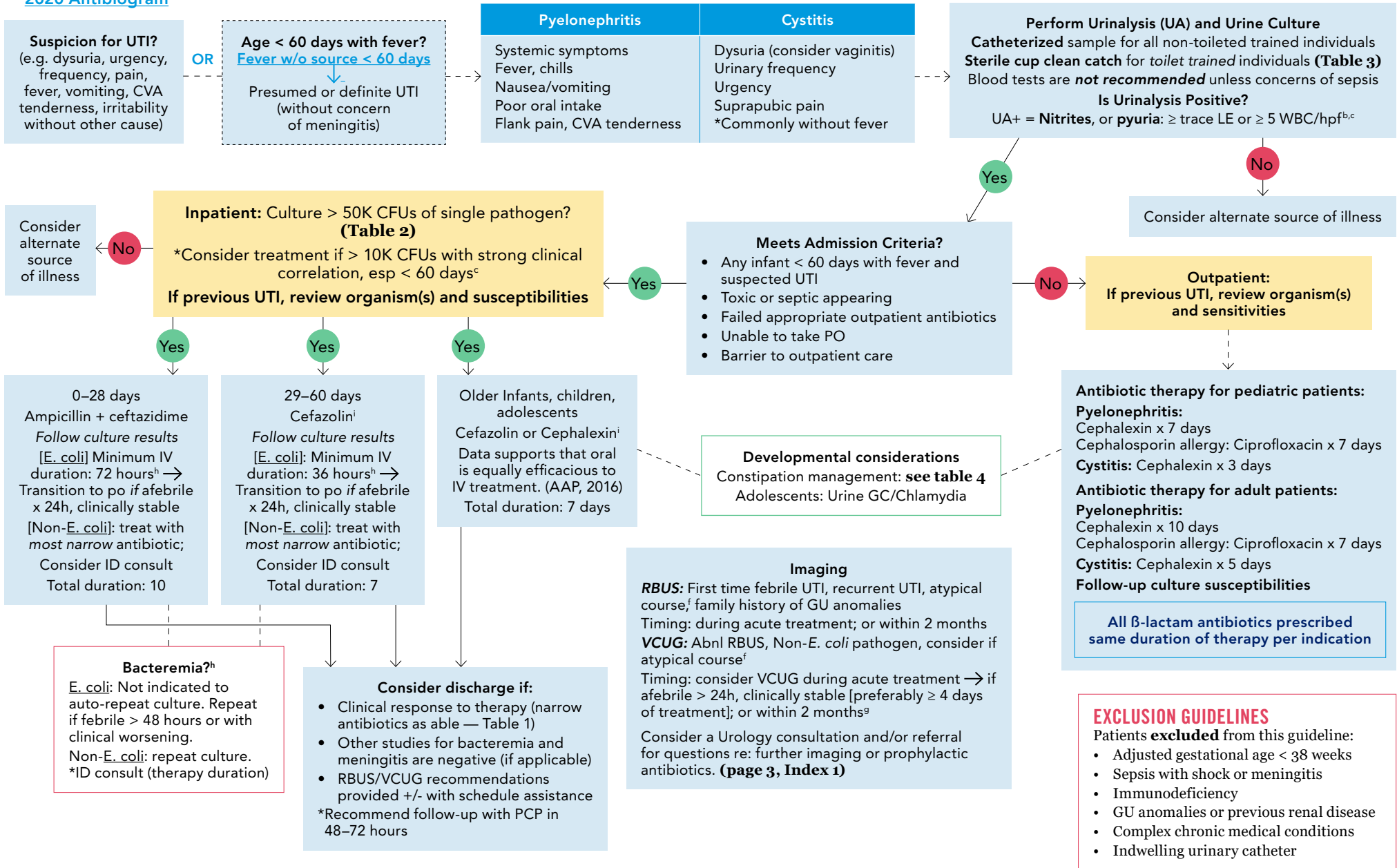


Aim: To decrease variation in management for uncomplicated UTI.

2020 Antibiogram



Aim: To decrease variation in management for uncomplicated UTI.

