Inclusion Criteria
- Birth to 18 years, with a postmenstrual age of at least 40 weeks, with presumed or definite UTI (not a recurrent UTI)

Exclusion Criteria
- Prior history of UTI
- Chronic kidney disease as defined by estimated glomerular filtration rate (GFR) by the original Schwartz formula < 80 mL/min/1.73m²
- Genitourinary abnormalities, including: previous genitourinary surgery (other than circumcision), neurogenic bladder conditions, known obstructive uropathy, known high-grade vesicoureteral reflux (Grades IV-V)
- Septic shock
- Presumed or definite meningitis
- Conditions requiring Intensive Care Unit care
- Immunocompromised host
- Pregnancy
- Recent history of sexual abuse

Atypical Versus Typical UTI
Atypical UTI is defined as a UTI with one of the following properties:
- Seriously ill
- Poor urine flow: oliguria not due to dehydration, or urinary retention; urine output less than 1 ml/kg/hour
- Abdominal or bladder mass
- Elevated creatinine (eGFR < 80 ml/min/1.73 m²)
- Septicemia
- Failure to respond to treatment with appropriate antibiotics within 48 hours
- Infection caused by organism other than Escherichia coli

Typical UTI is defined as a UTI without any of these conditions.
Urinary Tract Infection v5.0: Diagnosis

Decision to Test: Infants
- Febrile or prolonged jaundice
- > 8 days of age: irritable, emesis, failure to thrive

Decision to Test: Non-Toilet Trained Children
- Girl or uncircumcised boy: need ≥ 1 of the following.
- Circumcised boy: need ≥ 2 of the following OR suprapubic tenderness alone.
  Ill appearing, suprapubic tenderness, fever > 24 hrs, fever > 39°C, fever without source

Decision to Test: Toilet Trained Children & Adolescents
- Girl or uncircumcised boy: need ≥ 1 of the following.
- Circumcised boy: need ≥ 2 of the following.
  Abdominal pain, back pain, dysuria, frequency, new-onset incontinence, fever > 40°C (particularly if no source)

Decision to Test criteria met

Obtain Urinalysis and Urine Culture by the Following Method(s)
- Infants: Catheterization or suprapubic aspiration (SPA)
- Non-Toilet Trained Children: 2-6 months: consider SPA; otherwise catheterized
- Toilet Trained Children: Midstream clean catch
- Adolescents: Midstream clean catch + ‘dirty’ urine for Gonococcus (GC)/Chlamydia (Chl)

Additional Studies: Infants
- 0-60 days of age: refer to Neonatal Fever Pathway

Additional Studies: Non-Toilet Trained
- If ill appearing, consider blood culture and CSF studies

Additional Studies: Toilet Trained
- If ill appearing, consider blood culture

Additional Studies: Adolescents
- HSV testing: Culture visible lesions, or cervical culture as indicated.
- If GC/Chl positive: Consider Syphilis Screen
- Annual HIV testing
- Consider pregnancy testing in girls

Test of cure urine cultures not recommended

Potential poor sensitivity of U/As in infants

If an infant, also obtain
If an adolescent, also obtain
If non-toilet trained, also obtain
If toilet trained, also obtain

Return to Home
Admit Criteria

All Age Categories
- Toxic appearance
- Dehydration requiring IV fluids
- Adherence risk as defined by: 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
- Failed outpatient therapy as defined by: persistent clinical symptoms beyond 48 hours on appropriate therapy, or inability to maintain hydration status

Infants
- Admit all patients up to 30 days of age with presumed or definite UTI
- Admit all febrile patients 31-60 days of age with presumed or definite UTI

Adolescents
- Adherence risk is not an admission criteria for adolescents with cystitis

Outpatient Management: Non-Febrile Infants (31-60 days)
- Give ceftriaxone IM OR cephalaxin PO
- Follow up with primary care provider within 24 hours

Outpatient Management: Non-Toilet Trained Children, Toilet Trained Children & Adolescents
- Give cephalaxin PO, OR trimethoprim/sulfamethoxazole PO (if cephalosporin allergy) OR ceftriaxone IM

Culture results follow-up
- Call family to review culture results
- Narrow coverage when sensitivities return

Phase Change

Criteria for Urology Referral

Return to Home

For questions concerning this pathway, contact: UTI@seattlechildrens.org
© 2015 Seattle Children's Hospital; all rights reserved. Medical Disclaimer

Last Update: September 2015
Next Expected Review: April 2020
Urinary Tract Infection v5.0: Inpatient Management

**Inpatient Management: Infants (0-30 days)**
- Give IV ampicillin + gentamicin OR ampicillin + cefotaxime
- Give IV antibiotics 7 days minimum, then 7 days PO; 14 days total
- Switch to PO at 7 days if responding and after identification and sensitivities return; narrow coverage if possible

**Inpatient Management: Infants (31-60 days)**
- Give IV ceftriaxone OR ampicillin + gentamicin if cocci/enterococcus is suspected
- Give IV antibiotics until afebrile X 24 hrs (minimum 36 hours IV with negative initial blood cultures)
- Switch to PO if responding after identification and sensitivities return; narrow coverage if possible
- Total duration of antibiotics: 14 days

**Inpatient Management: Non-Toilet Trained Children, Toilet Trained Children & Adolescents**
- Give IV ceftriaxone OR ampicillin + gentamicin if cocci/enterococcus is suspected
- Give IV antibiotics until afebrile X 24 hrs (minimum 36 hours IV with negative initial blood cultures)
- Switch to PO if responding after identification and sensitivities return; narrow coverage if possible
- Total duration of antibiotics: adolescents (7 days), toilet trained (7-14 days), non-toilet trained (10-14 days), adolescent with cystitis (3 days)

**Discharge Criteria**

**General discharge criteria for all patients**
- Clinical response to therapy
- Able to maintain hydration status
- Social risk factors assessed and addressed
- Family education provided/completed
- Urine culture is negative on final report OR urine culture is positive and patient is on targeted antibiotics
- Other studies for bacteremia and meningitis are negative (if applicable), or if bacteremic have completed appropriate course of IV antibiotic therapy
- If indicated, renal ultrasound completed or pre-natal ultrasound reviewed
- If indicated, VCUG completed or scheduled
- Consultation (e.g., urology, nephrology, ID) completed if desired

**Infants: General criteria and**
- Afebrile (T < 38°C) for 24 hours
- Tolerating planned home therapy

**Non-toilet trained and toilet trained children**
- Afebrile (T < 38°C) for 12 hours

**Adolescents**
- Completion of or plan for additional sexually transmitted infection (STI) testing as indicated

---

*Criteria for Urology Referral*

---

*Consider imaging if no improvement in 48 hrs*
Urinary Tract Infection v5.0: Imaging Recommendations

Age Category?

