Date started: August 2018

Date completed:

**Objective:**
To create an OHSU Health System guideline for diagnosing and treating pediatric urinary tract infections

**Inclusion Criteria:**
- Pediatrics patients up to 18 years old with presumed urinary tract infection

**Exclusion Criteria:**
- Adult patients with urinary tract infections
- Known urinary tract abnormality
- Neurogenic bladder
- Prior history of urinary tract infection
- Chronic kidney disease
- Immunocompromised host
- Conditions requiring Intensive Care Unit care

**Definitions:**
Urinary tract infection (UTI): Defined as a common bacterial infection involving the low urinary tract (cystitis), the upper urinary tract (pyelonephritis), or both, causing illness in children.
Cystitis: Inflammation of the lower urinary bladder. It is often caused by infection and is usually accompanied by frequent, painful urination.
Pyelonephritis: Inflammation of the substance of the kidney in the upper urinary tract as a result of bacterial infection.
Fever: Because of normal variation in body temperature, there is no single value that is defined as fever. In general, a fever means a temperature above 100.4 °F (38°C). Temperature may vary slightly depending on how you take child's temperature – oral (mouth), axillary (armpit), ear, forehead, or rectal.
Urinalysis: Analysis of physical, chemical, microscopical means to test for the presence of disease, drugs, etc.

**Target Guideline Users:**
All clinicians caring for pediatric patients presenting with urinary tract infections within OHSU
Guideline Review:

1. a. In pediatric patients <2 months old with suspected urinary tract infection, which children should have urine testing? What testing should be done?
   b. In pediatric patients >2 months to 18 years old with suspected urinary tract infection, which children should have urine testing? What testing should be done?

2. a. In pediatric patients <2 months old with suspected urinary tract infection, how should the sample be obtained?
   b. In pediatric patients >2 months to 18 years old with suspected urinary tract infection, How should the sample be obtained?

3. a. In pediatric patients <2 months old with suspected urinary tract infection, how is the diagnosis made? What is the threshold for diagnosis?
   b. In pediatric patients >2 months to 18 years old with suspected urinary tract infection, how is the diagnosis made? What is the threshold for diagnosis?

4. a. In pediatric patients <2 months old with suspected urinary tract infection, How should UTIs be treated depending on age and upper or lower tract?
   b. In pediatric patients >2 months to 18 years old with suspected urinary tract infection, How should UTIs be treated depending on age and upper or lower tract?

In pediatric patients from birth to 18 years old with suspected urinary tract infection,

5. When do both urinalysis and microscopy need to be performed to diagnose a UTI
6. What imaging and follow-up are recommended after a diagnosis of UTI?
7. How should children be followed after a UTI has been diagnosed?
8. What are the clinical indicators to admit child for UTI?

Quality Measures:
Process:

Outcome:
- Admissions
- Length of Stay
- Imaging Rates
- Treatment Failures
- Antibiotics Use – Peds, ED, Pharmacy
### Existing External Guidelines/Pathways/Order Sets

#### Existing External Guidelines

<table>
<thead>
<tr>
<th>National Guidelines</th>
<th>Organization and Author</th>
<th>Last Update</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinary tract infection in under 16s: diagnosis and management</td>
<td>UK's National Institute for Health and Care Excellence (NICE)</td>
<td>2017</td>
</tr>
<tr>
<td>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</td>
<td>American Academy of Pediatrics</td>
<td>2016</td>
</tr>
<tr>
<td>Urinary Tract Infection - Child</td>
<td>American College of Radiology</td>
<td>2016</td>
</tr>
<tr>
<td>Clinical Policy for Well-Appearing Infants and Children Younger Than 2 Years of Age Presenting to the Emergency Department with Fever</td>
<td>American College of Emergency Physicians</td>
<td>2016</td>
</tr>
<tr>
<td>KHA-CARI guideline: Diagnosis and treatment of urinary tract infection in children</td>
<td>Kidney Health Australia – Caring for Australians with Renal Impairment</td>
<td>2015</td>
</tr>
<tr>
<td>Urinary Tract Infection: Clinical Practice Guideline for the Diagnosis and Management of the Initial UTI in Febrile Infants and Children 2 to 24 Months</td>
<td>American Academy of Pediatrics</td>
<td>2011</td>
</tr>
</tbody>
</table>

#### Health System Guidelines

<table>
<thead>
<tr>
<th>Health System Guidelines</th>
<th>Organization and Author</th>
<th>Last Update</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathway for the Evaluation and Treatment of Children with Febrile UTI</td>
<td>Children’s Hospital of Philadelphia (CHOP)</td>
<td>Revised 2018</td>
</tr>
<tr>
<td>Febrile Urinary Tract Infection (UTI)</td>
<td>Children’s Hospital of Chicago</td>
<td>2017</td>
</tr>
<tr>
<td>Urinary Tract Infection Diagnosis and Management</td>
<td>Nationwide Children’s Hospital</td>
<td>2017</td>
</tr>
<tr>
<td>Urinary Tract Infection: Criteria and Definitions</td>
<td>Seattle Children’s Hospital</td>
<td>Revised 2016</td>
</tr>
<tr>
<td>First Febrile Urinary Tract Infection – Imaging excerpt from AAP Guideline</td>
<td>Cincinnati Children’s Hospital</td>
<td>2012</td>
</tr>
<tr>
<td>UTI Algorithm</td>
<td>Mercy Children’s Kansas City</td>
<td>2006</td>
</tr>
<tr>
<td>Urinary Tract Infections (UTI) (Infants 2-24 months with fever &gt;38°C)</td>
<td>Children’s Minnesota</td>
<td>Unknown</td>
</tr>
</tbody>
</table>
The ten published clinical guidelines were evaluated for this review using the University of Pennsylvania’s Center for Evidence-Based Practice Trustworthy Guideline rating scale. The scale is based on the Institute of Medicine’s “Standards for Developing Trustworthy Clinical Practice Guidelines” (IOM), as well as a review of the AGREE Enterprise and Guidelines International Network domains.
See appendix B for full description of the Trustworthy Guideline grading system.

<table>
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</thead>
<tbody>
<tr>
<td>1. Transparency</td>
<td>A</td>
<td>B</td>
<td>C</td>
<td>A</td>
<td>B</td>
<td>B</td>
<td>B</td>
<td>A</td>
<td>A</td>
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<tr>
<td>2. Conflict of interest</td>
<td>C</td>
<td>C</td>
<td>NR</td>
<td>B</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>A</td>
</tr>
<tr>
<td>3. Development group</td>
<td>B</td>
<td>B</td>
<td>NR</td>
<td>B</td>
<td>B</td>
<td>B</td>
<td>B</td>
<td>A</td>
<td>A</td>
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<tr>
<td>4. Systematic Review</td>
<td>A</td>
<td>A</td>
<td>B</td>
<td>A</td>
<td>B</td>
<td>B</td>
<td>B</td>
<td>A</td>
<td>A</td>
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<tr>
<td>5. Supporting evidence</td>
<td>A</td>
<td>A</td>
<td>A</td>
<td>A</td>
<td>A</td>
<td>A</td>
<td>A</td>
<td>A</td>
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<tr>
<td>6. Recommendations</td>
<td>A</td>
<td>A</td>
<td>B</td>
<td>A</td>
<td>A</td>
<td>C</td>
<td>C</td>
<td>B</td>
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<tr>
<td>7. External Review</td>
<td>C</td>
<td>C</td>
<td>NR</td>
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<tr>
<td>Evidence evaluation system not described, no formal rating of recommendations</td>
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</tbody>
</table>

- **Level A recommendations.** Generally accepted principles for patient care that reflect a high degree of clinical certainty (e.g., based on evidence from 1 or more Class of Evidence I or multiple Class of Evidence II studies).

- **Level B recommendations.** Recommendations for patient care that may identify a particular strategy or range of strategies that reflect moderate clinical certainty (e.g., based on evidence from 1 or more Class of Evidence II studies or strong consensus of Class of Evidence III studies).

- **Level C recommendations.** Recommendations for patient care that are based on evidence from Class of Evidence III studies or, in the absence of any adequate published literature, based on expert opinion.
<table>
<thead>
<tr>
<th>CHOP Revised 2018</th>
<th>SCH Revised 2016</th>
<th>CCH 2012</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Evidence Evaluation</strong></td>
<td>The clinical pathways are based upon publicly available medical evidence and/or a consensus of medical practitioners at The Children’s Hospital of Philadelphia (“CHOP”) and are current at the time of publication. These clinical pathways are intended to be a guide for practitioners and may need to be adapted for each specific patient based on the practitioner’s professional judgment, consideration of any unique circumstances, the needs of each patient and their family, and/or the availability of various resources at the health care institution where the patient is located. Accordingly, these clinical pathways are not intended to constitute medical advice or treatment, or to create a consensus. In instances where consensus recommendations are made, “consensus” is placed in parentheses at the end of the recommendation.</td>
<td>SCH uses the GRADE method of rating evidence quality.</td>
</tr>
</tbody>
</table>

**Quality of Evidence**:
- High quality
- Moderate quality
- Low quality
- Very low quality
- Expert Opinion
The doctor-patient relationship between/among The Children’s Hospital of Philadelphia (“CHOP”), its physicians and the individual patients in question. CHOP does not represent or warrant that the clinical pathways are in every respect accurate or complete, or that one or more of them apply to a particular patient or medical condition. CHOP is not responsible for any errors or omissions in the clinical pathways, or for any outcomes a patient might experience where a clinician consulted one or more such pathways in connection with providing care for that patient.

Evaluating the Quality of Evidence

The GRADE criteria were used to evaluate the quality of evidence presented in research articles reviewed during the development of this guideline. The table below defines how the quality of the evidence is rated and how a strong versus weak recommendation is established. For more detailed information, see Appendix A.

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Type of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>STRONG</td>
<td>Desirable effects clearly outweigh undesirable effects or vice versa</td>
</tr>
<tr>
<td>WEAK</td>
<td>Desirable effects closely balanced with undesirable effects</td>
</tr>
<tr>
<td>Quality</td>
<td>Type of Evidence</td>
</tr>
<tr>
<td>High</td>
<td>Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies</td>
</tr>
<tr>
<td>Moderate</td>
<td>Evidence from RCTs with important limitations (e.g., inconsistent results, methodological flaws, indirect evidence, or imprecise results) or unusually strong evidence from unbiased observational studies</td>
</tr>
<tr>
<td>Level</td>
<td>Description</td>
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<td>------------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Low</td>
<td>Evidence for at least 1 critical outcome from observational studies, from RCTs with serious flaws or indirect evidence</td>
</tr>
<tr>
<td>Very Low</td>
<td>Evidence for at least 1 critical outcome from unsystematic clinical observations or very indirect evidence</td>
</tr>
</tbody>
</table>
Question #1.

a) In children less than 2 months old, which children should have urine testing? What testing should be done?

**Question 1a National/International Guideline Recommendations:**

In 2017, the National institute for Health and Care Excellence (NICE) provided the following recommendations in the update to the Urinary tract infection in under 16s: diagnosis and management guideline:

1.1.1 Symptoms and signs
   1.1.1.1 Infants and children presenting with unexplained fever of 38°C or higher should have a urine sample tested within 24 hours. [2007]
   1.1.1.2 Infants and children with an alternative site of infection should not have a urine sample tested. When infants and children with an alternative site of infection remain unwell, urine testing should be considered after 24 hours at the latest. [2007]
   1.1.1.3 Infants and children with symptoms and signs suggestive of urinary tract infection (UTI) should have a urine sample tested for infection. Table 1 is a guide to the symptoms and signs that infants and children present with. [2007]

Table 1 Presenting symptoms and signs in infants and children with UTI

<table>
<thead>
<tr>
<th>Age group</th>
<th>Symptoms and signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants younger than 3 months</td>
<td>Fever, Vomiting, Lethargy, Irritability</td>
</tr>
<tr>
<td></td>
<td>Poor feeding, Failure to thrive</td>
</tr>
<tr>
<td></td>
<td>Abdominal pain, Jaundice, Haematuria</td>
</tr>
<tr>
<td></td>
<td>Offensive urine</td>
</tr>
</tbody>
</table>
1.1.2 Assessment of risk of serious illness

1.1.2.1 The illness level in infants and children should be assessed in accordance with recommendations in the NICE guideline on fever in under 5s. [2007]

1.1.5 Urine testing

1.1.5.1 For all diagnostic tests there will be a small number of false negative results; therefore clinicians should use clinical criteria for their decisions in cases where urine testing does not support the findings. [2007]

1.1.5.2 Refer all infants under 3 months with a suspected UTI (see table 1) to paediatric specialist care, and
  - send a urine sample for urgent microscopy and culture
  - manage in line with the NICE guideline on fever in under 5s. [2017]

1.1.5.3 Use dipstick testing for infants and children 3 months or older but younger than 3 years with suspected UTI.
  - If both leukocyte esterase and nitrite are negative: do not start antibiotic treatment; do not send a urine sample for microscopy and culture unless at least 1 of the criteria in recommendation 1.1.6.1 apply.
  - If leukocyte esterase or nitrite, or both are positive: start antibiotic treatment; send a urine sample for culture. [2017]

Table 3 Guidance on the interpretation of microscopy results

<table>
<thead>
<tr>
<th>Microscopy results</th>
<th>Pyuria positive</th>
<th>Pyuria negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacteriuria positive</td>
<td>The infant or child should be regarded as having UTI</td>
<td>The infant or child should be regarded as having UTI</td>
</tr>
<tr>
<td>Bacteriuria negative</td>
<td>Antibiotic treatment should be started if clinically UTI</td>
<td>The infant or child should be regarded as not having UTI</td>
</tr>
</tbody>
</table>
1.1.7 History and examination on confirmed UTI

1.1.7.1 The following risk factors for UTI and serious underlying pathology should be recorded:

- poor urine flow
- history suggesting previous UTI or confirmed previous UTI
- recurrent fever of uncertain origin
- antenatally diagnosed renal abnormality
- family history of vesicoureteric reflux (VUR) or renal disease
- constipation
- dysfunctional voiding
- enlarged bladder
- abdominal mass
- evidence of spinal lesion
- poor growth
- high blood pressure. [2007]

In 2015, the Kidney Health Australia, Caring for Australians with Renal Impairment (KHA-CARI) recommended the following:

- Recommend that the diagnosis of urinary tract infection (UTI) only be made on the basis of clinical symptoms in association with a positive urine culture. (1B)
- Suggest that the presence of bacteriuria (by microscopy with gram stain) on an appropriately collected urine specimen can be used as the basis for a presumptive diagnosis of UTI. (2B)
- Recommend that culture of an appropriately collected urine specimen (see below) is required for definitive diagnosis of UTI (1B) and that UTI diagnosis not be made solely on the basis of:
  - Urinary dipstick testing for leucocyte esterase or nitrite (1B) or
  - The presence of white cells on microscopy, in the absence of bacteriuria. (1B)
- Suggest that the occurrence of a positive urine culture in the absence of clinical symptoms (asymptomatic bacteriuria) does not warrant treatment or further investigation for UTI. (2B)

The 2011 American Academy of Family Physicians guideline on the Diagnosis and Treatment of Urinary Tract Infections in Children recommended the following:

- UTI should be suspected in patients with leukocyte esterase and nitrite present on dipstick testing, or with pyuria of at least 10 white blood cells per high-power field and bacteriuria on microscopy. (Evidence Rating: C)
Guideline References:


Question 1a Health System Guidelines:

In 2017, Nationwide Children’s Hospital guideline on Urinary Tract Infection Diagnosis and Management recommended

General Management Principles

The following guidance will focus on uncomplicated UTIs in otherwise healthy children. Infections in children with underlying renal diseases, anatomic or functional anomalies of the urinary tract, urinary catheters, or immunocompromising conditions/therapies constitute complicated UTIs and must be approached on an individual basis.

