

- abnormalities of the urinary tract [on pre- or postnatal ultrasound scan (USS)]
- previous medical/surgical history
- voiding habits
- bowel habits, including history of constipation
- family history or nephrological/urological problems
- neonates and infants with urosepsis may present with nonspecific symptoms (fever without source, failure to thrive, jaundice, vomiting, hyperexcitability, lethargy, hypothermia and sometimes without fever)
- in older children upper urinary tract symptoms include fever, flank pain and vomiting
- in older children, lower urinary tract symptoms include dysuria, frequency, urgency, incontinence, hematuria and suprapubic pain
- malodorous urine may be a symptom of UTI, but it is nonspecific as other factors such as diet, hydration and medication may also cause this.

Additional blood tests^{47,48} and imaging can be useful depending on the subgroup of cUTI, both for initial diagnosis and subsequently (Table 2), with the rationale for their use often different at different stages in the infection. For example, USS of the kidneys and urinary tract during the acute phase can neither rule in nor rule out an upper UTI (pyelonephritis) or vesicoureteric reflux (VUR). Therefore, the role of acute USS in children with urosepsis, septic shock, poor urine flow, abdominal or bladder mass and increased creatinine is to determine whether there is acute obstruction that needs urgent surgical intervention.⁴⁹ USS may be performed for different reasons, including failure to respond with suitable antibiotics within 48 hours to investigate for renal abscess, or for recurrent UTI to assess for other urological abnormalities needing intervention.

All children should be reassessed 48 hours after diagnosis for (1) clinical response to treatment, (2) confirmation of the diagnosis and (3) potential targeting of antibiotics according to susceptibility (aim to the narrow antimicrobial spectrum).^{29,50}

Treatment should be stopped if the UTI diagnosis is not confirmed, that is, most cases with a negative urine culture with no prior antibiotics to explain this. If the response to treatment is atypical and does not follow the expected trajectory after 48 hours, reassessment for the cause is imperative, rather than simply switching to IV or broader-spectrum antibiotics (although either of these could be needed). Depending on the clinical situation, repeat urine culture, inflammatory markers, serum creatinine and renal USS may be needed to confirm the UTI diagnosis and assess for complications.⁵¹ Other investigations may be needed to seek an alternate/additional diagnosis.

How Should Children With cUTI be Treated?

Treatment of cUTI involves consideration of antibiotic route, choice and duration and supportive management. The majority of RCTs and meta-analyses of childhood UTIs exclude those with cUTIs, so recommendations largely rely on a synthesis of retrospective studies (see Table, Supplemental Digital Content 2, <http://links.lww.com/INF/G141>) and expert opinion to provide a practical empirical guideline to initiate treatment (Table 3). Due to the variability of complicating features even within subgroups, a further individualized approach is often needed, considering local antibiograms, past urine cultures, antibiotic exposure, hospital admissions, urine catheterization and other host factors, including allergies.

Initial Antibiotic Route

- For most children with cUTI, oral antibiotics can be trialed initially, including those who are not severely unwell, for isolated

urological abnormality (including post-surgery or urological implementation), isolated tachycardia and for most underlying conditions (GRADES C and D).

- The exceptions for whom at least initial IV is recommended are significant urological abnormality (VUR grades 4 and 5 or obstruction), clinical features of sepsis, renal nephronia/abscess, neonates and infants <2 months, post-renal transplant and immunocompromise with concomitant febrile neutropenia (GRADES B–D).

The primary rationale for administering IV antibiotics is to rapidly achieve high concentrations at the site of action in critical situations while bypassing the limitations of oral intake, absorption and bioavailability. There are few studies including children with significant anatomical and functional urologic abnormalities. The only high-grade evidence for route of antibiotic for VUR is from an RCT that included isolated VUR.⁵² For VUR grades 1 and 2, oral antibiotics were as effective as IV. For VUR grades 3–5, it appeared that there was less scarring if IV antibiotics were used: 8/24 (33%) scarring with oral versus 1/22 (5%) with IV, $P = 0.02$. However, only 16% of participants had VUR grades 3–5 so the study was underpowered for this group and the authors did not draw conclusions. There are no other IV versus oral studies for VUR grades 3–5. A prospective study found that half of 172 children with any urological abnormality were treated with oral antibiotics with good clinical outcomes, although this was not stratified by severity.^{53,54} Given the move towards oral antibiotic management over the last 2 decades since the above RCT, and assessing clinical outcomes rather than dimercaptosuccinic acid (DMSA) scans, we recommend that most children with VUR grade 3 can be managed with oral antibiotics. There are no studies comparing oral with IV post instrumentation or surgery in this group, but in a stable child, oral antibiotics are appropriate.

For children with multiple recurrent UTI, starting with IV antibiotics is not obligatory. Each episode should be managed according to presentation. This group is at risk of infection with antibiotic-resistant bacteria through increased antibiotic exposure.^{55,56} If a child has previously had a UTI with bacteria resistant to all oral options, initial antibiotics can be IV until culture results are available. Intravesical antibiotics, via the urethra or Mitrofanoff, are occasionally used to treat intractable recurrent UTI, with small studies showing successful outcomes with 7 days of treatment.^{57,58} Local irrigation may limit systemic antibiotic side effects and keep children out of hospital.

UTI with fever alone can be effectively treated with oral antibiotics.⁵⁹ Severe clinical presentations of UTI requiring initial IV include sepsis (features include hypotension and tachycardia when afebrile) and extensive parenchymal involvement.^{5,27,29,34,60} Vomiting can be a sign of sepsis, but on its own is rarely a reason to start IV: in an observational study, over 60% of children with vomiting were successfully treated with oral antibiotics.^{53,54} For extensive renal parenchymal involvement (nephronia/abscess), IV antibiotics ensure maximum concentration at the site.⁶¹

Nonurologic underlying conditions are renal and nonrenal. A review of UTI postrenal transplant recommended initial IV antibiotics for pyelonephritis to achieve rapid tissue saturation.⁶² Although there is a lack of studies of UTI management with other renal impairment, in the absence of severe VUR, oral antibiotics can usually be used. For immunocompromised children, treatment should be via febrile neutropenia pathways if relevant. Otherwise, unless presenting severely unwell, oral antibiotics may be appropriate in immunosuppression or other states of chronic disease (eg, diabetes and liver disease).

For neonates and infants <2 months, there are no RCTs and little comparative evidence to definitively guide the route of antibiotics for UTI. Major guidelines recommend IV antibiotics