AMBULATORY GUIDELINE

Urinary Tract Infections (UTIs): Primary Care/Outpatient



Neonatal to Adult Considerations

Aim: To decrease variation in management for uncomplicated UTI.

Suspicion for UTI? (e.g. dysuria, urgency, frequency, pain, fever, vomiting, CVA tenderness, irritability without other cause)

Pyelonephritis	Cystitis
Systemic symptoms	Dysuria (consider vaginitis)
Fever, chills	Urinary frequency
Nausea/vomiting	Urgency Suprapubic pain
Poor oral intake Flank pain, CVA tenderness	*Commonly without fever
\	,

Treatment:

If previous UTI, review organism(s) and sensitivities from last 12 months

Pain: If pain present, manage with appropriate medication: acetaminophen, ibuprofen, phenazopyridine hydrochloride (>12 yrs).

Resource: Patient & Family Education: Urinary Tract Infections

Perform Urinalysis (UA) and Urine Culture (UC)

Catheterized sample for all non-toileted trained individuals Sterile cup clean catch for *toilet trained* individuals (Table 3) Blood tests are *not recommended* unless concerns of sepsis

Is UA Positive? UA+ = Nitrites, or pyuria: ≥ trace LE or ≥ 5 WBC/hpf b,c

Developmental Considerations:

Constipation management (Table 4)
Adolescents: Urine GC/Chlamydia

No V

Consider alternate source of illness

Exclusion guidelines for Ambulatory Care

- Infants <60 days refer to <u>AAP Febrile Infant</u> <u>Guideline</u> or <u>Children's Minnesota Febrile</u> <u>Infant Guideline</u>
 - Refer to page 2 for infants days 8-60
- Concern for meningitis or other source
- · Sepsis with shock or meningitis
- Immunodeficiency
- · GU anomalies or previous renal disease
- · Complex chronic medical conditions
- · Indwelling urinary catheter



Consider sending to Children's Minnesota or nearest Emergency Department for evaluation

Educate family that evaluation does not guarantee admission

See Page 2 for ED/Inpatient Guideline

Empiric antibiotic therapy duration and frequency:*		Pediatric patients** (60 days - 18 yrs of age)	Adult patients (>18 yrs of age)
Pyelonephritis		Cephalexin for 7 days 25 mg/kg PO TID (max: 1000 mg/dose)	Cephalexin for 10 days 1000mg PO TID
	Cephalosporin allergy:*	Ciprofloxacin for 7 days 10mg/kg PO BID (max 500mg/dose)	Ciprofloxacin for 7 days 500 mg PO BID
Custitio		Cephalexin for 3 days 25mg/kg PO BID (max 1000mg/dose)	Cephalexin for 5 days 1000mg PO BID
Cystitis	Cephalosporin allergy:*	Ciprofloxacin for 3 days 10 mg/kg PO BID (max: 500 mg/dose)	Ciprofloxacin for 3 days 500 mg PO BID

*If cephalosporin allergy, use ciprofloxacin or guidance by culture results

**Avoid Ceftriaxone if has hyperbilirubinemia

Imaging:

RBUS: First time febrile UTI, recurrent UTI, atypical course, family history of GU anomalies