Antibiotic	Neonatal dosing	Pediatric dosing	Adult dosing
<b>Note: All β-lactam antibiotics prescribed same duration of therapy per indication</b>			
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) <sup>d</sup>	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)	IV: 400 mg q12h PO: 500 mg BID
Nitrofurantoin (PO)	Contraindicated in patients < 1 month of age	Do not use if CrCl < 30 mL/min Cystitis — Duration of therapy: 3 days <b>Immediate release formulation</b> (brand names: <b>Furadantin</b> , <b>Macrochantin</b> ) 5 to 7 mg/kg/day divided four times daily (max: 100 mg/dose); or fixed dosing as below: <ul style="list-style-type: none"> <li>• 7 to &lt; 12 kg: 12.5 mg PO four times daily</li> <li>• 12 to &lt; 22 kg: 25 mg PO four times daily</li> <li>• 22 to &lt; 31 kg: 37.5 mg PO four times daily</li> <li>• 31 to &lt; 42 kg: 50 mg PO four times daily</li> <li>• ≥ 42 kg: 50 to 100 mg PO four times daily</li> </ul> <b>Nitrofurantoin macrocrystal/monohydrate</b> (brand name <b>Macrobid</b> ) Adolescents: 100 mg BID	Do not use if CrCl < 30 mL/min or pregnant at term (38–42 weeks gestation) Cystitis – Duration of therapy: 5 days <b>Nitrofurantoin macrocrystal/monohydrate</b> (brand name: <b>Macrobid</b> ) 100 mg PO BID
TMP-SMX (IV/PO)	Avoid in infants < 2 months of age	Cystitis – Duration of therapy: 3 days Pyelo – Duration of therapy: 7 days 5 mg/kg/dose IV/PO q12h (max: 160 mg/dose)	Avoid during 3rd trimester of pregnancy Cystitis – Duration of therapy: 5 days Pyelo – Duration of therapy: 10 days 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 **cefepodoxime** can be used to predict susceptibility to **cefdinir**
- Susceptibility to cefepodoxime 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 cefepodoxime as surrogate) if the isolate is susceptible to cefepodoxime. Inferring susceptibility to cefixime using cefepodoxime susceptibility as surrogate is **not** advised.

Aim: To decrease variation in management for uncomplicated UTI.

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; <sup>c</sup> 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

Pre-continent children: contamination rates <sup>5</sup>		
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** Yusuf E, Van Herendael B, van Schaeren J. *J Clin Pathol* 2017;70:631–636.

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 and 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

Aim: To decrease variation in management for uncomplicated UTI.

### 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.)

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		1 cap (17 g) QD up to 2 caps (34 g) BID	5 mL or 1 tab QD (QHS) up to BID
> 10 years			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 <i>several months</i> of therapy. Recommend <b>interval follow-up(s)</b> with primary care provider and/or gastroenterologist.			

**Aim:** To decrease variation in management for uncomplicated UTI.

## NOTES

- a.) **Uropathogens:** Approximately 85% to 90% of uncomplicated UTIs are caused by *Escherichia coli*.<sup>15</sup> According to Children's Minnesota 2020 Antibiogram, *E. coli* urine isolates were 95% sensitive to Cefazolin (1st gen cephalosporin). [2020 Antibiogram](#)
- b.) **UA:** The 2011 American Academy of Pediatrics (AAP) guideline defines UTI by the presence of **at least 50,000 CFU/mL** 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).<sup>28</sup>
- 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, nephrolithiasis<sup>9</sup>
- 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.<sup>3</sup> 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.<sup>24</sup>
- d.) **Oral 3rd generation cephalosporins:** Susceptibility of *E. coli* and other gram-negative uropathogens to ceftriaxone should **not** be 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).<sup>32</sup> 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 cefdinir<sup>13</sup>, 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 pyuria were highly sensitive and specific screening in febrile infants <60 days, esp those with bacteraemia. Negative nitrites highly correlated with neonates without UTI.<sup>30</sup>
- 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: Oliguria, treatment failure, or AKI
- c.) *E. coli* 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.<sup>21</sup>
- 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<sup>11,16</sup> → 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.<sup>3,14</sup>
- 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.<sup>4,23</sup>
- 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.<sup>31</sup>
- 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](#).

