Chapter 2
Urinary Tract Infection: United Kingdom

Andrew Neilson and Stuart O’Toole

Key Points

› Urinary stasis due to anatomical or functional obstruction predisposes to UTI.
› Dysfunctional voiding is common, but underlying anatomical abnormalities of the urinary tract should be considered and excluded.
› Anatomical abnormalities can predispose to renal scarring, which can lead to hypertension, renal impairment or renal failure.
› UTI should be considered in all febrile infants and children where another cause is not clearly established.
› A renal tract ultrasound scan is the first line investigation after diagnosis of UTI but it can miss vesico-ureteric reflux and renal scarring.
› Try to prove the diagnosis of UTI before undertaking more invasive investigations, and target such investigations to those most at risk.

2.1 Introduction

Urinary tract infection (UTI) is common in childhood. Three percent of boys and eleven percent of girls have had at least one UTI before their 16th birthday. In the first
3 years of life the sex related incidence is approximately equal, but thereafter UTI becomes more common in girls. Correct diagnosis, treatment and subsequent targeted investigation of UTI in children is important because of the associations between UTI, underlying urological abnormalities, subsequent progressive renal damage and associated hypertension.

2.2 Pathogenesis

- The mode of infection in most cases is bacterial ascent into the urinary tract from below.
- The risk of infection is elevated if there is urinary stasis because organisms are cleared less efficiently from the urinary tract. Urinary stasis can be due to anatomical factors (anatomical obstruction, vesico-ureteric reflux), or functional interference with bladder emptying (neuropathic bladder, dysfunctional voiding, constipation).
- Dysfunctional voiding in girls, often in association with constipation, is a common clinical picture.
- The causative organism is *Escherichia coli* in the majority of cases.
- Other causative organisms include *Proteus vulgaris*, *Klebsiella*, *Enterobacter*, and *Pseudomonas*.
- Certain host factors modulate the risk of UTI. Breast feeding reduces the risk. Prematurity increases the risk, as does the presence of a foreskin in males.
  - In normal boys, circumcising 111 boys would prevent one UTI.\(^1\)
  - In boys with severe vesico-ureteric reflux, the number needed to treat (NNT) to prevent one UTI is 4.\(^1\)
  - In boys with posterior urethral valves, the NNT to prevent one UTI is less than one, therefore circumcision is recommended in these boys.\(^2\)
  - Circumcision should be considered in boys with “at risk” urinary tracts, and those having recurrent UTIs.
2.3 Establishing the Diagnosis

Clinical features:

- The clinical features of UTI vary with age\(^3\) (Table 2.1).
- A high index of suspicion is important, especially with pre-verbal children.
- UTI should be considered in any unwell infant and any child with failure to thrive or prolonged jaundice.

Upper tract or lower tract infection:

- Differentiating upper from lower tract infection can be difficult.
- The absence of fever does not preclude renal scarring, and children who have afebrile UTIs should also be treated and investigated.\(^4\)
- Features suggestive of upper or lower tract infection are shown in Table 2.2.

<table>
<thead>
<tr>
<th>Age group</th>
<th>Most common</th>
<th>Less common</th>
<th>Least common</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3 months</td>
<td>Fever, Vomiting, Lethargy, Irritability</td>
<td>Poor feeding, Failure to thrive</td>
<td>Abdominal pain, Prolonged jaundice, Hematuria, Offensive urine</td>
</tr>
<tr>
<td>&gt;3 months</td>
<td>Fever</td>
<td>Abdominal pain, Loin tenderness, Vomiting, Poor feeding</td>
<td>Lethargy, Irritability, Hematuria, Offensive urine, Failure to thrive</td>
</tr>
<tr>
<td>Preverbal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Verbal</td>
<td>Frequency, Dysuria, Nausea</td>
<td>Dysfunctional voiding, Changes to continence, Abdominal pain, Loin tenderness, Fever</td>
<td>Malaise, Vomiting, Hematuria, Offensive urine, cloudy urine, Suspected sexual abuse, Hypertension</td>
</tr>
</tbody>
</table>

Modified from NICE guideline: UTI in children, 2007\(^3\)
A. Neilson and S. O’Toole

Differential diagnosis:

- One fifth of children with appendicitis have urinary symptoms.\(^5\)
  - Most children with appendicitis have some abnormality on dipstick urinalysis.\(^6\)
  - The risk of perforation is elevated and the length of stay is prolonged in children who have received antibiotics for suspected UTI before a correct diagnosis of appendicitis is made.\(^6\)
  - The clinical signs of appendicitis become less obvious after antibiotics have been given.\(^7\)
- Foreskin problems in boys and vulvo-vaginitis in girls can mimic lower urinary tract infection.