· Timing: during acute treatment; or within 2 months

VCUG: Abnl RBUS, Non-*E. coli* pathogen, consider if atypical course^f

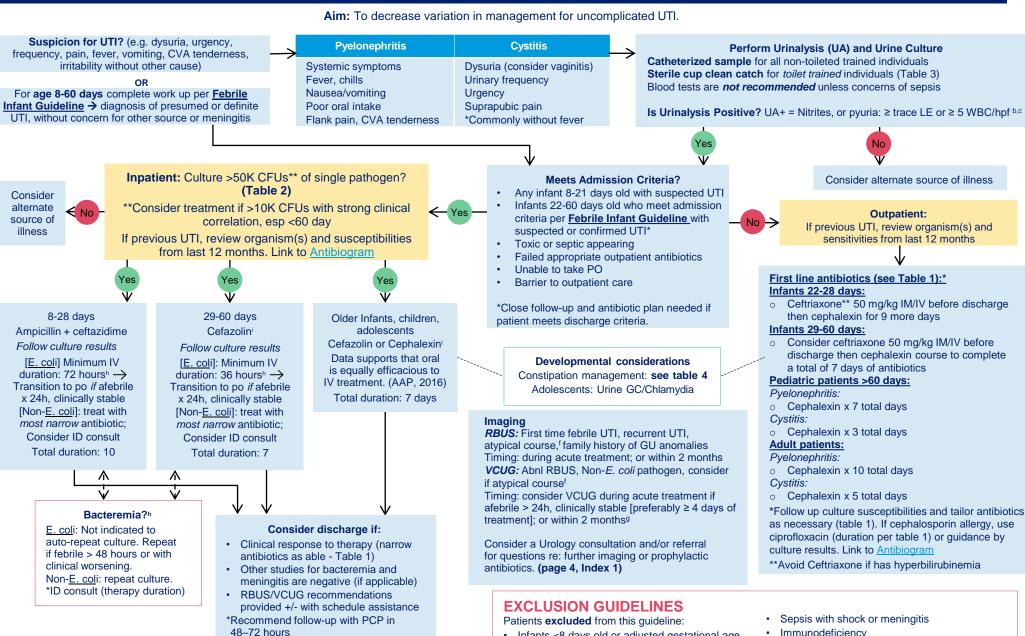
 Timing: consider VCUG during acute treatment if afebrile > 24h, clinically stable [preferably ≥ 4 days of treatment]; or within 2 months⁹



Symptom F/U: Instruct families to follow up with Clinic/ED if pain or fever not improved or new onset flank pain in 48-72 hours

UC/Antibiotic Selection: Upon receipt of urine culture results and adjust antibiotic choice based on the organism and susceptibilities (page 3, Table 1) Imaging F/U:
Consider a Urology consultation and/or referral for questions re: further imaging or prophylactic antibiotics. (page 4, Index 1)

Urinary Tract Infections (UTIs): ED and Inpatient Neonatal to Adult Considerations



Disclaimer: This quideline is designed for general use with most patients; each clinician should use their own independent judgment to meet the needs of each individual patient. This guideline is not a substitute for professional medical advice, diagnosis or treatment.

Immunodeficiency

Infants <8 days old or adjusted gestational age

Infants <60 days and concern for meningitis or

<37 weeks

other source

- · GU anomalies or previous renal disease
- Complex chronic medical conditions
- · Indwelling urinary catheter



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TABLE 1 - Antibiotics Neonatal, Pediatric and Adult Dosing