The management of suspected UTI in children involves six key steps:

1. Determine whether the pre-test probability of UTI is high enough to warrant testing.
2. Obtain an appropriate urine sample for urinalysis and urine culture (if urinalysis positive or clinical suspicion despite a negative urinalysis).
2016's Seattle Children's Hospital Urinary Tract Infection: Criteria and Definitions:
Health System Guideline References:


Question 1a. Primary Literature:

<table>
<thead>
<tr>
<th>Modality: Urinalysis</th>
<th>Outcome: Prevalence of UTI</th>
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</thead>
<tbody>
<tr>
<td><strong>PICO Question:</strong> In children less than 2 months old, which children should have urine testing? What testing should be done?</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th><strong>Study Acronym; Author; Year Published; Location</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Archives of Pediatrics &amp; Adolescent Medicine</td>
</tr>
<tr>
<td>Bachur R. and M.B. Harper</td>
</tr>
<tr>
<td>2001</td>
</tr>
<tr>
<td>Divisions of Emergency Medicine and Infectious Disease, Children's Hospital, Boston, Massachusetts</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Aim of Study; Study Type; Study Size (N)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>To determine how the sensitivity of the standard UA as a screening test for UTI varies with age, and to determine the clinical situation that necessitates the collection of a urine culture regardless of the UA result.</td>
</tr>
<tr>
<td>Retrospective medical record review</td>
</tr>
<tr>
<td>37,450 febrile children younger than 2 years were reviewed. 1,123 between the ages of 0 – 1 month; 3,426 between the ages of &gt;1 – 3 months</td>
</tr>
</tbody>
</table>

| **Inclusion Criteria:** Children younger than 2 years with fever (temperature >/= 38.0C) who were seen in the emergency department. |

<table>
<thead>
<tr>
<th><strong>Study Methods (# patients) / Study Comparator</strong></th>
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</thead>
<tbody>
<tr>
<td>Retrospective medical record review of patients younger than 2 years with fever (&gt;/=38 degrees C) seen in the emergency department during a period of 65 months. All urine cultures were reviewed for the collection method, isolates, and colony counts. A UA result was considered positive if the presence of 1 of the following was detected: leukocyte esterase, nitrite, or pyuria (&gt;=/=5 white blood cells per high power field). Patients who had a paired UA and urine culture were used to calculate the sensitivity, specificity, and likelihood ratios of the UA. The prevalence of UTIs was also subcategorized by age, race, sex, and fever.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Endpoint Results / Outcome (Absolute Event Rates, P values; OR or RR; &amp; 95% CI)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Study found that that sensitivity of UA to be 82% and constant for age subgroups among febrile children younger than 2 years.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Design Limitations</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Study found that that sensitivity of UA to be 82% and constant for age subgroups among febrile children younger than 2 years.</td>
</tr>
</tbody>
</table>

Data also demonstrates that the sensitivity and specificity, and thus the likelihood ratio for a negative rest result, do not vary by age.

However, because the prevalence of UTI is high in young infants, the absolute number of false-negative results is also high; so despite a constant sensitivity for UTI, the UA

Study Limitations:
- None
- Non-Randomized Studies
  - Failure to develop and apply appropriate eligibility criteria
  - Flawed measurement of both exposure and outcome
- Failure to adequately control confounding
- Incomplete or inadequately short follow-up
- Differences in important prognostic factors at baseline

Low Quality Rating if:
- Studies inconsistent (wide variation of treatment effect across studies, population, interventions, or outcomes varied)
  - Not Available
- Studies are indirect (PICO question is quite different from the available evidence in regard to population, intervention, comparison, or outcome)
- Studies are imprecise (when studies include few patients and few events, and thus have wide confidence intervals, and the results are uncertain)
- Publication Bias (e.g. pharmaceutical company sponsors study on effectiveness of drug only small, positive studies found)

Increase Quality Rating if:
- Large effect
- Dose-response gradient
PICO Question: In children less than 2 months old, which children should have urine testing? What testing should be done?

Modality: Urinary automated flow cytometry analysis and urinary dipstick
Outcome: Prevalence of UTI

<table>
<thead>
<tr>
<th>Study Acronym; Author; Year Published; Location</th>
<th>Aim of Study; Study Type; Study Size (N)</th>
<th>Patient Population</th>
<th>Study Methods (# patients) / Study Comparator</th>
<th>Endpoint Results / Outcome (Absolute Event Rates, P values; OR or RR; &amp; 95% CI)</th>
<th>Design Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Journal: Journal of Clinical Microbiology Author: Duong, H.P., et al. Year Published: 2016 Location: Department of Pediatric Nephrology, Hôpital Universitaire des Enfants Reine Fabiola, Université Libre de Bruxelles</td>
<td>To compare the diagnostic performance of urinary automated flow cytometry analysis and urinary dipstick analysis of nitrates and leukocyte esterase (LE) as screening tests for UTI in the pediatric population</td>
<td>CRT population</td>
<td>For every child screened for UTI, a fresh urine sample was sent to the local laboratory for dipstick and automated cytometer analyses as well as quantitative urine culture. For children younger than 24 months, urine samples were obtained by suprapubic aspiration or bladder</td>
<td>The prevalence of UTI was 25.56% in the 0 – 3 month age group. Compared to all age groups, children with UTI were significantly younger, more frequently were girls, and had higher fever and C-reactive protein (CRP) levels than those without.</td>
<td>Study Limitations: None Diagnostic Studies Patients not enrolled in consecutive or random manner Case-control study No independent, blind comparison between index test and reference test Not all patients received reference test</td>
</tr>
</tbody>
</table>

References:
**Study Type:** Prospective Cross-Sectional Study  
**Size:** 1,247 in all age groups, 133 aged between 0 – 3 months between July 2006 and July 2008 were included.

For older children, samples were obtained by clean catch or bladder catheterization. Dipstick urinalysis (Medi-Test Combi 11; Macherey-Nagel, Düren, Germany) was considered positive if there was a trace or more of LE and/or nitrite. Bacterial, RBC, and WBC counts were assessed on uncentrifuged urine using the automated flow cytometer Sysmex UF-100 (Merck-Eurolab, Leuven, Belgium). The threshold for abnormal leukocyturia was set at >/=35 leukocytes/ul of urine by the manufacturer. Urine osmolality was not taken into account in order to process or not process samples for culture. The laboratory staff was blinded to clinical information. UTI was confirmed in children having a urine culture growing >/=100,000 CFU/ml of a single pathogen. In urine samples obtained by suprapubic aspiration, any growth of pathogen was considered significant. Urine culture was realized in the routine of the hospital bacteriology laboratory by technicians who were unaware that the specimens were part of a clinical study.

**Automated flow cytometry results for all age groups:**  
The AUC for WBC counts was 0.99 (95% CI, 0.98 to 0.99), compared with 0.74 (95% CI, 0.70 to 0.78) for RBC counts and 0.89 (95% CI, 0.87 to 0.92) for bacterial counts. The overall diagnostic performance of urinary WBC counts was by far superior to that of RBC and bacterial counts (P<0.001 for both comparisons).

**Comparison of overall diagnostic performance between automated flow cytometry urinary WBC counts and urinary dipstick including all age groups.**  
Urinary WBC counts had an ROC AUC of 0.99 that was significantly higher than the ROC AUC for the LE dipstick (0.92), nitrite dipstick (0.83), or the combination of positive results for LE and/or nitrite (0.91) (P < 0.001 for all comparisons).

**Stratification of results by age:** The diagnostic performance of urinary dipstick and cytometry WBC count tests with a thus have wide confidence intervals, and the results are uncertain)
References:


PICO Question: In children less than 2 months old, which children should have urine testing? What testing should be done?

<table>
<thead>
<tr>
<th>Modality: Urine dipstick tests with clean-catch method</th>
<th>Outcome: Test performance</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Study Acronym; Author; Year Published; Location</strong></td>
<td><strong>Aim of Study; Study Type; Study Size (N)</strong></td>
</tr>
<tr>
<td><strong>Journal:</strong> Acta Paediatrica</td>
<td><strong>Aim:</strong> To evaluate using urine dipstick tests with clean-catch method to screen for urinary tract infection (UTI) in febrile infants under 90 days of age</td>
</tr>
</tbody>
</table>

| **Low Quality Rating if:** | - Studies inconsistent (wide variation of treatment effect across studies, population, interventions, or outcomes varied) |
| | - Not Available |
| | - Studies are indirect (PICO question is quite different from the available evidence in regard to population, intervention, comparison, or outcome) |
| | - Case-control study |
| | - No independent, blind comparison between index test and reference test |
| | - Not all patients received reference test |

Cutoff of 35 WBC/μl of urine was investigated after stratifying patients into five age categories. There were no differences in test performance as expressed by the AUC of ROC curves between the age categories for any of the tests. The analysis also demonstrated excellent diagnostic performance of cytometry WBC counts, which remained superior to dipstick analysis in all age categories.
### References:


### PICO Question: In children less than 2 months old, which children should have urine testing? What testing should be done?

<table>
<thead>
<tr>
<th>Modality: Urine Testing; Outcome: Predictors</th>
<th>Low Quality Rating if:</th>
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<td>Large effect</td>
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<td>Plausible confounders or other biases increase certainty of effect</td>
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</table>

#### Study Acronym; Author; Year Published; Location

**Journal**: Archives of Pediatrics & Adolescent Medicine  
**Author**: Newman, T.B. et al.  
**Year Published**: 2002  
**Location**: Departments of Epidemiology and Biostatistics, University of California, San Francisco

<table>
<thead>
<tr>
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<th>Patient Population</th>
<th>Study Intervention (# patients) / Study Comparator</th>
<th>Endpoint Results / Outcome (Absolute Event Rates, P values; OR or RR; &amp; 95% CI)</th>
<th>Design Limitations</th>
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<td>Newman, T.B. et al. (2002)</td>
<td>Prospective cohort study</td>
<td>3066 infants 3 months of younger</td>
<td>Inclusion Criteria: infants were eligible for inclusion if they (1) were no older than 3 months; (2) had axillary, rectal, or tympanic temperatures of at least 38°C if the office or in the previous 24 hours at home; and (3) were initially</td>
<td>Methods: PROS practitioners recorded clinical and demographic data on standard forms, including initial physical examination results, diagnostic impression, and assessment of overall severity of illness before the results of any laboratory tests were available.</td>
<td>Results: Fifty-four percent of the infants initially had urine tested, of whom 10% had a UTI. The height of the fever was associated with urine testing and a UTI among those tested (adjusted odds ratio per degree Celsius, 2.2 for both). Younger age, ill appearance, and lack of a</td>
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<td>Studies are indirect (PICO question is quite different from the available evidence in regard to population, intervention, comparison, or outcome)</td>
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<td>Studies are imprecise (when studies include few patients and few events, and thus have wide confidence)</td>
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</table>
with temperatures of 38°C or higher were evaluated and treated examined by a PROS practitioner fever source were associated with urine testing but not with a UTI, whereas lack of circumcision (adjusted odds ratio, 11.6), female sex (adjusted odds ratio, 5.4), and longer duration of fever (adjusted odds ratio, 1.8 for fever lasting > or = 24 hours) were not associated with urine testing but were associated with a UTI. Bacteremia accompanied the UTI in 10% of the patients, including 17% of those younger than 1 month. Among 807 infants not initially tested or treated with antibiotics, only 2 had a subsequent documented UTI; both did well.

### Journal: American Journal of Diseases of Children
Author: Krober, M.S., et al.
Year Published: 1985
Location: Department of Pediatrics, Tripler Army Medical Center, Honolulu and the John A. Burns School of Medicine, University of Hawaii, Honolulu

**Aim:** To report the results of extensive bacterial and viral cultures, chest roentgenograms, and lumbar punctures on febrile infants less than 3 months old with correlation of their clinical findings and diagnoses

**Study Type:** Prospective Study

**Size:** 182 sick, febrile (temperature >38 degree C) infants less than 3 months of age.

**Inclusion Criteria:** Study patients included all infants less than 3 months of age with fever (rectal temperature >/= 38 degrees C) seen during the periods from February 1982 through June 1982 and from September 1982 through January 1983.

**Methods:** Infants were hospitalized for observation and evaluation. Each had a chest roentgenogram and urinalysis (catheterized specimen) performed on admission. A clinical data sheet was completed for each infant recording symptoms, physical findings, hospital course and results of laboratory tests. Cerebrospinal fluid, blood, urine and stool (rectal swabs) specimens were cultured for bacterial pathogens using standard media and technique.

**Results:** The most common diagnoses in our study were aseptic meningitis, UTI, otitis media, and gastroenteritis. Twenty infants had catheterized urine samples yielding more than 10 colonies/mL. Urinary tract infection was more common in male infants (14/20; 70%), especially in the uncircumcised ones (12/14; 86%). A structural urinary tract anomaly (ureterocele) was found.

**Study Limitations:** None

**Non-Randomized Studies**
- Failure to develop and apply appropriate eligibility criteria
- Flawed measurement of both exposure and outcome
- Failure to adequately control confounding

<table>
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<tr>
<th>Study Limitations</th>
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<td>Quality (certainty) of evidence for studies as a whole:</td>
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<td>Low</td>
<td>Very Low</td>
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</table>
99 (54%) male and 83 (46%) female infants. There were 60 infants less than 1 month, 73 infants from 1 to 2 months and 49 infants from 2 to 3 months of age.

| Aim: To identify clinical and demographic factors associated with UTI in febrile infants who are < = 60 days of age using a prospective multicenter cohort | Inclusion Criteria: All infants who were aged 60 days or younger and presented with rectal temperatures > = 38 degree C by history of in the ED were eligible for enrollment. |
| Methods: Patients were evaluated with a standard history and physical examination on all enrolled patients, including completion of a Yale Observation Scale (YOS) score to assess ill appearance. Clinical factors that were hypothesized in advance to be associated with UTI and therefore collected and analyzed included age < = 28 days, female gender, circumcision status, ill appearance (defined as a YOS > 10), height of fever, and white race. A standardized laboratory evaluation was performed on all enrolled infants, including testing for respiratory syncytial virus (RSV) and bladder catheterization or suprapubic aspiration for urinalysis and urine culture. Standard laboratory screening for UTI varied among institutions; some performed microscopic analysis, whereas others used urine dipstick as an initial screen. |
| Results: Uncircumcised male infants had a higher rate of UTI (21.3%) compared with female (5.0%) and circumcised male (2.3%) infants. Infants with maximum recorded temperature of > = 39 degree C had a higher rate of UTI (16.3%) than other infants (7.2%). After multivariable adjustment, UTI was associated with being uncircumcised (odds ratio: 10.4; biased-corrected 95% confidence interval: 4.7-31.4) and maximum temperature (odds ratio: 2.4 per degree C; 95% confidence interval: 1.5-3.6). Factors that were reported previously to be associated with risk for UTI in infants and toddlers, such as white race and ill appearance, were not significantly associated with risk for UTI in this cohort of young infants. |
| Study Limitations: None |

Blood samples were cultured in aerobic, anaerobic, and hypertonic media, and stool specimens were cultured on Campylobacter medium in addition to standard media for isolation of enteric bacterial pathogens. In only one male infant. Pyuria (a count greater than ten white blood cells [WBC] per high-power field) was found in only five of the 20 infants with UTI.

