

# My Pee Pee Hurts

## Management of UTIs and VUR

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# Objectives

- 1. Describe treatment options for urinary tract infections
- 2. Discuss the rationale for imaging in pediatric patients with urinary tract infections
- 3. Discuss management strategies for vesicoureteral reflux

# Case

- A 2 month old presents to your office with a temperature of 102 F axillary that morning.
- Mom reports the patient was fussy while febrile, but has calmed down and is otherwise eating well and appropriately active.
- Your examination is unremarkable and you obtain a CBC, which is normal, a urine dip, which reveals (+) nitrites and leukocyte esterase, and blood and urine for culture.

# Questions

- How should this infection be managed?
  - Does the child need IV antibiotics and hospitalization?
- What imaging should be obtained?
  - What is the best predictor of renal scarring?
- How is vesicoureteral reflux best managed?

# Additional Topics

- Recurrent UTIs/Chronic pyelo
- Antibiotic prophylaxis
  - Grey areas
  - Side effects
  - Counseling/involving families
- ?

# Oral Versus Initial Intravenous Therapy for Urinary Tract Infections in Young Febrile Children

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**ABSTRACT.** *Background.* The standard recommendation for treatment of young, febrile children with urinary tract infection has been hospitalization for intravenous antimicrobials. The availability of potent, oral, third-generation cephalosporins as well as interest in cost containment and avoidance of nosocomial risks prompted evaluation of the safety and efficacy of outpatient therapy.

*Methods.* In a multicenter, randomized clinical trial, we evaluated the efficacy of oral versus initial intravenous therapy in 306 children 1 to 24 months old with fever and urinary tract infection, in terms of short-term clinical outcomes (sterilization of the urine and defervescence) and long-term morbidity (incidence of reinfection and incidence and extent of renal scarring documented at 6 months by <sup>99m</sup>Tc-dimercaptosuccinic acid renal scans). Children received either oral cefixime for 14 days (double dose on day 1) or initial intravenous cefotaxime for 3 days followed by oral cefixime for 11 days.

*Results.* Treatment groups were comparable regarding demographic, clinical, and laboratory characteristics. Bacteremia was present in 3.4% of children treated orally and 5.3% of children treated intravenously. Of the short-term outcomes, 1) repeat urine cultures were sterile within 24 hours in all children, and 2) mean time to defervescence was 25 and 24 hours for children treated orally and intravenously, respectively. Of the long-term outcomes, 1) symptomatic reinfections occurred in 4.6% of children treated orally and 7.2% of children treated intravenously, 2) renal scarring at 6 months was noted in 9.8% children treated orally versus 7.2% of children treated intravenously, and 3) mean extent of scarring was ~8% in both treatment groups. Mean costs were at least twofold higher for children treated intravenously (\$3577 vs \$1473) compared with those treated orally.

*Conclusions.* Oral cefixime can be recommended as a safe and effective treatment for children with fever and urinary tract infection. Use of cefixime will result in substantial reductions of health care expenditures.

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ABBREVIATIONS. UTI, urinary tract infection; APN, acute pyelonephritis; IV, intravenous; VCUG, voiding cystourethrogram; DMSA, dimercaptosuccinic acid; VUR, vesicoureteral reflux.

Management of urinary tract infection (UTI) requires early diagnosis and prompt antimicrobial treatment to minimize renal scarring that results from acute pyelonephritis (APN).<sup>1,2</sup> Most pediatric textbooks and review articles recommend that young children be hospitalized, at least initially, to receive intravenous (IV) antibiotics.<sup>3–6</sup> However, oral therapy, if effective in treating the acute infection and preventing the development of scars, would preclude both the costs and risks associated with hospitalization. We therefore undertook a multicenter, randomized clinical trial to compare the efficacy of oral antibiotic alone versus initial treatment with IV antibiotic followed by oral antibiotic, in young children with fever and UTI.

## METHODS

### Enrollment and Eligibility Criteria

The study was conducted at Children's Hospital of Pittsburgh, Columbus Children's Hospital, Fairfax Hospital for Children, and Children's Hospital, Boston, after approval by the Institutional Review Board at each of these participating institutions. Children aged 1 to 24 months were considered eligible if they 1) had a rectal temperature of  $\geq 38.3^{\circ}\text{C}$  at presentation or within 24 hours, and 2) were suspected to have a UTI because of the presence of pyuria ( $\geq 10$  white blood cells per cubic millimeter in an uncentrifuged urine sample) and bacteriuria ( $\geq 1$  Gram-negative rod per 10 oil immersion fields in a Gram-stained smear of uncentrifuged urine).<sup>7</sup> Final eligibility required that there be a positive urine

# Antibiotic treatment for pyelonephritis in children: multicentre randomised controlled non-inferiority trial

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## ABSTRACT

**Objective** To compare the efficacy of oral antibiotic treatment alone with treatment started parenterally and completed orally in children with a first episode of acute pyelonephritis.

**Design** Multicentre, randomised controlled, open labelled, parallel group, non-inferiority trial.

**Setting** 28 paediatric units in north east Italy.

**Participants** 502 children aged 1 month to <7 years with clinical pyelonephritis.

**Intervention** Oral co-amoxiclav (50 mg/kg/day in three doses for 10 days) or parenteral ceftriaxone (50 mg/kg/day in a single parenteral dose) for three days, followed by oral co-amoxiclav (50 mg/kg/day in three divided doses for seven days).

