Acute management, imaging, and prognosis of urinary tract infections in children

By: T. Faghihi

Pharm. D

Tehran University Of Medical Sciences

Introduction

- Urinary tract infections (UTI) are a common and important clinical problem in childhood.

- Upper urinary tract infections (ie, acute pyelonephritis) may lead to renal scarring, hypertension, and end-stage renal dysfunction.

- Although children with pyelonephritis tend to present with fever, it is often difficult on clinical grounds to distinguish cystitis from pyelonephritis, particularly in young children (those younger than two years).

- Thus, we have defined UTI broadly here without attempting to distinguish cystitis from pyelonephritis.

OVERVIEW

Goals — The goals of treatment for UTI include:

- Elimination of infection and prevention of urosepsis

- Prevention of recurrence and long-term complications including hypertension, renal scarring, and impaired renal growth and function

- Relief of acute symptoms (eg, fever, dysuria, frequency)

- **Acute management** of UTI in children entails antimicrobial therapy to treat the acute infection and evaluation for possible predisposing factors (eg, urologic abnormalities).

- **Long-term management** centers on prevention of recurrence and complications; it is discussed separately

- Decision to hospitalize
- Most infants older than two months with UTI can be safely managed as outpatients as long as close follow-up is possible.

Usual indications for hospitalization include:

- Age <2 months
- Clinical urosepsis or potential bacteremia
- Immunocompromised patient
- Vomiting or inability to tolerate oral medication
- Lack of adequate outpatient follow-up (eg, no telephone, live far from hospital, etc.)
- Failure to respond to outpatient therapy

- ANTIBIOTIC THERAPY
- The effectiveness of antimicrobial therapy for UTI is demonstrated by the change in mortality between the pre- and post-antibiotic eras.
- The mortality of UTI was as high as 20 percent in the preantibiotic era.
- In contrast, when UTI are appropriately treated with antibiotics, acute complications, including death, are uncommon.
- Antimicrobial therapy for children with presumed UTI depends upon a number of factors, including the age of the child, severity of illness, presence of vomiting, duration of fever before presentation, underlying medical and/or urologic problems, and the antimicrobial resistance patterns in the community.

Empiric therapy

- Early and aggressive antibiotic therapy (eg, within 72 hours of presentation) is necessary to prevent renal damage.

- Delayed therapy has been associated with increased severity of infection and greater likelihood of renal damage in experimental, retrospective, and small prospective studies.

Empiric therapy…

- Two large prospective studies found no association between the rate of renal scarring and the duration of fever before initiation of antimicrobial therapy.

- However, because the studies were observational, the lack of association may be related to confounding or selection bias.

- In addition, two prospective studies (including one of those cited above) demonstrate an association between delayed initiation of therapy and the development of acute pyelonephritis, as evidenced on abnormal renal scans in the acute phase of illness.

- These observations suggest that after infection has localized to the kidney, the development of renal scarring is independent of timing of antimicrobial therapy, further highlighting the need for prompt initiation of therapy.

Empiric therapy…

- Decisions regarding the initiation of empiric antimicrobial therapy for UTI are best made on a case-by-case basis based upon the probability of UTI, which is determined by demographic and clinical factors (table 1 and table 2) and the results of the dipstick and/or microscopic urinalysis (table 3 and algorithm 1A-C)

Prevalence of urinary tract infection in febrile* infants and children by demographic group

Demographic group	Prevalence or pretest probability (95% CI)
0 to 24 months	**7.0 percent (5.5-8.4)**
Girls	7.3 percent (5.0-9.6)
White girls with temperature ≥39°C	16 percent•
Boys	8.0 (5.5-10.4)
White children	8.0 percent (5.1-11)
Black children	4.7 percent (2.1-7.3)
0 to 3 months	**7.2 percent (5.8-8.6)**
Girls	7.5 percent (5.1-10)
Circumcised boys	2.4 percent (1.4-3.5)
Uncircumcised boys	20.1 percent (16.8-23.4)
3 to 6 months	**6.6 percent (1.7-11.5)**
Girls	5.7 percent (2.3-9.4)
Boys	3.3 percent (1.3-5.3)
6 to 12 months	**5.4 percent (3.4-7.4)**
Girls	8.3 percent (3.9-12.7)
Boys	1.7 percent (0.5-2.9)
12 to 24 months	**4.5 percent•**
Girls	2.1 percent•
Circumcised boys >1 year	<1 percent•
<19 years with urinary symptoms and/or feverΔ	**7.8 percent (6.6-8.9)**

* Temperature ≥38°C.
• 95% confidence interval not available.
Δ Most of these children were older than two years.
Data from: Shaikh, N, Morone, NE, Bost, JE, Farrell, MH. Prevalence of Urinary Tract Infection in Childhood: A Meta-Analysis. Pediatr Infect Dis J 2008; 27:302.

Likelihood ratios for selected symptoms and signs of urinary tract infection in children

