KHA-CARI Guideline

Guideline title: Diagnosis and Treatment of Urinary Tract Infection in Children

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Accepted Article

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KHA-CARI Guideline: Diagnosis and Treatment of Urinary Tract Infection in Children

Scope of Guidelines

Specialist assessment and management is required for children who are considered at high risk of serious illness (underlying structural urinary tract abnormalities or neurogenic bladder or kidney transplant recipients). These children are beyond the scope of these guidelines and it is important that they are excluded from the recommendations detailed below.

1. Diagnosis.

Guideline Recommendations:

a. We 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)

b. We 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)

c. We 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)

d. We 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 Collection

e. 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)

f. If positive urine culture by bag urine is obtained, we recommend it is confirmed on repeat urine culture by SPA, CSU, CCU or MSU. (1B)

g. We suggest that suprapubic aspirate (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 one hour or use of bladder ultrasound or both. (2B)

Urine Culture

h. We 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: >10^5 CFU/L (10^6 - 10^8 CFU/L; possible UTI)
   • MSU or CCU: >10^8 CFU/I (10^7 - 10^8 CFU/I; possible UTI)
   • Bag/ Pad/ Cotton ball: not recommended for definitive culture.
i. We 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.

j. If contamination is possible on initial urine culture, we 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

Ungraded Suggestions for Clinical Care:

a. UTI is more likely in girls and uncircumcised boys (especially between 3-6 months), infants <12 months, and if a fever has been present for >2 days and there is an absence of another source of fever on examination. No factor can predict with 100% accuracy the absence of serious bacterial illness in febrile infants <3months (ungraded).

b. In children with culture-proven UTI, a serum procalcitonin value >0.5 ng/mL predicts reasonably well the presence of renal parenchymal injury, as evidenced by early DMSA scintigraphy (within two weeks of diagnosis) (ungraded).

Background:

Urinary tract infection in children is common, about 6% of girls and 2% of boys will experience an episode before their 7th birthday [1]. Having had one infection the child is at a 13 -19% risk of having another UTI [2-4]. UTI causes pain, discomfort and irritability to the child, and anxiety, stress and inconvenience to the family. Prompt diagnosis and early treatment are central to good clinical care.

Summary of the evidence:

Initial treatment of urinary tract infection is guided by clinical presentation, however reliance on clinical symptoms may result in under treatment. The practical definition of UTI for clinical practice is the combination of symptomatic evidence of infection of the urinary tract (including one or more of: abdominal pain, dysuria, frequency, fever, loin pain and irritability in infants) in association with a urine sample containing a positive bacterial culture.

A pure growth of a single bacterial species with a significant colony number is generally regarded as evidence of a true UTI. Mixed growths, growth of skin commensals or low colony counts are regarded as evidence of contamination. However, there may be occasions when these may represent true UTIs, especially in individuals with abnormal urinary tracts.

There is no universal definition of a contaminated positive culture compared with a “true” UTI and none of the criteria for contamination are sufficient to exclude the possibility that the culture result does indeed reflect a true UTI. Culture results should therefore be interpreted in the context of the individual child. Pro-calcitonin may aid in the identification of children with UTI, warranting more intense evaluation and management.

Key references:

2. Acute Management

**Guideline Recommendations:**

**General**

a. We recommend starting treatment for presumed urinary tract infection (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**

b. 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, we recommend that oral treatment be used if the child:
   - Is at low risk of serious illness (as defined in the scope of guideline above);
   - Does not appear septic;
   - Is able to tolerate oral medications. (1C)

c. We do not recommend single dose therapy for the treatment of acute pyelonephritis in children. (1A)

d. We recommend a duration of therapy for acute pyelonephritis of 7-10 days. (1D)

**Lower urinary tract infection** (cystitis)

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

**Ungraded Suggestions for Clinical Care:**

a. In children who are younger than 1 month of age, or children older than 1 month that appear septic, dehydrated, or are unable to retain oral intake, initial antimicrobial therapy should be administered parenterally and hospitalization should be considered. (ungraded)

b. Published trials suggest that no particular antibiotic is superior for treatment of UTI. The choice of antibiotic should be guided by local microbiology patterns and sensitivities but amoxicillin should not be used as first line therapy. (ungraded)

c. Reassessment of a treated infant or child is indicated if they are still unwell after 48 hours. (ungraded)

**Background:**
Whilst a systematic review found that clinical and laboratory features generally performed poorly in localising the site of UTI \[1\], the majority of studies use either one or both of these characteristics to define patient populations. As such, evidence for the treatment of UTIs is generally based upon classifying the nature of urinary infection according to clinical characteristics. Acute pyelonephritis refers to infection within the kidney parenchyma and is characterised clinically by systemic symptoms such as fever (>38°C), malaise, vomiting, abdominal pain and loin tenderness. Cystitis refers to infection limited to the bladder that is not associated with systemic features but may present with localising symptoms such as frequency, urgency, dysuria and suprapubic discomfort.