The urine sample:

- A urine specimen should be collected and analyzed in all children with fever and in afebrile children with urinary symptoms.\(^8\)
- Older children can provide a mid-stream urine sample into a sterile bowl if clearly instructed. A clean catch sample can be obtained from younger children with patience and perseverance on their parents’ part. Catheter samples should be considered, but they may give false positive results. Bag samples have unacceptably high false positive rates. Samples from cotton wool or gauze placed in the nappy should be avoided.\(^9\)

**Table 2.2.** Clinical features used to distinguish upper tract from lower tract infection.

<table>
<thead>
<tr>
<th>Upper tract features</th>
<th>Lower tract features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temperature &gt;38°C</td>
<td>No systemic features</td>
</tr>
<tr>
<td>Loin pain</td>
<td>Frequency</td>
</tr>
<tr>
<td>Upper abdominal pain</td>
<td>Urgency</td>
</tr>
<tr>
<td>Malaise</td>
<td>Nocturia</td>
</tr>
<tr>
<td>Vomiting</td>
<td>Secondary enuresis</td>
</tr>
<tr>
<td></td>
<td>Dysuria</td>
</tr>
<tr>
<td></td>
<td>Hesitancy</td>
</tr>
<tr>
<td></td>
<td>Supra-pubic pain</td>
</tr>
</tbody>
</table>


• In unwell, hospitalized infants where empirical treatment is going to be commenced before culture the result is available, the sample should be obtained by supra-pubic aspiration (which should be ultrasound guided).
• If immediate culture cannot be performed, samples can be stored for up to 24 h at 4°C, or in a tube containing boric acid.

Dipstick urinalysis:

• Testing for protein and blood is not useful in the diagnosis of UTI. These abnormalities are frequently present with other pathologies (e.g., appendicitis).
• Testing for nitrites and leukocyte esterase is useful. Not all dipsticks test for the presence of these so beware if someone else runs the test and tells you the urine is “clear.” Did they test for nitrites and leukocyte esterase?
• When testing for nitrites, it is important to test a fresh urine sample.
• Nitrites are the product of bacterial conversion of nitrates. Many gram-positive cocci are not capable of this conversion, so give a false negative.
• Leukocyte esterase is an indirect marker of pyuria, but this too can be caused by conditions outside the urinary tract (e.g., appendicitis).
• If urine is positive for both nitrites and leukocyte esterase UTI is likely.
• If urine is negative for both nitrites and leukocyte esterase, UTI can be excluded and other causes of symptoms should be considered. The exception is children under 3, in whom a sample should still be sent for culture.
• Table 2.3 summarizes recommended actions to be taken based on clinical features and dipstick findings in children aged 3 years and older.

Urine microscopy and culture:

• Microscopy performed on fresh, unspun urine can reveal the presence of motile bacteria and the presence of pyuria. Significant pyuria is defined as >10 white cells/mm³.
<table>
<thead>
<tr>
<th>Dipstick urinalysis findings</th>
<th>Treat as a UTI with antibiotics?</th>
<th>Send urine for culture?</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukocyte esterase positive</td>
<td>Nitrite positive</td>
<td>Yes</td>
<td>Yes&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Leukocyte esterase negative</td>
<td>Nitrite positive</td>
<td>Yes&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Yes</td>
</tr>
<tr>
<td>Leukocyte esterase positive</td>
<td>Nitrite negative</td>
<td>Only if clinical evidence of UTI</td>
<td>Yes</td>
</tr>
<tr>
<td>Leukocyte esterase negative</td>
<td>Nitrite negative</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

Modified from NICE guideline: UTI in children, 2007<sup>3</sup>

<sup>a</sup> and <sup>b</sup> refer to the corresponding sentence in the comments column
• Pure growth of $>10^5$ bacterial colony forming units per ml is the traditional criteria used for diagnosis of UTI, though this was based on adult series.

• On SPA samples, any growth of gram negative bacteria, or $>500$ gram positive colony forming units per ml is significant.

• The necessity of performing culture in all cases has recently been questioned. However, in children, the benefit of confirming the diagnosis, and identifying the causative organism and its sensitivities should outweigh cost concerns.

2.4 Acute Management

• The choice of antibiotic, route of administration and duration of course are all controversial, and few studies have found significant differences when comparing regimes. Many units have their own local protocols; other units follow national guidelines.

Which antibiotic:

• Local patterns of sensitivity and resistance should guide your practice.

• Trimethoprim remains effective against many common organisms.