Symptoms and signs	Positive likelihood ratio*	Negative likelihood ratio●
Symptoms and signs in children aged 0 to 24 months		
Nonblack race	1.4 (95% CI 1.1-1.8)	0.52 (95% CI 0.29-0.73)
History of prior UTIΔ	2.3 (95% CI 0.3-17.4)	0.97 (95% CI 0.89-1.07)
	2.9 (95% CI 1.2-7.1)	0.95 (95% CI 0.89-1.02)
Temperature (T) >39°C	1.4 (95% CI 1.2-1.7)	0.78 (95% CI 0.65-0.81)
T >40°Δ	3.2 (95% CI 0.7-15.6)	0.93 (95% CI 0.8-1.08)
	3.3 (95% CI 1.3-8.3)	0.66 (95% CI 0.35-1.25)
Fever >24 hours	2.0 (95% CI 1.4-2.9)	0.90 (95% CI 0.83-0.97)
Fever >48 hours	1.3 (95% CI 0.8-1.9)	0.95 (95% CI 0.85-1.06)
Ill appearance (infants <3 months)Δ	0.59 (95% CI 0.22-1.59)	1.03 (95% CI 0.99-1.08)
	1.1 (95% CI 0.9-1.3)	0.95 (95% CI 0.84-1.08)
Ill appearance (children 3-24 months)	1.9 (95% CI 1.5-2.4)	0.68 (95% CI 0.53-0.88)
Suprapubic tenderness	4.4 (95% CI 1.6-12.4)	0.96 (95% CI 0.9-1.01)
No other source for fever on examination◇	1.4 (95% CI 1.1-1.8)	0.69 (95% CI 0.55-0.8)
Uncircumcised male infants	2.8 (95% CI 1.9-4.3)	0.33 (95% CI 0.18-0.63)
Combination of symptoms and signs		
T > 39°C for >48 hours and no potential source for fever◇	4 (95% CI 1.2-13)	
T >38°C for >48 hours and no potential source for fever◇	3.6 (95% CI 1.4-8.8)	
T >39°C and no potential source for fever◇	2 (95% CI 1.8-2.4)	
T >39°C for >48 hours	1.7 (95% CI 0.9-2.9)	
T >39°C with a potential source for fever◇	0.86 (95% CI 0.5-1.47)	
T <39°C and potential source for fever◇	0.37 (95% CI 0.16-0.85)	
Symptoms and signs in verbal children		
Abdominal pain	6.3 (95% CI 2.5-16)	0.8 (95% CI 0.65-0.99)
Back pain	3.6 (95% CI 2.1-6.1)	0.84 (95% CI 0.75-0.95)
Dysuria/frequency	2.2 (95% CI 1.1-4.3)	0.71 (95% CI 0.45-1.13)
New-onset urinary incontinence	4.6 (95% CI 2.8-7.6)	0.79 (95% CI 0.69-0.90)

* The positive likelihood ratio is the probability that a child with UTI will have the symptom or sign divided by the probability that a child without a UTI will have the symptom or sign (eg, true positive rate/ false positive rate).
● The negative likelihood ratio is the probability that a child with a UTI will not have the symptom or sign divided by the probability that a child without UTI will not have the symptom or sign (eg, the false negative rate/true negative rate).
Δ The likelihood ratios from individual studies are presented separately.
◇ Other potential sources of fever included illnesses such as upper respiratory infection, acute otitis media, and acute gastroenteritis.
Data from: Shaikh, N, Morone, NE, Lopez, J, et al. Does this child have a urinary tract infection? JAMA 2007; 298:2895.

Test characteristics of tests used to diagnose urinary tract infections in children

	Sensitivity	Specificity	Positive likelihood ratio*	Negative likelihood ratio●	Ref
Dipstick					
Leukocyte esterase (LE)	84 percent	78 percent	4	0.2	[1]
Nitrite	50 percent	98 percent	25	0.5	[1]
Nitrite or LE	88 percent	93 percent	13	0.1	[1]
Nitrite and LE	72 percent	96 percent	18	0.3	[1]
Microscopy					
Uncentrifuged					
Pyuria (>10/mm3) (all ages)	77 percent	89 percent	7	0.4	[1]
Pyuria (>10/mm3) (<2 yr)	90 percent	95 percent	18	0.1	[1,2]
Bacteriuria (gram stained)	93 percent	95 percent	19	0.1	[1]
Overall (P+B) = enhanced	85 percent	99.9 percent	85	0.1	[1]
Overall (P or B)	95 percent	89 percent	9	0.1	[1]
Centrifuged					
Pyuria (>5/hpf)	67 percent	79 percent	3	0.4	[1]
Bacteriuria	81 percent	83 percent	5	0.2	[3]
Overall (P+B)	66 percent	99 percent	7	0.4	[2]

* Positive likelihood ratio: The positive likelihood ratio is the probability that a child with a UTI will have a positive test divided by the probability that a child without a UTI will have a positive test (eg, true positive rate/false positive rate). The higher the positive likelihood ratio, the better the test.
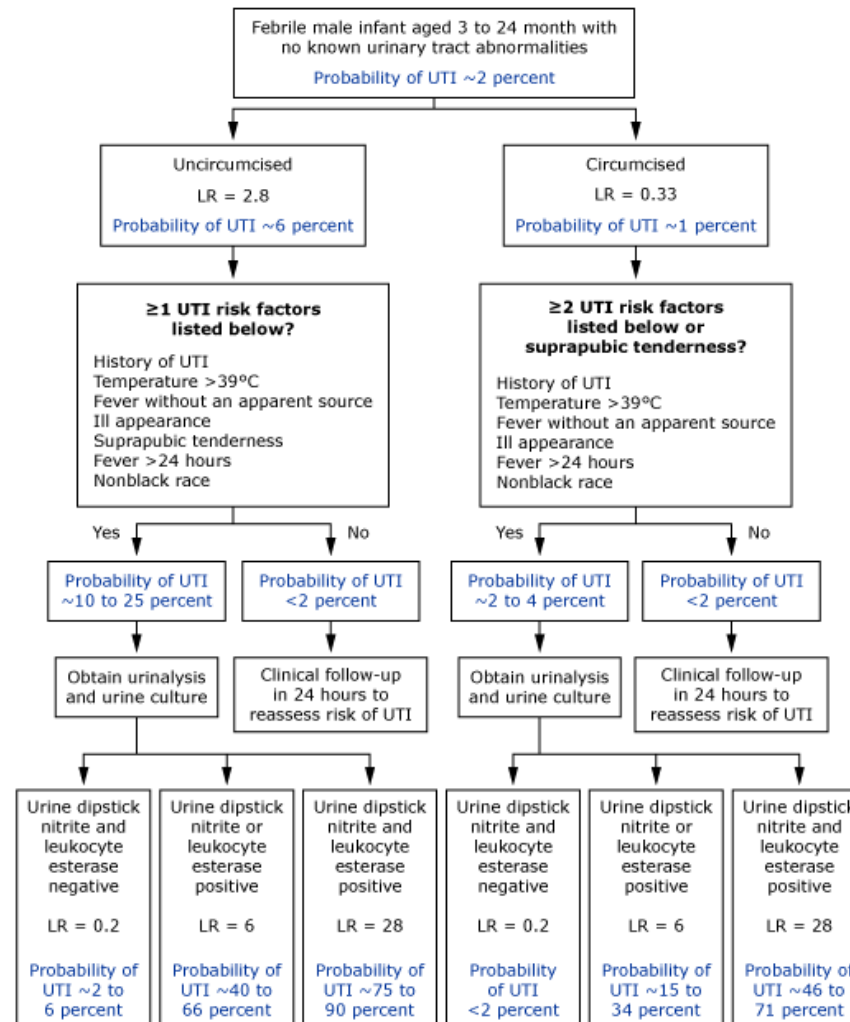
● Negative likelihood ratio: The negative likelihood ratio is the probability that a child with a UTI will have a negative test divided by the probability that a child without a UTI will have a negative test (eg, false negative rate/true negative rate). The lower the negative likelihood ratio, the better the test (a perfect test has a negative likelihood ratio of zero).