- Infant or non-toilet trained
  - Can skip RUS if high quality third trimester U/S is normal and < 1 month of age
  - If stones are present, refer to Nephrolithiasis Pathway
  - Atypical UTI (seriously ill, poor urine flow (< 1 ml/kg/hr), mass, increased creatinine (eGFR < 80), treatment failure, non-E. coli) OR
  - RUS shows: hydronephrosis (pelvocaliectasis), renal parenchymal loss, kidney size discrepancies independent of SFU grade
  - VCUG recommended when patient is stable, >24 hours afebrile, and prior to the end of antibiotic therapy if possible

- Toilet-trained or adolescent
  - For boys with first UTI, or girls with atypical UTI
  - If stones are present, refer to Nephrolithiasis Pathway
  - Atypical UTI (seriously ill, poor urine flow (< 1 ml/kg/hr), mass, increased creatinine (eGFR < 80), treatment failure, non-E. coli) OR
  - RUS shows: hydronephrosis (pelvocaliectasis), renal parenchymal loss, kidney size discrepancies independent of SFU grade
  - VCUG recommended when patient is stable, >24 hours afebrile, and prior to the end of antibiotic therapy if possible

Antibiotic prophylaxis not routinely recommended for Gr I-II vesicoureteral reflux

Give antibiotic prophylaxis prior to VCUG
Age Categories: Overview

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants</td>
<td>birth to 60 days of age</td>
</tr>
<tr>
<td>Non-toilet trained children</td>
<td>greater than 60 days of age</td>
</tr>
<tr>
<td>Toilet trained children</td>
<td>up to 12 years</td>
</tr>
<tr>
<td>Adolescents</td>
<td>13 years and older or sexually active</td>
</tr>
</tbody>
</table>
### ATYPICAL
Urinary Tract Infection

- UTI with one of the following properties:
  - Seriously ill
  - Poor urine flow: oliguria not due to dehydration, or urinary retention; urine output less than 1 ml/kg/hour
  - Abdominal or bladder mass
  - Elevated creatinine (eGFR < 80 ml/min/1.73 m²)
  - Septicemia
  - Failure to respond to treatment with suitable antibiotics within 48 hours
  - Infection caused by organism other than Escherichia coli

### TYPICAL
Urinary Tract Infection

- UTI without any of the above conditions

---

*This categorization of typical vs. atypical UTI is based on a descriptive study of 180 infants aged 1 to 24 months with acute pyelonephritis (Jantunen, 2001). This study found that risk factors for significant urinary tract abnormalities included: younger infants (1 to 6 months of age), urine infected with organisms other than Escherichia coli, infants with a positive blood culture, or a lack of papG adhesin genes in patients infected with Escherichia coli. The other findings appear to have been generated by NICE committee consensus as representing risk factors where further imaging would be warranted.*
# Presumed Versus Definite UTI Definitions

<table>
<thead>
<tr>
<th>Presumed Urinary Tract Infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants and non-toilet trained children: defined by a combination of clinical features where urinary tract infection is deemed likely, regardless of urinalysis result.</td>
</tr>
<tr>
<td>Toilet trained children and adolescents: defined by a combination of clinical features and a positive urine screening test (urinalysis shows nitrite or leukocyte esterase; microscopy shows bacteria or &gt;10 WBC/hpf).</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Definite Urinary Tract Infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>All age categories: defined by a combination of clinical features and a positive urine culture.</td>
</tr>
</tbody>
</table>

(Guideline, AAP 2011)
Sensitivity of U/As in Infants

- The distinction for infant and non-toilet trained children is based upon the observation that urine screening studies (urinalysis, urine dip and microscopy) in these age groups are felt to be insufficient to rule in or rule out urinary tract infection. (Wong, Lee & Han 2008) (Nys et al. 2006) (Antwi et al. 2008) (McIsaac, Moineddin & Ross 2007) (Little et al. 2006)

- As a result, the committee felt that these tests were insufficient to rule out urinary tract infection in this age group where clinical suspicion was otherwise high.

Diagnosis: Definite UTI

Culture results defining a definite UTI are:

- Single predominant organism (one organism meets criteria below, all other organisms do not meet criteria below) ( يونس, Seattle Children’s UTI Pathway 2011)
  - $\geq 10^5$ colony forming units (cfu) / ml for clean catch
  - $> 10^4$ cfu/ml for in and out catheterization
  - $> 10^3$ cfu/ml for suprapubic aspiration
Diagnosis: Suprapubic Aspiration

- Suprapubic aspiration (SPA) is an available option if there is difficulty obtaining a catheterized specimen.
- Additionally, UAs may be falsely (+) in uncircumcised infant boys.
- SPA may be offered to parents and performed in the following circumstances:
  - Uncircumcised infant boy with positive cath screening tests (urinalysis, microscopy)
  - Operationally difficult to obtain a catheterized specimen
- The following criteria must be met prior to performing SPA:
  - Provider with demonstrated competency available (consult Urology, Nephrology, or Neonatology for teaching or help performing SPA)
  - Ultrasound guidance available
  - With agreement of family after discussion of risks/benefits
# Diagnosis: Adolescent and Sexually Active Patients