Journal: Pediatrics
Author: Zorc, J.J., et al.
Year Published: 2005
Location: Department of Pediatrics, University of Pennsylvania School of Medicine, The Children’s Hospital of Philadelphia, Pennsylvania

Aim: To identify clinical and demographic factors associated with UTI in febrile infants who are < = 60 days of age using a prospective multicenter cohort

Study Type: Prospective Multicenter cohort

Size: 1025 (67%) of 1513 eligible patients were enrolled; 9.0% of enrolled infants received a diagnosis of UTI

Exclusion Criteria: Infants were excluded when they had received antibiotics within 48 hours of ED presentation or when a parent or guardian refused consent.
Question #1.

b) In pediatric patients >2 months to 18 years old with suspected urinary tract infection, which children should have urine testing? What testing should be done?

**Question 1b National/International Guidelines**

In 2016, the American Academy of Pediatrics (AAP) reaffirmed and updated the supporting evidence for the 2011 APP Practice Guideline: The Diagnosis and Management of the Initial Urinary Tract Infection in the Febrile Infants and Young Children 2 – 24 months of age. Recommendations remain the same from 2011 guideline and include the following action statements regarding urine testing:

- **Action Statement 1**: If a clinician decided that a febrile infant with no apparent source for the fever requires antimicrobial therapy to be administered because of ill appearance or another pressing reason, the clinician should ensure that a urine specimen is obtained for both culture and urinalysis before an antimicrobial is administered; the specimen needs to be obtained through catheterization or suprapubic aspiration (SPA), because of the diagnosis of UTI cannot be established reliably through culture of urine collected in a bag (evidence quality: A; strong recommendations).

- **Action Statement 2**: If a clinician assesses a febrile infant with an apparent source for the fever as not being so ill as to require immediate antimicrobial therapy, then the clinician should assess the likelihood of UTI.

- **Action Statement 2a**: If the clinician determines the febrile infant to have a low likelihood of UTI, then clinician follow-up monitoring without testing is sufficient (evidence quality: A; strong recommendation).

- **Action Statement 2b**: If the clinician determines that the febrile infant is not a low-risk group, then there are 2 choices (evidence quality: A; strong recommendation).
  - **Option 1** is to obtain a urine specimen through catheterization or SPA for culture and urinalysis.
  - **Option 2** is to obtain a urine specimen through the most convenient means and to perform a urinalysis. If the urinalysis results suggest a UTI (positive leukocyte esterase test results or nitrite test or microscopic analysis results for leukocytes or bacteria), then a urine specimen should be obtained through catheterization or SPA and cultured; if urinalysis of fresh (less than 1 hour since void) urine yields negative leukocyte esterase and nitrite results, then it is reasonable to monitor the clinical course without initiating antimicrobial therapy, recognizing that a negative urinalysis does not rule out a UTI with certainty.
AAP Clinical Practice Guideline Algorithm:
National Institute for Health and Care Excellence updated the 2017 Urinary tract infection in under 16s: diagnosis and management with the following recommendations for urine testing:

This guideline covers diagnosing and managing first or recurrent upper or lower urinary tract infections in infants, children and young people. It aims to achieve more consistent clinical practice, based on accurate diagnosis and effective management.

1.1 Diagnosis

1.1.1 Symptoms and signs

1.1.1.1 Infants and children presenting with unexplained fever of 38°C or higher should have a urine sample tested within 24 hours. [2007]

1.1.1.2 Infants and children with an alternative site of infection should not have a urine sample tested. When infants and children with an alternative site of infection remain unwell, urine testing should be considered after 24 hours at the latest. [2007]

1.1.1.3 Infants and children with symptoms and signs suggestive of urinary tract infection (UTI) should have a urine sample tested for infection. Table 1 is a guide to the symptoms and signs that infants and children present with. [2007]

Table 1 Presenting symptoms and signs in infants and children with UTI
1.1.2 Assessment of risk of serious illness

1.1.2.1 The illness level in infants and children should be assessed in accordance with recommendations in the NICE guideline on fever in under 5s. [2007]

1.1.5 Urine testing

1.1.5.1 For all diagnostic tests there will be a small number of false negative results; therefore clinicians should use clinical criteria for their decisions in cases where urine testing does not support the findings. [2007]

1.1.5.2 Refer all infants under 3 months with a suspected UTI (see table 1) to paediatric specialist care, and
   - send a urine sample for urgent microscopy and culture
   - manage in line with the NICE guideline on fever in under 5s. [2017]
1.1.5.3 Use dipstick testing for infants and children 3 months or older but younger than 3 years with suspected UTI.
   - If both leukocyte esterase and nitrite are negative: do not start antibiotic treatment; do not send a urine sample for microscopy and culture unless at least 1 of the criteria in recommendation 1.1.6.1 apply.
   - If leukocyte esterase or nitrite, or both are positive: start antibiotic treatment; send a urine sample for culture. [2017]

1.1.5.4 The urine-testing strategy shown in table 2 is recommended for children aged 3 years or older. [2007]

1.1.5.5 Follow the guidance in table 3 on interpreting microscopy results. [2007]

Table 2 Urine-testing strategies for children 3 years or older
1.1.6 Indication for culture

1.1.6.1 Urine samples should be sent for culture:
- in infants and children who are suspected to have acute pyelonephritis/upper urinary tract infection (see 1.1.8.1)
- in infants and children with a high to intermediate risk of serious illness
- in infants under 3 months
- in infants and children with a positive result for leukocyte esterase or nitrite
- in infants and children with recurrent UTI
- in infants and children with an infection that does not respond to treatment within 24–48 hours, if no sample has already been sent
- when clinical symptoms and dipstick tests do not correlate. [2017]

1.1.7 History and examination on confirmed UTI

1.1.7.1 The following risk factors for UTI and serious underlying pathology should be recorded:
- poor urine flow
- history suggesting previous UTI or confirmed previous UTI
- recurrent fever of uncertain origin
- antenatally diagnosed renal abnormality
- family history of vesicoureteric reflux (VUR) or renal disease
• constipation
• dysfunctional voiding
• enlarged bladder
• abdominal mass
• evidence of spinal lesion
• poor growth
• high blood pressure. [2007]

2016 American College of Emergency Physicians Clinical Policies Subcommittee on Pediatric Fever recommended:

Pain Management Recommendations:

Clinical Question: For well-appearing immunocompetent infants and children aged 2 months to 2 years presenting with fever (≥38.0°C [100.4°F]), are there clinical predictors that identify patients at risk for urinary tract infection?

• Infants and children at increased risk for urinary tract infection include females younger than 12 months, uncircumcised males, nonblack race, fever duration greater than 24 hours, higher fever (≥39°C), negative test result for respiratory pathogens, and no obvious source of infection. Although the presence of a viral infection decreases the risk, no clinical feature has been shown to effectively exclude urinary tract infection. Physicians should consider urinalysis and urine culture testing to identify urinary tract infection in well-appearing infants and children aged 2 months to 2 years with a fever ≥38°C (100.4°F), especially among those at higher risk for urinary tract infection. (Level C recommendations)

Clinical Question: For well-appearing febrile infants and children aged 2 months to 2 years undergoing urine testing, which laboratory testing method(s) should be used to diagnose a urinary tract infection?

• Physicians can use a positive test result for any one of the following to make a preliminary diagnosis of urinary tract infection in febrile patients aged 2 months to 2 years: urine leukocyte esterase, nitrites, leukocyte count, or Gram’s stain. (Level B recommendations)

  (1) Physicians should obtain a urine culture when starting antibiotics for the preliminary diagnosis of urinary tract infection in febrile patients aged 2 months to 2 years. (2) In febrile infants and children aged 2 months to 2 years with a negative dipstick urinalysis result in whom urinary tract infection is still suspected, obtain a urine culture. (Level C recommendations)

In 2015, the Kidney Health Australia, Caring for Australians with Renal Impairment (KHA-CARI) recommended the following:

• Recommend that the diagnosis of urinary tract infection (UTI) only be made on the basis of clinical symptoms (see below) in association with a positive urine culture. (1B)
• Suggest that the presence of bacteriuria (by microscopy with gram stain) on an appropriately collected urine specimen can be used as the basis for a presumptive diagnosis of UTI. (2B)

• Recommend that culture of an appropriately collected urine specimen (see below) is required for definitive diagnosis of UTI (1B) and that UTI diagnosis not be made solely on the basis of:
  o Urinary dipstick testing for leucocyte esterase or nitrite (1B) or
  o The presence of white cells on microscopy, in the absence of bacteriuria. (1B)

• Suggest that the occurrence of a positive urine culture in the absence of clinical symptoms (asymptomatic bacteriuria) does not warrant treatment or further investigation for UTI. (2B)
The 2011 American Academy of Family Physicians Guideline on Diagnosis and Treatment of Urinary Tract Infections in Children recommended the following:

- UTI should be suspected in patients with leukocyte esterase and nitrite present on dipstick testing, or with pyuria of at least 10 white blood cells per high-power field and bacteriuria on microscopy. (Evidence Rating: C)

- In young children, urine samples collected with a bag are unreliable in the evaluation of UTI. (Evidence Rating: C)

![Diagram of Urine Testing in Children with Suspected Urinary Tract Infection](image)
Guideline References:

Question 1b Health System Guidelines:

Children's Hospital of Philadelphia's revised 2018 Pathway for the Evaluation and Treatment of Children with Febrile UTI
Febrile UTI

This pathway is to be used for infants, children > 56 days through 18 years of age, with fever ≥ 38°C for evaluating and treating urinary tract infection.

Exclusions
8. Known urinary tract abnormality
9. Neurogenic bladder
10. Immune deficiency
11. Recent GU Surgery
12. Infants < 57 days
Urine Testing

13. Dipstick should be performed within 1 hour
14. Dipstick is the preferred screening method and is as good as a formal UA when done correctly, therefore it is unnecessary to send a specimen for a standard UA
15. Abnormal dipsticks should NOT be sent to the lab unless clinically indicated (casts, etc)

Cultures
16. Clean-catch specimens that have a negative dipstick should not be sent for culture
17. All specimens obtained by catheterization or suprapubic tap should be sent for culture
18. Send in grey top tube if > 3 ml of urine. If specimen is < 3 ml of urine, place in sterile container on ice and transport to lab
19. For febrile, symptomatic patients with isolated hematuria, it is reasonable to send a urine culture

Uncircumcised Males with Phimosis
20. Consider treatment with betamethasone 0.05% cream twice daily for four weeks or refer to Urology

ALL urine cultures need careful follow-up

Patients treated empirically
21. Check urine culture results
22. If positive, review sensitivities, change antibiotic as needed, assure response to therapy within 48 hours
23. Educate family about follow-up for future febrile illness
24. See imaging and prophylaxis recommendations
25. If negative, discontinue antibiotics, inform family that child did not have UTI

Positive urine cultures
26. Review sensitivities
27. Assure appropriate antibiotic therapy, and response to treatment within 48 hours
28. Educate family about follow-up for future febrile illness
29. See imaging and prophylaxis recommendations

Negative urine cultures
30. Inform family that the patient did not have a UTI
In 2017, Nationwide Children’s Hospital guideline on Urinary Tract Infection Diagnosis and Management recommended:

**General Management Principles**

The following guidance will focus on uncomplicated UTIs in otherwise healthy children. Infections in children with underlying renal diseases, anatomic or functional anomalies of the urinary tract, urinary catheters, or immunocompromising conditions/therapies constitute complicated UTIs and must be approached on an individual basis.

**The management of suspected UTI in children involves six key steps:**

1. Determine whether the pre-test probability of UTI is high enough to warrant testing.
2. Obtain an appropriate urine sample for urinalysis and urine culture (if urinalysis positive or clinical suspicion despite a negative urinalysis).
3. Decide whether empiric antibiotic therapy for presumed UTI is warranted.
4. When empiric therapy is given, prescribe the most appropriate antibiotic for the optimal duration.
5. Follow-up results of the urine culture and susceptibility testing and adjust therapy if needed (i.e. stop or change the antibiotic).
6. Assess and manage risk factors for recurrent UTI and UTI-related morbidity.

Steps 1 and 2 are beyond the scope of these guidelines, except to emphasize that it is essential to obtain an appropriate urine sample for culture given the impact on both the acute and subsequent management of a child with presumed UTI. Catheterization is recommended for urine cultures in pre-toilet trained children. The American Academy of Pediatrics’ recommendations allow bagged urine samples for initial urinalysis but NOT for culture due to potential for contamination. Thus, bagged urine samples with either A) positive leukocyte esterase or nitrite test results, or B) presence of white blood cells or bacteria on microscopy require collection of a second urine sample by catheterization or suprapubic aspiration for culture.

**Treatment of UTI in Children**

Once the clinician determines that the clinical presentation and urinalysis results are suggestive of an uncomplicated UTI, the decision whether to treat empirically, and if so, with which antibiotic depends on several factors:
2016's Seattle Children's Hospital Urinary Tract Infection: Criteria and Definitions:

**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 < 60 mL/min/1.73m²
- Genitourinary abnormalities, including: previous genitourinary surgery (other than circumcision), neurogenic bladder conditions, known obstructive uropathy, known high-grade vesicoureteral reflex (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 v8.0: 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 coagulase-negative is suspected
- Give IV antibiotics until sterile X 24 hrs (minimum 24 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 = pentalgin if coagulase-negative is suspected
- 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 pyelitis (14 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 (or 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 bacteremia 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
2017 Children's Hospital of Chicago's Febrile Urinary Tract Infection (UTI) Pathway
Children's Minnesota:
Health System Guideline References:


Question #2.

a. In pediatric patients < 2 months old with suspected urinary tract infection, how should the sample be obtained?

**Question 2a National/International Guideline Recommendations:**

**National Institute for Health and Care Excellence** updated in 2017 Urinary tract infection in under 16s: diagnosis and management with the following recommendations:

1.1.3 Urine collection

1.1.3.1 A clean catch urine sample is the recommended method for urine collection. If a clean catch urine sample is unobtainable:
   a. Other non-invasive methods such as urine collection pads should be used. It is important to follow the manufacturer’s instructions when using urine collection pads. Cotton wool balls, gauze and sanitary towels should not be used to collect urine in infants and children.
   b. When it is not possible or practical to collect urine by non-invasive methods, catheter samples or suprapubic aspiration (SPA) should be used.
   c. Before SPA is attempted, ultrasound guidance should be used to demonstrate the presence of urine in the bladder. [2007]

1.1.3.2 In an infant or child with a high risk of serious illness it is highly preferable that a urine sample is obtained; however, treatment should not be delayed if a urine sample is unobtainable. [2007]

1.1.4 Urine preservation

1.1.4.1 If urine is to be cultured but cannot be cultured within 4 hours of collection, the sample should be refrigerated or preserved with boric acid immediately. [2007]

1.1.4.2 The manufacturer's instructions should be followed when boric acid is used to ensure the correct specimen volume to avoid potential toxicity against bacteria in the specimen. [2007]

In 2015, the Kidney Health Australia, Caring for Australians with Renal Impairment (KHA-CARI) recommended the following:

**Urine collection**

d. Suprapubic aspirate (SPA) is the most definitive method of urine culture but is regarded as more invasive than other methods. We recommend the use of clean catch urine (CCU), mid-stream urine (MSU) or in–out catheter specimen urine (CSU) as satisfactory alternate methods for urine collection. **(1B)**

e. If positive urine culture by bag urine is obtained, recommend it is confirmed on repeat urine culture by SPA, CSU, CCU or MSU. **(1B)**
f. Suggest that SPA collection follow a protocol that ensures a full bladder prior to the procedure. This may involve either clinical assessment of good hydration and delay after voiding by 1 hour or use of bladder ultrasound or both. (2B)

Guideline References:


Question 2a Health System Guidelines:

2016's Seattle Children's Hospital Urinary Tract Infection: Criteria and Definitions:
Health System Guideline References:


**Question 2a Primary Literature:**

<table>
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<tr>
<th>PICO Question: In patients &lt; 2 months old with suspected urinary tract infection, how should the sample be obtained?</th>
<th>Modality: Urine dipstick tests with clean-catch method; Outcome: Test performance</th>
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<tr>
<td><strong>Study Acronym; Author; Year Published; Location</strong></td>
<td><strong>Aim of Study; Study Type; Study Size (N)</strong></td>
</tr>
<tr>
<td>Journal: Acta Paediatrica Author: Herreros, M.L., et al. Year Published: 2018 Location: Department of Pediatrics, Infanta Sofia University Hospital, San Sebastian de los Reyes, Madrid, Spain</td>
<td><strong>Aim:</strong> To evaluate using urine dipstick tests with clean-catch method to screen for urinary tract infection (UTI) in febrile infants under 90 days of age</td>
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<td><strong>Diagnosis Studies</strong></td>
<td><strong>Patients not enrolled in consecutive or random manner</strong></td>
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PICO Question: In patients < 2 months old with suspected urinary tract infection, how should the sample be obtained?