1. Data from: Gorelick, MH, Shaw, KN. Screening tests for urinary tract infection in children: A meta-analysis. Pediatrics 1999; 104:e54.
2. Data from: Huicho, L, Campos-Sanchez, M, Alamo, C. Metaanalysis of urine screening tests for determining the risk of urinary tract infection in children. Pediatr Infect Dis J 2002; 21:1.
3. Data from: Downs, SM. Technical report: urinary tract infections in febrile infants and young children. The Urinary Tract Subcommittee of the American Academy of Pediatrics Committee on Quality Improvement. Pediatrics 1999; 103:e54.
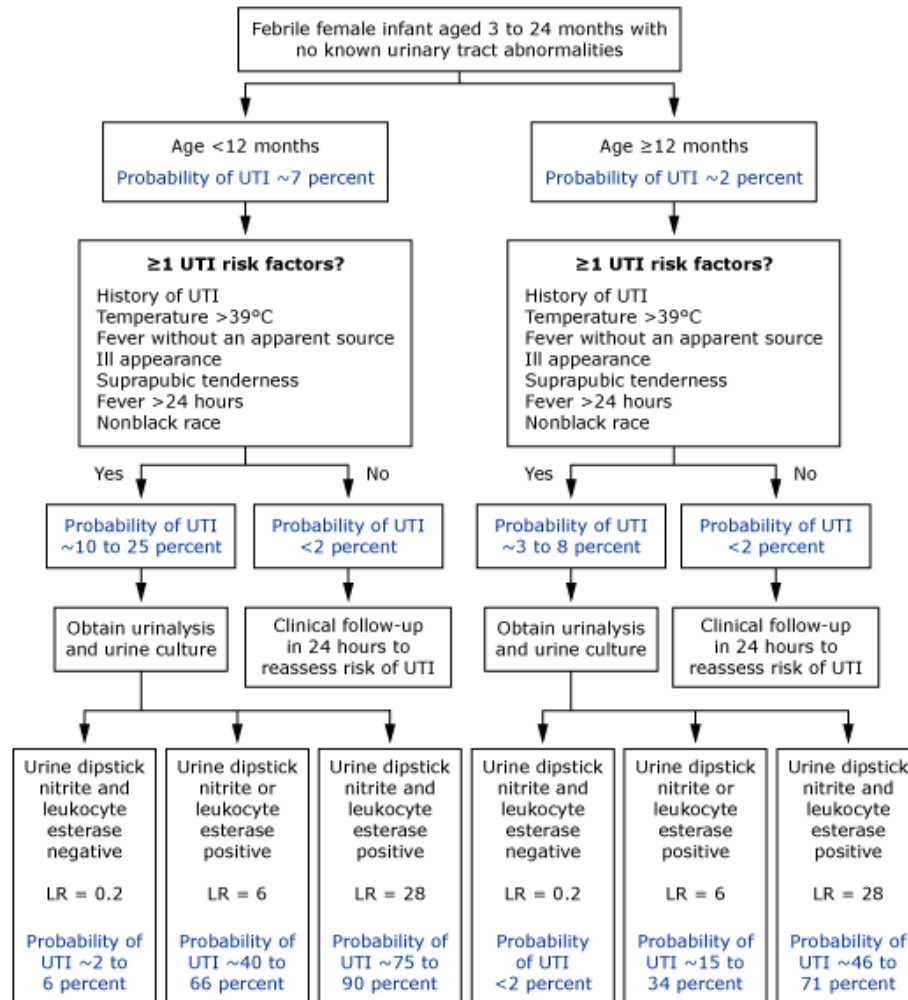
UpToDate

Diagnostic algorithm for febrile male infants aged 3 to 24 months suspected of having a UTI

Febrile male infant aged 3 to 24 month with no known urinary tract abnormalities

Probability of UTI ~2 percent

Uncircumcised

LR = 2.8

Probability of UTI ~6 percent

≥1 UTI risk factors listed below?

History of UTI
Temperature >39ºC
Fever without an apparent source
Ill appearance
Suprapubic tenderness
Fever >24 hours
Nonblack race

Yes → Probability of UTI ~10 to 25 percent → Obtain urinalysis and urine culture

No → Probability of UTI <2 percent → Clinical follow-up in 24 hours to reassess risk of UTI

Urine dipstick nitrite and leukocyte esterase negative	Urine dipstick nitrite or leukocyte esterase positive	Urine dipstick nitrite and leukocyte esterase positive
LR = 0.2	LR = 6	LR = 28
Probability of UTI ~2 to 6 percent	Probability of UTI ~40 to 66 percent	Probability of UTI ~75 to 90 percent

---

Circumcised

LR = 0.33

Probability of UTI ~1 percent

≥2 UTI risk factors listed below or suprapubic tenderness?