Summary of the evidence:

Initial treatment of urinary tract infection is guided by the clinical presentation. Children with significant systemic symptoms (fever, loin pain) have a clinical diagnosis of pyelonephritis but can be treated with oral antibiotics providing they are older than 1 month of age, don’t appear septic and able to tolerate oral medications. The optimal duration of therapy is unknown but 7-10 days is currently recommended.

Children without systemic features can be managed as cystitis and treated with oral antibiotic therapy for 2-4 days.

Key references:


3. Radiological Investigation

Guideline Recommendations:

a. We do not recommend routine renal tract imaging following a first urinary tract infection (UTI) except in the circumstances described below. (1B)

Renal Ultrasound

b. We suggest that children who have had a first UTI and who haven’t had a second or third trimester antenatal ultrasound that includes the urinary tract, have a renal ultrasound performed to assess the kidney and urinary collecting system (2B).

c. We suggest that a renal ultrasound be considered in children who:
   • Have concurrent bacteraemia; (2B)
   • Are less than 3 months of age; (2C)
   • Have a urine culture with atypical organisms (e.g. Staphlococcus aureus or Pseudomonas); (2C)
   • Lack a clinical response to 48 hours of antibiotic if sensitive organism; (2C)
   • Have renal impairment or significant electrolyte derangement; (2D)
   • Have an abdominal mass; (2D)
   • Have a poor urinary stream. (2D)

Micturating Cystourethrogram (MCUG)

d. We suggest that MCUG to detect vesicoureteric reflux (VUR) is performed in children with recurrent pyelonephritis. (2D)
e. We suggest that MCUG is performed in male children with bilateral hydroureteronephrosis or bladder wall thickening on ultrasound, to exclude urethral pathology (2D).

f. We suggest that prophylactic antibiotics should be given at the time of MCUG. (2B)

dimercaptosuccinic acid scan (DMSA)

g. We do not recommend DMSA in the acute phase (0 - 4 weeks) of a UTI (1D)

h. We suggest that DMSA in the follow-up phase (at least 3 months after UTI) may be undertaken if there is clinical concern over reduced kidney function (2D)

Ungraded Suggestions for Clinical Care:

Renal Ultrasound

a. Minimum requirements for renal ultrasound should include high resolution scanning, imaging kidneys in 3 planes and bladder in 2 planes. Report should include measurements of maximum renal length, maximum transverse pelvic dimension at the exit of the pelvis from the renal parenchyma, the presence of calyceal dilatation, bladder wall thickness and pre-and post-void bladder volumes if possible. (ungraded)

Micturating Cystourethrogram

b. In older children sedation/anxiolysis with midazolam or nitrous oxide may reduce distress associated with the procedure (ungraded).

Background:

Renal tract imaging after urinary tract infection aims to identify children with renal tract abnormalities that increase their risk of repeated infections. This is based firstly on the assumption that recurrent infections damage the kidneys which in the long term, leads to high blood pressure and end stage kidney failure and secondly that preventative treatments are effective. Preventative treatment options include low dose antibiotics for long periods of time, surgical interventions to correct VUR and complementary therapies such as cranberry products.

The first assumption on which renal tract imaging has been justified is the detrimental long term effect of repeated urinary tract infections. Evidence on which this assumption is made is not convincing because retaining a large and representative sample of children with a relatively minor illness for long term follow-up is difficult. In general, studies that have managed to follow children over long periods tend to retain those with more serious illness which leads to over estimation of rates of hypertension due to selection bias. A systematic review of the prevalence of hypertension following reflux nephropathy showed that 6-28% had hypertension [1]. The risk of hypertension after childhood UTI is likely to be small. Registry data demonstrates that the frequency of end stage renal failure following pyelonephritic scarring or reflux nephropathy is around 0.5% in the USA, 4% in Australia and Sweden, 7.3% in England and Wales and around 15% in some European countries [2]. It is difficult to be precise about a risk of end stage renal failure after UTI but it would appear quite low given the available data.