## In adolescents and sexually active pre-adolescents:

- Clinicians must document a sexual history and an external genital examination.
- Clinicians should perform a bimanual examination in females if clinically indicated (e.g., in cases of pelvic pain). (○○○○, Seattle Children’s UTI Pathway 2011)

## Additional lab testing to consider in this population:

- “Dirty” urine for Gonococcus (GC) and Chlamydia
- If GC/Chlamydia positive, consider Syphilis Screen
- HSV: Culture Visible lesions or cervical culture if indicated
- Annual HIV Screen
- Pregnancy Testing in females

---

One ED study of adolescents 12 to 25 years of age presenting with urinary complaints found that 49% of sexually active patients were not tested (Musacchio, Gehani & Garofalo 2009). Of those tested, 12/43 had chlamydia or gonorrhea, and 13/43 had a positive urine culture. Another study of sexually active females aged 14-22 ascertained through teen health centers and emergency rooms ((Huppert et al. 2007) found the prevalence of UTI and sexually transmitted infection (STI) to be 17 and 33%, respectively.
# Treatment: Overview

Treatment guidelines are summarized in the following table:

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Empiric therapy for presumed UTI</th>
<th>Treatment strategy</th>
<th>Treatment duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants (0-30 days)</td>
<td>IV ampicillin + gentamicin or IV ampicillin + cefotaxime</td>
<td>7 days IV antibiotics, then 7 days PO</td>
<td>14 days **</td>
</tr>
<tr>
<td></td>
<td><strong>If admitted</strong> (e.g., febrile): IV ceftriaxone OR IV ampicillin + gentamicin if cocci / Enterococcus suspected</td>
<td><strong>If outpatient:</strong> IM ceftriaxone OR po cephalaxin</td>
<td>14 days **</td>
</tr>
<tr>
<td>Infants (31-60 days)</td>
<td><strong>If admitted:</strong> IV ceftriaxone OR IV ampicillin + gentamicin if cocci / Enterococcus suspected</td>
<td><strong>If outpatient:</strong> IV antibiotics until afebrile x 24 hours (minimum 36 hours IV with negative blood cultures), then switch to PO to complete course if responding</td>
<td>10-14 days ** **</td>
</tr>
<tr>
<td></td>
<td><strong>If outpatient:</strong> PO cephalaxin OR PO cefuroxime OR if cephalosporin allergy, PO trimethoprim-sulfamethoxazole OR IM ceftriaxone</td>
<td><strong>For inpatients:</strong> IV antibiotics until identification and sensitivities return, then switch to targeted PO to complete course if responding</td>
<td>7-14 days ** **</td>
</tr>
<tr>
<td>Non-toilet trained children</td>
<td><strong>If admitted:</strong> IV ceftriaxone OR IV ampicillin + gentamicin if cocci / Enterococcus suspected</td>
<td><strong>For outpatients:</strong> target antibiotics when identification and sensitivities return</td>
<td>7 days **</td>
</tr>
<tr>
<td>Toilet trained children</td>
<td><strong>If outpatient:</strong> PO cephalaxin OR PO cefuroxime OR if cephalosporin allergy, PO trimethoprim-sulfamethoxazole OR IM ceftriaxone</td>
<td></td>
<td>3 days if cystitis</td>
</tr>
</tbody>
</table>

* When there is a treatment range, use longer courses if slower to respond to therapy
** Refer to UTI + bacteremia slides for treatment duration and switch to oral recommendations
Treatment: Empiric Antibiotic Choice

- Overuse of broad spectrum antibiotics has lead to emergence of resistant *E. coli* and other Gram-negatives
  - ~80% of first-time UTIs are due to *E. coli*
  - 3rd generation cephalosporins such as oral cefixime are *NOT* recommended as first-line empiric therapy.
  - Narrow spectrum (1st generation) cephalosporin such as cephalexin is recommended.
    - Note: cephalosporins should not be used where *enterococci* are suspected, due to intrinsic resistance.
    - In case of cephalosporin allergy, trimethoprim/sulfamethoxazole is an alternative.
  - Antibiotic therapy should always be targeted to the sensitivities of the organism when those sensitivities are known.

- Further rationale for recommending empiric cephalexin therapy included factors such as cost and percent of antibiotic excreted unchanged in the urine.

<table>
<thead>
<tr>
<th></th>
<th>Cephalexin (Keflex)</th>
<th>Cefuroxime (Ceftin)</th>
<th>Cefixime (Suprax)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Approximate Daily Dosing</strong></td>
<td>50 mg/kg/day (divided QID)</td>
<td>30 mg/kg/day (divided BID)</td>
<td>Day 1: 16 mg/kg/day Subsequent days: 8 mg/kg/day</td>
</tr>
<tr>
<td><strong>Cost (suspension)</strong></td>
<td>$29.55 or $0.148/ml</td>
<td>$166.64 or $1.67/ml</td>
<td>$168.37 or $3.37/ml</td>
</tr>
<tr>
<td><strong>Cost/ day for a 10 kg patient</strong></td>
<td>10 ml x $0.148 = $1.48</td>
<td>6 ml x $1.67/ml = $10.02</td>
<td>8 ml x $3.37/ml = $26.96 (day 1) 4 ml x $3.37/ml = $13.48 (subsequent)</td>
</tr>
<tr>
<td><strong>% excreted unchanged in urine</strong></td>
<td>90%</td>
<td>50%</td>
<td>50%</td>
</tr>
</tbody>
</table>
Treatment: Antibiotic Stewardship

- Current epidemiology differs dramatically from that during the Hoberman study (1992-1997) which recommended empiric cefixime. (Hoberman, 1999)

- Resistance to 3rd generation cephalosporins is rising around the world.

- The UTI Pathway recommends a susceptible narrow-spectrum agent. Avoiding routine use of broad-spectrum antibiotics for empiric treatment of infections helps prevent further resistant and promotes antibiotic stewardship.