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<tr>
<td>Journal: Pediatric Nursing Author: Burke, N. Year Published: 1995 Location: South Miami Hospital, Miami, FL</td>
<td><strong>Aim:</strong> To investigate the accuracy of laboratory results of urine samples collected from cotton balls as compared with paired samples collected from catheterization, Preemie Pampers, and Newborn Pampers</td>
<td><strong>Inclusion Criteria:</strong> Infants from birth to 28 days of age. Infants whose parents consented to their participation and who had intact skin were included in the study. The first 20 infants who were admitted to the NICU for a septic work-up (blood culture, CBC, and urine for LPA) were entered into the sample. The first 30 clinically stable infants cared for in the NICU whose urine samples could be collected within a 12-hour period of time were also entered.</td>
<td><strong>Methods:</strong> Urine samples were collected from 30 infants by aspirating urine from a cotton ball placed over the meatus. An additional urine sample was obtained from the same infants by aspiration from the diaper. The samples were tested by labstick analysis and results were compared by t-test. An additional sample of 20 infants had urine collected by cotton ball and catheterization for detection of Group B strep antigen and the results were correlated.</td>
<td><strong>Results:</strong> Samples obtained from cotton balls and Preemie Pampers yielded equivalent results. Significant differences were found in the pH and specific gravity of Newborn Pampers and Preemie Pampers. No redness nor skin breakdown was observed with the cotton ball application. Three positive Group B strep results were detected by both methods of urine collection. The remainder of the samples were negative by both methods.</td>
<td><strong>Study Limitations:</strong> None Non-Randomized Studies Failure to develop and apply appropriate eligibility criteria Flawed measurement of both exposure and outcome Failure to adequately control confounding Incomplete or inadequately short follow-up Differences in important prognostic factors at baseline</td>
</tr>
</tbody>
</table>

Quality (certainty) of evidence for studies as a whole:
- High
- Moderate
- Low
- Very Low

Increase Quality Rating if:
- Studies inconsistent (wide variation of treatment effect across studies, population, interventions, or outcomes varied)
- Studies are indirect (PICO question is quite different from the available evidence in regard to population, intervention, comparison, or outcome)
- Studies are imprecise (when studies include few patients and few events, and thus have wide confidence intervals, and the results are uncertain)
- Publication Bias (e.g. pharmaceutical company sponsors study on effectiveness of drug only small, positive studies found)
**Exclusion Criteria:** Infants with renal anomalies, urinary tract infections, and those who were receiving transfusions of blood or blood product.


**PICO Question:** In patients < 2 months old with suspected urinary tract infection, how should the sample be obtained?

**Modality:** Suprapubic aspiration and transurethral bladder catheterization; **Outcome:** Pain

<table>
<thead>
<tr>
<th>Study Acronym; Author; Year Published; Location</th>
<th>Aim of Study; Study Type; Study Size (N)</th>
<th>Patient Population</th>
<th>Study Intervention (# patients) / Study Comparator</th>
<th>Endpoint Results / Outcome (Absolute Event Rates, P values; OR or RR; &amp; 95% CI)</th>
<th>Design Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Journal: Pediatrics Author: Kozer, E., et al. Year Published: 2006 Location: Assaf Harofeh Medical Center, Tel Aviv University, Tel Aviv, Israel</td>
<td>Aim: To compare the pain that is experienced during these 2 procedures when performed in young infants  <strong>Study Type:</strong> RCT  <strong>Size:</strong> 58 infants were recruited; 29 to suprapubic aspiration and 29 to transurethral catheterization.</td>
<td>Inclusion Criteria: Infants who were 0 to 2 months of age and presented to the emergency department with fever and therefore required urine collection for culture  <strong>Exclusion Criteria:</strong> Patients born prematurely or had had a previous sepsis workup or other painful procedures or an anomaly of the urogenital system or abdominal wall.</td>
<td>Methods: Infants were randomly assigned evenly into 2 sample collections groups: suprapubic aspiration or transurethral catheterization. Eutectic mixture of local anesthetic cream that contained lidocaine and prilocaine was applied 1 hour before the procedure. The urethra was catheterized using a 5-Fr latex-free feeding tube that was lubricated with sterile water-soluble jelly that contained 2% lidocaine hydrochloride. Pediatric residents who were experienced with the procedures performed both suprapubic aspiration</td>
<td>Results: Seven infants were excluded because of consent withdrawal (3 patients), because of technical difficulties during videotaping (3 patients), or because the child voided during the procedure (1 patient). Twenty-seven infants in the suprapubic aspiration group and 24 in the transurethral catheterization group completed the study. All male infants were circumcised. An adequate urine sample was obtained in 18 (66%) of 27 patients in the suprapubic aspiration</td>
<td>Low Quality Rating if:  □ Studies inconsistent (wide variation of treatment effect across studies, population, interventions, or outcomes varied)  -Not Available  □ Studies are indirect (PICO question is quite different from the available evidence in regard to population, intervention, comparison, or outcome)  □ Studies are imprecise (when studies include few patients and few events, and thus have wide confidence intervals, and the results are uncertain)  □ Publication Bias (e.g. pharmaceutical company sponsors study on effectiveness of drug only small, positive studies found)</td>
</tr>
</tbody>
</table>

Reference:

and transurethral catheterization. The parents were instructed to use any comfort strategies that they wished, including verbal or physical comforting and pacifiers. Pain during collection was assessed on a 100-mm visual analog scale by a nurse and a parent. In addition, the infant’s upper part of the body was videotaped during the procedure. An investigator, who was blinded to the procedure, assigned a point score according to the Douleur Aigue du Nouveaune neonatal acute pain scale. For ensuring a successful blinding process, the following steps were taken. First, camera recording started 30 seconds before the procedure to prevent the possibility of distinguishing between the procedures on the basis of their duration. Second, the physician and the nurse were asked not to speak during the procedure to avoid revealing the nature of the procedure. Third, the person who videotaped the procedure watched the tape before it was analyzed to ensure the impossibility of identifying the procedure from the tape. The Student’s t test was used to compare the group and in 20 (83.3%) of 24 in the transurethral catheterization group. The mean Douleur Aigue du Nouveaune score was significantly higher in patients who were randomly assigned to suprapubic aspiration compared with patients who were randomly assigned to transurethral catheterization (7 and 4.5, respectively). The differences in Douleur Aigue du Nouveaune score also were significant in a subgroup analysis of boys and girls. Mean visual analogue scale scores by parents was higher in the suprapubic aspiration group compared with transurethral catheterization (63 +/- 27 mm vs 46 +/- 26, respectively). Similarly, mean visual analogue scale scores by nurses was higher in the suprapubic aspiration group compared with transurethral catheterization (3 +/- 18 mm vs 43 +/- 25 mm, respectively).

Increase Quality Rating if:
- Large effect
- Dose-response gradient
- Plausible confounders or other biases increase certainty of effect

Quality (certainty) of evidence for studies as a whole:
- High
- Moderate
- Low
- Very Low
Question #2.
b. In pediatric patients >2 months to 18 years old with suspected urinary tract infection, how should the sample be obtained?

**Question 2b National/International Guideline Recommendations:**

In 2016, the American Academy of Pediatrics (AAP) reaffirmed and updated the supporting evidence for the 2011 APP Practice Guideline: The Diagnosis and Management of the Initial Urinary Tract Infection in the Febrile Infants and Young Children 2 – 24 months of age. Recommendations remain the same from 2011 guideline and include the following action statements for obtaining sample:

- **Action Statement 1:** If a clinician decided that a febrile infant with no apparent source for the fever requires antimicrobial therapy to be administered because of ill appearance or another pressing reason, the clinician should ensure that a urine specimen is obtained for both culture and urinalysis before an antimicrobial is administered; the specimen needs to be obtained through catheterization or suprapubic aspiration (SPA), because of the diagnosis of UTI cannot be established reliably through culture of urine collected in a bag (evidence quality: A; strong recommendations).

- **Action Statement 2a:** If the clinician determines the febrile infant to have a low likelihood of UTI, then clinician follow-up monitoring without testing is sufficient (evidence quality: A; strong recommendation).

- **Action Statement 2b:** If the clinician determines that the febrile infant is not a low-risk group, then there are 2 choices (evidence quality: A; strong recommendation).
  1. **Option 1** is to obtain a urine specimen through catheterization or SPA for culture and urinalysis.
  2. **Option 2** is to obtain a urine specimen through the most convenient means and to perform a urinalysis. If the urinalysis results suggest a UTI (positive leukocyte esterase test results or nitrite test or microscopic analysis results for leukocytes or bacteria), then a urine specimen should be obtained through catheterization or SPA and cultured; if urinalysis of fresh (less than 1 hour since void) urine yields negative leukocyte esterase and nitrite results, then it is reasonable to monitor the clinical course without initiating antimicrobial therapy, recognizing that a negative urinalysis does not rule out a UTI with certainty.
National Institute for Health and Care Excellence updated in 2017 Urinary tract infection in under 16s: diagnosis and management with the following recommendations:

1.1.3 Urine collection

1.1.3.1 A clean catch urine sample is the recommended method for urine collection. If a clean catch urine sample is unobtainable:
   2. Other non-invasive methods such as urine collection pads should be used. It is important to follow the manufacturer's instructions when using urine collection pads. Cotton wool balls, gauze and sanitary towels should not be used to collect urine in infants and children.
   3. When it is not possible or practical to collect urine by non-invasive methods, catheter samples or suprapubic aspiration (SPA) should be used.
   4. Before SPA is attempted, ultrasound guidance should be used to demonstrate the presence of urine in the bladder. [2007]

1.1.3.2 In an infant or child with a high risk of serious illness it is highly preferable that a urine sample is obtained; however, treatment should not be delayed if a urine sample is unobtainable. [2007]

1.1.4 Urine preservation

1.1.4.1 If urine is to be cultured but cannot be cultured within 4 hours of collection, the sample should be refrigerated or preserved with boric acid immediately. [2007]

1.1.4.2 The manufacturer's instructions should be followed when boric acid is used to ensure the correct specimen volume to avoid potential toxicity against bacteria in the specimen. [2007]

In 2015, the Kidney Health Australia, Caring for Australians with Renal Impairment (KHA-CARI) recommended the following:

Urine collection

- Suprapubic aspirate (SPA) is the most definitive method of urine culture but is regarded as more invasive than other methods. We recommend the use of clean catch urine (CCU), mid-stream urine (MSU) or in–out catheter specimen urine (CSU) as satisfactory alternate methods for urine collection. (1B)
- If positive urine culture by bag urine is obtained, recommend it is confirmed on repeat urine culture by SPA, CSU, CCU or MSU. (1B)
- Suggest that SPA collection follow a protocol that ensures a full bladder prior to the procedure. This may involve either clinical assessment of good hydration and delay after voiding by 1 hour or use of bladder ultrasound or both. (2B)
The 2011 American Academy of Family Physicians Guideline on Diagnosis and Treatment of Urinary Tract Infections in Children recommended the following:

- UTI should be suspected in patients with leukocyte esterase and nitrite present on dipstick testing, or with pyuria of at least 10 white blood cells per high-power field and bacteriuria on microscopy. (Evidence Rating: C)

- In young children, urine samples collected with a bag are unreliable in the evaluation of UTI. (Evidence Rating: C)

Guideline References:

Question 2b Health System Guidelines:

Children's Hospital of Philadelphia’s revised 2018 Pathway for the Evaluation and Treatment of Children with Febrile UTI

Cleansing the Perineum

- Baby wipes are the preferred method to reduce contamination for clean-catch or urine bag specimens
- Supervision of cleansing and mid-stream clean catch reduce contamination (rates can be as high as 50% in children 2-6 years old)
- Ensure foreskin retraction in uncircumcised male
Use of the Urine Bag

- Discuss need for possible urine testing with the family as per script (Learn More)
- Cleanse the perineum with baby wipes prior to bag application
- Choose appropriately sized urine bag and utilize no-sting barrier to improve adhesion
- For prompt recognition of urine, assure bag is visible outside the diaper
- If specimen is contaminated with stool, discard and collect a new sample
- After placing the bag, provide beverage if PO status allows and check for urine in 30 minutes × 2
- If there is no urine after 1 hour, consult MD for further plan

In 2017, Nationwide Children’s Hospital guideline on Urinary Tract Infection Diagnosis and Management recommended:

- Catheterization is recommended for urine cultures in pre-toilet trained children. The American Academy of Pediatrics’ recommendations allow bagged urine samples for initial urinalysis but NOT for culture due to potential for contamination.1 Thus, bagged urine samples with either A) positive leukocyte esterase or nitrite test results, or B) presence of white blood cells or bacteria on microscopy require collection of a second urine sample by catheterization or suprapubic aspiration for culture.
2016’s Seattle Children’s Hospital Urinary Tract Infection: Criteria and Definitions:

![Diagram of Urinary Tract Infection v7.1: Diagnosis]

- **Decision to Test: Infants**
  - Febrile or prolonged jaundice
  - > 4 weeks of age: irritability, stress, failure to thrive

- **Decision to Test: Non-Toilet Trained Children**
  - Urine or upper respiratory tract infection
  - Circumcised boy: need ≥ 1 of the following OR suprapubic tenderness
    - Fever ≥ 38°C, fever ≥ 38°C, fever ≥ 38°C
    - Abdominal pain, dysuria, frequency, perineal tenderness, fever ≥ 38°C

- **Decision to Test: Toilet-Trained Children & Adolescents**
  - Urine or upper respiratory tract infection
  - Circumcised boy: need ≥ 2 of the following
    - Abdominal pain, dysuria, frequency, perineal tenderness, fever ≥ 38°C

- **Obtain Urinalysis and Urine Culture by the Following Methods:**
  - Infants: Catheterization or suprapubic aspiration (SPA)
  - Non-Toilet Trained Children: 2-6 months: consider SPA, otherwise catheterization
  - Toilet-Trained Children: Midstream clean catch
  - Adolescents: Midstream clean catch + 5-day urine culture (CDC/ChangePCH)

- **Test of cure urine cultures not recommended**

- **Potential poor sensitivity of UA's in infants**

- **Additional Studies: Infants**
  - < 48 days of age: refer to Invasive Fever Pathogens

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

- **Additional Studies: Toilet Trained**
  - If ill appearing, consider blood culture
**Diagnosis: Suprapubic Aspiration**

- Suprapubic aspiration (SPA) is an available option if there is difficulty obtaining a catheterized specimen.
- Additionally, UA's 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

[Suprapubic Aspiration Technique](http://www.baus.org.uk)
INPATIENT GUIDELINE | URINARY TRACT INFECTIONS (UTI)
(Infants 2-24 months with fever >38°C)

Aim: To improve compliance with AAP published guidelines for the management of urinary tract infections in infants.

