DIAGNOSIS AND TREATMENT OF URINARY TRACT INFECTION IN CHILDREN: ACUTE MANAGEMENT

Date written: September 2014
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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.

GUIDELINES

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)

UNGRATED 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). Refer to Table 1 for commonly used antibiotics.

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

IMPLEMENTATION AND AUDIT

Units should consider an audit of current practices of assessment and treatment of children with symptoms of UTI that includes a review of patient outcomes and alignment of current procedures with the guideline recommendations. Following audit and review, key areas for focus of an implementation strategy should be identified and a site specific plan developed.

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.

Whilst a systematic review found that clinical and laboratory features generally performed poorly in localising the site of UTI [5], the majority of studies use either one or both of these characteristics to define patient populations. As such, evidence for the treatment of urinary tract infections is generally based upon classifying the nature of urinary infection according to clinical characteristics. The diagnosis of UTI is addressed in a separate sub-topic of these guidelines (KHA-CARI Diagnosis and Treatment of Urinary Tract Infection in Children: Diagnosis). 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.

SEARCH STRATEGY

Databases searched: MeSH terms and text words for UTI, bacteriuria, bacterial infection, pyuria or pyelonephritis with MeSH terms and text words for anti-bacterial-agents, intravenous infusions, intravenous injections, or oral administration combined with MeSH terms and text words for paediatric populations. The search was carried out in Medline. The Cochrane Renal Group Trials Register was also searched for trials not indexed in Medline.

Date of search/es: 1950 to 15 August 2014.

WHAT IS THE EVIDENCE?

A summary of the key studies identified below are presented in Table 2.

Management of Acute Pyelonephritis

Intravenous vs Oral Therapy

A systematic review published in 2007 [6] identified three randomised controlled trials that dealt with route of administration of antibiotics in acute pyelonephritis in children. In each of these studies, there was no difference in efficacy for intravenous compared to oral therapy. Subsequent randomised controlled trials support these earlier trials, having reported no significant difference in important clinical outcomes (scarring, time to defervescence, percentage with sterile urine after 72 hours) in children treated with oral antibiotics compared to those treated initially with intravenous antibiotics followed by oral therapy [7, 8]. However, all of these studies excluded infants under 1 month of age and children who appeared septic or who were vomiting. As such, in keeping with current clinical experience it is recommended that infants under 1 month of age and those unable to tolerate oral therapy should be treated at least initially with intravenous antibiotics. For those children who are initially treated with
intravenous antibiotics, evidence indicates that short duration (2-4 days) of intravenous therapy, followed by oral therapy is as efficacious as longer courses of intravenous therapy [9, 10].

**Choice of Antibiotic Agent**

A number of different antibiotics have been recommended as suitable for the treatment of acute pyelonephritis [11]. A Cochrane systematic review [6] found only six randomised controlled trials that compared different antibiotic regimens and concluded that no particular agent was superior to any other for the treatment of acute pyelonephritis in children. The authors of this review also noted that none of the included trials compared widely available and commonly used antibiotics. While there is a paucity of properly conducted RCTs, clinical experience suggests that most antibiotics are effective in children with uncomplicated pyelonephritis and the best choice of agent should be guided by local urine culture and sensitivity results (Table 1).

**Duration of Therapy**

Three randomised control trials comparing the effectiveness of single dose versus standard (7-10 days) duration of antibiotic treatment in children with urinary tract infections were performed in the 1980s [10, 12, 13]. Each of these trials reported no difference between the single and multiple-dose therapy groups in the number of children with persistent bacteriuria or recurrent UTI suggesting that single dose therapy may be feasible for the treatment of urinary tract infections. However, the number of patients with acute pyelonephritis in each study was small (17 patients [10], 11 patients [12], not reported [13]) precluding definitive conclusions on the effectiveness of single dose therapies for acute pyelonephritis. In children with cystitis, systematic reviews that included trials of single dose therapy compared to longer duration treatment have demonstrated increased failure rates for single dose therapy [14, 15]. In light of this data and given the lack of adequately powered randomised controlled trials we do not currently recommend single dose therapy for the treatment of pyelonephritis in children.

The Cochrane systematic review [6] found no eligible studies comparing short course (1-4 days) antibiotic treatment with standard duration therapy for children with acute pyelonephritis and only one retrospective study has been published since that time [9]. In summary, there is currently insufficient evidence to determine the optimal duration of therapy for children with pyelonephritis.