The second assumption that preventative treatment is effective is also questionable (refer to Section 4 of these guidelines).

Available research findings for renal tract imaging assessment can determine which modality is optimal for identifying various aspects of the urinary tract. Renal ultrasound is useful for identifying structural abnormalities of the urinary tract. Structural abnormalities detected by ultrasound occur in 10 to 75% (median around 30%) of children scanned after a UTI [2]. Abnormalities tend to be seen more often in younger children. Renal ultrasound may suggest an obstructive uropathy which can be diagnosed with a MAG3 renal scan (pelvi-ureteric or uretro-vesical obstruction) or MCU (posterior urethral valves or other urethral pathology). Micturating cystourethrogram is the preferred test to detect VUR and between 30 and 40% of children with a UTI will have VUR detected [2]. A DMSA scan is considered the most appropriate test for detection of renal parenchymal abnormalities. The
National Institute for Health and Clinical Excellence (NICE) evidence compilation concludes that 5% of children who have had a UTI have renal parenchymal abnormalities [2]. A later systematic review of 33 studies [3] showed that 57% of children had changes when measurements were made in the acute phase (< 15 days after UTI) and 15% had renal parenchymal changes when measured during the follow-up phase (> 5 months post UTI). There is insufficient evidence to conclude whether performing a DMSA scan to detect these abnormalities is beneficial to the patient in the long term [2, 4].

Summary of the evidence:
There is insufficient evidence to demonstrate a clinical benefit for renal tract imaging after first UTI in children. Renal ultrasound can detect structural integrity of the renal tract system, while MCUG is the test of choice for detecting VUR and DMSA is the best test for identifying renal parenchymal abnormalities. Abnormalities of the renal tract are identified in 10 - 75% of children following a UTI. Few children with renal tract obstruction or grades 4 and 5 VUR will have normal ultrasound findings. Grades 4 and 5 VUR increase the risk of repeat UTI. Very few children (<5%) with UTI will develop hypertension and end stage renal failure.

Key references:

4. Long Term Management – Recurrent Urinary Tract Infection and Vesicoureteric Reflux

Guideline Recommendations:

Antibiotic prophylaxis
a. We do not recommend the routine use of prophylactic antibiotics for children after a first urinary tract infection (UTI). (1A)

b. We suggest that antibiotic prophylaxis be considered in young infants with a severe index UTI and for children with recurrent UTI and/or Grades III-V vesicoureteric reflux (VUR). (2B)

Surgical interventions for recurrent UTI

c. We do not recommend routine circumcision for boys after a first UTI. (1B)

d. We suggest that circumcision be considered for boys with recurrent UTI or high grade VUR. (2C).

e. We do not recommend surgical interventions to correct VUR as a means of preventing UTI (1C)

Alternative therapies

f. We suggest that Cranberry concentrate not be used for the prevention of UTI. (2C)
Ungraded Suggestions for Clinical Care:

Antibiotic Prophylaxis

a. Some children at high risk of morbidity relating to further UTI may benefit from the use of prophylactic antibiotics. (ungraded)

b. There is no data that determines the appropriate duration of antibiotic prophylaxis. Most studies have administered prophylaxis for 6 months to 2 years. (ungraded).

c. For those children offered prophylaxis, based on results of the PRIVENT and RIVUR trials [1, 2], the following dose and duration is considered appropriate: (ungraded)

- 6 months of cotrimoxazole at a dose of 2mg of trimethoprim plus 10 mg of sulphamethoxazole per kilogram of body weight per day; or
- 0.25mL of suspension [containing 40 mg of trimethoprim and 200 mg of sulphamethoxazole per 5mL] per kilogram to the nearest 0.5mL.

Surgical interventions for recurrent UTI

d. Surgical interventions to correct VUR can correct the anatomical abnormality but there are too few robust data to support this intervention as being preventative for repeat UTI (ungraded).