• Many organisms are resistant to amoxicillin alone, but are sensitive to co-amoxiclav.

• Aminoglycosides or cephalosporins are appropriate alternatives.

Route of administration:

• IV is preferred in early infancy because infants are at the greatest risk of renal scarring.

• In older infants and children, oral antibiotics are appropriate so long as they are tolerated.

• Initial IV therapy followed by subsequent oral therapy once the child is tolerating enteral feeds may be required.
Duration of course:

- Short courses are appropriate where lower tract infection is suspected.
- Longer courses should be prescribed where upper tract infection is suspected.
- Any systemically unwell child should have a longer course.

Failure of initial management:

- Parents or carers should seek medical advice if their child fails to respond to treatment within 24–48 h. They may be on the wrong antibiotic, or the wrong diagnosis may have been made initially.
- If there is failure of treatment whilst on the correct antibiotic, an intervention to drain the infected urine may be required. In bladder outlet obstruction and vesico-ureteric reflux this can be achieved by urethral or suprapubic catheter insertion. In VUJ or PUJ obstruction, a nephrostomy may be required.

2.5 Once the Diagnosis Is Established

The urological history:

1. Voiding history: volume, frequency, stream, urgency, incomplete emptying
2. Fluid intake: volume, type
3. Bowel habit: constipation, dietary information
4. Drug history: prophylaxis, breakthrough UTI on prophylaxis, laxatives
5. Antenatal history: any abnormal antenatal scans
6. Family history: renal disease

The urological examination:

1. Abdomen: renal masses, palpable bladder, fecal loading
2. Anus: inspection for position and fissure if constipation or fecal loading
3. Spine: any stigmata of spina bifida occulta, palpable sacral abnormality
4. Lower limbs: neurology
5. Blood pressure

Radiological investigations:

- Investigation of UTI places a burden on the child, their family and health care services. However, investigation of UTI in children allows:
  1. Identification of anatomical anomalies that require treatment
  2. Identification and documentation of scarring & damage to the kidneys
  3. Identification of dysfunctional voiding that predisposes to further UTI
- Renal tract ultrasound should routinely include pre-void and post-void images if the child is able to comply.
- Ultrasound can demonstrate gross renal scarring, obstruction, high grade vesico-ureteric reflux and dysfunctional voiding. It fails to detect lower grades of vesico-ureteric reflux, and lesser degrees of renal scarring.
- DMSA is the gold standard investigation for renal scarring. It also measures differential function. Scarring is more likely to be present in children who have had upper tract infections, recurrent infections, and those with a family history of vesico-ureteric reflux. Remember, it is difficult to differentiate upper from lower tract infection in younger children.
- Clinicians can target DMSA scans to those most at risk.
- In children under 2 years of age who have a single febrile UTI, ultrasound and cystogram alone are poor predictors of long-term renal damage. A DMSA scan is therefore recommended in this group. It should be considered in older children.\textsuperscript{10,11}
- Children over a year of age who have a normal DMSA and normal ultrasound do not require cystogram investigation for reflux because any reflux in these children is likely to be low grade, is likely to resolve spontaneously, and is unlikely to cause subsequent renal scarring.
• A catheter cystogram is the gold standard investigation for vesico-ureteric reflux, though it is invasive and may be poorly tolerated.
• An indirect cystogram using MAG3 can also detect vesico-ureteric reflux in children able to void upon request, although low grade reflux may be missed on this investigation. The MAG3 also measures differential function.

2.6 Long Term Management

Underlying abnormalities:
• A small number of children with history of UTI have an underlying urinary tract abnormality, some of which will require follow-up or intervention.

Modifiable risk factors:
• It is important to identify and manage poor fluid intake, constipation and dysfunctional voiding.
• This is the most important conservative measure in prevention of recurrent UTIs in children.

Prophylactic antibiotics:
• Which children should receive prophylactic antibiotics is controversial.12
• The objective of their use is to prevent renal scarring associated with UTIs.
• Prophylaxis should be considered in all children who have had a UTI, especially those who experienced upper tract symptoms.
• Prophylaxis is often continued until investigations are complete.
• Children with an underlying renal tract abnormality may continue on prophylaxis for several years.
• The timing of a trial off antibiotics often involves an element of parental preference, and may be postponed until the child is toilet trained.
Other measures:

- Cranberry juice has been shown to be as effective as anti-
  biotic prophylaxis in children with vesico-ureteric reflux,
  though large studies are lacking.\textsuperscript{13}
- Probiotics may have a role in prophylaxis of UTIs in chil-
  dren, but robust evidence is lacking.

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