**Management of Cystitis**

**Choice of Antibiotic Agent**

As with the treatment of pyelonephritis, no specific oral antibiotic has been shown to be superior in the treatment of cystitis. Empiric antibiotics that may be used in the treatment of acute cystitis are shown in Table 1.

**Duration of Therapy**

Three systematic reviews have compared single dose or short-course therapy with standard duration therapy [14-16] (Table 2). While each of these systematic reviews has used slightly different study inclusion criteria and outcomes, all have shown that there is no difference in the efficacy of short (2-4 days) versus standard duration (7-10 days) antibiotic therapy for the treatment of lower UTI. Of note, in two reviews [14, 15] sub-group analysis showed that single dose treatment was associated with a greater risk of treatment failure when compared to longer duration therapy. Taken together, the studies analysed in these three reviews suggest that 2-4 days of antibiotic therapy should be given for treatment of children with cystitis.

**SUMMARY OF THE EVIDENCE**

In summary, 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.
WHAT DO THE OTHER GUIDELINES SAY?


*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 ‘Feverish illness in children’ (NICE Clinical Guideline 47).

*For infants and children 3 months or older with acute pyelonephritis/upper urinary tract infection:*
  - Consider referral to secondary care.
  - Treat with oral antibiotics for 7–10 days. The use of an oral antibiotic with low resistance patterns is recommended, for example cephalosporin or amoxicillin-clavulanic acid.
  - 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.

*For infants and children 3 months or older with cystitis/low-grade 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.

For infants and children who receive aminoglycosides (gentamicin or amikacin), once-daily dosing is recommended.

If parenteral treatment is required and IV treatment is not possible, intramuscular treatment should be considered.

If an infant or child is receiving prophylactic medication and develops an infection, treatment should be with a different antibiotic, not a higher dose of the same antibiotic.

Asymptomatic bacteriuria in infants and children should not be treated with antibiotics.

Labsatories should monitor resistance patterns of urinary pathogens and make this information routinely available to prescribers.

American Academy of Pediatrics. Urinary tract infection: clinical practice guideline for the diagnosis and management of the initial UTI in febrile infants and children 2 to 24 months (September 2011). [18]

*Action Statement 4a:* When initiating treatment, the clinician should base the choice of route of administration on practical considerations. Initiating treatment orally or parenterally is equally efficacious. The clinician should base the choice of agent on local antimicrobial sensitivity patterns (if available) and should adjust the choice according to sensitivity testing of the isolated uropathogen (evidence quality: A; strong recommendation).

*Action Statement 4b:* The clinician should choose 7 to 14 days as the duration of antimicrobial therapy (evidence quality: B; recommendation).

Most children can be treated orally, children whom clinicians judge to be “toxic” or who are unable to retain oral intake, should receive parenteral treatment until they exhibit clinical improvement (generally 24 to 48 hours) and are able to retain orally administered fluids and medications. Parenteral administration of an antimicrobial agent also should be considered when compliance is uncertain.
There is evidence that 1 to 3 day courses of treatment for febrile UTIs are inferior to 7 to 14 day courses. Data comparing 7, 10 and 14 days of treatment directly are not available: Therefore, the minimal duration of treatment should be 7 days.


The patient’s age, features suggesting toxicity and dehydration, ability to retain oral intake and the likelihood of compliance with medication help in deciding between outpatient therapy and hospitalization. Therapy should be prompt to reduce the morbidity of infection, minimize renal damage and subsequent complications.

*Children less than 3 months of age and those with complicated UTI* should be hospitalized and treated with parenteral antibiotics. The choice of antibiotic should be guided by local sensitivity patterns. A third generation cephalosporin is preferred. Therapy with a single daily dose of aminoglycoside may be used in children with normal renal function. Once the result of antimicrobial sensitivity is available, the treatment may be modified. Intravenous therapy is given for the first 2-3 days followed by oral antibiotics once the clinical condition improves.

*Children with simple UTI and those above 3 months of age* are treated with oral antibiotics. With adequate therapy, there is resolution of fever and reduction of symptoms by 48-72 hours. Failure to respond may be due to presence of resistant pathogens, complicating factors or noncompliance; these patients require re-evaluation.

Duration of therapy is 10-14 days for *infants and children with complicated UTI*, and 7-10 days for *uncomplicated UTI*. *Adolescents with cystitis* may be treated with shorter duration of antibiotics, lasting 3 days. Following the treatment of the UTI, prophylactic antibiotic therapy is initiated, in children below 1 year of age, until appropriate imaging of the urinary tract is completed.