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: Katie Brunsberg, Jodi O'Neill, Andrew Rose, Gloria Swanson
  - Infectious Disease: Bill Pomputius
  - Pharmacy: Christina Koutsari
  - Primary Care: Kent Wegmann
  - Urology: Erica Lundberg, Judy Reitmeyer-Hunt, Katie Willihnganz-Lawson
- Organizational Stakeholders
  - Medical-Surgical: Courtney Herring
  - Quality Improvement: Gabi Hester



**Aim:** To decrease variation in management for uncomplicated UTI.

## REFERENCES

1. Bonsu BK, Shuler L, Sawicki L et al. Susceptibility of recent bacterial isolates to cefdinir and selected antibiotics among children with urinary tract infections. *Acad Emerg Med.* 2006 Jan;13(1):76-81.
2. Buettcher M, Trueck J, Niederer-Loher A, et al. Swiss consensus recommendations on urinary tract infections in children. *Eur J Pediatr.* 2021 Mar;180(3):663-674.
3. Chang et al. Diagnosis and Management of UTI in Febrile Infants age 0-2 Months: Applicability of the AAP Guideline. *Journal of Hospital Medicine* 2020;15:176-180.
4. Desai S, Aronson PL, Shabanova V, et al. Parenteral Antibiotic Therapy Duration in Young Infants With Bacteremic Urinary Tract Infections. *Pediatrics.* 2019; 144(3):e20183844
5. Eliakim-Raz N, Yahav D, Paul M, et al. Duration of antibiotic treatment for acute pyelonephritis and septic urinary tract infection-- 7 days or less versus longer treatment: systematic review and meta-analysis of randomized controlled trials. *J Antimicrob Chemother.* 2013 Oct;68(10):2183-91.
6. Erba L, Furlan L, Monti A et al. Short vs long-course antibiotic therapy in pyelonephritis: a comparison of systematic reviews and guidelines for the SIMI choosing wisely campaign. *Intern Emerg Med.* 2021 Mar;16(2):313-323.
7. Fox MT, Amoah J, Hsu AJ, et al. Comparative Effectiveness of Antibiotic Treatment Duration in Children With Pyelonephritis. *JAMA Netw Open.* 2020 May 1;3(5):e203951.
8. Fox MT, Melia MT, Same RG, et al. A Seven-Day Course of TMP-SMX May Be as Effective as a Seven-Day Course of Ciprofloxacin for the Treatment of Pyelonephritis. *Am J Med.* 2017 Jul;130(7):842-845.
9. Glen P, Prashar A, Hawary A. Sterile pyuria: a practical management guide. *Br J Gen Pract.* 2016;66(644):e225-e227
10. Gupta K, Hooton TM, Naber KG, et al; Infectious Diseases Society of America; European Society for Microbiology and Infectious Diseases. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: A 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. *Clin Infect Dis.* 2011 Mar 1;52(5):e103-20.
11. Kassis I, et al. Early Performance of Voiding Cystourethrogram after Urinary Tract Infection in Children. *IMAJ* 2008;10:453-456
12. Kaufman J, et al. Urinary tract infections in children: an overview of diagnosis and management. *BMJ Paediatrics Open* 2019;3:e000487. doi:10.1136/bmjpo-2019-000487
13. Leigh AP, Nemeth MA, Keyserling CH, et al. Cefdinir versus cefaclor in the treatment of uncomplicated urinary tract infection. *Clin Ther.* 2000 Jul;22(7):818-25
14. Lewis-de los Angeles WW, Thurm C, Hersh AL, et al. Trends in Intravenous Antibiotic Duration for Urinary Tract Infections in Young Infants. *Pediatrics.* 2017;140(6): e20171021
15. Mattoo TK, Shaikh N, Nelson CP. Contemporary Management of Urinary Tract Infection in Children. *Pediatrics.* 2021;147(2): e2020012138,