Antibiogram

Antibiotic	Neonatal dosing	Pediatric dosing	Adult dosing
Dosing for all antibiotics unless otherwise stated: Pediatric: cystitis x 3 days, pyelonephritis x 7 days; Adult: cystitis x 5 days, pyelonephritis x 10 days			
Ampicillin (IV)	> 2 kg: 50 mg/kg IV q8h	50 mg/kg IV q6h (max: 2000 mg/dose)	2000 mg IV q6h
Amoxicillin (PO)	> 2 kg: 15 mg/kg PO BID	40 mg/kg/day PO divided TID (max: 500 mg/dose)	500 mg PO TID
Amoxicillin-clavulanate (PO)	> 2 kg: 15 mg/kg of amoxicillin PO BID (Use 25 mg/mL or 50 mg/mL suspension)	40 mg/kg/day of amoxicillin PO divided TID (max: 500 mg/dose) (Use 25 mg/mL or 50 mg/mL suspension or 500 mg tablet)	500 mg of amoxicillin PO TID
Cefazolin (IV)	> 2 kg and PNA ≤ 7 days: 50 mg/kg IV q12h > 2 kg and PNA > 7days: 50 mg/kg IV q8h	33 mg/kg IV q8h (max: 2000 mg/dose)	2000 mg IV q8h
Cefdinir (PO)d	7 mg/kg PO BID	7 mg/kg PO BID (max 300 mg/dose)	300 mg PO BID
Cephalexin (PO)	50 mg/kg/day PO divided TID	25 mg/kg PO BID (cystitis) 25 mg/kg PO TID (pyelonephritis) (max: 1000 mg/dose)	1000 mg PO BID (cystitis) 1000 mg PO TID (pyelonephritis)
Ceftazidime (IV)	PNA ≤ 7 days: 50 mg/kg IV q12h PNA > 7days: 50 mg/kg IV q8h	50 mg/kg IV q8h (max: 2000 mg/dose)	2000 mg IV q8h
Ceftriaxone (IV)	N/A	50 mg/kg IV q24h (max: 2000 mg/dose)	2000 mg IV q24h
Ciprofloxacin (IV/PO)	25 mg/kg/day IV divided q12h	IV: 10 mg/kg q12h (max: 400 mg/dose) PO: 10 mg/kg BID (max: 500 mg/dose) x 3 days (cystitis) or x 7 days (pyelonephritis)	IV: 400 mg q12h PO: 500 mg BID x 3 days (cystitis) or x 7 days (pyelonephritis)
Nitrofurantoin (PO) (Do not use for pyelonephritis)	Contraindicated in patients < 1 month of age	Do not use if CrCl < 60 mL/min or for pyelonephritis Cystitis — Duration of therapy: 3 days Immediate release formulation (brand names: Furadantin, Macrodantin) 5 to 7 mg/kg/day divided four times daily (max: 100 mg/dose); or fixed dosing as below: • 7 to < 12 kg: 12.5 mg PO four times daily • 12 to < 22 kg: 25 mg PO four times daily • 22 to < 31 kg: 37.5 mg PO four times daily • 31 to < 42 kg: 50 mg PO four times daily • ≥ 42 kg: 50 to 100 mg PO four times daily Nitrofurantoin macrocrystal/monohydrate (brand name Macrobid) Adolescents: 100 mg BID	Do not use if CrCl < 30 mL/min, for pyelonephritis or pregnant at term (38–42 weeks gestation) Cystitis – Duration of therapy: 5 days Nitrofurantoin macrocrystal/monohydrate (brand name: Macrobid) 100 mg PO BID
TMP-SMX (IV/PO)	Avoid in infants < 2 months of age	5 mg/kg/dose IV/PO q12h (max: 160 mg/dose)	Avoid during 3rd trimester of pregnancy 5 mg/kg/dose IV/PO q12h (max: 160 mg/dose)

SUSCEPTIBILITY SURROGATE INFORMATION:

- Susceptibility of urinary E. Coli, Klebsiella pneumoniae, and Proteus mirabilis isolates to cefazolin can be used to predict susceptibility to cephalexin
- · Susceptibility of urinary E. Coli, Klebsiella pneumoniae, and Proteus mirabilis isolates to cefpodoxime can be used to predict susceptibility to cefdinir
- Susceptibility to cefpodoxime will be tested in urinary *E. Coli, Klebsiella pneumoniae, and Proteus mirabilis* isolates that are resistant to cefazolin and are not ESBL producers. This allows use of cefdinir (with cefpodoxime as surrogate) if the isolate is susceptible to cefpodoxime. Inferring susceptibility to cefixime using cefpodoxime susceptibility as surrogate is **not** advised.



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REFERENCE TABLES, UROLOGY REFERRAL

Table 2: Urine culture			
Culture results		Post-test likelihood UTI	Treatment considerations
Negative Mixed flora < 50,000 cfu/mL clean catch		Unlikely	Do not treat *Likely contaminant
Abnormal UA (+), and	> 10,000 cfu/ mL catheterized specimen	Possible	Young infants: consider treating if no other source for fever found; clinically correlate
	> 50,000 cfu/ mL clean catch		Clinically correlate
Abnormal UA (+), and > 50,000 cfu/mL catheterized > 100,000 cfu/mL clean catch		Probable	Empirically treat Follow up speciation and sensitivities
UA+ = nitrites , or pyuria : ≥ trace LE or ≥ 5 WBC/hpf		Narrow/adjust antibiotics as able	