EXCLUSION GUIDELINES
Patients excluded from this guideline:
- Severe with shock or meningitis
- Immunodeficiency
- Major genitourinary abnormalities
- Hardware/instrumentation of the urinary tract
- History of renal disease

NOTE 2
Admission Criteria:
- IL, toxic or septic appearing
- Failed outpatient antibiotics
- Inability to be cared for as an outpatient
- Dehydrated with inability to take PO

Discharge Criteria:
- Improving fever curve
- Tolerating PO
- Discharge education complete
- IFU plan in place

SUSPICION OF UTI
Obtain urine by catheterization: perform UA and culture

Pyuria (>5 WBC/HPF) and/or bacteriuria OR UA + for LE and/or nitrites

NOTE 3
For patients with UTI + bacteremia without septic shock or meningitis:
May still use oral therapy (7 days total abs) if it is a single positive blood culture that grow E. coli and subsequent cultures were negative. If not, consider ID consult.

NOTE 4
For cephalosporin allergy give:
Ciprofloxacin 20 mg/kg/dose PO bid (max: 750 mg/dose) If unable to take PO:
Gentamicin 2.5 mg/kg/dose IV q12h

NOTE 5
Signs of an abnormal renal US
- Hydronephrosis
- Scarring
- Evidence of high grade VUR
- Obstructive uropathy
- Signs of congenital renal abnormalities

Children’s Minnesota:

UTI Guidelines | Reviewer: Swanson | Revised V16 | Page 1
Health System Guideline References:

Question 3:

a. In pediatric patients <2 months old with suspected urinary tract infection, how is the diagnosis made? What is the threshold for diagnosis?

**Question 3a National/International Guidelines:**

National Institute for Health and Care Excellence updated in 2017 Urinary tract infection in under 16s: diagnosis and management with the following recommendations:

1.1.5 Urine testing

1.1.5.1 For all diagnostic tests there will be a small number of false negative results; therefore clinicians should use clinical criteria for their decisions in cases where urine testing does not support the findings. [2007]

1.1.5.2 Refer all infants under 3 months with a suspected UTI (see table 1) to paediatric specialist care, and

- send a urine sample for urgent microscopy and culture
- manage in line with the NICE guideline on fever in under 5s. [2017]

1.1.5.3 Use dipstick testing for infants and children 3 months or older but younger than 3 years with suspected UTI.

- If both leukocyte esterase and nitrite are negative: do not start antibiotic treatment; do not send a urine sample for microscopy and culture unless at least 1 of the criteria in recommendation 1.1.6.1 apply.
- If leukocyte esterase or nitrite, or both are positive: start antibiotic treatment; send a urine sample for culture. [2017]

1.1.5.4 The urine-testing strategy shown in table 2 is recommended for children aged 3 years or older. [2007]

1.1.5.5 Follow the guidance in table 3 on interpreting microscopy results. [2007]

Table 2 Urine-testing strategies for children 3 years or older
Dipstick testing for leukocyte esterase and nitrite is diagnostically as useful as microscopy and culture, and can safely be used.

<table>
<thead>
<tr>
<th>If both leukocyte esterase and nitrite are positive</th>
<th>The child should be regarded as having UTI and antibiotic treatment should be started. If a child has a high or intermediate risk of serious illness and/or a past history of previous UTI, a urine sample should be sent for culture.</th>
</tr>
</thead>
<tbody>
<tr>
<td>If leukocyte esterase is negative and nitrite is positive</td>
<td>Antibiotic treatment should be started if the urine test was carried out on a fresh sample of urine. A urine sample should be sent for culture. Subsequent management will depend upon the result of urine culture.</td>
</tr>
<tr>
<td>If leukocyte esterase is positive and nitrite is negative</td>
<td>A urine sample should be sent for microscopy and culture. Antibiotic treatment for UTI should not be started unless there is good clinical evidence of UTI (for example, obvious urinary symptoms). Leukocyte esterase may be indicative of an infection outside the urinary tract which may need to be managed differently.</td>
</tr>
<tr>
<td>If both leukocyte esterase and nitrite are negative</td>
<td>The child should not be regarded as having UTI. Antibiotic treatment for UTI should not be started, and a urine sample should not be sent for culture. Other causes of illness should be explored.</td>
</tr>
</tbody>
</table>
Table 3 Guidance on the interpretation of microscopy results

<table>
<thead>
<tr>
<th>Microscopy results</th>
<th>Pyuria positive</th>
<th>Pyuria negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacteriuria positive</td>
<td>The infant or child should be regarded as having UTI</td>
<td>The infant or child should be regarded as having UTI</td>
</tr>
<tr>
<td>Bacteriuria negative</td>
<td>Antibiotic treatment should be started if clinically UTI</td>
<td>The infant or child should be regarded as not having UTI</td>
</tr>
</tbody>
</table>

1.1.6 Indication for culture

1.1.6.1 Urine samples should be sent for culture:
- in infants and children who are suspected to have acute pyelonephritis/upper urinary tract infection (see 1.1.8.1)
- in infants and children with a high to intermediate risk of serious illness
- in infants under 3 months
- in infants and children with a positive result for leukocyte esterase or nitrite
- in infants and children with recurrent UTI
- in infants and children with an infection that does not respond to treatment within 24–48 hours, if no sample has already been sent
- when clinical symptoms and dipstick tests do not correlate. [2017]

1.1.7 History and examination on confirmed UTI

1.1.7.1 The following risk factors for UTI and serious underlying pathology should be recorded:
- poor urine flow
- history suggesting previous UTI or confirmed previous UTI
- recurrent fever of uncertain origin
• antenatally diagnosed renal abnormality
• family history of vesicoureteric reflux (VUR) or renal disease
• constipation
• dysfunctional voiding
• enlarged bladder
• abdominal mass
• evidence of spinal lesion
• poor growth
• high blood pressure. [2007]

In 2015, the Kidney Health Australia, Caring for Australians with Renal Impairment (KHA-CARI) recommended the following:

• Recommend that the diagnosis of urinary tract infection (UTI) only be made on the basis of clinical symptoms (see below) in association with a positive urine culture. (1B)
• Suggest that the presence of bacteriuria (by microscopy with gram stain) on an appropriately collected urine specimen can be used as the basis for a presumptive diagnosis of UTI. (2B)
• Recommend that culture of an appropriately collected urine specimen (see below) is required for definitive diagnosis of UTI (1B) and that UTI diagnosis not be made solely on the basis of:
  o Urinary dipstick testing for leucocyte esterase or nitrite (1B) or
  o The presence of white cells on microscopy, in the absence of bacteriuria. (1B)
• Suggest that the occurrence of a positive urine culture in the absence of clinical symptoms (asymptomatic bacteriuria) does not warrant treatment or further investigation for UTI. (2B)

Urine culture
• Recommend the following minimum counts of colony forming units (CFU) grown on urine culture be considered as diagnostic of UTI (1B):
  o SPA: any growth
  o CSU: > 108 CFU/L (106–108 CFU/L; possible UTI)
  o MSU or CCU: > 108 CFU/L (107–108 CFU/L; possible UTI)
  o Bag/pad/cotton ball: not recommended for definitive culture.
• Suggest that the following be taken as indicators of possible contamination (2C):
  o Any growth from a bag specimen
  o Growth of more than one organism from any method of urine collection
  o Growth of skin commensals
• CFU counts less than the recommended minimum counts.

If contamination is possible on initial urine culture, suggest repeat urine culture if any of the following conditions apply (2C):
  o Convincing urinary symptoms are present.
  o The child has a structurally abnormal urinary tract.
  o There is a history of complicated UTIs.

The 2011 American Academy of Family Physicians Guideline on Diagnosis and Treatment of Urinary Tract Infections in Children recommended the following:

• UTI should be suspected in patients with leukocyte esterase and nitrite present on dipstick testing, or with pyuria of at least white blood cells per high-power field and bacteriuria on microscopy. (Evidence Rating: C)

• In young child, urine samples collected with a bag are unreliable in the evaluation of UTI. (Evidence Rating: C)
Urine Testing in Children with Suspected Urinary Tract Infection.

Children < 3 months of age
- Urine sample should be sent for urgent microscopy and culture
- Initiate treatment

Children 3 months to 3 years of age
- Specific urinary symptoms
  - Initiate antibiotic treatment, and send urine sample for urgent microscopy and culture
- Symptoms nonspecific for UTI
  - High risk of serious illness
    - Initiate antibiotic treatment, and send urine sample for urgent microscopy and culture
  - Intermediate or low risk of serious illness
    - Urine sample should be sent for microscopy and culture
    - Initiate treatment if microscopy or culture results are positive

Children > than 3 years of age
- Perform urine dipstick test
  - Positive for leukocyte esterase and nitrite
    - Diagnose UTI
      - Initiate antibiotic treatment; send urine sample for culture only if patient is at intermediate or high risk of serious illness or has a history of UTI
    - Initiate antibiotic treatment; send urine sample for culture
      - Treat depending on urine culture results
  - Negative for leukocyte esterase and positive for nitrite
    - Initiate antibiotic treatment
      - Send urine sample for microscopy and culture; initiate antibiotic treatment only if there is good clinical evidence of UTI
      - Treat depending on urine culture results
  - Positive for leukocyte esterase and negative for nitrite
    - Send urine sample for microscopy and culture
    - Treat depending on urine culture results
  - Negative for leukocyte esterase and nitrite
    - Explore other causes of illness

Figure 1.
Algorithm for urine testing in children with suspected urinary tract infection (UTI).
Guideline References:

**Question 3a Health System Guidelines**

**2016’s Seattle Children’s Hospital** Urinary Tract Infection: Criteria and Definitions:

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

(Guideline, AAP 2011)
Sensitivity of U/A 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) (Molseed, 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) (O O O, Seattle Children's UTI Pathway 2011)
  - $\geq 100,000$ colony forming units (CFU)/ml for clean catch
  - $\geq 50,000$ CFU/ml for in- and out-catheterization and suprapubic aspiration
### Diagnosis: Adolescent and Sexually Active Patients

| In adolescents and sexually active pre-adolescents: | • Clinicians must document a sexual history and an external genitourinary examination.  
• Clinicians should perform a bimanual examination in females if clinically indicated (e.g., in cases of pelvic pain). (GΩΩ, 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.
### 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

---

**Health System Guideline References:**

### Question 3a Primary Literature

**PICO Question:** How is the diagnosis made? What is the threshold for diagnosis?

<table>
<thead>
<tr>
<th>Study Acronym; Author; Year Published; Location</th>
<th>Study Type; Study Size (N)</th>
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<tbody>
<tr>
<td>Journal: Journal of Clinical Microbiology; Author: Duong, H. P., et al.; Year Published: 2016; Location: Belgium</td>
<td>Aim: To compare the predictive values of flow cytometry and a dipstick test as initial diagnostic tests for UTI in febrile children  <strong>Study Type:</strong> cross sectional  <strong>Size:</strong> 1,106 children (133 children less than 3 months of age)</td>
<td>Inclusion Criteria: children with body temperature of ≥38°C recorded in the emergency department or a history of fever of ≥38°C recorded within the previous 24 h. All consecutive eligible infectious episodes between July 2006 and July 2008 were included.  <strong>Exclusion Criteria:</strong> incomplete urinalysis and/or clinical data.</td>
<td>Intervention: urinary automated flow cytometry analysis  <strong>Comparator:</strong> urinary dipstick analysis</td>
<td><strong>Results:</strong>  <strong>Children 0-3 months old:</strong> The AUC for cytometry white blood cell (WBC) count was 0.99 (0.99–1.00)  The AUC for dipstick analysis for leukocyte esterase (LE) was 0.93 (0.91–0.95), for nitrites was 0.81 (0.80–0.84) and 0.93 (0.90–0.95) for LE and/or nitrites</td>
<td><strong>Study Limitations:</strong>  None  <strong>Diagnostic Studies</strong>  Patients not enrolled in consecutive or random manner  Case-control study  No independent, blind comparison between index test and reference test  Not all patients received reference test</td>
</tr>
</tbody>
</table>
### PICO Question: How is the diagnosis made? What is the threshold for diagnosis?

<table>
<thead>
<tr>
<th>Modality: Dipstick combined with Urine Microscopy vs Dipstick alone</th>
<th>Outcome: Test Performance Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Performance Characteristics / Endpoint Results / Outcome (Absolute Event Rates, P values; OR or RR; &amp; 95% CI)</td>
<td>Design Limitations</td>
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</tbody>
</table>

#### Study Acronym; Author; Year Published; Location
- Aim of Study; Study Type; Study Size (N)
- Patient Population
- Study Intervention (# patients) / Study Comparator
- Endpoint Results / Outcome (Absolute Event Rates, P values; OR or RR; & 95% CI)

### Journal: Pediatrics
- Author: Glissmeyer, E. W., et al.
- Year Published: 2014
- Location: United States

#### Aim: To compare the performance of urine dipstick alone with urine microscopy and with both tests combined as a screen for urinary tract infection (UTI) in febrile infants aged 1 to 90 days.

#### Study Type: Retrospective cohort study

#### Size: 6,394 febrile infant encounters (770 had UTI)

#### Inclusion Criteria: all infants with a catheterized urine dipstick, microscopic urinalysis, and urine bacterial cultures performed simultaneously

#### Exclusion Criteria: any child who had a urine collection method other than catheterization

#### Intervention: dipstick combined with urine microscopy

#### Comparator: urine dipstick alone

#### Results: The negative predictive value (NPV) was >98% for all tests. The combined urinalysis NPV was 99.2% (95% confidence interval; 99.1%-99.3%) and was significantly greater than the dipstick NPV of 98.7% (98.6%-98.8%). The dipstick positive predictive value was significantly greater than combined urinalysis (66.8% [66.2%-67.4%] vs 51.2% [50.6%-51.8%]).

### Design Limitations
- None

### Study Limitations:
- None

### Diagnostic Studies
- Patients not enrolled in consecutive or random manner
- Case-control study
- No independent, blind comparison between index test and reference test
- Not all patients received reference test

### Non-Randomized Studies
- Failure to develop and apply appropriate eligibility criteria
- Flawed measurement of both exposure and outcome
- Failure to adequately control confounding
- Incomplete or inadequately short follow-up

### Increase Quality Rating if:
- Large effect
|---------------------------------------------|--------------------------|------------------|-------------------|

**Aim:** to determine whether point-of-care (POCT) urinalysis (UA) is as accurate as laboratory-performed UA in diagnosing urinary tract infections (UTIs) in the pediatric emergency department (PED).

**Study Type:** retrospective series

**Size:** 4072 infants <2mo

**Inclusion Criteria:** both a UA and urine culture were obtained

**Exclusion Criteria:** Urine culture specimens collected via a bag, Foley catheter, indwelling stent, or urinary tract fistula were excluded.

