine culture with bacteria known to be resistant to oral antibiotics
- Poor follow up
- Failure to respond to outpatient therapy
- Positive blood culture

Empiric Antibiotic Treatment ^[3, 4, 8]

NOTE: Treatment of asymptomatic bacteriuria is discouraged.

Empiric antibiotics should be started promptly if clinical suspicion for UTI is high and UA is suggestive of infection (ie, presence of pyuria, with or without nitrites). The empiric antibiotics recommended in this guideline are based on our local susceptibility data. Cook Children's Antibiogram can be found in EPIC or on CookNet under the Antimicrobial Stewardship webpage or the Laboratory Services webpage [Cook Children's Antibiogram](#).

Based on most recent CCMC local susceptibility data for urine specimens, the reported susceptibility of *E. coli* to Ceftriaxone is 88% and 87% susceptible to Cefazolin. The reported susceptibility of *K. pneumoniae* is 84% and 82% to Ceftriaxone and Cefazolin, respectively. Susceptibility to Cefazolin for uncomplicated UTI predicts susceptibility to all oral cephalosporins.

Empiric Antibiotic Therapy

Diagnosis	Preferred 1 st Line Treatment	Beta-Lactam Allergy	Duration of Therapy/Comments
Uncomplicated Cystitis	Cephalexin (50mg/kg/day divided Q8h max dose 500mg)	History of severe penicillin allergy, consider cefuroxime, cefixime or cefdinir. Avoid cephalexin (due to cross reactivity with penicillin)	5 days 3 days for TMP/SMX

	If IV therapy needed, Cefazolin 50mg/kg/day divided q8h (max dose 1000mg)	History of severe allergy to beta-lactams (penicillin and cephalosporin): Nitrofurantoin (1.25-1.75 mg/kg/dose divided q6h; max dose 100mg) or TMP/SMX (5mg/kg/dose BID; max dose 160mg)	
Pyelonephritis – previously healthy	Cefazolin (50mg/kg/day divided q8h, max dose 1000mg) If tolerating oral: Cephalexin (50mg/kg/day divided q8h, max dose 500mg)	History of severe penicillin allergy, consider cefuroxime, cefixime or cefdinir. Avoid cephalexin (due to cross reactivity with penicillin) Note: Cefazolin does not cross react with any penicillins History of severe allergy to beta-lactams (penicillin and cephalosporin): Ciprofloxacin IV/PO (10mg/kg/dose q12h, max PO dose 750mg, max IV dose 400mg)	7 days Tailor therapy to culture results and transition to oral therapy following clinical improvement, as evidenced by improving fever curve and ability to tolerate PO. Note: Nitrofurantoin is NOT an alternative for pyelonephritis due to low parenchymal concentrations
Pyelonephritis – history of prior UTI and ill appearing	Review prior culture results and susceptibilities from last 3 cultures, to determine empiric treatment. If no prior results: Ceftriaxone (50mg/kg/dose q24h, max dose 2000mg)	History of severe allergy to beta-lactams (penicillin and cephalosporin): Ciprofloxacin IV/PO (10mg/kg/dose q12h, max PO dose 750mg, max IV dose 400mg)	7 days* Tailor therapy to culture results and transition to oral therapy following clinical improvement, as evidenced by improving fever curve and ability to tolerate PO.

TMP/SMX = trimethoprim/sulfamethoxazole

*10-14 days if slow clinical improvement

Extended Spectrum Beta-Lactamase Producing Enterobacterales (ESBL-E)^[10]

Diagnosis	Preferred 1 st Line Treatment	Alternative	Duration of Therapy/Comments
Uncomplicated Cystitis	TMP/SMX (5mg/kg/dose BID; max dose 160mg) or Nitrofurantoin (1.25-1.75 mg/kg/dose divided q6h; max dose 100mg)	Ciprofloxacin IV/PO (10mg/kg/dose q12h, max PO dose 750mg, max IV dose 400mg) or	5 days 3 days for TMP/SMX Carbapenems are discouraged when