During an episode of UTI, it is important to maintain adequate hydration. A sick, febrile child with inadequate oral intake or dehydration may require parenteral fluids. Routine alkalization of the urine is not necessary. Paracetamol is used to relieve fever; therapy with non steroidal anti-inflammatory agents should be avoided. A repeat urine culture is not necessary, unless there is persistence of fever and toxicity despite 72 hours of adequate antibiotic therapy.


A *severe UTI* requires adequate parenteral antimicrobial treatment, preferably with cephalosporins (third generation). Antimicrobial treatment has to be initiated on an empirical basis, but should be adjusted according to culture results as soon as possible. In patients with an allergy to cephalosporins, aztreonam or gentamicin may be used. When aminoglycosides are necessary, serum levels should be monitored for dose adjustment. Chloramphenicol, sulphonamides, tetracyclines, rifampicin, amphotericin B and quinolones should be avoided. For a safety period of 24-36 hours, parenteral therapy should be administered. When the child becomes afebrile and is able to take fluids, he/she may be given an oral agent to complete the 10-14 days of treatment, which may be continued on an outpatient basis. The preferred oral antimicrobials are: trimethoprim, cotrimoxazole, an oral cephalosporin, or amoxyccillin/clavulanate.

In children less than 3 years of age, who have difficulty taking oral medications, parenteral treatment for 7-10 days seems advisable, with similar results to those with oral treatment. A *simple UTI* is considered to be a low-risk infection in children. Oral treatment with cephalosporin or amoxyccillin/clavulanate according to the local resistance pattern is recommended. The duration of treatment in uncomplicated UTIs treated orally should be 5-7 days. A single parenteral dose may be used in cases of doubtful compliance and with a normal urinary tract. If the response is poor or complications develop, the child must be admitted to hospital for parenteral treatment.

If there is an increased risk of pyelonephritis, e.g. VUR, and recurrent UTI, low-dose antibiotic prophylaxis is recommended. It may also be used after an acute episode of UTI until the diagnostic work-up is completed.
In a febrile child with suggestive clinical signs, positive urine microscopy and/or dipstick, antibiotic treatment has to be initiated after a urine specimen for culture has been obtained.

If the UTI is complicated, i.e. when the child appears toxic or severely dehydrated or is vomiting, or if there are concerns regarding compliance, treatment should be started parenterally and continued with an oral antibiotic after 2-4 days (grade A). If the UTI is not complicated, i.e. when the febrile child is in good clinical conditions, only slightly dehydrated and a good compliance is expected, treatment should be given orally (grade A). While awaiting the results of antibiotic sensitivity testing, the antibiotic treatment has to be chosen on an empiric basis.

There is no consensus in the literature on the optimal duration of antimicrobial therapy. 7-14 days of antimicrobial therapy is generally recommended, while a 10-day course seems reasonable and appropriate (grade C). However, parenteral therapy can be limited to 3 days in most cases, followed by a 7-day oral course, as treatment failure does not appear to be associated with the duration of intravenous antibiotic treatment (grade B).

Hospital admission is indicated in the following situations (grade C): infants younger than 3 months, severely ill children (sepsis, dehydration and vomiting), concerns of noncompliance, and fever persisting after 3 days of appropriate antibiotic treatment as shown by the sensitivity testing.

**Kidney Disease Improving Global Outcomes:** No recommendation.

**UK Renal Association:** No recommendation.

**Canadian Society of Nephrology:** No recommendation.

**European Best Practice Guidelines:** No recommendation.

**International Guidelines:** No recommendation.

**SUGGESTIONS FOR FUTURE RESEARCH**

Randomised controlled trials are required to determine the optimal duration of antibiotic treatment for both acute pyelonephritis and cystitis.

**CONFLICT OF INTEREST**

Drs McTaggart and Trnka have no relevant financial affiliations that would cause a conflict of interest according to the conflict of interest statement set down by KHA-CARI.

**REFERENCES**


### Empirical IV antibiotics for treatment of UTI in children

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Dose</th>
</tr>
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<tbody>
<tr>
<td>Gentamicin</td>
<td>&lt;10 years: 7.5 mg/kg; ≥10 years: 6 mg/kg for one dose, then determine dosing interval for a maximum of either 1 or 2 further doses based on renal function</td>
</tr>
<tr>
<td>PLUS</td>
<td></td>
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<tr>
<td>Amoxy/ampicillin</td>
<td>50 mg/kg up to 2 grams, 6 hourly</td>
</tr>
</tbody>
</table>

In children hypersensitive to penicillin, gentamicin alone will usually suffice. If gentamicin is contraindicated as a single drug, use:

- **Cefotaxime**: 25 mg/kg up to 1 gram, 8 hourly
- **OR**
- **Ceftriaxone**: 25 mg/kg up to 1 gram, once daily

Subsequent treatment should be guided by susceptibility results and clinical response, with early conversion to oral therapy. Other than short-term empirical use, gentamicin is no longer recommended except for directed therapy in specific circumstances. If susceptibility results are not available by 72 hours and empirical IV therapy is still required, cease the gentamicin-containing regimen and use cefotaxime or ceftriaxone as above.