Seattle Children’s Hospital produces a yearly antibiogram of our urinary isolates that can be found here: Antibiograms
Treatment: Rationale for Cephalexin

- Cephalexin is highly concentrated in the urine (~100 fold)
- Most *E. coli* are susceptible to cephalexin (=cefazolin) in the urine, even when susceptibility testing based on treatment for *bloodstream* infections report intermediate or resistant susceptibility.
- Some children would be expected to respond to treatment with cephalexin even when their *urinary isolate* was reported intermediate or resistant to cefazolin.
- Questions can be directed to the ID service if questions about antibiotic choice for resistant organisms.

In January 2011, the Clinical and Laboratory Standards Institute (CLSI) published new minimum inhibitory concentration (MIC) breakpoints for cefazolin against Enterobacteriaceae. These new breakpoints were largely based on data from *bloodstream infections in adults*. Following adoption of this new standard in March 2011, Seattle Children's antibiograms gave the false impression that intrinsic resistance of *E. coli* to cefazolin was increasing. Because of this, the Microbiology lab now includes a comment for *E. coli* isolates from the urine discussing this issue.
Treatment: "Switch Therapy" (IV to Oral Antibiotics)

- Strong evidence supports the equivalence of long-course IV therapy, "switch" therapy of 2-4 days of IV therapy followed by PO therapy, and PO therapy alone. (Guideline, NICE 2013)
- Limited data available for early “switch” therapy in infants 0-30 days of age.
- Because of small numbers of infants and children with bacteremia in these studies, results are also not easily generalizable to this specific patient population.

Treatment: “Switch Therapy”
(infants <30 days of age)

- Given the high incidence of bacteremia (12.4%) and potential for suboptimal blood culture volumes in infants, the committee recommended 7 days of IV therapy followed by 7 days of oral therapy for this age group regardless of blood culture results.
- The assumed pathogenesis of UTI in infants 0-30 days of age is an initial bloodstream infection independent of blood culture result. (Expert Opinion)
- Given this relatively short course of IV antibiotics, Peripherally Inserted Central Catheters (PICCs) are not necessary. (Expert Opinion)
Treatment: UTI With Positive Blood Cultures
Children >30 days of age

- Given limited evidence to guide duration of therapy in patients with UTI with associated bacteremia, local expert consensus was reached after literature review and discussion by Infectious Disease Division
- Increasing evidence suggests that early transition to orals antibiotics in patients with bacteremia may be equally effective as prolonged IV therapy

Current pathway recommendation for patients >30 days of age with bacteremia:
- 7d IV + 7d PO therapy = total duration 14 days
- May consider early transition to oral antibiotics if clinically back to baseline, afebrile x 24hrs, repeat blood culture negative x 48hrs, and good oral option available
- Only 1 repeat blood culture is necessary following initial positive as this is negative in the majority of cases
- Consider ID Consult in case of atypical UTI, early transition to orals in children 1-6 months old, any other ID related questions
A systematic review conducted to examine the appropriate treatment of cystitis concluded that in children 3 months to 18 years of age, a 2-4 day course of systemic antibiotics appeared as effective as a 7-14 day course of systemic antibiotics in eradicating lower tract UTI in children (Michael, 2009), however, it was noted that this analysis pooled many small studies with wide age ranges. The committee felt that given the difficulty in definitively distinguishing between lower and upper tract UTI in the younger age groups, this recommendation was most appropriate.
## Treatment: No Clinical Improvement in 48 Hours

<table>
<thead>
<tr>
<th>Expect clinical improvement within 48 hours</th>
<th>Fever should resolve by 72 hours. In patients that have not clinically improved in 48 hours despite appropriate antibiotic therapy, ensure renal ultrasound has occurred and consider specialty consult. (Guideline, AAP 2011)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient persistently febrile</td>
<td>CT is considered gold standard, as RUS does not always detect perinephric abscess. However, depending on patient characteristics, RUS may be more appropriate first line imaging study. (Expert Opinion)</td>
</tr>
<tr>
<td>Further imaging</td>
<td>If considering further imaging, consult radiology to discuss ultrasound vs. CT scan and need for contrast in CT scan. (Expert Opinion)</td>
</tr>
</tbody>
</table>

[Return to Inpatient Management](#)

[Return to Outpatient Management](#)
Follow-up urine cultures for test of cure are not routinely indicated. (☆☆☆O, Seattle Children's UTI Pathway 2011)

- Two retrospective reviews support the lack of usefulness of follow-up urine cultures at 48 hours. One study of 364 children < 18 years of age showed that of 291 follow-up urine cultures, none were positive (Currie, 2003). Another study of 599 children hospitalized and treated with UTI with 328 having a urine culture at 48 hours found only one positive culture (Oreskovic, 2007).
Diagnostic Imaging: Renal Ultrasound (RUS)

- It is felt that a RUS is a radiation free, high yield initial screen for identifying anatomical abnormalities in children up to 36 months of age (Guideline, AAP 2011)

- Studies suggest that third-trimester prenatal ultrasounds were highly likely to identify the anatomical abnormalities on postnatal ultrasound (Guideline, AAP 2011)

- If third-trimester prenatal ultrasound images could be obtained and reviewed by radiology, may be sufficient to preclude obtaining a repeat ultrasound at the time of infection if patient under 30 days of age (Expert Opinion)
VCUG is the definitive test for vesicoureteral reflux (VUR).

Although VCUG is felt to be the best imaging study for detection of VUR, it is no longer necessary for most patients. (Guideline, AAP 2011).

VCUG is not a good study for detection of acute pyelonephritis or to delineate renal parenchymal anatomy.

VCUG is an invasive test that involves fluoroscopy. Children may need sedation to tolerate the procedure.

OPTION:

- Radionuclide VCUG may be used in place of fluoroscopic VCUG for initial detection of VUR in females. This study offers a lower radiation dose, although with lesser anatomic detail and limited spatial resolution.

- If considering a Radionuclide Study, consult Radiology to discuss appropriateness of this test

Although VCUG is felt to be the best imaging study for detection of VUR, it is no longer necessary for most patients.