History of UTI
Temperature >39ºC
Fever without an apparent source
Ill appearance
Fever >24 hours
Nonblack race

Yes → Probability of UTI ~2 to 4 percent → Obtain urinalysis and urine culture

No → Probability of UTI <2 percent → Clinical follow-up in 24 hours to reassess risk of UTI

Urine dipstick nitrite and leukocyte esterase negative	Urine dipstick nitrite or leukocyte esterase positive	Urine dipstick nitrite and leukocyte esterase positive
LR = 0.2	LR = 6	LR = 28
Probability of UTI <2 percent	Probability of UTI ~15 to 34 percent	Probability of UTI ~46 to 71 percent

UTI: urinary tract infection; LR: likelihood ratio.

Reproduced with permission from: Shaikh, N, Morone, NE, Lopez, L, et al. Does this child have a urinary tract infection? JAMA 2008; 298:2895. Copyright ©2008 American Medical Association.
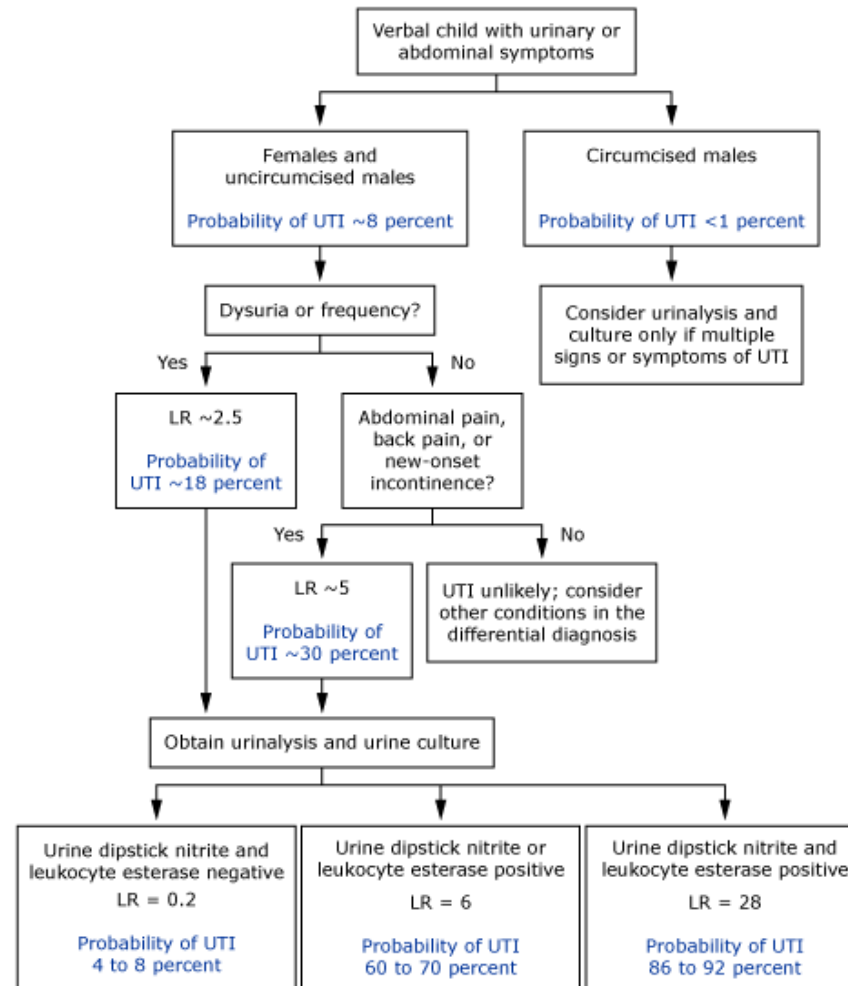
UpToDate

Diagnostic algorithm for febrile female infants aged 3 to 24 months suspected of having a UTI

```
                    ┌──────────────────────────────────────────┐
                    │ Febrile female infant aged 3 to 24 months │
                    │    with no known urinary tract             │
                    │           abnormalities                    │
                    └──────────────────────────────────────────┘
```

Age <12 months	Age ≥12 months
Probability of UTI ~7 percent	Probability of UTI ~2 percent

≥1 UTI risk factors?	≥1 UTI risk factors?
History of UTI Temperature >39°C Fever without an apparent source Ill appearance Suprapubic tenderness Fever >24 hours Nonblack race	History of UTI Temperature >39°C Fever without an apparent source Ill appearance Suprapubic tenderness Fever >24 hours Nonblack race

Yes	No	Yes	No
Probability of UTI ~10 to 25 percent	Probability of UTI <2 percent	Probability of UTI ~3 to 8 percent	Probability of UTI <2 percent
Obtain urinalysis and urine culture	Clinical follow-up in 24 hours to reassess risk of UTI	Obtain urinalysis and urine culture	Clinical follow-up in 24 hours to reassess risk of UTI

Urine dipstick nitrite and leukocyte esterase negative	Urine dipstick nitrite or leukocyte esterase positive	Urine dipstick nitrite and leukocyte esterase positive	Urine dipstick nitrite and leukocyte esterase negative	Urine dipstick nitrite or leukocyte esterase positive	Urine dipstick nitrite and leukocyte esterase positive
LR = 0.2	LR = 6	LR = 28	LR = 0.2	LR = 6	LR = 28
Probability of UTI ~2 to 6 percent	Probability of UTI ~40 to 66 percent	Probability of UTI ~75 to 90 percent	Probability of UTI <2 percent	Probability of UTI ~15 to 34 percent	Probability of UTI ~46 to 71 percent

UTI: urinary tract infection; LR: likelihood ratio.