### Empirical oral antibiotics for treatment of UTI in children

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Amoxycillin+clavulanate</td>
<td>22.5+3.2 mg/kg up to 875+125 mg, 12 hourly for 5 days</td>
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<td>OR</td>
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<tr>
<td>Cephalexin</td>
<td>12.5 mg/kg up to 500 mg, 6 hourly for 5 days</td>
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<tr>
<td>OR</td>
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<tr>
<td>Trimethoprim</td>
<td>4 mg/kg up to 150 mg, 12 hourly for 5 days</td>
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<td>OR</td>
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<tr>
<td>Trimethoprim/sulfamethoxazole</td>
<td>4+20 mg/kg up to 160+800 mg, 12 hourly for 5 days</td>
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</tbody>
</table>

If resistance to all the above drugs is proven or the causative organism is *Pseudomonas aeruginosa*, use:

| Norfloxacin                           | 10 mg/kg up to 400 mg, 12 hourly for 5 days                         |
| OR                                     |                                                                      |
| Ciprofloxacin                         | 12.5 mg/kg up to 500 mg, 12 hourly for 5 days                      |

Avoid norfloxacin and ciprofloxacin in children unless required on microbiological grounds.

### Table 2. Summary of included studies

<table>
<thead>
<tr>
<th>Study ID</th>
<th>N</th>
<th>Study design and setting</th>
<th>Participants and Interventions</th>
<th>Follow up</th>
<th>Comments and results</th>
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<tbody>
<tr>
<td><strong>Acute Pyelonephritis - Intravenous vs Oral Therapy</strong></td>
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<tr>
<td>Hodson et al (2011) [6]</td>
<td>3 studies. 960 children.</td>
<td>Systematic review of RCTs.</td>
<td>Children aged 1 month to 16 years with acute pyelonephritis. 1. Oral -cefixime or amoxicillin/clavulanic acid vs. 2. IV -cefotaxime or ceftriaxone.</td>
<td>6, 7 and 12 months</td>
<td>Time to resolution of fever (2 studies):  - MD 2.05 hours (95% CI: 0.84, 4.94) Rate of recurrence of bacteriuria (1 study)  - RR 0.65 (95% CI: 0.28, 1.51) [Control rate: 5.7%] Rate of recurrence of symptomatic UTI within 6 months (1 study)  - RR 0.67 (95% CI: 0.27, 1.67) [Control rate: 5%] Risk of persistence of UTI at 72 hours (1 study)  - RR 1.10 (95% CI 0.07 to 17.41) [Control rate: 0.5%] Risk of persistent renal parenchymal defects on DSMA scan (3 studies).  - In children: RR 0.80 (95% CI: 0.50, 1.26). [Control rate: 15%]  - In children who had defects on initial DMSA scan: RR 0.77 (95% CI: 0.53 to 1.11) [Control rate: 17%] Limitations:  - All studies excluded infants under 1 month of age and those who appeared septic or were vomiting.  - Significant heterogeneity and wide confidence intervals for risk of renal parenchymal damage assessed by DMSA.  - Data on VUR restricted to post hoc subgroup analysis of one study.  - RCTs generally not powered to detect significant side effects at low reported incidence of adverse events.</td>
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<tr>
<td>Montini et al (2007) [7]</td>
<td>502</td>
<td>RCT (non-inferiority). Multicentre (Italy)</td>
<td>Children aged 1 month to 16 years with acute pyelonephritis. 1. Oral - co-amoxiclav vs. 2. Parenteral –ceftaxime for 3 days followed by oral co-amoxiclav.</td>
<td>12 months</td>
<td>Scarring at 12 months:  - MD –4% (95% CI: -11.1, 3.1) Time to defervescence:  - MD – 2.6 hours (95% CI: -0.9, 6.0) Sterile urine at 72 hours  - MD -0.05% (95% CI: -1.5, 1.4) Limitations  - Excluded children with severe clinical sepsis, dehydration or vomiting.  - High loss to follow-up at 12 months (20%), however similar between groups.  - Repeat scintigraphy only conducted in children at risk of scarring.</td>
</tr>
<tr>
<td>Study ID</td>
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<tr>