Table 3: Urine collection considerations			
Pre-continent children: contamination rates ⁵			
Bagged urine	Clean catch	Catheterization	
50%	> 25%	10%	
Continent children (link for directions):			
Mid-stream clean catch urine specimen collection			

INDEX 1: CRITERIA FOR UROLOGY REFERRAL

[Consider Inpatient consultation if patient evaluation is time-sensitive]

- Children with recurrent febrile UTIs
- Abnormal imaging: anatomic abnormality detected on ultrasound or VCUG, including complex congenital urologic problems such as:
 - Renal parenchymal loss or kidney size discrepancies
 - Ureterocele
 - Any grade vesicoureteral reflux with febrile UTI
 - Posterior urethral valves
 - Other structural abnormalities of genitourinary development, such as persistent genitourinary sinus or cloacal abnormalities
- Children with neurogenic bladder (excluded in this clinical pathway)

Performance of nitrite and leucocyte esterase as determined by automated test strip analyser, and bacteria and leucocyte count as determined by flow cytometer measured in against gold standard urine culture in various patient population. Columns represent sensitivity, specificity, PPV, and NPV, respectively.

Urine samples from paediatric patients aged <24 months (n=361) using paediatric-specific gold standard to define positive urine cultures				
Nitrite	27.1	98.6	76.5	89.2
Leucocyte esterase	68.9	80.0	35.2	94.1
Bacteria count	76.7	96.5	76.7	96.5
Leucocyte count	62.5	83.0	37.5	93.1
Urine samples from paediatric	patients aged between 3 an	d 17 years (n=216)		
Nitrite	40.0	99.5	50.0	97.1
Leucocyte esterase	85.5	90.0	23.7	99.4
Bacteria count	95.1	100.0	50.0	100.0
Leucocyte count	89.2	80.0	26.7	98.9
Urine samples from adult patients between 18 and 60 years old (n=818)				
Nitrite	38.3	99.7	92.0	94.9
Leucocyte esterase	80.0	74.7	22.2	98.1
Bacteria count	91.5	77.8	26.1	99.1
Leucocyte count	79.7	74.0	20.7	97.7

Table from Yusuf E, Van Herendael B, van Schaeren J. J Clin Pathol 2017;70:631-636

Urinary Tract Infections (UTIs)



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CONSTIPATION MANAGEMENT

WHAT IS FUNCTIONAL CONSTIPATION?

Delay or difficulty in defecation that is present for 2 weeks or more and sufficient to cause excessive straining and/or pain.

Rome III criteria:

- No organic pathology/RED FLAGS
- 2 or more of the following lasting for 1 month (< 4 years of age) or 2 months (> 4 years of age)
 - 2 or fewer defecations per week
 - One episode of incontinence per week
 - History of excessive stool retention
 - Painful or hard bowel movements
 - Large fecal mass in rectum
 - Large diameter stools that may obstruct the toilet

RED FLAGS

- · No stool in the first 48 hrs of life
- Signs of constipation in < 1 month olds
- Narrow diameter stool (ribbon or toothpaste) suggestive of anal atresia
- Anatomic abnormality (back/coccyx; position of the anus)
- New-onset weakness in legs, locomotor delay
- · Abdominal distension with bilious vomiting
- Faltering growth and/or other signs suggestive of congenital hypothyroidism versus other metabolic etiologies

DIETARY AND LIFESTYLE RECOMMENDATIONS

- Develop daily habit of sitting on the toilet for 5–10 minutes 20–30 minutes after a meal
- · Use positive reinforcement for good habits
- · Increase water
- Increase fiber with goal of 5 gm + years in age (use this until child reaches 20–25 grams)
- · Increase fresh fruits and vegetables
- Limit milk to 16–24 oz per day in child > 1 year (any additional dairy restriction should be done under a specialist's advice and care.)