**Intervention:** POCT urinalysis and laboratory-performed UA

**Comparator:** urine culture

**Results:**
- **4,033 lab performed UA**
  - Sensitivity 86.1% (95% CI 80.9-90.1)
  - Specificity 89.3% (95% CI 88.2-90.2)
  - PPV 33.5% (95% CI 29.8-37.4)
  - NPV 99% (95% CI 98.6-99.3)
- **39 POCT-UAs**
  - Sensitivity 75.0% (95% CI 35.6-95.5)
  - Specificity 90.3% (95% CI 73.1-97.5)
  - PPV 66.7% (95% CI 30.9-91.0)
  - NPV 93.3% (95% CI 76.5-98.8)

**Study Limitations:**
- None
- Non-Randomized Studies
  - Failure to develop and apply appropriate eligibility criteria
  - Flawed measurement of both exposure and outcome
  - Failure to adequately control confounding
  - Incomplete or inadequately short follow-up
  - Differences in important prognostic factors at baseline

**Quality (certainty) of evidence for studies as a whole:**
- High
- Moderate
- Low
- Very Low

**Diagnostic Studies**
- Patients not enrolled in consecutive or random manner
- Case-control study
- No independent, blind comparison between index test and reference test
- Not all patients received reference test

**References:**

**PICO Question:** How is the diagnosis made? What is the threshold for diagnosis?

**Modality:** Urinalysis  
**Outcome:** Test Performance Characteristics  
**Low Quality Rating If:** Differences in important prognostic factors at baseline  
**Dose-response gradient**  
Plausible confounders or other biases increase certainty of effect
<table>
<thead>
<tr>
<th>Study Acronym; Author; Year Published; Location</th>
<th>Aim of Study; Study Type; Study Size (N)</th>
<th>Patient Population</th>
<th>Study Intervention (# patients) / Study Comparator</th>
<th>Endpoint Results / Outcome (Absolute Event Rates, P values; OR or RR; &amp; 95% CI)</th>
<th>Design Limitations</th>
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<tr>
<td>Journal: Pediatrics Author: Schroeder, A. R., et al. Year Published: 2015 Location: United States</td>
<td>Aim: To calculate the sensitivity of the urinalysis (UA) in a multicenter sample of infants &lt;3 months with bacteremic UTI. <strong>Study Type</strong>: cross-sectional <strong>Size</strong>: 245 infants with bacteremic UTI and 115 infants with negative urine cultures.</td>
<td>Inclusion Criteria: &lt;3 months of age and had the same pathogenic organism isolated from blood and urine. <strong>Exclusion Criteria</strong>: if they had major comorbidities, if they were managed in the ICU, or if they had indwelling urinary or central venous catheters at the time the cultures were drawn or if no UA was performed or if the urine culture grew below the AAP threshold for UTI.</td>
<td>Intervention: Sensitivity was calculated on infants who had at least a partial UA performed and had &gt;=5000 colony-forming units per milliliter from the urine culture. Specificity was determined by using a random sample of infants from the central study site with negative urine cultures.</td>
<td>Results: The sensitivity of leukocyte esterase was 97.6% (95% CI 94.5%-99.2%) and of pyuria (&gt;3 white blood cells) was 96% (95% CI 92.5%-98.1%). In infants with negative urine cultures, leukocyte esterase specificity was 93.9% (95% CI 87.9 - 97.5) and of pyuria was 91.3% (84.6%-95.6%).</td>
<td>Studies inconsistent (wide variation of treatment effect across studies, population, interventions, or outcomes varied)</td>
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<td>Studies are indirect (PICO question is quite different from the available evidence in regard to population, intervention, comparison, or outcome)</td>
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<td>Studies are imprecise (when studies include few patients and few events, and thus have wide confidence intervals, and the results are uncertain)</td>
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<td>Publication Bias (e.g. pharmaceutical company sponsors study on effectiveness of drug only small, positive studies found)</td>
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<td>Dose-response gradient</td>
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<td>Plausible confounders or other biases increase certainty of effect</td>
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<td>Quality (certainty) of evidence for studies as a whole: High</td>
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</table>

References:
**PICO Question:** How is the diagnosis made? What is the threshold for diagnosis?

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<tr>
<th>Study Acronym / Author; Year Published; Location</th>
<th>Aim of Study; Study Size (N)</th>
<th>Patient Population</th>
<th>Study Intervention (# patients) / Study Comparator</th>
<th>Endpoint Results / Outcome (Absolute Event Rates, P values; OR or RR; &amp; 95% CI)</th>
<th>Design Limitations</th>
</tr>
</thead>
</table>
| Journal: Pediatric Emergency Care  
Author: Velasco, R., et al.  
Year Published: 2016  
Location: Spain | Aim: to evaluate the adequacy of the UTI diagnosis cutoff point of > 50,000 cfu/mL of a single bacterium in a urine culture with a positive urine dipstick or with a urinalysis in young febrile infants.  
Study Type: prospective multicenter study  
Size: 3333 infants | Inclusion Criteria: all infants younger than 90 days presenting in the pediatric emergency department with a fever without symptoms who had a CRP, WBC count, urine dipstick and urine and blood culture performed | Intervention: young febrile infants with a urine culture growth of 0-50,000 colony-forming units per milliliter (cfu/mL)  
Comparator: growth greater than 50,000 cfu/mL, both compared to a positive or negative urine dipstick | Results: Of a total of 3333 infants younger than 90 days with fever without focus which were included in the study, 538 were classified as UTI in accordance with American Academy of Pediatrics' guidelines.  
These patients were similar to those who had a positive urine dipstick and a urine culture yielding 10,000 to 50,000 ufc/mL, and they were different from those who had a normal urine dipstick and a urine culture >50,000 cfu/mL, being focused on the isolated bacteria and blood biomarkers values. | Study Limitations: None  
Non-Randomized Studies:  
Failure to develop and apply appropriate eligibility criteria  
Flawed measurement of both exposure and outcome  
Failure to adequately control confounding  
Incomplete or inadequately short follow-up  
Differences in important prognostic factors at baseline |

| Journal: Pediatrics  
Author: Chaudhari, P. P., et al  
Year Published: 2016  
Location: United States | Aim: To determine the optimal urine WBC threshold for UTI in young infants by using an automated urinalysis system, stratified by urine concentration.  
Inclusion Criteria: infants with paired urinalysis and urine culture  
Exclusion Criteria: urine culture grew mixed urogenital organisms or nonpathogenic organisms; urine | Intervention: UTI was defined as ≥50 000 colony-forming units/mL from catheterized specimens. Test characteristics were calculated across a range of WBC and leukocyte esterase (LE) cut-points, dichotomized into | Microscopic Urinalysis  
A cut-point of 3 WBC/ high powered field(HPF) in dilute urine resulted in LR+ 9.9 (CI, 8.5–11.5) and LR− 0.15 (CI, 0.10–0.21), whereas a cut-point of 6 WBC/HPF resulted in LR+ 10.1 (CI, 7.1–14.4) and LR− 0.17 (CI, 0.06–0.49) in concentrated urine. The AUC for both specific gravity groups are equal (0.93).  
**Dipstick** | | Increase Quality Rating if:  
Large effect  
Dose-response gradient  
Plausible confounders or other biases increase certainty of effect  
**Quality (certainty) of evidence for studies as a whole:**  
High  
Moderate |
## References:


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### Study Details:

**Study Type:** Retrospective cross-sectional study  
**Size:** 2700

**Diagnostic Studies**

- Patient Population: culture was obtained from a bag, clean void sample, or indwelling catheter; the urine source was missing; or the specific gravity was missing.
- **Study Intervention (# patients) / Study Comparator:** specific gravity groups (dilute < 1.015; concentrated ≥ 1.015)
- **Results:** A cut-point of any (positive) LE (small or 1+) resulted in LR+ 22.1 (CI, 17.7–27.6) and LR− 0.12 (0.09–0.18) in dilute urine, and LR+ 31.6 (CI, 17.2–57.6) and LR− 0.22 (CI, 0.09–0.52) in concentrated urine

**Author's conclusion:** Pyuria thresholds of 3 WBC/HPF in dilute urine and 6 WBC/HPF in concentrated urine are recommended for the presumptive diagnosis of UTI. Without correction of specific gravity, positive LE by automated dipstick is a reliably strong indicator of UTI.

**Study Limitations:**

- Low
- Very Low

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### PICO Question:

**How is the diagnosis made? What is the threshold for diagnosis?**

**Low Quality Rating if:**

- Studies inconsistent (wide variation of treatment effect across studies, population, interventions, or outcomes varied)
- Studies are indirect (PICO question is quite different from the available evidence in regard to population, intervention, comparison, or outcome)
- Studies are imprecise (when studies include few patients and few events,
**Question 3:**

b. In pediatric patients >2 months to 18 years old with suspected urinary tract infection, how is the diagnosis made? What is the threshold for diagnosis?

### Question 3b National/International Guidelines

In 2016, the American Academy of Pediatrics (AAP) reaffirmed and updated the supporting evidence for the 2011 APP Practice Guideline: The Diagnosis and Management of the Initial Urinary Tract Infection in the Febrile Infants and Young Children 2 – 24 months of age. Recommendations remain the same from 2011 guideline and include the following action statements:

- **Action Statement 1:** If a clinician decided that a febrile infant with no apparent source for the fever requires antimicrobial therapy to be administered because of ill appearance or another pressing reason, the clinician should ensure that a urine specimen is obtained for both culture and urinalysis before an antimicrobial is
administered; the specimen needs to be obtained through catheterization or suprapubic aspiration (SPA), because of the diagnosis of UTI cannot be established reliably through culture of urine collected in a bag (evidence quality: A; strong recommendations).

- Action Statement 2: If a clinician assesses a febrile infant with an apparent source for the fever as not being so ill as to require immediate antimicrobial therapy, then the clinician should assess the likelihood of UTI.
- Action Statement 2a: If the clinician determines the febrile infant to have a low likelihood of UTI, then clinician follow-up monitoring without testing is sufficient (evidence quality: A; strong recommendation).
- Action Statement 2b: If the clinician determines that the febrile infant is not a low-risk group, then there are 2 choices (evidence quality: A; strong recommendation).
  - Option 1 is to obtain a urine specimen through catheterization or SPA for culture and urinalysis.
  - Option 2 is to obtain a urine specimen through the most convenient means and to perform a urinalysis. If the urinalysis results suggest a UTI (positive leukocyte esterase test results or nitrite test or microscopic analysis results for leukocytes or bacteria), then a urine specimen should be obtained through catheterization or SPA and cultured; if urinalysis of fresh (less than 1 hour since void) urine yields negative leukocyte esterase and nitrite results, then it is reasonable to monitor the clinical course without initiating antimicrobial therapy, recognizing that a negative urinalysis does not rule out a UTI with certainty.
- Action Statement 3: To establish the diagnosis of UTI, clinicians should require both urinalysis results that suggest infection (pyuria and/or bacteriuria) and the presence of at least 50,000 colony-forming units (cfu) per milliliter of a uropathogen cultured from a urine specimen obtained through transurethral cauterization or SPA (evidence quality: C; recommendation).

**National Institute for Health and Care Excellence** updated in 2017 Urinary tract infection in under 16s: diagnosis and management with the following recommendations:

1.1.5 Urine testing

1.1.5.1 For all diagnostic tests there will be a small number of false negative results; therefore clinicians should use clinical criteria for their decisions in cases where urine testing does not support the findings. [2007]

1.1.5.3 Use dipstick testing for infants and children 3 months or older but younger than 3 years with suspected UTI.
  - If both leukocyte esterase and nitrite are negative: do not start antibiotic treatment; do not send a urine sample for microscopy and culture unless at least 1 of the criteria in recommendation 1.1.6.1 apply.
  - If leukocyte esterase or nitrite, or both are positive: start antibiotic treatment; send a urine sample for culture. [2017]

1.1.5.4 The urine-testing strategy shown in table 2 is recommended for children aged 3 years or older. [2007]

1.1.5.5 Follow the guidance in table 3 on interpreting microscopy results. [2007]
### 1.1.5.6 Table 2 Urine-testing strategies for children 3 years or older

<table>
<thead>
<tr>
<th>Condition</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>If both leukocyte esterase and nitrite are positive</td>
<td>The child should be regarded as having UTI and antibiotic treatment should be started. If a child has a high or intermediate risk of serious illness and/or a past history of previous UTI, a urine sample should be sent for culture.</td>
</tr>
<tr>
<td>If leukocyte esterase is negative and nitrite is positive</td>
<td>Antibiotic treatment should be started if the urine test was carried out on a fresh sample of urine. A urine sample should be sent for culture. Subsequent management will depend upon the result of urine culture.</td>
</tr>
<tr>
<td>If leukocyte esterase is positive and nitrite is negative</td>
<td>A urine sample should be sent for microscopy and culture. Antibiotic treatment for UTI should not be started unless there is good clinical evidence of UTI (for example, obvious urinary symptoms). Leukocyte esterase may be indicative of an infection outside the urinary tract which may need to be managed differently.</td>
</tr>
<tr>
<td>If both leukocyte esterase and nitrite are negative</td>
<td>The child should not be regarded as having UTI. Antibiotic treatment for UTI should not be started, and a urine sample should not be sent for culture. Other causes of illness should be explored.</td>
</tr>
</tbody>
</table>
Table 3 Guidance on the interpretation of microscopy results

<table>
<thead>
<tr>
<th>Microscopy results</th>
<th>Pyuria positive</th>
<th>Pyuria negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacteriuria positive</td>
<td>The infant or child should be regarded as having UTI</td>
<td>The infant or child should be regarded as having UTI</td>
</tr>
<tr>
<td>Bacteriuria negative</td>
<td>Antibiotic treatment should be started if clinically UTI</td>
<td>The infant or child should be regarded as not having UTI</td>
</tr>
</tbody>
</table>

1.1.6 Indication for culture

1.1.6.1 Urine samples should be sent for culture:
- in infants and children who are suspected to have acute pyelonephritis/upper urinary tract infection (see 1.1.8.1)
- in infants and children with a high to intermediate risk of serious illness
- in infants under 3 months
- in infants and children with a positive result for leukocyte esterase or nitrite
- in infants and children with recurrent UTI
- in infants and children with an infection that does not respond to treatment within 24–48 hours, if no sample has already been sent
- when clinical symptoms and dipstick tests do not correlate. [2017]

1.1.7 History and examination on confirmed UTI

1.1.7.1 The following risk factors for UTI and serious underlying pathology should be recorded:
- poor urine flow
- history suggesting previous UTI or confirmed previous UTI
- recurrent fever of uncertain origin
antenatally diagnosed renal abnormality
family history of vesicoureteric reflux (VUR) or renal disease
constipation
dysfunctional voiding
enlarged bladder
abdominal mass
evidence of spinal lesion
poor growth
high blood pressure. [2007]
AAP Clinical Practice Guideline Algorithm:

1. Risk of urinary tract infection (UTI) is ~7%
2. A decision to delay a confirmatory urine sample if antimicrobial therapy is being administered because of UTI symptoms or other overt urinary tract infection.
3. UTI should be considered if the patient is febrile and unable to urinate, has a history of UTI, and has a positive urinalysis or positive urine culture.
4. Obtain a urine specimen for culture and sensitivity (C&S).
5. Obtain a urine specimen for culture and sensitivity (C&S).
6. If the urine specimen is negative for infection, the patient may not have a UTI.
7. UTI may be diagnosed if the patient is febrile, has a history of UTI, and has a positive urinalysis or positive urine culture.
8. UTI may be diagnosed if the patient is febrile, has a history of UTI, and has a positive urinalysis or positive urine culture.
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40. UTI may be diagnosed if the patient is febrile, has a history of UTI, and has a positive urinalysis or positive urine culture.
In 2015, the Kidney Health Australia, Caring for Australians with Renal Impairment (KHA-CARI) recommended the following:

- Recommend that the diagnosis of urinary tract infection (UTI) only be made on the basis of clinical symptoms (see below) in association with a positive urine culture. *(1B)*
- Suggest that the presence of bacteriuria (by microscopy with gram stain) on an appropriately collected urine specimen can be used as the basis for a presumptive diagnosis of UTI. *(2B)*
- Recommend that culture of an appropriately collected urine specimen (see below) is required for definitive diagnosis of UTI *(1B)* and that UTI diagnosis not be made solely on the basis of:
  - Urinary dipstick testing for leucocyte esterase or nitrite *(1B)* or
  - The presence of white cells on microscopy, in the absence of bacteriuria. *(1B)*
- Suggest that the occurrence of a positive urine culture in the absence of clinical symptoms (asymptomatic bacteriuria) does not warrant treatment or further investigation for UTI. *(2B)*

**Urine culture**

- Recommend the following minimum counts of colony forming units (CFU) grown on urine culture be considered as diagnostic of UTI *(1B)*:
  - SPA: any growth
  - CSU: > 108 CFU/L (106–108 CFU/L; possible UTI)
  - MSU or CCU: > 108 CFU/L (107–108 CFU/L; possible UTI)
  - Bag/pad/cotton ball: not recommended for definitive culture.
- Suggest that the following be taken as indicators of possible contamination *(2C)*:
  - Any growth from a bag specimen
  - Growth of more than one organism from any method of urine collection
  - Growth of skin commensals
  - CFU counts less than the recommended minimum counts.
- If contamination is possible on initial urine culture, suggest repeat urine culture if any of the following conditions apply *(2C)*:
  - Convincing urinary symptoms are present.
  - The child has a structurally abnormal urinary tract.
  - There is a history of complicated UTIs.