Reproduced with permission from: Shaikh, N, Morone, NE, Lopez, L, et al. Does this child have a urinary tract infection? JAMA 2008; 298:2895. Copyright ©2008 American Medical Association.

UpToDate

Diagnostic algorithm for verbal children older than 24 months with urinary or abdominal symptoms

```
                    ┌─────────────────────────────┐
                    │ Verbal child with urinary or │
                    │     abdominal symptoms       │
                    └─────────────────────────────┘
                          │                    │
          ┌───────────────┘                    └──────────────┐
          ▼                                                   ▼
┌─────────────────────────┐              ┌─────────────────────────┐
│     Females and         │              │    Circumcised males    │
│  uncircumcised males    │              │                         │
│                         │              │ Probability of UTI <1 percent │
│ Probability of UTI ~8 percent │        └─────────────────────────┘
└─────────────────────────┘                          │
          │                                           ▼
          ▼                              ┌─────────────────────────┐
┌─────────────────────────┐              │ Consider urinalysis and │
│   Dysuria or frequency? │              │  culture only if multiple │
└─────────────────────────┘              │ signs or symptoms of UTI │
   Yes │          │ No                   └─────────────────────────┘
       ▼          ▼
┌──────────┐  ┌──────────────┐
│ LR ~2.5  │  │ Abdominal pain, │
│          │  │  back pain, or  │
│Probability of│ new-onset    │
│UTI ~18 percent│ incontinence? │
└──────────┘  └──────────────┘
       │        Yes │      │ No
       │            ▼      ▼
       │     ┌──────────┐ ┌──────────────┐
       │     │ LR ~5    │ │ UTI unlikely; consider │
       │     │          │ │ other conditions in the │
       │     │Probability of│ differential diagnosis │
       │     │UTI ~30 percent│└──────────────┘
       │     └──────────┘
       │            │
       └────────────┤
                    ▼
        ┌─────────────────────────────┐
        │ Obtain urinalysis and urine culture │
        └─────────────────────────────┘
          │            │            │
          ▼            ▼            ▼
```

Urine dipstick nitrite and leukocyte esterase negative LR = 0.2	Urine dipstick nitrite or leukocyte esterase positive LR = 6	Urine dipstick nitrite and leukocyte esterase positive LR = 28
Probability of UTI 4 to 8 percent	Probability of UTI 60 to 70 percent	Probability of UTI 86 to 92 percent

UTI: urinary tract infection; LR: likelihood ratio.
Reproduced with permission from: Shaikh, N, Morone, NE, Lopez, L, et al. Does this child have a urinary tract infection? JAMA 2008; 298:2895. Copyright ©2008 American Medical Association.

UpToDate

Empiric therapy…

- We suggest that empiric antimicrobial therapy be initiated while awaiting culture results in infants and young children who are at increased risk for UTI on the basis of demographic and clinical factors (table 1 and table 2) and in children with underlying urologic abnormalities.

- In children who are not at increased risk for UTI, we suggest that empiric antibiotic therapy be initiated if the results of urine dipstick or microscopic examination indicate a high likelihood of UTI (table 3)

Empiric therapy…

- Choice of agent — Gram staining of the urine, if readily available, can help guide decisions regarding empiric therapy. The ultimate choice of antimicrobial therapy is based upon the sensitivities of the patient's urine culture isolate.

- Escherichia coli is the most common bacterial cause of UTI; it accounts for approximately 80 percent of UTI in children.

- Other gram-negative bacterial pathogens include Klebsiella, Proteus, Enterobacter, and Citrobacter.

- Gram-positive bacterial pathogens include Staphylococcus saprophyticus, Enterococcus, and, rarely, Staphylococcus aureus

Empiric therapy…

- We recommend that empiric therapy for UTI in children include an antibiotic that provides adequate coverage for E. coli. The agent of choice should be guided by local resistance patterns.

- Approximately 50 percent of E. coli are resistant to amoxicillin or ampicillin.

- In addition, increasing rates of E. coli resistance to first-generation cephalosporins (eg, cephalexin), amoxicillin-clavulanate or ampicillin-sulbactam, and trimethoprim-sulfamethoxazole (TMP-SMX) have been reported in some communities.

- Increased resistance to extended-spectrum cephalosporins has been reported in children receiving prophylactic antibiotics.

Empiric therapy…

- Second- and third-generation cephalosporins (eg, cefprozil, cefpodoxime, cefixime, cefotaxime, ceftriaxone) and aminoglycosides (eg, gentamicin, amikacin) are appropriate first-line agents for empiric treatment of UTI in children.

- However, these drugs are not effective in treating Enterococcus and should not be used for patients in whom enterococcal UTI are suspected (eg, those with a urinary catheter in place, instrumentation of the urinary tract, or an anatomical abnormality). In such patients, amoxicillin or ampicillin should be added.

Empiric therapy...

- Oral therapy
- Infants and young children older than two months who are treated in the outpatient setting can be treated orally as long as oral intake is tolerated .
- In children who are treated orally, the initial dose should be administered in the outpatient setting to confirm tolerability.
- Close contact with the family should be maintained for the first two to three days of therapy .
- The seriousness of the infection and the need for completion of the entire course of therapy should be stressed [25].
- We suggest cefixime or another oral third-generation cephalosporin (eg, cefdinir, ceftibuten) as the first-line oral agent in the treatment of UTI in children .
- In a randomized, controlled trial of 306 children 1 to 24 months of age with a febrile UTI, oral therapy with cefixime for 14 days was as effective as intravenous therapy with cefotaxime for three days followed by oral therapy with cefixime [3]. The rates of symptom resolution, sterilization of the urine, reinfection, and renal scarring did not differ between groups.

