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OHSU HEALTH SYSTEM
OFFICE OF CLINICAL INTEGRATION AND EVIDENCE-BASED PRACTICE

GUIDELINE FOR PEDIATRIC URINARY TRACT INFECTIONS

Background: Urinary tract infections (UTI) are the most common bacterial infections encountered in ambulatory and long-term care settings in the United States.[1] UTIs are common infections of childhood that may affect any part of the urinary tract, from the urethra to the kidneys. Anomalies, such as those resulting in urinary reflux, can result in urinary tract infections that can cause serious morbidity.[2]

Prevalence: Acute urinary tract infections are relatively common in children, with 8 percent of girls and 2 percent of boys having at least one episode by seven years of age.[3,4] For boys, UTIs are more likely during the first year of life, with uncircumcised boys at 10 times the risk of circumcised boys.[5] UTIs affect approximately 3 percent of all U.S. children each year and result in up to 1 million office visits annually.[2,6] In a study of febrile infants younger than 60 days presenting to pediatric emergency departments, the prevalence of UTI was 9 percent.[7]

Risks: It is important for clinicians to appropriately diagnose and treat UTIs in children. Some consequences of untreated UTIs include renal scarring and renal disease, which can lead to considerable morbidity later in life.[4] Pediatric UTI can range from simple cystitis to severe febrile infections that, if left untreated, can lead to kidney damage and the many sequelae of chronic kidney disease (CKD).[8]

Definitions:
Urinary tract infection (UTI): A common bacterial infection involving the low urinary tract (cystitis), the upper urinary tract (pyelonephritis), or both, causing illness in children.
Cystitis: Inflammation of the urinary bladder. It is often caused by infection and is usually accompanied by frequent, painful urination.
Pyelonephritis: Inflammation of the substance of the kidney in the upper urinary tract as a result of bacterial infection.
Fever: Because of normal variation in body temperature, there is no single value that is defined as fever. In general, a fever means a temperature above 100.4 ºF (38ºC). Temperature may vary slightly depending on how child's temperature is taken – oral (mouth), axillary (armpit), ear, forehead, or rectal.
Urinalysis: Analysis of physical, chemical, and/or microscopic properties of urine to test for the presence of disease. Urinalysis includes dipstick and/or microscopy. Urinalysis with or without microscopy will depend on age of patient and/or results of dipstick test.
Urine Culture: A test to find bacteria in the urine that can cause an infection.
Clean Catch Urine Specimen: The clean catch method is used to avoid contaminating the urine sample with bacteria that are normally present in the urethra and appear in a voided urine sample. It is used for a routine urinalysis, urine culture, or other urine tests that require uncontaminated urine for accurate results.

Guideline Eligibility Criteria:
-Pediatric patients up to 18 years old with suspected urinary tract infections

Guideline Exclusion Criteria:
-Adult patients with suspected urinary tract infections
-Known urinary tract abnormality
-Neurogenic bladder
-Prior history of recurrent urinary tract infections
-Chronic kidney disease
-Immunocompromised host

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Clinical Practice Recommendations:

UTI Symptoms and Signs to consider during assessment

Birth to <2 months[9] **(Consensus-Adapted)**

Most common ⟶ Least Common		
Fever (38ºC) Vomiting Lethargy Irritability	Poor Feeding Failure to thrive	Abdominal pain Jaundice Hematuria Unusual urine odor

2 months or older[9] **(Consensus-Adapted)**

Most common ⟶ Least Common			
Preverbal	Fever (38ºC).	Abdominal pain Flank tenderness Vomiting Poor feeding	Lethargy Irritability Hematuria Unusual urine Failure to thrive
Verbal	Frequency Dysuria	Dysfunctional voiding Changes to continence Abdominal pain Flank tenderness	Fever Malaise Vomiting Hematuria Unusual Urine Cloudy Urine

Risk factors include: uncircumcised males, females younger than 12 months, high fever, and prolonged fever.[9-12] **(Conditional Recommendation; Low Quality Evidence)**

Admission Criteria

Strongly consider admission if one or more of the following criteria is met:[10,19] **(Consensus-Adapted)**

- < 28 days old
- Ill, toxic, septic appearing
- Dehydration requiring IV fluids
- Failed outpatient antibiotic therapy
- Adherence risk such as unable to take previously prescribed regimen, no reliable caregivers at home, inability to follow recommended care plan, or at risk for loss to follow-up.