		Levofloxacin IV/PO (≤5 years old: 10mg/kg q12h, >5 years old: 10mg/kg q24h, max dose 750mg) or Meropenem (20mg/kg q8h, max dose1000mg) Or Ertapenem (≤12 years old: 15mg/kg q12h, mas dose 1000mg, >12 years old, 1000mg q24h)	<i>nitrofurantoin or TMP/SMX are active unless toxicities or resistance preclude use of other antibiotics</i> Note: Nitrofurantoin is NOT an alternative for pyelonephritis due to low parenchymal concentrations Consult ID as needed
Pyelonephritis	TMP/SMX (5mg/kg/dose BID; max dose 160mg) or Ciprofloxacin IV/PO (10mg/kg/dose q12h, max PO dose 750mg, max IV dose 400mg)	Meropenem (20mg/kg q8h, max dose1000mg) Or Ertapenem (≤12 years old: 15mg/kg q12h, mas dose 1000mg, >12 years old, 1000mg q24h)	7 days* <i>Carbapenems are discouraged when TMP/SMX or ciprofloxacin are active unless toxicities or resistance preclude use of other antibiotics</i> Consult ID as needed

TMP/SMX = Trimethoprim/Sulfamethoxazole

*10-14 days if slow clinical improvement

NOTE: Nitrofurantoin is NOT recommended to treat febrile infants with UTI because it does not achieve therapeutic concentrations in the blood stream and may be insufficient to treat pyelonephritis or sepsis due to a urinary tract infection.

For empiric IV therapy, add Ampicillin if *Enterococcus* is suspected. In neonates, *Enterococcus* has been reported to occur in approximately 10-16% of UTIs.^[11] In older children, *Enterococcus* is not a particularly invasive organism and is rarely a cause of UTI in healthy children. It does, however, account for up to 15% of nosocomially acquired UTIs in children. *Enterococcus* can also be associated with urinary catheterization or underlying anatomic abnormalities, such as vesicoureteral reflux.^[12, 13]

For empiric step down therapy in the absence of culture results, consider Cephalexin as first line. If cultures return before the patient is discharged, always tailor therapy based on the results, using the narrowest spectrum agent (eg, 1st generation cephalosporin).

Multiple other large pediatric institutions have a similar step down approach to empiric cephalexin, if culture results are not back prior to discharge, without complications, though it is important to follow-up any pending culture results at the time of discharge.

**** Always de-escalate and tailor therapy according to cultures and susceptibilities for patients who remain in the hospital.**

Duration [4, 8, 14-20]

Although controversy persists, 3-7 days of antibiotic treatment for cystitis is often recommended. Consider shorter courses in those children who are toilet trained and longer courses in those children who are not toilet trained. For pyelonephritis, the recommended treatment duration is 7-14 days. [16-18, 20]

While the American Academy of Pediatrics (AAP) guidelines recommend a treatment course of 7-14 days for children 2 to 24 months of age with UTI, there is evidence that shorter treatment courses of 2-4 days may be just as effective in this age group. For those individuals wishing to remain consistent with AAP guidance, a treatment course closer to 7 days in uncomplicated patients is considered appropriate and adequate. [8, 14, 15]

In a systematic review, short course antibiotic therapy (2 to 4 days) was as effective as standard duration (7 to 14 days) in children with lower UTI. [15] A single-dose or single-day therapy may be less effective than longer courses and is not recommended. [14]

It is NOT recommended that routine follow-up urine cultures be obtained after treatment for any age. Emphasis is on urine testing with subsequent febrile illnesses.

Procalcitonin in combination with clinical assessment can be a useful tool for guiding the discontinuation of antibiotics in pediatric patients in specific clinical scenarios, contributing to antimicrobial stewardship and potentially reducing the risk of antibiotic resistance and other adverse effects associated with antibiotic overuse. [21]

Work-Up/Evaluation of Patient with UTI

1. Children < 24 months of age or patients who are not toilet trained or if 1st UTI in a male
 - a. 1st Febrile UTI
 - i. Evaluation should begin with renal and bladder US.
 1. If patient is significantly ill, consider obtaining US within the first 1-2 days of illness to evaluate for possible presence of renal or perirenal abscess. [8, 22]
 2. US does not need to be done on an emergency basis (e.g., at night or during weekends) unless specific clinical concerns.
 3. For those patients who respond well to therapy, it is acceptable to defer US until they have recovered from their acute illness. [8, 22]
 - a. Animal models have demonstrated that *E. coli* endotoxin produced during an acute infection can produce dilation that can be confused for hydronephrosis. Changes in size, shape and echogenicity that can occur within kidneys during an acute infection also make it impossible to use renal US results obtained during an acute infection to establish a baseline for the patient. [8, 22]
 - ii. Those patients with an abnormal renal US, that is concerning for high-grade VUR or obstructive uropathy, should undergo VCUG. [22] Findings that are suggestive of this and should prompt follow-up VCUG include hydronephrosis, scarring, notable size difference between kidneys, urothelial thickening or Urinary Tract Dilation (UTD) P2 or P3. Isolated UTD P1 or pelviectasis is not necessarily an indication for VCUG.
 1. While the decision to obtain VCUG inpatient vs outpatient should be made based on individual patient circumstances, it is preferable to obtain VCUG

testing as an outpatient, once the patient has recovered from their acute illness.