Empiric therapy…

- A similar trial in children 6 months to 16 years, albeit limited by imbalances in treatment group comparability at baseline and high drop-out rates, found once-daily therapy with ceftibuten to be comparable to initial therapy with ceftriaxone followed by ceftibuten.

Empiric therapy…

- Oral amoxicillin-clavulanate (50 mg/kg per day in three divided doses) also was shown to be as effective as parenteral therapy followed by oral therapy in a multicenter, randomized trial in Italy.

- However, amoxicillin-clavulanate, as discussed below, is associated with increasing rates of resistance.

Empiric therapy…

- Cefixime, cefdinir, and ceftibuten are dosed as follows:

- Cefixime (16 mg/kg per day by mouth in two divided doses on the first day, followed by 8 mg/kg once per day to complete therapy). (See 'Duration of therapy' below.)
- Cefdinir (14 mg/kg per day by mouth divided in two doses)
- Ceftibuten (9 mg/kg by mouth once per day)
- Other second- or third-generation cephalosporins that may be used for oral therapy include cefprozil and cefpodoxime [29]. However, no large trials have specifically examined the efficacy of these agents for pediatric UTI

Empiric therapy…

- Amoxicillin and ampicillin are not routinely recommended for empiric therapy because of the high rate of resistance of E. coli.

- Similarly, amoxicillin-clavulanate, first-generation cephalosporins (eg, cephalexin), and TMP-SMX should be used with caution because of the increasing rates of resistance to these drugs.

Empiric therapy…

- Fluoroquinolones (eg, ciprofloxacin) are effective for E. coli, and resistance is rare.

- Ciprofloxacin is licensed by the United States Food and Drug Administration for use in complicated UTI and pyelonephritis in children.

- However, the safety of quinolones in children is still under study.

- In addition, the widespread use of fluoroquinolones is leading to increased resistance among other bacteria.

Empiric therapy…

- [Ciprofloxacin](#) should not be used as a first-line agent. The American Academy of Pediatrics (AAP) Committee on Infectious Diseases recommends that the use of ciprofloxacin for UTI in children be limited to UTI caused by Pseudomonas aeruginosa or other multidrug-resistant, gram-negative bacteria.

Empiric therapy…

- Oral agents that are excreted in the urine but do not achieve therapeutic serum (eg, nalidixic acid, nitrofurantoin) should not be used to treat UTI in febrile infants and young children in whom renal involvement is likely.

Empiric therapy…

- Parenteral therapy
- Third- or fourth-generation cephalosporins (eg, cefotaxime, ceftriaxone, cefepime) and aminoglycosides (eg, gentamicin) are appropriate first-line parenteral agents for empiric treatment of UTI in children.
- Definitive therapy is based upon the results of urine culture and sensitivities.
- Acceptable inpatient treatment regimens include the combination of ampicillin and gentamicin, gentamicin alone, or a third- or fourth-generation cephalosporin.
- Ampicillin should be included if enterococcal UTI is suspected.

Empiric therapy...

- The doses are as follows:
- Ampicillin (100 mg/kg/day IV divided in four doses)
- Gentamicin (7.5 mg/kg/day divided in three doses)
- Cefotaxime (150 mg/kg per day IV divided in three doses)
- Ceftriaxone (50 to 100 mg/kg per day IV)
- Cefepime (100 mg/kg per day divided in two doses for children weighing ≤40 kg, maximum daily dose 1 g; 500 mg twice per day for children weighing >40 kg)

Empiric therapy...

- Outpatient parenteral therapy
- Once-daily parenteral administration of gentamicin or ceftriaxone in a day treatment center may avoid the need for hospital admission in select patients (eg, children who are ≥3 months old who are unable to tolerate oral therapy and are nontoxic appearing, well hydrated, without urologic abnormalities, and whose caretakers will be able to adhere to the outpatient regimen)

Empiric therapy…

In children receiving antibiotic prophylaxis

- Whether the child has been receiving antibiotic prophylaxis (for urinary tract infection or other medical problems) is another factor to consider in the choice of empiric antibiotics.

- This was illustrated in a review of antibiotic resistance patterns among 361 children hospitalized for UTI at a tertiary-care children's hospital between 1997 and 2001.

- **E. coli** was the causative organism in 87 percent of cases overall but was less frequent among children receiving prophylactic antibiotics (58 percent) and in children with a history of previous UTI (47 percent).

Empiric therapy…

- **Antibiotic resistance patterns** of isolated organisms differed according to whether the child was receiving prophylactic antibiotics.

- Among the isolates from 26 children receiving prophylaxis (with amoxicillin, TMP-SMX, penicillin, or nitrofurantoin), the following findings were noted:
- Resistance to cefotaxime was 27 percent, compared to 4 percent overall
- Resistance to ceftazidime and cefepime were 19 and 16 percent, respectively (compared to 4 and 2 percent overall)
- Sensitivity to aminoglycosides remained high (98 and 95 percent for amikacin and gentamicin, respectively)

- It is not clear whether the increased resistance to third- and fourth-generation cephalosporins among patients receiving prophylaxis is caused by altered bacterial flora, a predisposition to acquisition of resistant organisms, and/or previous exposure to third-generation cephalosporins.

Empiric therapy…

- **This report highlights the importance of consideration of antibiotic resistance patterns when choosing empiric therapy .**

- **It also suggests that aminoglycoside therapy may be indicated pending sensitivity results for certain children who are hospitalized with UTI, particularly those who are highly febrile or clinically unstable.**

Empiric therapy…

- Duration of therapy
- The total duration of therapy depends upon the age of the child and the clinical scenario.

