**National Collaborative Sites **

- Children’s Hospital of Philadelphia
  Philadelphia, PA
- Children’s Hospital of Pittsburgh
  Pittsburgh, PA
- Children’s Hospital of Michigan
  Detroit, MI
- Johns Hopkins Children’s Center
  Baltimore, MD
- Women and Children’s Hospital of Buffalo
  Buffalo, NY
- Children’s National Medical Center
  Washington, DC
- Oregon Health and Science University
  Portland, OR
- Univ. of Oklahoma Health Science Center
  Oklahoma City, OK
- Children’s Hospital
  Boston, MA
- Nationwide Children’s Hospital
  Columbus, OH
- Children’s Mercy Hospital and Clinics
  Kansas City, MO
- Emory Children’s Center
  Atlanta, GA
- The Hospital of Sick Children
  Toronto, CA
- Texas Children’s Hospital
  Houston, TX
- University of Alabama
  Birmingham, AL

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**Randomized Intervention for Children with Vesicoureteral Reflux (RIVUR)**

**Research Study Overview**

- National Institute of Diabetes and Digestive and Kidney Diseases
- www.rivur.net

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**When to Contact the Study**

As soon as your patient, aged between 1 month and 6 years, is diagnosed with a first or second UTI, please contact:

**Potential Participants**

Potential participants will need to have a renal ultrasound, VCUG, and DMSA within 16 weeks of the first or second UTI.

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**Version Date**: 1/7/2008
Background and Rationale

Vesicoureteral Reflux (VUR), the retrograde flow of urine from the bladder to the ureters, is the most common functional abnormality of the urinary tract in children. VUR is found in 30-50% of children with a urinary tract infection (UTI).

The goal of current management of VUR has been to prevent UTI’s, theoretically decreasing the risk of permanent renal scarring. Renal scarring has been associated with proteinuria, hypertension, eclampsia and end-stage renal disease (ESRD) in later life. Most children with VUR outgrow it by adolescence. Current management consists of either long-term antimicrobial prophylaxis while VUR is present, or surgical correction.

The current management of VUR has been based on an international study which compared antimicrobials vs. surgery, but did not include a control group. Because of this design flaw, the need for either antimicrobial prophylaxis or surgery in all children with VUR has been questioned. The cost and potential harm of current diagnostic and therapeutic studies to detect VUR, as well as the development of antimicrobial resistance, resulting from the long term use of prophylactic antibiotics has also caused concern.

A great need exists for evidence-based recommendations for the management of children with VUR.

Specific Aim of the Study

This is a multicenter, randomized, double-blind, placebo-controlled study to determine whether daily antimicrobial prophylaxis, in the setting of prompt evaluation and treatment of UTI, is superior to placebo in preventing recurrence UTI and/or the occurrence of, or worsening, of renal scarring in children with vesicoureteral reflux (VUR).

Six hundred children diagnosed with VUR will be recruited from across the United States and Canada after their first or second UTI. They will be followed for 2 years in one of two double blinded treatment arms, antimicrobial prophylaxis or placebo.

The primary study endpoint is recurrent urinary tract infection. Secondary endpoints include renal scarring and development of antimicrobial resistance.

Patient Screening Criteria

Inclusion:
- Children ages 1 month- (<)6 years
- Documented 1st or 2nd UTI within 112 days of study enrollment
- VUR Grade I-IV, based on VCUG
- Appropriately-treated 1st or 2nd UTI

Exclusion:
- More than 2 previous UTIs at time of enrollment
- Small kidneys on Ultrasound
- Syndromes associated with UTI
- Sulfa Allergy
- Renal injury or disease

Study Design

Recruitment and Screening:
Children will be evaluated to determine if they meet the entry criteria for the RIVUR study.

Treatment:
Children will be randomized to daily antimicrobial prophylaxis or placebo. Long-term antimicrobial prophylaxis therapy will consist of a single daily dose of trimethoprim/sulfamethoxazole (TMP/SMZ) at a trimethoprim dose of 3 mg/kg/day administered orally.

Follow-up:
- Parents contacted every 2 months via telephone
- Clinic visits at enrollment, 6, 12, 18, and 24 months.
- Quality of Life assessments at baseline, 12 and 24 months.
- DMSA renal scans at enrollment, 12 and 24 month visits to closely monitor for any renal scarring.

Clinical Safety Monitoring:
The local IRB and the study Data and Safety Monitoring Board will monitor the clinical course of patients in this study. Some children who develop recurrent febrile or symptomatic infections and/or new renal scarring will be changed from randomization treatment to routine care and referred to an appropriate specialist. They will also continue to be observed for their remaining time of the 2-year follow-up period.