TABLE 4: Constipation Oral (enteral) Maintenance Management			
Age groups	Prune juice	Polyethylene glycol (Miralax) Dosing: 0.4-1 g/kg/day	Senna (8.8 mg/5 mL, 8.6 mg/tab)
2-6 months	1-2 ounces/day	¼ cap (4 g) QD up to BID	
7–12 months	2-6 ounces/day	½ cap (8.5 g) QD up to BID	2.2 mg QD up to BID*
1-5 years		½ cap (8.5 g) QD up to 1 cap (17 g) BID	4.4. mg QD up to BID
6–10 years		4 con (47 m) OD un to 2 cons (24 m) DID	5 mL or 1 tab QD (QHS) up to BID
> 10 years		1 cap (17 g) QD up to 2 caps (34 g) BID	10 mL or 2 tabs QD (QHS) up to BID

Goal of treatment is 1–2 soft/mushy stools (Bristol 4–6) per day depending on symptoms.

*May consider glycerin suppositories instead of stimulant laxative in infants.

Constipation maintenance treatment could require up to several months of therapy.

Recommend interval follow-up(s) with primary care provider and/or gastroenterologist.

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NOTES

- a) Uropathogens: Approximately 85% to 90% of uncomplicated UTIs are caused by Escherichia coli. 15 According to Children's Minnesota 2022 Antibiogram, *E. coli* urine isolates were 92% sensitive to Cefazolin (1st gen cephalosporin). Antibiogram
- b) UA: The 2011 American Academy of Pediatrics (AAP) guideline defines UTI by the presence of <u>at least 50 000 CFU/mL</u> of a uropathogen in a specimen obtained by *bladder catheterization* in a child with either a positive result on a **leukocyte esterase** test or with **white blood cells** in the urine on microscopy (ie, pyuria).²⁸
 - a) The nitrite test on the urine reagent strip detects the presence of nitrate-reducing bacteria (ie, gram-negative bacteria); however, not all GN organisms convert nitrates well and it is time sensitive test leading to false negative results. Therefore, nitrites on UA are considered specific but not sensitive in general.
 - b) Possible signs of contamination: epithelial cells; LE+ alone may represent vaginal source → clinically correlate
 - c) Sterile pyuria: associated with partially treated UTI, appendicitis, tuberculosis, or fungal, viral, or parasitic infections. Immunologic conditions such as APGN, SLE, and Kawasaki disease; AIN, nephrolithiasis⁹
- c) Urine Culture bacteriuria (CFUs):
 - a) Neonates: In one retrospective study of infants < 60 days with fUTI, a proportion with *E. coli* bacteremia had urine cultures with < 50,000 CFU/mL plus pyuria (WBC or LE) in the UA, indicating that true UTIs may occur with <50,000 CFU/mL.³ Consider clinical correlation including UA results.
 - b) Asymptomatic bacteriuria (ABU): In a systematic review of the literature (2020), the prevalence of asymptomatic bacteriuria is very low relative to the prevalence of UTI it is likely that, in a sample of preverbal children being tested for UTI, the number of those with true UTI that have a negative leukocyte esterase test far exceeds the number of children with asymptomatic bacteriuria.²⁴
- d.) Oral 3rd generation cephalosporins: Susceptibility of E coli and other gram-negative uropathogens to ceftriaxone should not be

A team drafted from across the continuum of care at Children's MN took part in the revisionary processes of these guidelines.