<td>Acute Pyelonephritis - Duration of IV Therapy</td>
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<tr>
<td>Hodson et al (2011) [6]</td>
<td>5 studies. 534 children</td>
<td>Systematic review of RCTs.</td>
<td>Children aged 1 month to 16 years with acute pyelonephritis. 1. Short duration IV – 3 to 4 days. 2. Long duration IV – 7 to 14 days.</td>
<td>20 days to 3 months</td>
<td>Persistent bacteriuria after treatment short IV then oral vs. long IV (4 studies): • RR 0.78 (95%CI: 0.24, 2.55) [Control rate 2.6%] Recurrent UTI at 6 months after treatment short IV then oral vs. long IV (4 studies): • RR 1.15 (95%CI: 0.52, 2.51) [Control rate 5.8%] Persistent renal damage at 3-6 months short IV then oral vs. long IV (3 studies): • All children RR 1.13 (95%CI: 0.86, 1.49) [Control rate 36%] • Children with damage on initial DMSA scan RR 1.10 (95% CI: 0.84,1.45) [Control rate 39%]. Limitations • All studies excluded infants under 1 month of age and those who appeared septic or were vomiting. • Data on VUR restricted to post hoc subgroup analysis of one study. • RCTs generally not powered to detect significant side effects at low reported incidence of adverse events. • Optimal IV duration not able to be defined.</td>
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<tr>
<td>Brady et al (2010) [9]</td>
<td>12,333</td>
<td>Retrospective medical records review Multicentre (US)</td>
<td>All &quot;healthy&quot; children &lt; 6 months of age with a primary or secondary discharge diagnosis code for acute UTI or pyelonephritis. Primary exposure variable was short-course (≤3 days) versus long-course (&gt;4 days).</td>
<td>NA</td>
<td>After adjustment there was no significance association between treatment failure and long versus short duration IV therapy. (OR 1.02 95%CI 0.77-1.35) [Control rate 1.6%]. Limitations • Excluded: children with secondary diagnosis codes suggestion comorbid chronic conditions; secondary or catheter associated UTI; &gt;14 days IV antibiotic treatment; and &gt;14 days hospitalisation. • The longer duration therapy group were younger and sicker. • Overall treatment failure rate was 1.9%. • Retrospective cohort study based on administrative data and resultant potential for misclassification of exposure. • Potential for different patterns of or criteria for readmission may have led to different treatment failure rates.</td>
</tr>
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</table>
### Acute Pyelonephritis - Choice of Antibiotic Agent

<table>
<thead>
<tr>
<th>Study ID</th>
<th>N</th>
<th>Study design and setting</th>
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</tr>
</thead>
</table>
  1. Third generation cephalosporins vs other antibiotics (3 studies).  
  2. Third generation cephalosporins vs fourth generation cephalosporins (1 study).  
  3. Ceftriaxone vs cefotaxime (1 study).  
  4. Isepamicin vs amikacin (1 study). | 3 weeks to 6 months. | Third generation cephalosporins vs other antibiotic (2 studies):  
  - Persistent bacteriuria after 48 hours RR 5.50 (95% CI: 0.30, 101.28) [Control rate 6%].  
  - Recurrent UTI at 5-10 days RR 0.42 (95% CI: 0.03, 6.23) [Control rate 1.4%].  
  Third generation vs fourth generation cephalosporins (1 study)  
  - Persistence or recurrence of initial organism at 4-6 weeks RR 0.13 (95% CI: 0.02, 1.04) [control rate 1%].  
  - Unsatisfactory clinical response at 4-6 weeks RR 0.28 (95% CI: 0.06, 1.27) [control rate 2%].  
  Ceftriaxone vs cefotaxime (1 study)  
  - Bacteriuria 10 days after treatment, all patients RR 0.87 (95% CI: 0.37, 2.03) [control rate 19%].  
  - UTI 1 month after treatment, all patients RR 0.68 (95% CI: 0.30, 1.50) [control rate 19%].  
  Limitations  
  - No study was identified which compared widely available oral antibiotics or compared commonly used IV therapies.  
  - Small number of studies.  
  - Excluded: children with secondary diagnosis codes suggesting comorbid chronic conditions; secondary or catheter associated UTI; >14 days IV antibiotic treatment; and >14 days hospitalisation. |