Urine Testing

Obtain a urine specimen to perform urinalysis with dipstick.[9, 12-13] **(Strong Recommendation, Low Quality Evidence)**

Catheterization is the preferred method to obtain urine cultures in not fully toilet-trained children. The American Academy of Pediatrics' recommendations allow bagged urine samples for initial urinalysis but NOT for culture due to potential for

contamination. Thus, bagged urine samples with positive leukocyte esterase or nitrite test results require collection of a second urine sample by catheterization or suprapubic aspiration for culture.[8] **(Consensus-Adapted)** *See Table 1 for preferred and alternate urine sample collection methods.*

Table 1. Urine Collection Methods[18] **(Consensus-Adapted)**

Patients who are not fully toilet-trained	
Catheterization	**Preferred method** to obtain urine for culture in children who are not fully toilet-trained
Bagged Urine Specimens	**Alternative method** to obtain urine for urinalysis in children who are not fully toilet-trained. However, urine catheterization should be performed if urine sample has positive leukocyte esterase or nitrite test results.
Suprapubic aspiration (SPA)	Requires ultrasound (US) guidance **May be useful in children when catheterization fails**, for example, uncircumcised, abnormal urethra or fused labia
Patients who are fully toilet-trained	
Clean-catch	Fully toilet trained defined as daytime dryness without accidents

For infants less than 28 days old presenting with unexplained fever and signs and symptoms of a UTI, perform full urinalysis (dipstick and microscopy) and urine culture.[9, 14-17] **(Conditional Recommendation; Very Low Quality Evidence)**

For Infants and children older than 28 days old with signs and symptoms of a UTI, perform at minimum a urinalysis with dipstick; further testing is needed depending on following results:[9,14,18] **(Conditional Recommendation; Very Low Quality Evidence)**

- Positive for leukocyte esterase and nitrites, or positive for nitrites alone, and send urine sample for culture
- Positive for leukocyte esterase and negative for nitrite, send urine sample for microscopy and culture
- Negative for leukocyte esterase and nitrite, explore other causes of illness

For all diagnostic tests there will be a small number of false negative results, which is even higher in infants <28 days old; therefore clinicians should use clinical criteria for their decisions in cases where urine testing does not support the findings.[9,15] **(Conditional Recommendation; Low Quality Evidence)**

Practice Implications

For all febrile or ill-appearing infants and children, additional testing for other serious bacterial illnesses may be warranted.

Diagnosis

To establish the diagnosis of UTI, clinicians should require both urinalysis results that suggest infection and the presence of at least 50,000 colony-forming units (cfu) per milliliter of a uropathogen cultured from a urine specimen obtained through transurethral catheterization or SPA.[10,13, 20-21] **(Strong Recommendation, Low Quality Evidence)**

When urine culture is performed, infants and children with the presence of 10,000 cfu – 50,000 cfu should be closely followed for UTI.[20] **(Conditional Recommendation, Very Low Quality Evidence)**

Specimen (cfu/mL)	Definite (cfu/mL)	Possible (Cfu/mL)
Catheterization	>50,000 cfu/mL	>10,000 cfu/mL
Clean-Catch	>100,000 cfu/mL	>50,000 cfu/mL

Infants and children who have bacteriuria and temperature of 38°C or higher should be considered to have acute pyelonephritis. Infants and children presenting with temperature lower than 38°C with flank pain/tenderness and bacteriuria should also be considered to have acute pyelonephritis. All other infants and children who have bacteriuria but no systemic symptoms or signs should be considered to have cystitis.[8-9] **(Conditional Recommendation, Low Quality Evidence)**

Initial Treatment Considerations

For infants less than 28 days old presenting with unexplained fever and signs and symptoms of a UTI, antibiotics should be initiated empirically.[8,9,13,18] **(Strong Recommendation; Moderate Quality Evidence)** See Table 2 for empirical selection of antibiotic therapy.

For Infants and children older than 28 days old with signs and symptoms of a UTI, and an abnormal urinalysis, antibiotics can be initiated empirically. [8,9,13,18] **(Strong Recommendation; Moderate Quality Evidence)** See Table 2 for empirical selection of antibiotic therapy.