**Main outcomes measures** Primary outcome was the rate of renal scarring. Secondary measures of efficacy were time to defervescence ( $37^{\circ}\text{C}$ ), reduction in inflammatory indices, and percentage with sterile urine after 72 hours. An exploratory subgroup analysis was conducted in the children in whom pyelonephritis was confirmed by dimercaptosuccinic acid (DMSA) scintigraphy within 10 days after study entry.

**Results** Intention to treat analysis showed no significant differences between oral ( $n=244$ ) and parenteral ( $n=258$ ) treatment, both in the primary outcome (scarring scintigraphy at 12 months 27/197 (13.7%) v 36/203 (17.7%), difference in risk -4%, 95% confidence interval -11.1% to 3.1%) and secondary outcomes (time to defervescence 36.9 hours (SD 19.7) v 34.3 hours (SD 20), mean difference 2.6 (-0.9 to 6.0); white cell count  $9.8 \times 10^9/\text{l}$  (SD 3.5) v  $9.5 \times 10^9/\text{l}$  (SD 3.1), mean difference 0.3 (-0.3 to 0.9); percentage with sterile urine 185/186 v 203/204, risk difference -0.05% (-1.5% to 1.4%)). Similar results were found in the subgroup of 278 children with confirmed acute pyelonephritis on scintigraphy at study entry.

**Conclusions** Treatment with oral antibiotics is as effective as parenteral then oral treatment in the management of the first episode of clinical pyelonephritis in children.

**Trial registration** Clinical Trials NCT00161330.

## INTRODUCTION

Acute pyelonephritis is one of the most common serious bacterial infections in childhood, particularly in young children,<sup>1,3</sup> because of the potential renal scarring.<sup>4,8</sup> The diagnosis is based on the clinical presentation (clinical pyelonephritis), with fever and raised inflammatory indices, active urinary sediment, and subsequent positive results on urine culture. Published guidelines recommend initial treatment with a parenteral third generation cephalosporin followed by oral antibiotics.<sup>9-11</sup>

A recent Cochrane review of antibiotic treatment for acute pyelonephritis in children identified 18 randomised trials that for the most part compared different antibiotic regimens given parenterally.<sup>11</sup> There were no significant differences in the risk of persistent renal damage (three trials, 315 children: relative risk 0.99, 95% confidence interval 0.72 to 1.37) between initial intravenous (three to four days) followed by oral treatment and completely intravenous treatment (seven to 14 days). Only one previous randomised controlled trial (306 children) compared oral treatment (cefixime) only with antibiotics started parenterally.<sup>12</sup> There was no significant difference between the two groups in terms of renal scarring at six months (1.45, 0.69 to 3.03). Hoberman et al expressed some concern regarding the low rate of scarring in both groups in the study compared with the rates reported elsewhere.<sup>12</sup> Furthermore, 90% of children studied were girls. This was despite the mean age of the children being 8 months, and studies have shown that the sex distribution in the first 6 months is about equal, with a significant predominance in girls only after 12 months of age.<sup>13</sup>

# Antibiotics for acute pyelonephritis in children (Review)

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# Efficacy of Short-Term Intravenous Antibiotic in Neonates With Urinary Tract Infection

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**Background:** Recent studies have questioned the use of prolonged intravenous treatment in neonates with urinary tract infection (UTI). The aim of the present study was to examine the clinical course of neonates with UTI with special attention paid to the rates of bacteremia and meningitis and to determine the efficacy of short-term intravenous antibiotic.

**Methods:** Retrospective review of clinical charts of neonates admitted for UTI. Patients were treated first intravenously with a  $\beta$ -lactam antibiotic and gentamicin. Treatment was completed orally.

**Results:** One hundred seventy-two neonates (median age, 19 days) were included. Of 129 blood cultures carried out, 16 (12.4%) were positive. Analysis of cerebrospinal fluid was performed in 75 patients; none of the cultures was positive. Forty-nine patients (28.5%) were treated with ampicillin and gentamicin and 105 (61%) with amoxicillin-clavulanate and gentamicin. The median length of intravenous treatment was 4 days (P25: 3; P75: 6). Oral amoxicillin-clavulanate was used in the continuation phase in 75%. No treatment failure or relapse was detected. Eleven (8.7%) of 126 patients had renal scarring at 6 months.

**Conclusions:** The clinical course in neonates with UTI treated with short-term intravenous antibiotic followed by oral treatment is highly favorable, both in short and long terms. The absence of meningitis and the good evolution of the associated bacteremias argue in favor of a review of the habitual diagnostic-therapeutic protocol in neonates.

protocol.<sup>5-7</sup> For 1 thing, the frequency of associated meningitis is low, which calls into question the routine practice of lumbar puncture.<sup>4-10</sup> Furthermore, the percentage of bacteremia is quite variable among the series considered (ranging from 0% to 31%), and the significance of this bacteremia remains to be determined.<sup>5,7,8,11-14</sup> Finally, the clinical course in neonates with UTI is usually favorable after the first doses of intravenous antibiotics, such that more than 80% of patients are afebrile for 24 hours, so it would be possible the management of those patients in short-stay units.<sup>8</sup>

We carried out a retrospective study with the aim of learning about the clinical course among neonates diagnosed with UTI in the emergency department, with special attention paid to the rates of bacteremia and meningitis, and of determining the efficacy of a short-term intravenous antibiotic followed by oral antibiotic.

## METHODS

The clinical charts of patients between 1 and 31 days of age attended in the emergency department of our hospital during the period of January 1997 to December 2002 were reviewed. Those hospitalized with a diagnosis of UTI or acute pyelonephritis were examined. Excluded were those patients with urine cultures showing multiple organisms.