- Approximate prevalences of VUR among girls age 0 to 18 yrs are: (Grade I: 7%; Grade II: 22%; Grade III: 6%; Grade IV: 1%; Grade V: < 1%). Antibiotic prophylaxis is not felt to be helpful for patients with no reflux or grade I-III reflux (AAP 2011; Cincinnati 2006, Chand 2003)

- This suggests that over 30 VCUGs would need to be performed to find a patient with high grade (IV-V) reflux.
The Society for Fetal Urology (SFU) developed an ultrasonography grading system for hydronephrosis in 1993 based on renal sinus splitting patterns and dilation of the renal pelvis and calyces.

Though SFU grading is currently being applied to RUS interpretation at Seattle Children's, local expert consensus recommends using all RUS findings to guide clinicians in VCUG decision making rather than SFU grade alone.

Per the 2011 AAP Recommendation on imaging following first urinary tract infection, "VCUG is indicated if renal and bladder ultrasonography reveals hydronephrosis, scarring, or other findings that would suggest either high-grade VUR or obstructive uropathy and in other atypical or complex clinical circumstances."
Imaging: Procalcitonin

- Leroy 2013 and 2011 studies address the issues of utility of Procalcitonin in guiding decision making for imaging following first febrile UTI, specifically VCUG vs DMSA
- Procalcitonin may help predict upper vs lower tract disease and may help identify which patients are at risk for scarring
- However, procalcitonin may not be useful if drawn after start of therapy. Additionally, it is a send-out test with a lengthy turnaround time

Local consensus: Procalcitonin is not recommended at this time. Will re-evaluate in setting of further evidence.

<table>
<thead>
<tr>
<th>Variable</th>
<th>VUR &lt;3</th>
<th>VUR ≥3</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCT</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥0.5</td>
<td>272 (58)</td>
<td>44 (83)</td>
<td>83%</td>
<td>42%</td>
<td>14%</td>
<td>96%</td>
</tr>
<tr>
<td>&lt;0.5</td>
<td>201 (42)</td>
<td>9 (17)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCT</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥1</td>
<td>201 (43)</td>
<td>39 (74)</td>
<td>74%</td>
<td>57%</td>
<td>16%</td>
<td>95%</td>
</tr>
<tr>
<td>&lt;1</td>
<td>265 (57)</td>
<td>14 (26)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCT</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥2</td>
<td>134 (28)</td>
<td>31 (58)</td>
<td>58%</td>
<td>72%</td>
<td>18.8%</td>
<td>94%</td>
</tr>
<tr>
<td>&lt;2</td>
<td>339 (72)</td>
<td>22 (42)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dilation on RUS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>60 (13)</td>
<td>19 (38)</td>
<td>38%</td>
<td>87%</td>
<td>24%</td>
<td>93%</td>
</tr>
<tr>
<td>No</td>
<td>402 (87)</td>
<td>31 (62)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(Leroy, 2011)
Diagnostic Imaging: Antibiotic Prophylaxis Prior to VCUG

When a VCUG is indicated, clinicians should prescribe antibiotic prophylaxis for patients until VCUG is performed.

Infants <2 months:
- amoxicillin 20 mg/kg, up to 500 mg once daily

Infants >2 months to children <18 years:
- trimethoprim-sulfamethoxazole 2 mg/kg of trimethoprim up to 80 mg once daily, OR
- nitrofurantoin 1 mg/kg up to 100 mg once daily

Return to Imaging
Antibiotic Prophylaxis if VUR is Found

- Ongoing antibiotic prophylaxis is NOT routinely recommended for patients with first febrile urinary tract infection, or with low grade (I-III) vesicoureteral reflux (VUR). In setting of Grade III VUR, please discuss need for antibiotic prophylaxis with Urology.

- Multiple randomized trials examined the relationship between the effectiveness of antibiotic prophylaxis in different patient populations. This recommendation was reaffirmed by the 2014 RIVUR Study (★★★★★).

- Children with high grade VUR should be referred to Urology.

Summaries of literature evidence

- A trial of 336 randomized children with first febrile UTI showed no benefit of prophylaxis (Montini et al. 2008).

- A trial of 100 randomized patients showed no benefit in children under 30 months with grade II-IV reflux (Pennesi et al. 2008).

- A study of 225 randomized patients 1 month to 3 years of age with Grade I-III reflux showed no benefit of prophylaxis. (Roussey-Kesler et al. 2008).

- An retrospective review suggested that recurrent UTIs were associated with high-grade (IV, V) reflux, Caucasian race, and ages 3-5; and that antibiotic prophylaxis was associated with increasing resistance of organisms. (Conway et al. 2007).

- Another prospective randomized study of 218 children aged 3 months to 18 years of age suggests that grade I-III reflux does not increase the incidence of UTI / pyelonephritis, and that antibiotic prophylaxis does not appear to prevent the recurrence of UTI nor the development of renal scarring. (Garin et al. 2006).

- The RIVUR study was a randomized control study that assigned children ages 2 to 71 months of age with grade I-IV VUR to receive placebo vs. antibiotic prophylaxis. The study found fewer symptomatic recurrences in the placebo group (RR: 0.55; 95% CI: 0.38-0.78) but no significant difference in renal scarring at 2 years of follow-up. Antimicrobial resistance rates were higher in the prophylaxis group compared to placebo (63% vs. 19%). (Hoberman et al. 2014).
Criteria for Referral to Urology

• Children under 6 years of age with recurrent UTIs
• Abnormal imaging: Anatomic abnormality detected on Ultrasound or VCUG including complex congenital urologic problems such as:
  o Renal parenchymal loss or kidney size discrepancies
  o duplex systems
  o ureterocele
  o bladder or cloacal exstrophy
  o grade III-V vesicoureteral reflux
  o posterior urethral valves
  o other structural abnormalities of genitourinary development, such as persistent genitourinary sinus or cloacal abnormalities

• If uncertain if patient’s medical condition requires Urology management please consult Urology to discuss further
• DMSA Scan is an imaging study used to assess renal scarring approximately 12 months post-UTI and should be ordered via consultation with Urology
Executive Summary

Objective
Improve quality of care in patients with a first-time UTI birth to 18 years of age with a standardized approach to the diagnosis, management, and follow-up.