- Children younger than two years and children with febrile or recurrent UTI are usually **treated for 10 days .**

  It is suggested that **prophylactic antibiotics** (eg, TMP-SMX, nitrofurantoin) be initiated after completion of treatment and continued until the results of the imaging tests are available, unless images are obtained immediately following therapy.

- Children older than two years who are afebrile and without abnormalities of the urinary tract or previous episodes of UTI are usually treated **for five days**; such children have a low risk of recurrence or complications.

Response to therapy

Clinical response

- The clinical condition of most patients improves within 24 to 48 hours of initiation of appropriate antimicrobial therapy.

Response to therapy…

- The mean time to resolution of **fever** is 24 hours, but fever may persist beyond 48 hours.

- In one review of 288 children younger than two years who were admitted to a tertiary-care children's hospital with febrile UTI, 89 percent were afebrile within 48 hours of antimicrobial therapy .

- No differences were noted between those who remained febrile >48 hours and those who were afebrile within 48 hours with respect to bacteremia (42 and 35 percent, respectively), hydronephrosis (3 and 8 percent, respectively) and significant VUR (19 and 14 percent, respectively).

Response to therapy…

- In children whose **clinical condition (other than persistent fever)** worsens or fails to improve as expected within 24 to 48 hours of initiation of antimicrobial therapy**:**

- **Broadening antimicrobial therapy may be indicated if the culture and sensitivity results are not yet available.**

  Most of the empiric regimens suggested above do not provide adequate coverage for enterococcus.

- Renal ultrasonography (RUS) or computed tomography should be performed as soon as possible (to evaluate the presence of renal abscess, urinary calculi, or surgically correctable anatomic abnormalities or obstruction) ; voiding cystourethrogram (VCUG) or radionuclide cystogram (RNC) should be performed at the earliest convenient time

Repeat urine culture

- Several observational studies suggest there is little utility in repeating the urine culture in children with UTI who are treated with an antibiotic to which their uropathogen is susceptible.

- It is not necessary to routinely obtain repeat urine cultures during antimicrobial therapy to document sterilization of the urine, provided that the child has had the expected clinical response and the uropathogen is susceptible to the antibiotic that is used for treatment.

- However, urine cultures should be repeated after 48 hours of therapy if the uropathogen is not susceptible (intermediate or resistant) to the antibiotic that is being used for treatment or if susceptibility testing is not performed.

- **Data are not available to determine that clinical response ensures bacteriologic cure.**

IMAGING

- The rationale for imaging in young children with UTI is to identify abnormalities of the genitourinary tract, including VUR and obstructive uropathies.

- If such abnormalities are detected, steps can be taken to modify the risk of subsequent renal damage (eg, surgical intervention or antibiotic prophylaxis to prevent recurrent UTI).

- Urinary tract anomalies are more frequent among children with UTI caused by pathogens other than Escherichia coli.

IMAGING…

Indications

- Evidence to support the utility of routine imaging in reducing long-term sequelae (renal scarring, hypertension, renal failure) is limited, and there is some controversy about the optimal imaging strategy, particularly the role of ultrasonography.

- The **AAP practice parameter on UTI** suggests routine imaging with renal ultrasonography (RUS) and voiding cystourethrogram (VCUG) in the evaluation of febrile infants and young children (two months to two years) with UTI.

- Others suggest that VCUG is the most important (and perhaps the only) study necessary in young children with a first UTI.

IMAGING…

- suggest routine imaging (RUS and VCUG) for:
- Girls younger than three years of age with a first UTI (children older than three years are more reliably able to verbalize urinary symptoms).
- Boys of any age with a first UTI
- Children of any age with a febrile UTI
- Children with recurrent UTI (if they have not been imaged previously)
- First UTI in a child of any age with a family history of renal disease, abnormal voiding pattern, poor growth, hypertension, or abnormalities of the urinary tract.

IMAGING…

- We do not repeat RUS in children in whom prenatal ultrasonography was performed at a reputable center at >30 to 32 weeks of gestation.

IMAGING…

- Ultrasonography — Renal ultrasonography (RUS) is a non-invasive test that can demonstrate the size and shape of the kidneys, the presence of duplication and dilatation of the ureters, and the existence of gross anatomic abnormalities. It is not reliable in detecting renal scarring or VUR.

- The yield of RUS in detecting clinically significant obstructive anomalies is limited

IMAGING…

- Voiding cystourethrogram — Approximately 40 percent of young children with a first febrile UTI have VUR on VCUG .

- The VCUG is the test of choice to establish the presence and degree of VUR. The procedure involves catheterization to fill the bladder with a radioopaque or radioactive liquid and recording of VUR during voiding.

- Two tests are available to detect VUR: the fluoroscopic contrast voiding cystourethrogram (VCUG) and radionuclide cystogram (RNC). The RNC is more sensitive than the contrast VCUG (sensitivity 45 to 47 percent versus 78 to 91 percent, respectively) and is less expensive. However, contrast VCUG provides better anatomic resolution, which makes it more suited to grading VUR. The radiation exposure depends upon the technique and equipment used.

- The utility of the routine VCUG in the evaluation of children with UTI has been questioned.

- The controversy centers on the changing view of the role of VUR in the development of renal damage and progressive renal failure

IMAGING…

- However, until clinical studies showing that similar renal outcomes (chronic renal failure and renal scarring) are observed in children with VUR who are treated with antimicrobial prophylaxis or placebo, we continue to suggest VCUG to evaluate possible VUR as described above.

- Although VCUG is often scheduled several weeks after UTI, it may be performed as soon as the patient is asymptomatic.

- Early imaging (as early as the first week) does not appear to falsely increase the detection of VUR.

IMAGING...

- Renal scintigraphy — Renal scintigraphy using dimercaptosuccinic acid (DMSA) can be used to detect acute pyelonephritis and renal scarring in the acute and chronic settings, respectively.

- DMSA is injected intravenously, and uptake by the kidney is measured two to four hours later. Areas of decreased uptake represent pyelonephritis or scarring.