Alternative therapies

e. Probiotics, Vitamin A, nasturtium and horseradish, methenamine hippurate and UroVaxom have no well demonstrated efficacy in prevention of recurrent UTI (ungraded).

f. Avoidance of constipation, increasing fluid intake, avoiding bubble baths and improving cleaning methods after bowel motions are harmless and possibly beneficial for preventing UTI (ungraded).

Background:

Having had one infection the child is at a 13 - 19% risk of having another UTI [3-5]. UTI causes pain, discomfort and irritability to the child, and anxiety, stress and inconvenience to the family. Preventing further infections would be considered beneficial from a families perspective and may also protect the child’s kidneys from damage.

For many years long term, low dose antibiotics were given to children at risk of recurrent infection under the assumption this treatment would prevent further UTI. Little evidence existed to support the practice and systematic reviews published in 2000 and 2001 [6, 7] highlighted the poor quality and insufficient evidence to justify this practice. A number of larger, better designed trials were commenced and the most recent systematic reviews [8, 9] analysed these and demonstrated a change in the evidence to show a small benefit of low dose antibiotics in the larger rigorously conducted trials. The small scale of the benefit (6% absolute risk reduction) and considerably increased rate of antibiotic resistance to the prophylactic drug suggests this treatment might best be reserved for those children at most risk of recurrent UTI.

Studies of children with UTI [3, 5] have shown that those with VUR are at increased risk of repeat infection. Interventions that focus on this abnormality include open and laparoscopic surgery to reimplant the ureter in an attempt to prevent the backward flow of urine toward the kidney. Later techniques include injecting a bulking agent that increases the stiffness of the ureter to prevent backward flow of urine. To date, evidence that stopping reflux by correction of the anatomical abnormality prevents morbidity from UTI and prevents kidney damage or hypertension is unconvincing. Such invasive treatment should be considered only for those with recurring symptomatic infections unimproved by other preventative treatment.

Complementary therapies such as cranberry products, probiotics, methenamine hippurate, nasturtium and horseradish along with immuno active bacterial fractions have been trialled for the purpose of preventing recurrent UTI to some extent although primarily in adults. These trials generally
demonstrate a benefit however rigour and power in study design are usually lacking. Practitioners working with children with UTI, often recommend treating constipation, increasing fluid intake, avoiding bubble baths, hygiene issues and addressing dysfunctional voiding patterns to prevent further UTI. Trials to explore the efficacy of these interventions are absent, but given the harmless nature and possible benefits of these options, parents may appreciate awareness of them.

Summary of the evidence:

There is a small benefit in low dose antibiotics for preventing further urinary tract infection in children, but the benefit should be weighed against harms such as increased bacterial resistance to the prophylactic drug. Cranberry product may be helpful if tolerated. Circumcision may be warranted in boys with high grade VUR or recurrent UTI.

Key references:

**Explanation of grades**

The evidence and recommendations in this KHA-CARI guideline have been evaluated and graded following the approach detailed by the GRADE working group (www.gradeworkinggroup.org). A description of the grades and levels assigned to recommendations is provided in Tables 1 and 2.

### Table 1. Final grade for overall quality of evidence

<table>
<thead>
<tr>
<th>Overall Evidence Grade</th>
<th>Description</th>
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<tbody>
<tr>
<td>A</td>
<td>High quality of evidence. We are confident that the true effect lies close to that of the estimate of the effect.</td>
</tr>
<tr>
<td>B</td>
<td>Moderate quality of evidence. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.</td>
</tr>
<tr>
<td>C</td>
<td>Low quality of evidence. The true effect may be substantially different from the estimate of the effect.</td>
</tr>
<tr>
<td>D</td>
<td>Very low quality of evidence. The estimate of effect is very uncertain, and often will be far from the truth.</td>
</tr>
</tbody>
</table>

### Table 2. Nomenclature and description for grading recommendations

<table>
<thead>
<tr>
<th>Grade</th>
<th>Implications</th>
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</thead>
<tbody>
<tr>
<td><strong>Level 1 “We recommend”</strong></td>
<td>Patients: Most people in your situation would want the recommended course of action and only a small proportion would not.</td>
</tr>
<tr>
<td><strong>Level 2 “We suggest”</strong></td>
<td>Patients: The majority of people in your situation would want the recommended course of action, but many would not.</td>
</tr>
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</table>

**Access to the full text version**

For a full text version of the guideline, readers need to go to the KHA-CARI website [go to the Guidelines section (www.cari.org.au)]