Additional Objectives
- Decrease unnecessary exposure to broad-spectrum antibiotics (i.e. 3rd generation cephalosporins).
- Decrease unnecessary radiation exposure, patient discomfort, and cost by reducing VCUGs performed.
- Decrease unnecessary length-of-stay and readmission by appropriate antibiotic selection and timely transition to oral antibiotics.

Recommendations

Diagnosis
a) Diagnose non-toilet trained children via high quality specimen (not a bag).

Empiric Therapy
- c) Start empiric therapy when there is clinical suspicion of UTI in non-toilet trained children.
- d) Start empiric therapy when there is clinical suspicion of UTI in toilet trained children when there are clinical findings in addition to a positive urinalysis/urine dip or microscopy.
- e) Target antibiotic therapy to sensitivities once available.
- f) For admitted children ≥31 days, use ceftriaxone IV. Use ampicillin + gentamicin IV if Enterococcus species is suspected.
- g) For infants 31-60 days of age not meeting admission criteria, give ceftriaxone IM or cepahlexin PO.
- h) For outpatient PO therapy, use cepahlexin. Use trimethoprim-sulfamethoxazole if cephalosporin allergy is a concern.

Treatment Route and Duration
- i) For infants 0-30 days, treat for 7 days IV followed by 7 days PO (total course is 14-days) regardless of blood culture result.
- j) For infants 31-60 days meeting admission criteria, treat IV until afebrile for 24 hours and initial blood cultures negative for 36 hours, then treat PO (total course is 14-days).
- k) For infants and children > 60 days (not bacteremic), meeting admission criteria, treat IV and switch to PO if responding; narrow coverage after sensitivities return. Total duration of antibiotics: adolescents (7 days), toilet trained (7-14 days), non-toilet trained (10-14 days).
- l) For adolescents with uncomplicated cystitis, treat PO for 3 days.
- m) For all infants and children >30 days with documented bacteremia, treat for a 7 days IV followed by 7 days PO. May consider early transition to PO if meeting switch criteria.
Imaging & Follow-up

- For infants and non-toilet trained children, perform renal ultrasound. For infants under 30 days, can review high quality third trimester ultrasound if available.
- For toilet trained children and adolescents, perform renal ultrasound on boys diagnosed with a first-time UTI and girls with atypical UTI.
- DO NOT routinely perform a VCUG. VCUG is indicated for abnormal ultrasound findings or atypical UTI (see guideline for definition).
- DO NOT routinely perform a follow-up urine culture for test of cure.
- DO NOT prescribe antibiotic prophylaxis for patients with first-time UTI diagnosed with low-grade (I-II) vesicoureteral reflux. Antibiotic prophylaxis to be started in conjunction with discussion with Urology in Grades III-V.
- Due to limited evidence, procalcitonin is not recommended to guide decisions about follow-up imaging.

Rationale

At the time of the initial inception of this pathway there was new data regarding the diagnosis and management of first time UTI, particularly as it pertained to diagnostic imaging. The original intent of this pathway was to establish an evidence and consensus-based standardized approach to diagnosis and management of first-time UTI for patients aged 0 to 18 years. This current version is the product of a scheduled periodic review and aims to provide updated recommendations based on recent literature.

- Safety may be enhanced by reducing unnecessary radiation exposure (e.g. VCUG) and medication administration, thereby reducing opportunities for error related to variations in practice.
- Costs may be reduced by streamlining and reducing the number of diagnostic studies while standardizing therapy, potentially decreasing length of stay. For this periodic review, the team reviewed the utility of the original pathway recommendations to identify opportunities to increase value. Some examples include not recommending procalcitonin, due to its low positive predictive value, and recommending cefpodoxime over cefixime in cases of resistant organisms requiring treatment with a 3rd generation cephalosporin, due to its lower cost.
- Delivery of care will be improved by expediting patient flow through the inpatient setting and facilitating close follow up with primary care providers.
- Quality of care will improve by promoting timely diagnosis and management of initial UTI while reducing unnecessary diagnostic tests and prophylactic therapy, including improved follow-up with families and PCPs for ER and Urgent Care patients.
- Engagement is based on the fact that the pathway was developed by providers from multiple disciplines and practice settings, as well as feedback from families.

Evidence

Studies were identified by searching electronic databases using search strategies developed and executed by a medical librarian. Two searches were performed for different topics, looking back to 2010 (the end date of the last literature search), and additional articles were identified...
by team members and added to results. The results were systematically reviewed by the clinical pathway team, and 19 articles total were included to inform the recommendations.

**Implementation Items**
- Revision of training module and learning assessment
- Development of Emergency Department / Urgent Care tools to support new workflow

**Metrics Plan**
- Count of inpatient and observation discharges
- Median Length of Stay
- Percent of patients with any of the specified powerplans
- Average charges per case
- Readmission
- Overall VCUG use
- Antibiotic resistance rates
- Antibiotic selection (in particular to track the use of targeted therapy)

**PDCA Plan**
The CSW owner and committee will follow metrics, continue to review medical literature, and make alterations to the pathway and associated tools as needed.