When initiating treatment, the clinician should base the choice of route of administration on practical considerations: initiating treatment orally or parenterally in children >/= 2 months is equally efficacious. Initiate parenteral antibiotics for age < 28 days, inability to tolerate oral administration, failed oral outpatient antibiotics, or septic appearance.[13] **(Strong Recommendation; Moderate Quality Evidence**). Consider initiating parenteral antibiotics if the patient is between 29 days and 2 months. See Table 2 for empirical selection of antibiotic therapy.

For all infants less than 28 days old and children with acute pyelonephritis, treat with antibiotics for a total duration of 7–14 days.[8-9,13,22] **(Strong Recommendation; Moderate Quality Evidence)**

For children with cystitis, treat with short duration oral antibiotics for 3-7 days (dependent on antibiotic selection). [8-9,13,22] **(Strong Recommendation; Moderate Quality Evidence)**

Ongoing antibiotic prophylaxis is not routinely recommended for patient's first febrile urinary tract infection. Contact Urology to discuss need for antibiotic prophylaxis for patients with recurrent urinary tract infections.[9,13,22] **(Strong Recommendation; Moderate Quality Evidence)**

Table 2: Empirical antibiotic therapy for children with suspected UTI [8,10,14,18,]

Based on local antibiotic susceptibility, consider the following antibiotic therapy based on age of patient, suspected diagnosis, and location (inpatient or outpatient) during treatment:					
Age	**Location**	**Suspected Diagnosis**	**Preferred Antibiotic**	**Alternative Antibiotic**	**Duration**
0-28 days	Inpatient	Pyelonephritis	- Ampicillin + gentamicin		7-14 days

			- Ampicillin + 3rd generation cephalosporin		
28-60 days	Inpatient	Pyelonephritis	Ceftriaxone	- Ampicillin + gentamicin - Severe beta-lactam allergy: ciprofloxacin	7-14 days
	Outpatient	Pyelonephritis	Cephalexin	- Mild penicillin allergy: cefdinir - Severe beta-lactam allergy: ciprofloxacin	7-14 days
>60 days – 18 years	Inpatient	Pyelonephritis	Ceftriaxone	- Ampicillin + gentamicin - Severe beta-lactam allergy: ciprofloxacin	7-14 days
	Inpatient	Cystitis	Nitrofurantoin	Cephalexin	5-7 days
	Outpatient	Pyelonephritis	Cephalexin	- Mild penicillin allergy: cefdinir - Severe beta-lactam allergy: ciprofloxacin	7-14 days
	Outpatient	Cystitis	Nitrofurantoin	Cephalexin	5-7 days
Patients who grow an organism susceptible to a reasonable oral antibiotic option may be safely discharged on oral antibiotics					

Follow-up and Targeted Therapy

After confirmation of UTI, the clinician should determine if the current therapy adequately treats the identified organism; therapy should be adjusted as necessary, including discontinuation of therapy if no organism is identified. If intravenous therapy was initiated, clinicians can consider transitioning to oral therapy to complete the course, provided that the patient's signs and symptoms have improved and can reliably take oral medication, and an adequate oral therapy is available. No minimum duration of intravenous therapy for UTI has been identified. Additionally, the clinician should instruct parents or guardians to seek prompt medical evaluation (ideally within 48 hours) for future febrile illnesses to ensure that recurrent infections can be detected and treated promptly.[13] **(Conditional Recommendation, Very Low Quality Evidence)**

If urine culture is not pre-treated and indicate no growth or contamination, consider discontinuation of therapy.[8,18] **(Consensus-Adapted)**

Practice Implications

Refer to Urology if:

- VUR with Grades III-V
- Abnormal ultrasound
- Reoccurrence of UTI

Imaging

Infants and children with pyelonephritis and infants less than 6 months old with first febrile UTI should undergo renal and bladder ultrasonography (RBUS). When the clinical illness is severe or substantial clinical improvement does not occur with initiation of antibiotic therapy, RBUS is recommended within 2 days to identify obstructive uropathy, pyonephrosis, or renal/perirenal abscesses. If substantial clinical improvement occurs with therapy, RBUS is performed after resolution of the acute infection (within 4-6 weeks).[8-9,13-14,18,24] **(Conditional Recommendation, Low Quality Evidence)**