**2016 American College of Emergency Physicians** Clinical Policies Subcommittee on Pediatric Fever recommended:

**Clinical Question:** For well-appearing febrile infants and children aged 2 months to 2 years undergoing urine testing, which laboratory testing method(s) should be used to diagnose a urinary tract infection?
Physicians can use a positive test result for any one of the following to make a preliminary diagnosis of urinary tract infection in febrile patients aged 2 months to 2 years: urine leukocyte esterase, nitrites, leukocyte count, or Gram’s stain. (Level B recommendations)

(1) Physicians should obtain a urine culture when starting antibiotics for the preliminary diagnosis of urinary tract infection in febrile patients aged 2 months to 2 years. (2) In febrile infants and children aged 2 months to 2 years with a negative dipstick urinalysis result in whom urinary tract infection is still suspected, obtain a urine culture. (Level C recommendations)

The 2011 American Academy of Family Physicians Guideline on Diagnosis and Treatment of Urinary Tract Infections in Children recommended the following:

- UTI should be suspected in patients with leukocyte esterase and nitrite present on dipstick testing, or with pyuria of at least white blood cells per high-power field and bacteriuria on microscopy. (Evidence Rating: C)
- In young child, urine samples collected with a bag are unreliable in the evaluation of UTI. (Evidence Rating: C)
Urine Testing in Children with Suspected Urinary Tract Infection.

Children < 3 months of age
- Urine sample should be sent for urgent microscopy and culture
- Initiate treatment

Children 3 months to 3 years of age
- Specific urinary symptoms
  - Initiate antibiotic treatment, and send urine sample for urgent microscopy and culture
- Symptoms nonspecific for UTI
  - High risk of serious illness
    - Initiate antibiotic treatment, and send urine sample for urgent microscopy and culture
  - Intermediate or low risk of serious illness
    - Urine sample should be sent for microscopy and culture
    - Initiate treatment if microscopy or culture results are positive

Children > than 3 years of age
- Perform urine dipstick test
  - Positive for leukocyte esterase and nitrite
    - Diagnose UTI
      - Initiate antibiotic treatment; send urine sample for culture only if patient is at intermediate or high risk of serious illness or has a history of UTI
  - Negative for leukocyte esterase and positive for nitrite
    - Initiate antibiotic treatment, and send urine sample for culture
    - Treat depending on urine culture results
  - Positive for leukocyte esterase and negative for nitrite
    - Send urine sample for microscopy and culture; initiate antibiotic treatment only if there is good clinical evidence of UTI
    - Treat depending on urine culture results
  - Negative for leukocyte esterase and nitrite
    - Explore other causes of illness

Figure 1.
Algorithm for urine testing in children with suspected urinary tract infection (UTI).
Guideline References:

Febrile UTI
This pathway is to be used for infants, children > 56 days through 18 years of age, with fever ≥ 38°C for evaluating and treating urinary tract infection.

Exclusions
- Known urinary tract abnormality
- Neurogenic bladder
- Immune deficiency
- Recent GU Surgery
- Infants < 57 days

### History and Physical Examination

#### History
- Duration of fever
- Symptoms that suggest an alternative source of fever
- Hydration status
- History of recurrent fever without identifiable source
- History of UTI
- History of constipation
- Dysfunctional voiding by history
- FH of vesicoureteral reflux (VUR) or renal disease

#### Physical Examination
- VS, consider BP, growth
- Suprapubic, flank tenderness
- Abdominal mass, palpable bladder
- Evidence of spinal lesion
- Other GU abnormality

### Age Group

#### Symptoms and Signs of UTI: Most Common to Least Common

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Preverbal</th>
<th>Verbal</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 56 days – 18 years</td>
<td>Fever</td>
<td>Abdominal pain</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vomiting</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Poor feeding</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Flank pain/tenderness</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lethargy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Irritability</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hematuria</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Malodorous urine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Failure to thrive</td>
</tr>
</tbody>
</table>

|                | Frequency |
|                | Dysuria |
|                | Hesitancy |
|                | Urgency |

|                | Incontinence |
|                | Abdominal pain |
|                | Flank pain/tenderness |

|                | Fever |
|                | Vomiting |
|                | Malaise |
|                | Nausea |
|                | Hematuria |
|                | Malodorous urine |
|                | Cloudy urine |
Cleansing the Perineum

- Baby wipes are the preferred method to reduce contamination for clean-catch or urine bag specimens
- Supervision of cleansing and mid-stream clean catch reduce contamination (rates can be as high as 50% in children 2-6 years old)
• Ensure foreskin retraction in uncircumcised male

![When RN Should Consider Placing a Bag for Urine Collection](image)

**Use of the Urine Bag**
- Discuss need for possible urine testing with the family as per script (Learn More)
- Cleanse the perineum with baby wipes prior to bag application
- Choose appropriately sized urine bag and utilize no-sting barrier to improve adhesion
- For prompt recognition of urine, assure bag is visible outside the diaper
- If specimen is contaminated with stool, discard and collect a new sample
- After placing the bag, provide beverage if PO status allows and check for urine in 30 minutes x 2
- If there is no urine after 1 hour, consult MD for further plan

**Urine Testing**
- Dipstick should be performed within 1 hour
- Dipstick is the preferred screening method and is as good as a formal UA when done correctly, therefore it is unnecessary to send a specimen for a standard UA
- Abnormal dipsticks should NOT be sent to the lab unless clinically indicated (casts, ect)

**Cultures**
- Clean-catch specimens that have a negative dipstick should not be sent for culture
- All specimens obtained by catheterization or suprapubic tap should be sent for culture
- Send in grey top tube if > 3 ml of urine. If specimen is < 3 ml of urine, place in sterile container on ice and transport to lab
- For febrile, symptomatic patients with isolated hematuria, it is reasonable to send a urine culture
Uncircumcised Males with Phimosis

- Consider treatment with betamethasone 0.05% cream twice daily for four weeks or refer to Urology

Urine Pathogens

- *E. coli, Proteus sp.*
• Enterococcus sp.
• Pseudomonas sp.
• Serratia sp.
• Corynebacterium Urealyticum
• Klebsiella sp.
• Enterobacter sp.
• Group B streptococci
• Staphylococcus aureus

Common Contaminants
• Lactobacillus sp.
• Corynebacterium sp.
• Coagulase-negative staphylococci
• Alpha-hemolytic streptococci

In 2017, Nationwide Children's Hospital guideline on Urinary Tract Infection Diagnosis and Management recommended:

General Management Principles

The following guidance will focus on uncomplicated UTIs in otherwise healthy children. Infections in children with underlying renal diseases, anatomic or functional anomalies of the urinary tract, urinary catheters, or immunocompromising conditions/therapies constitute complicated UTIs and must be approached on an individual basis.

The management of suspected UTI in children involves six key steps:

3. Determine whether the pre-test probability of UTI is high enough to warrant testing.
4. Obtain an appropriate urine sample for urinalysis and urine culture (if urinalysis positive or clinical suspicion despite a negative urinalysis).
2016’s Seattle Children’s Hospital Urinary Tract Infection: Criteria and Definitions:

**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.
### 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>
Urinary Tract Infection (UTI) v4.0: Atypical vs Typical UTI Definitions

**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>
<th>DEFINITE 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>
<td>• All age categories: defined by a combination of clinical features and a positive urine culture.</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>
<td></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) (Molsaas, 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) (O.O.O. Seattle Children's UTI Pathway 2011)
  - ≥ 100,000 colony forming units (CFU)/ml for clean catch
  - ≥ 50,000 CFU/ml for in- and out- catheterization and suprapubic aspiration
**Diagnosis: Adolescent and Sexually Active Patients**

<table>
<thead>
<tr>
<th>In adolescents and sexually active pre-adolescents:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Clinicians must document a sexual history and an external genitourinary examination.</td>
</tr>
<tr>
<td>• Clinicians should perform a bimanual examination in females if clinically indicated (e.g., in cases of pelvic pain). (Goo, Seattle Children’s UTI Pathway 2011)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Additional lab testing to consider in this population:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• &quot;Dirty&quot; urine for Gonococcus (GC) and Chlamydia</td>
</tr>
<tr>
<td>• If GC/Chlamydia positive, consider Syphilis Screen</td>
</tr>
<tr>
<td>• HSV: Culture Visible lesions or cervical culture if indicated</td>
</tr>
<tr>
<td>• Annual HIV Screen</td>
</tr>
<tr>
<td>• Pregnancy Testing in females</td>
</tr>
</tbody>
</table>

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 (Muscchio, 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.
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
2017 Children's Hospital of Chicago's Febrile Urinary Tract Infection (UTI) Pathway
Health System Guideline References:
Question 4:

a. In pediatric patients <2 months old with suspected urinary tract infection, how should UTIs be treated depending on age and upper or lower tract?

**Question 4a National/International Guidelines:**

**National Institute for Health and Care Excellence** updated in 2017 Urinary tract infection in under 16s: diagnosis and management with the following recommendations:

1.1.8 Clinical differentiation between acute pyelonephritis/upper urinary tract infection and cystitis/lower urinary tract infection

1.1.8.1 Infants and children who have bacteriuria and fever of 38°C or higher should be considered to have acute pyelonephritis/upper urinary tract infection. Infants and children presenting with fever lower than 38°C with loin pain/tenderness and bacteriuria should also be considered to have acute pyelonephritis/upper urinary tract infection. All other infants and children who have bacteriuria but no systemic symptoms or signs should be considered to have cystitis/lower urinary tract infection. [2007]

1.1.9 Laboratory tests for localising UTI

1.1.9.1 C-reactive protein alone should not be used to differentiate acute pyelonephritis/upper urinary tract infection from cystitis/lower urinary tract infection in infants and children. [2007]

1.1.10 Imaging tests for localising UTI

1.1.10.1 The routine use of imaging in the localisation of a UTI is not recommended. [2007]

1.1.10.2 In the rare instances when it is clinically important to confirm or exclude acute pyelonephritis/upper urinary tract infection, power Doppler ultrasound is recommended. When this is not available or the diagnosis still cannot be confirmed, a dimercaptosuccinic acid (DMSA) scintigraphy scan is recommended. [2007]

1.2 Acute management
Note that the antibiotic requirements for infants and children with conditions that are outside the scope of this guideline (for example, infants and children already known to have significant preexisting uropathies) have not been addressed and may be different from those given here.

1.2.1.1 Infants and children with a high risk of serious illness should be referred urgently to the care of a paediatric specialist. [2007]

1.2.1.2 Infants younger than 3 months with a possible UTI should be referred immediately to the care of a paediatric specialist. Treatment should be with parenteral antibiotics in line with the NICE guideline on fever in under 5s. [2007]

1.2.1.3 For infants and children 3 months or older with acute pyelonephritis/upper urinary tract infection:
   - consider referral to a paediatric specialist
   - treat with oral antibiotics for 7–10 days. The use of an oral antibiotic with low resistance patterns is recommended, for example cephalosporin or co-amoxiclav
   - if oral antibiotics cannot be used, treat with an intravenous (IV) antibiotic agent such as cefotaxime or ceftriaxone for 2–4 days followed by oral antibiotics for a total duration of 10 days. [2007]

1.2.1.4 For infants and children 3 months or older with cystitis/lower urinary tract infection:
   - Treat with oral antibiotics for 3 days. The choice of antibiotics should be directed by locally developed multidisciplinary guidance. Trimethoprim, nitrofurantoin, cephalosporin or amoxicillin may be suitable.
   - The parents or carers should be advised to bring the infant or child for reassessment if the infant or child is still unwell after 24–48 hours. If an alternative diagnosis is not made, a urine sample should be sent for culture to identify the presence of bacteria and determine antibiotic sensitivity if urine culture has not already been carried out. [2007]

In 2015, the Kidney Health Australia, Caring for Australians with Renal Impairment (KHA-CARI) recommended the following:

**General**
- Recommend starting treatment for presumed UTI in children who have clinical symptoms suggestive of UTI and who have positive leukocyte esterase or nitrite on urinary dipstick testing or bacteriuria on microscopy. (1D)

**Acute pyelonephritis**
- In children older than 1 month of age with acute pyelonephritis, defined as bacteriuria in the presence of fever (>38°C) plus or minus loin pain/tenderness, recommend that oral treatment be used if the child:
  - Is at low risk of serious illness
  - Does not appear septic
Is able to tolerate oral medications. (1C)

- Do not recommend single-dose therapy for the treatment of acute pyelonephritis in children. (1A)
- Recommend a duration of therapy for acute pyelonephritis of 7–10 days. (1D)

**Lower UTI (cystitis)**

- Recommend short-duration oral therapy (2–4 days) for treating lower UTI, defined as bacteriuria without fever or loin pain but with localizing signs such as dysuria, frequency, urgency and lower abdominal discomfort, as it is as effective as standard duration therapy (7–14 days). (1A)

**Guideline References:**

Question 4:

b. In pediatric patients >2 months to 18 years old with suspected urinary tract infection, how should UTIs be treated depending on age and upper or lower tract?