**Revision History**
Date Approved: April 2015
Next Review Date: April 2020
Approved by the CSW Urinary Tract Infection (UTI) Team on April 8th, 2015

CSW Urinary Tract Infection (UTI) Team:

Hospital Medicine, Owner
Emergency Medicine, Owner
Emergency Medicine, CNS
Hospital Medicine, CNS
Radiology
Urology
Rebecca Taxier, MD
Derya Caglar, MD
Sara Fenstermacher, RN
Kristi Klee, MSN, RN-BC
Randy Otto, MD
Richard Grady, MD

Clinical Effectiveness Team:

Consultant:
Project Leader
KM Analyst:
CIS Informatician:
CIS Analyst:
Librarian:
Program Coordinator:
Claudia Crowell, MD
Elizabeth Austin, MPH
Susan Stanford, MPH, MSW
Michael Leu, MD, MS, MHS
Heather Marshall
Susan Klawansky, MLS
Ashlea Tade
Title: Urinary Tract Infections (UTI)

Authors:
- Seattle Children’s Hospital
- Rebecca Taxier
- Elizabeth Austin
- Derya Caglar
- Claudia Crowell
- Sara Fenstermacher
- Richard Grady
- Kristi Klee
- Michael Leu
- Randolph Otto
- Sahar Rooholamini

Date: April 2015

Retrieval Website: http://www.seattlechildrens.org/pdf/UTI-pathway.pdf

Example:
• Completion qualifies you for 1 hour of Category II CME credit. If you are taking this self-assessment as a part of required departmental training at Seattle Children's Hospital, you MUST logon to Learning Center.

1. Which of the following is NOT an exclusion criterion?
   a. Chronic kidney disease (decreased GFR)
   b. Sepsis/ Meningitis
   c. Neurogenic bladder/ obstructive uropathy
   d. Known Grade IV-V reflux
   e. Circumcision
   f. 2nd episode of pyelonephritis

2. Which of the following statements is/are TRUE about sexually active adolescents?
   a. Symptoms of UTI mimic those of STI
   b. Additional testing should be considered in this population including HIV, Syphilis Screen, Gonorrhea/Chlamydia, HSV, and pregnancy screen.
   c. A sexual history and a bimanual exam (if pelvic pain is present) should be done
   d. All of the above

3. Which of the following statements is/are TRUE regarding admission criteria?
   a. All infants < 30 days of age with presumed or definite UTI should be admitted
   b. Only infants < 30 days of age who are febrile should be admitted
   c. Admit all febrile patients 31-60 days of age with presumed or definite UTI
   d. a and c

4. Patients with presumed urinary tract infection do not need empiric treatment, treatment should only be started if the urine culture is (+)
   a. True
   b. False

5. Which of the following is/are TRUE regarding empiric antibiotic therapy?
   a. Cefixime is the only choice that is acceptable for outpatient therapy
   b. The majority of infections are caused by e.coli, most of which are susceptible to 1st and 2nd generation cephalosporins
   c. There is no need to tailor antibiotics once the sensitivities are known
   d. If gram (+) cocci are primarily identified on urine culture, cephalosporins are not indicated as empiric therapy due to the intrinsic resistance of enterococci to cephalosporins
   e. Answer a and c are correct
   f. Answer b and d are correct

6. Given the high incidence of bacteremia (12.4%) and potential for suboptimal blood culture volumes in infants, the committee recommended 7 days of IV therapy followed by 7 days of oral therapy for all infants < 30 days of age with pyelonephritis.
   a. True
   b. False
7. Which of the following statements is TRUE regarding renal ultrasounds?
   a. They evaluate the lower tract (bladder and urethra) well
   b. They are able to reliably detect the presence of a perinephric abscess
   c. They are indicated for all toilet trained or adolescent girls with UTI
   d. They are indicated for all infants and non-toilet trained children with pyelonephritis

8. Which of the following statements is/are FALSE regarding VCUGs
   a. It provides detailed images of the upper urinary tract
   b. It is the definitive test for VUR
   c. Most reflux is grade IV or higher, therefore VCUGs are always indicated
   d. Studies have shown that there is no advantage to antibiotic prophylaxis in patients with Grades I-II reflux
   e. a and c
   f. b and d

9. Which of the following patients would not be a good candidate for early transition to oral therapy?
   a. A 15 year-old female with *E. coli* pyelonephritis and bacteremia now hospital day 4 who defervesced after 24 hours of antibiotics, is tolerating PO, and has a negative repeat blood culture.
   b. A 3 week-old female with urine culture positive for pan-susceptible *E. coli* who is now hospital day 4, afebrile for the last 72 hours, tolerating PO, and who had a negative initial blood culture.
   c. A 6 month-old male with urine culture positive for *E. coli* resistant to all cephalosporins, susceptible to trimethoprim-sulfamethoxazole, on hospital day 4, afebrile for the last 24 hours, tolerating PO, and with a negative initial blood culture.
   d. A 2 month-old uncircumcised male with urine culture positive for pan-susceptible *E. coli* with SFU Grade 2 on renal ultrasound, who is now hospital day 4, afebrile for the last 24 hours, tolerating PO, and who had a negative initial blood culture.

10. Which of the following statement is/are TRUE regarding antibiotic stewardship?
    a. Infections should be treated with the narrowest-spectrum antibiotic possible.
    b. The number of isolates of extended spectrum beta-lactamase (ESBL) producing *E. coli* is increasing.
    c. The use of broad spectrum antibiotics selects for resistant organisms in the intestinal flora.
    d. All of the above
Answer Key

1) The correct answer is (e); all other choices except circumcision are exclusion criteria.

2) The correct answer is (d); all of the above statements are true about sexually active adolescents.

3) The correct answer is (d); both infants <30 days with presumed or definite UTI AND all febrile patients 31-60 days of age with presumed or definite UTI should be admitted to the hospital.

4) The correct answer is (b); patients with presumed UTI should receive empiric antibiotic treatment.

5) The correct answer is (f); it is true that the majority of infections are caused by e. coli, most of which are susceptible to 1st and 2nd generation cephalosporins. It is also true that if gram (+) cocci are primarily identified on urine culture, cephalosporins are not indicated as empiric therapy due to the intrinsic resistance of enterococci to cephalosporins.

6) The correct answer is (a); 7 days of IV therapy followed by 7 days of oral therapy for infants < 30 days of age with pyelonephritis is recommended.

7) The correct answer is (d); renal ultrasounds are indicated for all infants and non-toilet trained children with pyelonephritis, the remainder of the statements are false.

8) The correct answer is (e); VCUGs do not provide detailed images of the upper urinary tract. Most reflux is grade I-III, not grade IV or higher.