### Acute Pyelonephritis - Duration of Therapy

<table>
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<tr>
<th>Study ID</th>
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</table>
  1. Single dose gentamicin vs 2.7 day course of appropriate antibiotic. | 6 weeks | Single dose parenteral vs 7-10 days oral.  
  - Persistent bacteriuria 1-2 days after treatment, all patients RR 5.13 (95% CI: 0.29, 89.57) [control rate 21%].  
  - UTI 6 weeks after treatment, all patients RR 0.24 (95% CI: 0.03, 1.97) [control rate 7%].  
  Limitation  
  - As only 17 patients had acute pyelonephritis it is not possible to make definitive conclusion with respect to the effectiveness of single dose therapy.  
  - Single centre small trial. |
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<tr>
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</tr>
</thead>
</table>
| Repetto and MacLoughlin (1984) [12] | 37 | RCT, Single centre (Argentina) | Children with UTI and median age of 5 years (1 month to 14 years).  
   1. Single intramuscular dose of cefotaxime vs.  
   2. Conventional 10 day treatment. | 4 weeks   | Single dose parenteral vs 7-10 days oral.  
   • Persistent bacteriuria 1-2 days after treatment, all patients RR 0.53 (95% CI: 0.03, 10.70) [control rate 0%].  
   • UTI 6 weeks after treatment, all patients RR 0.  
   Limitations  
   • As only 11 patients had acute pyelonephritis it is not possible to make definitive conclusion with respect to the effectiveness of single dose therapy.  
   • Single centre small trial. |
   1. Single dose of trimethoprim-sulphamethoxazole vs.  
   2. 7 day treatment. | Not stated | Cure rate was 100% in both single dose and 7 day treatments 2 days after treatment.  
   Relapse at day 7:  
   • RR 2.50 (95% CI: 0.11, 58.06) [Control rate 1 in 23].  
   Limitations  
   • The number of patients who had acute pyelonephritis was not reported.  
   • Small single centre trial. |
| Cystitis - Duration of Therapy |    |                          |                                                                                                 |           |                                                                                                                                                                                                                      |
   1. Short duration therapy ≤3 days.  
   2. Long duration therapy 7-14 days. | Not stated | • Relative risk of treatment failure:  
   o All trials (12) 1.94 (95% CI 1.19,3.15)  
   o Lower tract UTI trials (9) 1.74 (95% CI 1.05,2.88)  
   • Relative risk of reinfection:  
   o All trials (12) 0.76 (95% CI 0.39,1.47)  
   o Lower tract UTI trials (9) 0.69 (95% CI 0.32-1.52)  
   Limitations  
   • Excluded studies that included children with recurrent or asymptomatic UTI.  
   • Three studies included lower and upper tract UTI patients.  
   • No report of heterogeneity provided.  
   • Low quality of available studies. |
   1. Short duration therapy ≤4 days.  
   2. Long duration therapy ≥5 days (7 to 14 days actual). | Not stated | • Difference in cure rates between single dose/short course therapy and long course therapy: 6.38% (95% CI 1.88,10.89%) with NNT of 16 (95% CI 9.53) to prevent 1 treatment failure.  
   Limitations  
   • Significant heterogeneity across all 22 studies and after exclusion of trials that used different antibiotic agents between treatment arms.  
   • Low quality of available studies. |
<table>
<thead>
<tr>
<th>Study ID</th>
<th>N</th>
<th>Study design and setting</th>
<th>Participants and Interventions</th>
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</thead>
</table>
| Michael et al  | 12 studies| Systematic review of RCTs | - Children with acute lower tract UTI aged 3 months to 18 years.  
1. Short duration therapy 2-4 days.  
2. Long duration therapy 7-14 days. | 33 days to 12 months | - All trials excluded children with acute pyelonephritis.  
- Primary outcomes: treatment failure (persisting symptoms, significant bacteriuria 0-7 days after completion of treatment. Recurrent UTI 10 days or more after completion of treatment.  
- Non significant heterogeneity for primary outcomes.  
- Relative risk of treatment failure (8 studies):  
  - 1.06 (95% CI 0.64,1.76) [control rate 14.7%]  
- Relative risk of recurrent UTI (12 studies):  
  - 1.01 (95% CI 0.77,1.33) [control rate 23.5%]  
Limitations  
- Excluded studies that used different antibiotics in the short and long treatment arms.  
- Low quality of available studies.  
- Wide confidence intervals indicating residual imprecision.  
- Limited information of information relevant to clinical care in available studies. |