**Question 4b National/International Guidelines:**

**National Institute for Health and Care Excellence** updated in 2017 Urinary tract infection in under 16s: diagnosis and management with the following recommendations:

1.1.8 Clinical differentiation between acute pyelonephritis/upper urinary tract infection and cystitis/lower urinary tract infection

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   - Treat with oral antibiotics for 3 days. The choice of antibiotics should be directed by locally developed multidisciplinary guidance. Trimethoprim, nitrofurantoin, cephalosporin or amoxicillin may be suitable.
   - The parents or carers should be advised to bring the infant or child for reassessment if the infant or child is still unwell after 24–48 hours. If an alternative diagnosis is not made, a urine sample should be sent for culture to identify the presence of bacteria and determine antibiotic sensitivity if urine culture has not already been carried out. [2007]

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- In children older than 1 month of age with acute pyelonephritis, defined as bacteriuria in the presence of fever (>38°C) plus or minus loin pain/tenderness, recommend that oral treatment be used if the child:
  - Is at low risk of serious illness
Does not appear septic

Is able to tolerate oral medications. (1C)

- Do not recommend single-dose therapy for the treatment of acute pyelonephritis in children. (1A)
- Recommend a duration of therapy for acute pyelonephritis of 7–10 days. (1D)

Lower UTI (cystitis)

- Recommend short-duration oral therapy (2–4 days) for treating lower UTI, defined as bacteriuria without fever or loin pain but with localizing signs such as dysuria, frequency, urgency and lower abdominal discomfort, as it is as effective as standard duration therapy (7–14 days). (1A)

Guideline References:


The 2011 American Academy of Family Physicians Guideline on Diagnosis and Treatment of Urinary Tract Infections in Children recommended the following:

- A two- to four-day course of oral antibiotics is as effective as a seven- to 14-day course in children with a lower UTI. A single-dose or single-day course is not recommended. (Evidence Rating: A)
- Children with acute pyelonephritis can be treated effectively with oral antibiotics (e.g., amoxicillin/clavulanate, cefixime, cefitubuten [Cedax] for 10 to 14 days or with short courses (two to four days) of intravenous therapy following by oral therapy. (Evidence Rating: A)

Guideline References:

Question 4b Health System Guidelines:

In 2017, Nationwide Children's Hospital guideline on Urinary Tract Infection Diagnosis and Management recommended:

1. Does the child have presumed cystitis or pyelonephritis?
   The presence of vomiting, flank pain or costovertebral angle tenderness suggests a diagnosis of pyelonephritis and warrants prompt empiric antibiotic therapy. Although the presence of fever is not an absolute indicator of pyelonephritis, approximately 60 percent of children with a febrile UTI have evidence of pyelonephritis on a DMSA scan. Because no routine clinical test adequately distinguishes cystitis from pyelonephritis, we consider all febrile UTIs the equivalent of pyelonephritis for management. A recent study confirmed prior data that delay in initiation of antibiotics for febrile UTIs is associated with increased risk for renal scarring. In contrast, treatment of children without signs or symptoms of pyelonephritis is less urgent, and the clinician should consider waiting for results of the urine culture to make a definitive diagnosis and provide optimal management.

2. Which antibiotics achieve adequate concentration at the site of infection?
   Nitrofurantoin is an excellent antibiotic for cystitis, but it does not achieve adequate concentrations in the bloodstream or in tissues and is not appropriate when pyelonephritis is a concern. The other antibiotics discussed below may be used for both cystitis and pyelonephritis.

In 2015, Nationwide Children's Hospital off-campus urgent care providers initiated a quality improvement project aimed to optimize treatment of uncomplicated cystitis. In a review of urine E. coli isolates from Nationwide Children's Hospital urgent care patients, resistance to TMP-SMX was 20 percent, while resistance to cefazolin (a surrogate marker in the lab that predicts susceptibility to all oral cephalosporins) and nitrofurantoin were <5 percent. For this reason and considering additional factors discussed above, the following approach to antibiotic choice was developed:

<table>
<thead>
<tr>
<th>AGE RANGE</th>
<th>SUSPECTED DIAGNOSIS</th>
<th>PREFERRED ANTIBIOTIC</th>
<th>ALTERNATE ANTIBIOTIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;12 years</td>
<td>Cystitis or pyelonephritis</td>
<td>cephalexin 25 mg/kg/dose TID</td>
<td>cefdinir 14 mg/kg/dose daily</td>
</tr>
<tr>
<td>≥12 years</td>
<td>Cystitis</td>
<td>nitrofurantoin macrocrystal/monohydrate 100 mg BID</td>
<td>cephalexin 500 mg BID</td>
</tr>
<tr>
<td>≥12 years</td>
<td>Pyelonephritis</td>
<td>cephalexin 500 mg TID</td>
<td>cefdinir 600 mg daily</td>
</tr>
</tbody>
</table>
The preferred antibiotics may be different for populations with different rates of bacterial resistance.

The optimal duration of therapy for UTI is controversial and based on limited data. Single-dose or single-day therapy is inferior to more prolonged (7-14 day) courses. However, for treatment of cystitis, two meta-analyses showed no statistical differences in treatment failure or reinfection when short courses (3 days in most studies) were compared to long courses (7-14 days). Although controversy persists, 3-5 days for cystitis is often recommended. For pyelonephritis, 7-10 days is likely sufficient. An ongoing clinical trial is comparing 5 days to 10 days for UTI in children aged 2 months to 10 years with and without fever; however, the results of this trial are currently unknown.

For follow-up management, adjust the antibiotic therapy as indicated depending on the results of the urine culture and susceptibilities. If the urine culture does not suggest a UTI, stop the antibiotic and consider other diagnoses. Be aware that low colony counts may occur in unusual circumstances. For children who improve with treatment, test-of-cure urine cultures are NOT routinely recommended after treatment. For children who do not demonstrate improvement in pyelonephritis symptoms after 48-72 hours of appropriate antibiotic therapy, consider obtaining a renal/bladder ultrasound to evaluate for complications such as renal or perirenal abscess.

Cincinnati Children’s Hospital in 2012 developed guideline on imaging in pediatric patients with first time febrile urinary tract infection (UTI)

Note 3: The APP’s meta-analysis of antimicrobial prophylaxis demonstrated that antimicrobial prophylaxis was not effective in preventing reoccurrence of febrile UTI/pyelonephritis. If prophylaxis is not beneficial, then the rationale for performing VCUG routinely after an initial febrile UTI must be questioned.
2016’s Seattle Children’s Hospital Urinary Tract Infection: Criteria and Definitions:

Urinary Tract Infection v8.0: 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; name coverage if possible.

- **Infants (31-60 days):**
  - Give IV ceftriaxone OR ampicillin + gentamicin if sensitivity is suspected.
  - Give IV antibiotics until sterile X 24 hrs (minimum 36 hours IV and negative initial blood cultures).
  - Switch to PO if responding after identification and sensitivities return; name coverage if possible.
  - Total duration of antibiotics: 14 days.

- **Non-Toilet Trained Children, Toilet Trained Children & Adolescents:**
  - Give IV ceftriaxone OR ampicillin + gentamicin if sensitivity is suspected.
  - Switch to PO if responding after identification and sensitivities return; name coverage if possible.
  - Total duration of antibiotics: 14 days (7 days), total 14 days (0-14 days), multiple therapy (10-14 days), adolescent with positive UI.

**Positive Blood Culture:**
- If positive, give IV + 7 days PO.
- Take urine culture if clinically suspected.
- If negative, can treat empirically.
- If positive, repeat culture and report sensitive.
- If positive, consult infectious disease.
- If positive, use 20-30 days of antibiotics.

**Discharge Criteria:**
- General discharge criteria for all patients:
  - Clinical improvement.
  - Able to maintain hydration status.
  - Social for home discharge addressed.
  - Family education provided/understood.
  - Urine culture is negative or final report shows culture is positive and patient is on targeted antibiotic.
  - Other findings by bedside criteria and results are negative (if applicable), or if bedside criteria have completed appropriate course of IV antibiotic therapy.
  - If indicated, social discharges accompanied by pre-discharge clearance.
  - If indicated, VUR cleared).
  - Ultrasound, urinalysis.
  - ID completed if desired.

- Infants: General criteria and:
  - Urine culture less than 200,000.
  - Total urine discharge.
  - Non-traineed and toilet-trained children.
  - Admitting 7-14 days.

- Adolescents:
  - Completion of plan for additional sexually transmitted infection (STI) testing.
Health System Guideline References:


**Appendix A. GRADE criteria for rating a body of evidence on an intervention**

Developed by the GRADE Working Group

**Grades and interpretations:**
- **High:** Further research is very unlikely to change our confidence in the estimate of effect.
- **Moderate:** Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
- **Low:** Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
- **Very low:** Any estimate of effect is very uncertain.

**Type of evidence and starting level**
- Randomized trial–high
- Observational study–low
- Any other evidence–very low

**Criteria for increasing or decreasing level**

**Reductions**
- Study quality has serious (−1) or very serious (−2) problems
- Important inconsistency in evidence (−1)
- Directness is somewhat (−1) or seriously (−2) uncertain
- Sparse or imprecise data (−1)
- Reporting bias highly probable (−1)

**Increases**
- Evidence of association† strong (+1) or very strong (+2)
- Dose-response gradient evident (+1)
- All plausible confounders would reduce the effect (+1)
†Strong association defined as significant relative risk (factor of 2) based on consistent evidence from two or more studies with no plausible confounders. Very strong association defined as significant relative risk (factor of 5) based on direct evidence with no threats to validity.
Appendix B. Trustworthy Guideline rating scale

The University of Pennsylvania’s Center for Evidence-Based Practice Trustworthy Guideline rating scale is based on the Institute of Medicine’s “Standards for Developing Trustworthy Clinical Practice Guidelines” (IOM), as well as a review of the AGREE Enterprise and Guidelines International Network domains.

The purpose of this scale is to focus on the weaknesses of a guideline that may reduce the trust a clinical user can have in the guideline, and distinguish weaknesses in documentation (e.g. guideline does not have a documented updating process) from weaknesses in the guidance itself (e.g. recommendations are outdated). Current quality scales like AGREE emphasize documentation. They are important checklists for developers of new guidelines, but are less useful for grading existing guidelines. These scales also are harder for clinicians and other persons who are not methodology experts to apply, and their length discourages their use outside formal technology assessment reports. This new scale is brief, balanced, and easy and consistent to apply.

We do not attempt to convert the results of this assessment into a numeric score. Instead we present a table listing the guidelines and how they are rated on each standard. This facilitates qualitative understanding by the reader, who can see for what areas the guideline base as a whole is weak or strong as well as which guidelines are weaker or stronger.

1. Transparency

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Guideline development methods are fully disclosed.</td>
</tr>
<tr>
<td>B</td>
<td>Guideline development methods are partially disclosed.</td>
</tr>
<tr>
<td>C</td>
<td>Guideline development methods are not disclosed.</td>
</tr>
</tbody>
</table>

The grader must refer to any cited methods supplements or other supporting material when evaluating the guideline. Methods should include:

- Who wrote the initial draft
- How the committee voted on or otherwise approved recommendations
- Evidence review, external review and methods used for updating are not addressed in this standard.

2. Conflict of interest
A Funding of the guideline project is disclosed, disclosures are made for each individual panelist, and financial or other conflicts do not apply to key authors of the guideline or to more than 1 in 10 panel members).

B Guideline states that there were no conflicts (or fewer than 1 in 10 panel members), but does not disclose funding source.

C Lead author, senior author, or guideline panel members (at least 1 in 10) have conflict of interest, or guideline project was funded by industry sponsor with no assurance of independence.

NR Guideline does not report on potential conflict of interests.

For purposes of this checklist, conflicts of interest include employment by, consulting for, or holding stock in companies doing business in fields affected by the guideline, as well as related financial conflicts. This definition should not be considered exclusive. As much as anything, this is a surrogate marker for thorough reporting, since it may be assumed that guideline projects are funded by the sponsoring organization and many authors think it unnecessary to report a non-conflict.

### 3. Guideline development group

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Guideline development group includes 1) methodological experts and clinicians and 2) representatives of multiple specialties.</td>
</tr>
<tr>
<td>B</td>
<td>Guideline development group includes one of the above, but not both.</td>
</tr>
<tr>
<td>C</td>
<td>Guideline developers all from one specialty or organization, and no methodologists.</td>
</tr>
<tr>
<td>NR</td>
<td>Affiliations of guideline developers not reported</td>
</tr>
</tbody>
</table>

The purpose of this standard is to ensure that supporters of competing procedures, or clinicians with no vested interest in utilization of one procedure or another, are involved in development of the guideline. Both AGREE II and IOM call for patient or public involvement: very few guideline panels have done so to date, so this is not necessary for guidelines to be rated A. Involvement of methodologists or HTA specialists in the systematic review is sufficient involvement in the guideline development group for our purposes. In the absence of any description of the guideline group, assume the named authors are the guideline group.

### 4. Systematic review

<p>| | |</p>
<table>
<thead>
<tr>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Guideline includes a systematic review of the evidence or links to a current review.</td>
</tr>
<tr>
<td>B</td>
<td>Guideline is based on a review which may or may not meet systematic review criteria.</td>
</tr>
<tr>
<td>C</td>
<td>Guideline is not based on a review of the evidence.</td>
</tr>
</tbody>
</table>

In order to qualify as a systematic review, the review must do all of the following:

Describe itself as systematic or report search strategies using multiple databases
Define the scope of the review (including key questions and the applicable population)
Either include quantitative or qualitative synthesis of the data or explain why it is not indicated

Note: this element does not address the quality of the systematic review: simply whether or not it exists. Concerns about quality or bias of the review will be discussed in text, where the analyst will explain whether the weaknesses of the review weaken the validity or reliability of the guideline.
Note: a guideline may be rated B on this domain even if the review on which it is based is not available to us. This potential weakness of the guideline should be discussed in text of the report.

5. Grading the supporting evidence

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Specific supporting evidence (or lack thereof) for each recommendation is cited and graded</td>
</tr>
<tr>
<td>B</td>
<td>Specific supporting evidence (or lack thereof) for each recommendation is cited but the recommendation is not graded.</td>
</tr>
<tr>
<td>C</td>
<td>Recommendations are not supported by specific evidence.</td>
</tr>
</tbody>
</table>

To score a B on this domain there should be specific citations to evidence tables or individual references for each relevant recommendation in the guideline, or an indication that no evidence was available. Any standardized grading system is acceptable for purposes of this rating. If a guideline reports that there is no evidence available despite a thorough literature search, it may be scored B on this domain, or even A if evidence for other recommendations is cited and graded.

6. Recommendations

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Considerations for each recommendation are documented (i.e. benefits and harms of a particular action, and/or strength of the evidence); and recommendations are presented in an actionable form.</td>
</tr>
<tr>
<td>B</td>
<td>Either one or the other of the above criteria is met.</td>
</tr>
<tr>
<td>C</td>
<td>Neither of the above criteria are met</td>
</tr>
</tbody>
</table>

In order to be actionable, the guideline should specify the specific population to which the guideline applies, the specific intervention in question, and the circumstances under which it should be carried out (or not carried out). The language used in the recommendations should also be consistent with the strength of the recommendation (e.g. directive and active language like “should” or “should not” for strong recommendations, and passive language like “consider” for weak recommendations). A figure
or algorithm is considered actionable as long as it is complete enough to incorporate all the applicable patients and interventions. Please see the forthcoming NICE manual (24) for a good discussion of actionability in guidelines.

7. External review

<table>
<thead>
<tr>
<th></th>
<th>Guideline was made available to external groups for review.</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>Guideline was reviewed by members of the sponsoring body only.</td>
</tr>
<tr>
<td>C</td>
<td>Guideline was not externally reviewed.</td>
</tr>
<tr>
<td>NR</td>
<td>No external review process is described.</td>
</tr>
</tbody>
</table>

8. Updating and currency of guideline

<table>
<thead>
<tr>
<th></th>
<th>Guideline is current and an expiration date or update process is specified.</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>Guideline is current but no expiration date or update process is specified.</td>
</tr>
<tr>
<td>C</td>
<td>Guideline is outdated.</td>
</tr>
</tbody>
</table>

A guideline is considered current if it is within the developers’ stated validity period, or if no period or expiration data is stated, the guideline was published in the past three years (NOTE: the specific period may be changed at the analyst’s discretion, based on whether the technology is mature and whether there is a significant amount of recent evidence). A guideline must address new evidence when it is updated. A guideline which is simply re-endorsed by the panel without searching for new evidence must be considered outdated.