- b. 2nd Febrile UTI
 - i. Those patients with recurrent febrile UTIs should undergo VCUG (if not previously done), regardless of their initial renal and bladder US findings. As mentioned previously, while the decision to obtain VCUG inpatient vs outpatient should be made based on individual patient circumstances, it is preferable to obtain VCUG testing as an outpatient, once the patient has recovered from their acute illness.
 - c. 1st Febrile UTI and 1st Degree Relative with history of High-Grade VUR that required surgery
 - i. Renal and bladder US should be obtained. Similar to the above recommendations, if the patient responded well to therapy, this can be deferred until after the acute illness.
 - ii. Regardless of the renal and bladder US results, VCUG should also be obtained, as US can miss up to 33% of patients with VUR and these patients are considered high risk. ^[20, 23] Additionally, familial clustering of VUR has been observed in 27-51% of siblings of patients with VUR and 66% of children of parents with VUR.^[24] As mentioned previously, while the decision to obtain VCUG inpatient vs outpatient should be made based on individual patient circumstances, it is preferable to obtain VCUG testing as an outpatient, once the patient has recovered from their acute illness.
 - d. Ultrasound alternatives to VCUG.
 - i. Voiding urosonography with ultrasound contrast is increasingly becoming more available. Studies evaluating its effectiveness have demonstrated high sensitivity and specificity and it is seen as a reasonable alternative to VCUG in Europe. ^[25-27] It is just beginning to emerge in American healthcare and while it may eventually be seen as an alternative to VCUG in the United States, it remains too early to make a recommendation regarding its use.
2. Children > 24 months of age or patients who are toilet trained
 - a. Children with 2 or more febrile UTIs over the age of 24 months (or those who are toilet trained) should be assessed for the presence of bowel and bladder dysfunction. Those patients with bowel and bladder dysfunction have a high incidence of renal scarring and treatment of bowel and bladder dysfunction can dramatically reduce the incidence of febrile UTIs in this population. ^[28]
 - b. Children with 2 or more febrile UTIs should undergo a renal and bladder US, if not previously obtained.
 - c. Children with an abnormal renal US or 2 or more febrile UTIs do not necessarily need a VCUG, but should be referred to Urology for further management.

Prevention of Recurrent Febrile UTIs

1. Children < 24 months of age or patients who are not toilet trained
 - a. Continuous Antibiotic Prophylaxis
 - i. One of the largest studies to evaluate the effectiveness of continuous antibiotic prophylaxis was the Randomized Intervention for Children with Vesicoureteral Reflux (RIVUR) study. This study found that continuous antibiotic prophylaxis resulted in a 50% reduction in the recurrence of febrile UTI in children with VUR.

Despite this, the study found no difference in the rate of renal scarring between the prophylaxis and non-prophylaxis groups. Additionally, the study did find increased drug resistance in the prophylaxis group. While interpreting these findings, it is important to note that the study period was only 2 years, so follow-up was relatively short. ^[29]

- ii. Despite the controversy surrounding continuous antibiotic prophylaxis, expert consensus at Cook Children's supports prophylaxis for those patients with a first time UTI who were found to have Grade II or higher VUR. Those patients who have recurrent febrile UTIs and any grade of VUR should also be started on continuous antibiotic prophylaxis. Those patients with no history of febrile UTI who were incidentally found to have VUR do not need to be started on continuous antibiotic prophylaxis.
 - iii. Continuous Antibiotic Prophylaxis Regimen (based on local antibiotic resistance patterns)
 1. Children < 2 months of life
 - a. Amoxicillin 15 mg/kg PO once daily
 2. Children > 2 months of life
 - a. Nitrofurantoin 1-2 mg/kg PO once daily
 - i. Nitrofurantoin is contraindicated in those patients with renal insufficiency.
 - b. Sulfamethoxazole-trimethoprim 2 mg TMP/kg PO once daily
 - c. Based on the CCMC 2023 Antibiogram, *E. coli* was susceptible to Bactrim in 63% of isolates, while it was susceptible to Nitrofurantoin in 98% of isolates. Based on this data, Nitrofurantoin should be considered first line therapy in this age group for continuous antibiotic prophylaxis.
2. Children > 24 months of age or patients who are toilet trained
 - a. Bowel and Bladder Dysfunction (BBD) Treatment is the mainstay of treatment in this group. ^[30] At least 50% of children in this group have been shown to experience improvement with only urotherapy and constipation management.
 - i. Urotherapy
 1. Adequate Hydration
 - a. While actual fluid requirements will vary from child to child, a general recommendation would for a child to drink a cup of water after every timed void, listed below.
 2. Timed Voiding
 - a. Holding behaviors increase the risk for UTIs
 - b. Children should be encouraged to void every 2-3 hours, during the day. A school excuse may be necessary for schools to allow adequate restroom and drinking breaks. An easy and practical way of wording this to patients is, "Every 2 hours, attempt to void, wash hands and drink a cup of water."
 3. Pelvic Floor Awareness and Retraining
 - a. Voiding is a passive process and children should be encouraged to relax during the entire void. This allows for better relaxation of the external urethral sphincter and bladder neck and promotes complete bladder emptying.
 - i. Urotherapy