- · Interdisciplinary Stakeholders
 - Emergency Medicine: Kelly Bergmann
 - Hospital Medicine: Jodi O'Neill, Andrew Rose, Gloria Swanson
 - Infectious Disease: Bill Pomputius
 - Pharmacy: Mary Ullman (original content Christina Koutsari)
 - Primary Care: Kent Wegmann
 - Urology: Erica Lundberg, Judy Reitmeyer-Hunt, Katie Willihnganz-Lawson
 - Children's Health Network (CHN): Rachel Bies, Chelsy Meier, John Hollerud, Steve Inman
- Organizational Stakeholders
 - Medical-Surgical: Courtney Herring
 - Quality Improvement: Katie Brunsberg (original content Gabi Hester)

used as a surrogate for susceptibility to oral 3rd generation cephalosporins (e.g. cefixime, cefpodoxime, cefdinir) due to risk of overestimating susceptibility to the latter (false susceptible).³² The Children's Minnesota Microbiology Lab provides susceptibility results to cefpodoxime, which can be reliably used as surrogate for susceptibility to cefdinir but not to cefixime. Given a) inconsistent insurance coverage and commercial availability of cefpodoxime and cefixime, and b) non-inferior clinical outcomes of cefdinir¹³, cefdinir can be used as the oral 3rd generation cephalosporin of choice for the small proportion of patients for whom cefazolin/cephalexin is not an option.

- e) Tzimentatos L, et al. (2018) described characteristics of urinalysis for 289 neonates with culture confirmed UTI. LE, nitrites, OR pyruia were highly sensitive and specific screening in febrile infants <60 days, esp those with bacteraemia. Negative nitiries highly correlated with neonates without UTI.30
- f) VCUG indications (explained):
 - a) If RBUS reveals *hydronephrosis, *scarring, or other findings that would *suggest either high-grade VUR or *obstructive uropathy
 - b) Atypical clinical course: Oliquria, treatment failure, or AKI
 - c) <u>E. coli</u> pathogen: In infants aged 0–3 months with a first febrile UTI, the presence of *E. coli* and normal renal US findings allow to safely avoid VCUG; with a very low risk (< 1%) of missing a high-grade VUR.²¹
 - d) Recurrent fUTIs: if recurrence < 12 months of age, recommend VGUG; if > 12 months, investigate and address any bowel & bladder dysfunction (BBD); consider VCUG
- g) Timing of VCUG: growing evidence reports obtaining VCUG within the first week of diagnosis and in concurrent treatment of fUTI does not impact results or raise risk to infant/child^{11,16} -> consider if: a) afebrile > 24 hours, b) Blood culture negative (if obtained), c) Barriers to refer later; preferably following a minimal 4 days of treatment
- h) < 60 day old considerations:
 - a.) Parenteral (IV) treatment: Multiple studies demonstrating that short-course IV treatment (≤ 4 days) as effective as long-course and without increased readmission rates.3.14
 - b.) Bacteremia: Adverse outcomes are rare in infants with bacteremic UTIs and not associated with parenteral antibiotic duration -> recommend short parenteral courses with conversion to oral therapy once infants have clinically improved.^{4,23}
 - c.) Consideration of longer treatment duration for patients who are persistently bacteremic and/or demonstrate slow clinical response following initiation of antibiotics.
- i) Discordant therapy (empiric antibiotics): Retrospective study of children < 18 yo with 3rd generation cephalosporin-resistant UTIs who were started on discordant antibiotics

 A total of 7/316 (2.2%) required escalation of care while 192/230 experienced clinical improvement. Repeat urine cultures in 16/19 showed improvement or resolution of pyuria and sterilized in 11/17. Conclusion: Results suggest that narrow-spectrum empiric therapy is appropriate while awaiting final urine culture results.³¹
- j) Antibiotic resistance considerations: Third generation cephalosporins (e.g. ceftriaxone, ceftazidime, cefdinir) are not recommended for treatment of infections due to Enterobacter spp (including Klebsiella (formerly Enterobacter) aerogenes), and certain Citrobacter spp. For more information, please refer to the corresponding guideline on Star Net Treatment for Infections due to AmpC- and ESBL-Producing Gram-Negative Bacteria. For outpatient treatment of UTIs due to ESBL-producing organisms, please refer to the corresponding guideline on Star Net ESBL UTI treatment: Outpatient.

CLINICAL GUIDELINE

Urinary Tract Infections (UTIs)



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Aim: To decrease variation in management for uncomplicated UTI.

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 Disclaimer: This quideline is designed for general use with most patients; each clinician should use their own independent judgment to