- The role of renal scintigraphy in the management of children with acute UTI is controversial.

- Scintigraphy at the time of an acute UTI provides information about the extent of renal parenchymal involvement.

- Moreover, most (>80 percent) children with moderate to severe VUR (grade III or higher) will have a positive DMSA scan.

- As such, some have advocated DMSA be used instead of a VCUG to identify children at higher risk for renal scarring.

IMAGING…

- On the other hand, use of the DMSA as a screening strategy to identify high-risk children has not been systematically studied.

- Furthermore, since most young febrile children with UTI have pyelonephritis and a positive DMSA, this strategy may lead to identification of a large number of children who may or may not be at risk for future UTI.

- Most initial DMSA defects resolve on follow-up.

- Careful clinical follow-up of all children with UTI may obviate the need for routine DMSA

PROGNOSIS

- *Recurrent UTI*
- *Long-term sequelae*

Recurrent UTI

- Approximately 14 percent of children younger than six years with UTI have a subsequent UTI.

- A large retrospective study found that white race, age three to five years , and VUR of grade IV to V were associated with a higher risk of UTI recurrence.

- Importantly, treatment with antimicrobial prophylaxis was not associated with a lower risk of UTI recurrence.

- Furthermore, children treated with antimicrobial prophylaxis had a higher risk of resistant organisms with their subsequent UTI.

Long-term sequelae

- The effects of UTI in young children were identified in a prospective study evaluating various imaging modalities after a first febrile urinary tract infection in children who underwent RUS, DMSA scan within 72 hours of diagnosis, VCUG one month later, and follow-up DMSA scan six months later :

- Approximately 40 percent had VUR (identified with VCUG); among children with VUR, 96 percent had VUR of grade I, II, or III, which typically resolves spontaneously over time.

- Renal scars (identified by DMSA scan) developed in approximately 8 percent of patients overall, 15 percent of those who had abnormal DMSA scan at the time of diagnosis, and none of the children who had normal renal scans at the time of diagnosis. The long-term significance of scarring, as identified by DMSA, remains to be determined.

Long-term sequelae…

- Predicting which children with UTI will develop long-term sequelae remains difficult.
- The large majority of children with UTI have no long-term sequelae, as illustrated by the following observations:
- In a study of 111 high-risk girls who were followed for 6 to 32 years after their initial UTI, only seven (6 percent) had decreased glomerular filtration rate (GFR).
- In another study of 68 children with history of urographic renal scarring who were followed for 16 to 26 years after their index UTI, median GFR and mean 24-hour ambulatory blood pressure were no different in children with and without urographic renal scarring.
- However, in seven patients with a history of bilateral urographic scarring, GFR decreased over time and was significantly less than in children who had a history of unilateral scarring.
- The prognosis for children with nonfebrile UTI is discussed separately

SUMMARY AND RECOMMENDATIONS

- Most children with urinary tract infection (UTI) can be managed as outpatients.

- Indications for hospitalization include age <2 months, clinical urosepsis or potential bacteremia, immunocompromised patient, vomiting or inability to tolerate oral medication, lack of outpatient follow-up, and failure to respond to outpatient therapy.

- We suggest that empiric antimicrobial therapy be initiated while awaiting culture results in infants and young children who are at increased risk for UTI on the basis of demographic and clinical factors (table 1 and table 2 and algorithm 1A-C) and children with underlying urologic abnormalities.

- In children who are not at increased risk for UTI, we suggest that empiric antibiotic therapy be initiated if the results of urine dipstick or microscopic examination indicate a high likelihood of UTI (table 3).

SUMMARY AND RECOMMENDATIONS...

- We recommend that empiric therapy for UTI in children include an antibiotic that provides adequate coverage for Escherichia coli (Grade 1B).

- The agent of choice should be guided by local resistance patterns.

- Second- and third- generation cephalosporins or gentamicin are appropriate alternative first-line empiric agents for the treatment of UTI in infants and children.

- We suggest cefixime or another third-generation cephalosporin as the first-line oral agent for empiric treatment.

- Amoxicillin or ampicillin should be added if enterococcal infection is suspected.

SUMMARY AND RECOMMENDATIONS…

- The duration of therapy depends upon the age of the child and the clinical scenario.

- Children younger than two years and children with febrile or recurrent UTI are usually treated for 10 days.

- We suggest that prophylactic antibiotics be initiated after completion of the treatment course and continued until the results of the imaging tests are available (Grade 2B).

- Children older than two years who are afebrile and without abnormalities of the urinary tract or previous episodes of UTI are usually treated for shorter periods.

SUMMARY AND RECOMMENDATIONS...

- The clinical condition of most patients improves within 24 to 48 hours of initiation of appropriate antimicrobial therapy.

- In children whose clinical condition worsens or fails to improve as expected within 24 to 48 hours of initiation of antimicrobial therapy, broadening of empiric therapy may be indicated.

- Renal ultrasonography (RUS) or computed tomography should be performed to evaluate the presence of renal abscess, urinary calculi, or surgically correctable anatomic abnormalities or obstruction).

SUMMARY AND RECOMMENDATIONS…

- We suggest routine imaging (renal ultrasonography and voiding cystourethrogram for (Grade 2C):

- Girls younger than three years of age with a first UTI
- Boys of any age with a first UTI
- Children of any age with a febrile UTI
- Children with recurrent UTI (if they have not been imaged previously)
- First UTI in a child of any age with a family history of renal disease, abnormal voiding pattern, poor growth, hypertension, or abnormalities of the urinary tract

- We do not repeat renal ultrasonography in children in whom prenatal ultrasonography was performed in a reputable center at >30 to 32 weeks of pregnancy

- The majority of children with UTI have no long-term sequelae.

- Prediction of long-term sequelae in children with UTI remains difficult.