- b. Reminding children not to “push”, strain, or force urine out is important. Valsalva voiding, straining, or pushing increases the resistance in the urethra at the bladder neck from a closed pelvic floor and external sphincter, increases high pressure voiding and decreases bladder emptying potential.
 - c. Girls, or boys who are sitting to void, should use a wide legged posture or sit backwards on a typical adult size toilet.
 - ii. Constipation Management – Every child with bowel and bladder dysfunction should be assumed to be constipated, at least initially.^[30]
 - 1. Dietary Changes
 - a. Patients should be encouraged to increase their amount of dietary fiber and water.
 - 2. Stool Softener
 - a. Patients should also be started on a stool-softener. The most common stool-softener used is Polyethylene Glycol 3350 (MiraLax®). Dosing should be personalized to the patient so that they are having one soft bowel movement once daily.
 - 3. Timed Stooling
 - a. Patients should be encouraged to sit on the toilet for approximately 15 minutes, twice daily after meals to establish more regular stooling patterns.
 - iii. Hygiene
 - 1. Female patients should be reminded of the importance of wiping themselves from front to back.
 - 2. Male and female patients should be reminded of the importance of regular bathing of their genitals.
- b. Continuous Antibiotic Prophylaxis
 - i. This is not recommended as first line treatment for the prevention of recurrent febrile UTI's in this group of patients. Continuous antibiotic prophylaxis should only be considered in those patients who have failed a BBD treatment regimen.

Circumcision Status

The majority of male UTIs occur in the first year of life. There is good evidence that the incidence of UTI is decreased under two years of age in circumcised vs. uncircumcised boys. ^[31-33] Decreased UTI incidence ranges from threefold to tenfold. Thus, the benefits of male circumcision are likely to be higher in boys with higher risk of recurrent UTIs. Vesicoureteral reflux, bowel and bladder dysfunction, posterior urethral valves, and neurogenic bladder are significant risk factors for recurrent UTI in the pediatric male population. ^[34-36]

Circumcision status and diagnosis of phimosis should be assessed and documented in males with a UTI. After the first UTI, education should be provided to the family about options for circumcision and its potential benefits for decreasing the risk of future UTIs without recommendation or advocacy for such. Alternatives to circumcision for males with the diagnosis of phimosis are to use mild steroid cream (i.e. - Betamethasone) and foreskin retraction after each void.

Uncircumcised males with phimosis and recurrent febrile UTIs, especially those with underlying urologic abnormalities that put them at an increased risk for recurrent UTIs, or high risk for renal dysfunction in the setting of a febrile UTI, should have the recommendation made for a circumcision with a urology consult.

When to Refer to Urology

The following are recommendations from Cook Children's Urology, as to when a patient should be referred to urology for further management.

1. Patient not previously seen by Urology
 - a. It is recommended that any child with more than 2 febrile UTIs be referred to urology for further evaluation and management.
2. Patient previously seen by Urology
 - a. It is recommended that Urology be notified of any patient they follow for recurrent UTIs, VUR or other significant urologic pathology who has been admitted to the hospital and found to have a febrile UTI.
 - b. For any patient diagnosed with a febrile UTI in the ambulatory setting, it is recommended that they be referred back to Urology for additional evaluation.

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This guideline is intended to assist providers in decision making by providing the current state of evidence and recommendations for the management of pediatric UTI. This guideline is not meant to replace clinical judgement and will not be appropriate for all cases of pediatric UTI.

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