9) The correct answer is (b); Infants < 30 days must have a 7 day course of IV therapy before switching to PO regardless of blood culture result.

10) The correct answer is (d); all three statements about antibiotic stewardship are true.
This pathway was developed through local consensus based on published evidence and expert opinion as part of Clinical Standard Work at Seattle Children’s. Pathway teams include representatives from Medical, Subspecialty, and/or Surgical Services, Nursing, Pharmacy, Clinical Effectiveness, and other services as appropriate.

When possible, we used the GRADE method of rating evidence quality. Evidence is first assessed as to whether it is from randomized trial or cohort studies. The rating is then adjusted in the following manner (from: Guyatt G et al. J Clin Epidemiol. 2011;4:383-94.):

- **Quality ratings are downgraded** if studies:
  - Have serious limitations
  - Have inconsistent results
  - If evidence does not directly address clinical questions
  - If estimates are imprecise OR
  - If it is felt that there is substantial publication bias

- **Quality ratings are upgraded** if it is felt that:
  - The effect size is large
  - If studies are designed in a way that confounding would likely underreport the magnitude of the effect OR
  - If a dose-response gradient is evident

Guideline – Recommendation is from a published guideline that used methodology deemed acceptable by the team.

Expert Opinion – Our expert opinion is based on available evidence that does not meet GRADE criteria (for example, case-control studies).

**Note about periodic reviews:** The CSW team conducts a full literature search for pathways every 3-5 years, reviewing literature since the previous pathway version and updating all recommendations with new evidence as applicable. The evidence ratings shown on pathway pages represent literature graded across pathway iterations:

- If the newer evidence is higher than the previous, the grade reflects the new evidence.
- If the evidence level is the same as the previous pathway iteration, the grade remains the same (representing a combination of old and new literature).
- If the evidence level is lower in the new literature, both the new literature and the old pathway may be cited (graded separately).
- If there is no new evidence, the previous pathway evidence and grade are cited.
Summary of Version Changes

**Version 2 (12/03/2011):** Expanded recommendation for empiric outpatient antibiotics to include oral cephalexin or oral cefuroxime

**Version 2.3 (4/3/2013):** Removed race from the decision to treat parameter; included information on timing of obtaining a VCUG; expanded discussion about cephalexin still being first-line treatment for E. coli in UTI

**Version 3.0 (6/3/2014):** Added additional content/information regarding the VCUG and SFU grade with a link to the SFU grade training slide

**Version 4.0 (4/8/2015):** Periodic review, full literature search completed, multiple changes made to algorithm and power plan

**Version 4.1 (7/6/2015):** Formatting updates to bibliography

**Version 5.0 (9/29/15):** Updated inclusion/exclusion criteria to coincide with Nephrolithiasis pathway go live. Addition to imaging section specifically renal ultrasound to consider Nephrolithiasis pathway if stones are present.
Medical Disclaimer

Medicine is an ever-changing science. As new research and clinical experience broaden our knowledge, changes in treatment and drug therapy are required.

The authors have checked with sources believed to be reliable in their efforts to provide information that is complete and generally in accord with the standards accepted at the time of publication.

However, in view of the possibility of human error or changes in medical sciences, neither the authors nor Seattle Children’s Healthcare System nor any other party who has been involved in the preparation or publication of this work warrants that the information contained herein is in every respect accurate or complete, and they are not responsible for any errors or omissions or for the results obtained from the use of such information.

Readers should confirm the information contained herein with other sources and are encouraged to consult with their health care provider before making any health care decision.
Literature Search
Literature Search Strategy

Search Methods, Urinary Tract Infection (UTI), Clinical Standard Work

Studies were identified by searching electronic databases using search strategies developed and executed by a medical librarian, Susan Klawansky. Searches were performed in May and October, 2014. The May 2014 search was performed in the following databases: on the Ovid platform – Medline (July 2010 to date), Cochrane Database of Systematic Reviews (2010 to date); elsewhere – Embase (July 2010 to date), Clinical Evidence, National Guideline Clearinghouse and TRIP (all 2010 to date). Retrieval was limited to English language and ages 0-18, except for the question relating to VCUG, which was limited to infants ages 0-2. In Medline and Embase, appropriate Medical Subject Headings (MeSH) and Emtree headings were used respectively, along with text words, and the search strategy was adapted for other databases using textwords alone. Concepts searched were urinary tract infection, pyelonephritis, cystitis, bacteriuria, pyuria and vesico-ureteral reflux/VCUG. All retrieval was further limited to certain evidence categories such as relevant publication types, Clinical Queries, index terms for study types and other similar limits.

An additional search was conducted in October 2014 in the following databases: on the Ovid platform – Medline and Central Register of Controlled Clinical Trials; elsewhere – Embase. All were searched from 2010 to current, results limited to English and ages 0-18. Search strategies were constructed as above, using index terminology and textwords as appropriate. Concepts searched were anti-bacterial agents, drug administration routes, intravenous injections or infusions, oral administration, drug administration schedule, bacteremia and blood culture – searched independently of urinary tract infections. All retrieval was further limited to certain evidence categories such as relevant publication types, Clinical Queries, index terms for study types and other similar limits.

Additional articles were identified by team members and added to results.
Identification (Question 1-4)

485 records identified through database searching

2 additional records identified through other sources

Screening

439 records after duplicates removed

439 records screened

406 records excluded

Eligibility

33 records assessed for eligibility

18 full-text articles excluded, 2 did not answer clinical question, 9 did not meet quality threshold, 7 outdated relative to other included study

Included

15 studies included in pathway

Flow diagram adapted from Moher D et al. BMJ 2009;339:bmj.b2535

Identification (Question 5)

192 records identified through database searching

4 additional records identified through other sources

Screening

196 records after duplicates removed

196 records screened

192 records excluded

Eligibility

4 records assessed for eligibility

0 full-text articles excluded

Included

4 studies included in pathway

Flow diagram adapted from Moher D et al. BMJ 2009;339:bmj.b2535