16. Mazzi S, Rohner K, Hayes W, et al. Timing of voiding cystourethrogram after febrile urinary tract infection in children: a systematic review. *Arch Dis Child.* 2020;105:264-269.
17. Michael M, Hodson EM, Craig JC, et al. Short versus standard duration oral antibiotic therapy for acute urinary tract infection in children. *Cochrane Database Syst Rev.* 2003;(1):CD003966.
18. National Institute for Health and Care Excellence (NICE). Urinary tract infections. <https://pathways.nice.org.uk/pathways/urinary-tract-infections> Accessed 6.18.21
19. Nelson's Pediatric Antimicrobial Therapy 2021, 27th Ed., edited by John S. Bradley, MD, Elizabeth D. Barnett, MD and Joseph B. Cantey, MD
20. Oishi T, Ueno K, Fukumoto K et al. Prophylactic cefdinir for pediatric cases of complicated urinary tract infection. *Pediatr Int.* 2011 Feb;53(1):57-61.
21. Pauchard J-Y, Chehade H, Kies CZ, et al. Avoidance of voiding cystourethrography in infants younger than 3 months with Escherichia coli urinary tract infection and normal renal ultrasound. *Arch Dis Child.* 2017;102:804-808.
22. Sader HS, Biedenbach DJ, Streit JM et al. Cefdinir activity against contemporary North American isolates from community-acquired urinary tract infections. *Int J Antimicrob Agents.* 2005 Jan;25(1):89-92.
23. Schroeder AR, Shen MW, Biondi EA, et al. Bacteraemic urinary tract infection: management and outcomes in young infants. *Arch Dis Child.* 2016;101(2):125-130. doi:10.1136/archdischild-2014-307997
24. Shaikh N, et al. Prevalence of Asymptomatic Bacteriuria in Children: A Meta-Analysis. *J Pediatr* 2020;217:110-7
25. Shaikh N, et al. Predictors of antimicrobial resistance among pathogens causing urinary tract infection in children *J Pediatr* 2016;171:116-21.
26. Shaikh N, Shope TR, Hoberman A, et al. Association Between Uropathogen and Pyuria. *Pediatrics.* 2016; 138(1):e20160087
27. Stultz JS, Francis N, Ketron S, et al. Analysis of Community-Acquired Urinary Tract Infection Treatment in Pediatric Patients Requiring Hospitalization: Opportunity for Use of Narrower Spectrum Antibiotics. *Journal of Pharmacy Technology.* 2021;37(2):79-88. doi:10.1177/8755122520964435
28. SUBCOMMITTEE ON URINARY TRACT INFECTION. Reaffirmation of AAP Clinical Practice Guideline: The Diagnosis and Management of the Initial Urinary Tract Infection in Febrile Infants and Young Children 2-24 Months of Age. *Pediatrics.* 2016;138(6):e20163026.
29. Tamma PD, Sklansky DJ, Palazzi DL, et al. Antibiotic susceptibility of common pediatric uropathogens in the United States. *Clin Infect Dis.* 2014 Sep 1;59(5):750-2.
30. Tzimenatos L, Mahajan P, Dayan PS, et al. Accuracy of the Urinalysis for Urinary Tract Infections in Febrile Infants 60 Days and Younger. *Pediatrics.* 2018;141(2):e20173068
31. Wang ME, Lee V, Greenhow TL, et al. Clinical Response to Discordant Therapy in Third-Generation Cephalosporin-Resistant UTIs. *Pediatrics.* 2020;145(2):e20191608
32. Watson JR, Burch C, Leber AL. Surrogate testing of oral third-generation cephalosporin susceptibility to common uropathogens. *Diagn Microbiol Infect Dis.* 2021 Apr;99(4):115299. doi: 10.1016/j.diagmicrobio.2020.115299.
33. Yahav D, Franceschini E, Koppel F et al. M; Bacteremia Duration Study Group. Seven Versus 14 Days of Antibiotic Therapy for Uncomplicated Gram-negative Bacteremia: A Noninferiority Randomized Controlled Trial. *Clin Infect Dis.* 2019 Sep 13;69(7):1091-1098.