After the first febrile UTI, voiding cystourethrography (VCUG) should not be performed routinely but is indicated if RBUS reveals hydronephrosis, scarring, or other findings that would suggest either high-grade VUR or obstructive uropathy, as well as in other atypical or complex clinical circumstances. VCUG is also indicated if there is a recurrence of febrile UTI. Patients should be afebrile for at least 24 hours before VCUG.[8-9,13-14,22-23] **(Conditional Recommendation, Low Quality Evidence)**

Quality Measures:

Process:

- Imaging Rates
- Referral to Urology

Outcome:

- Patients <18 years old diagnosed with UTI
- Admissions
- Length of Stay
- Antibiotics Prescribed across Departments (Pediatrics, Emergency Department, Family Medicine)
- Treatment Failures

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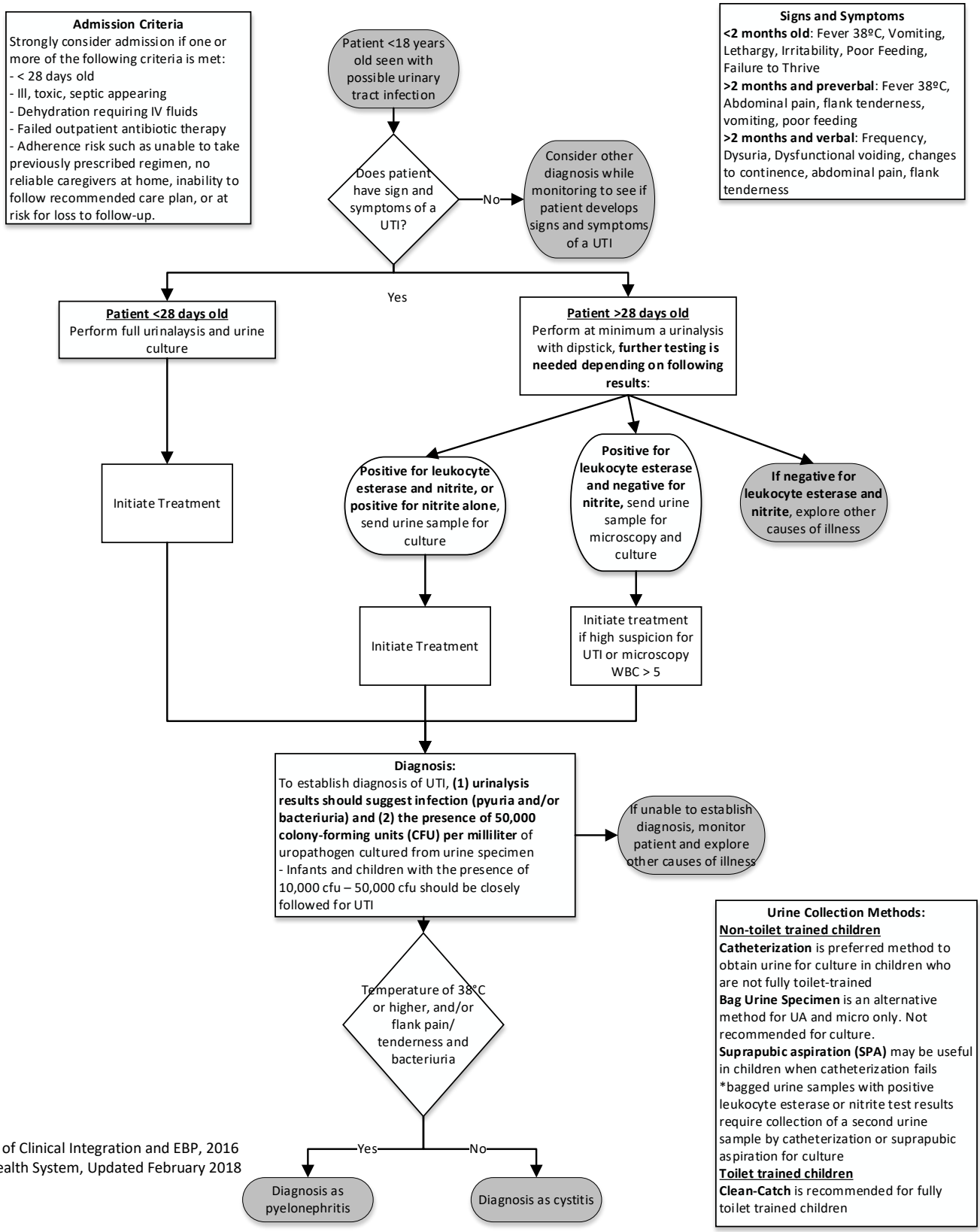
OHSU Office of Clinical Integration and EBP
Pediatric Urinary Tract Infection Diagnosis Management Algorithm



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Guideline Preparation

This guideline was prepared by the Office of Clinical Integration (CI) and Evidence-Based Practice (EBP) in collaboration with content experts at Oregon Health and Science University.

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Development Process

This guideline was developed using the process outlined in the CI and EBP Manual (2016). The review summary documents the following steps:

1. Review Preparation
   - PICO questions established
   - Evidence search confirmed with content experts
2. Review of Existing Internal and External Guidelines
   - Literature Review of Relevant Evidence
3. Critically Analyze the Evidence
4. Summarize the Evidence by preparing the guideline, and order sets
   - Materials used in the development of the guidelines, review summaries are maintained in a Pediatric Urinary Tract Infection EB review manual with the Office of CI and EBP.

Evaluating the Quality of the Evidence

Published clinical guidelines were evaluated for this review using the **University of Pennsylvania's Trustworthy Guideline Rating Scale**. The summary of these guidelines are included in the evidence summary. The rating scale is based on the Institute of Medicine's "Standards for Developing Trustworthy Clinical Practice Guidelines" (IOM), as well as a review of the AGREE Enterprise and Guidelines International Network domains. This scale evaluates a guideline's transparency, conflict of interest, development group, systematic review, supporting evidence, recommendations, external review and currency and updates. The purpose of this scale is to focus on the weaknesses of a guideline that may reduce the trust a clinical user can have in the guideline, and distinguish weaknesses in documentation (e.g. guideline does not have a documented updating process) from weaknesses in the guidance itself (e.g. recommendations are outdated).

The **GRADE (Grading of Recommendations, Assessment, Development and Evaluation)** criteria were utilized to evaluate the body of evidence used to make clinical recommendations. The table below defines how the quality of the evidence is rated and how a strong versus conditional recommendation is established. The evidence summary reflects the critical points of evidence.

Recommendation	
STRONG	Desirable effects clearly outweigh undesirable effects or vice versa
CONDITIONAL	Desirable effects closely balanced with undesirable effects
Quality	**Type of Evidence**
High	Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies

Moderate	Evidence from RCTs with important limitations (e.g., inconsistent results, methodological flaws, indirect evidence, or imprecise results) or unusually strong evidence from unbiased observational studies
Low	Evidence for at least 1 critical outcome from observational studies, from RCTs with serious flaws or indirect evidence
Very Low	Evidence for at least 1 critical outcome from unsystematic clinical observations or very indirect evidence

Recommendations

Recommendations for the guidelines were directed by the existing evidence, content experts, and consensus. Patient and family preference were included when possible. When evidence is lacking, options in care are provided in the guideline and the order sets that accompany the guideline.

Approval Process

Guidelines are reviewed and approved by the Content Expert Team, Office of CI and EBP, Knowledge Management and Therapeutics Committee, Professional Board, and other appropriate hospital committees as deemed appropriate for the guideline's intended use. Guidelines are reviewed and updated as necessary every 2 to 3 years within the Office of CI and EBP at OHSU. Content Expert Teams will be involved with every review and update.

Disclaimer

Guideline recommendations are made from the best evidence, clinical expertise and consensus, in addition to thoughtful consideration for the patients and families cared for within the Integrated Delivery System. When evidence was lacking or inconclusive, content experts made recommendations based on consensus. Expert consensus is implied when a reference is not otherwise indicated.

The guideline is not intended to impose standards of care preventing selective variation in practice that is necessary to meet the unique needs of individual patients. The physician must consider each patient and family's circumstance to make the ultimate judgment regarding best care.