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What Urinary Colony Count Indicates a Urinary Tract Infection in children?

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Abstract

Post-hoc analysis of the Randomized Intervention for Children with Vesicoureteral Reflux (RIVUR) study suggests that, in concordance with European guidelines, using bacteriologic criterion of 10,000 CFU/ml of a single organism does not decrease diagnostic specificity of a UTI in children aged 2 months to 6 years in a properly collected urine if symptoms/fever and pyuria are present.

Keywords

vesicoureteral reflux; suprapubic aspiration; urinary catheterization; pyuria; guideline

The RIVUR (Randomized Intervention for Children with Vesicoureteral Reflux [VUR])¹ study showed that antibiotic prophylaxis with trimethoprim/sulfamethoxazole decreased the number of recurrent urinary tract infections (UTIs) in children 2 months to 6 years of age with VUR. In order to ensure rigorous diagnosis of a recurrent UTI, the study protocol required 3 criteria: fever and/or symptoms, pyuria, and growth of a single organism 100,000 colony forming units/ml (CFU/ml) for clean catch or 50,000 CFU/mL for a catheterized specimen. Since 2007 when the RIVUR trial was designed², uncertainty has arisen as to the threshold for organism growth to appropriately diagnose a UTI in children^{3–4}. Swerkersson recently showed that 12% of 430 children less than 12 months of age with a carefully diagnosed first UTI had colony counts of 10,000 to 50,000 CFU/ml.⁴ Current European and Canadian guidelines in infants and young children suggest that any growth on suprapubic aspiration (SPA) is abnormal^{5–7}. European guidelines state that growth of 10,000 CFU/mL or even 1,000 CFU/ml are sufficient to diagnose a UTI from a catheterized urine^{5–7}, while US and Canadian guidelines use 50,000 CFU/mL as the cut-off^{5–7,10}.

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Since the work of Kass et al in adult women in the 1950's,⁸ 100,000 CFU/mL of a single organism has been the diagnostic criterion for diagnosing a UTI in older children and adults. However, based in part on the work by Hoberman et al in children⁹, the recently reaffirmed American Academy of Pediatrics 2011 UTI guideline recommends that 50,000 CFU/mL of a single organism and pyuria be present in urine collected by SPA or catheterization in children 2–24 months of age in order to diagnosis a UTI¹⁰. We have reanalyzed RIVUR data in order to determine whether use of a lower criterion for bacterial growth, consistent with most international guidelines, would significantly change the number of children diagnosed with a recurrent UTI in this cohort. We hypothesize that lowering the bacteriologic threshold to 10,000 CFU/ml in order to diagnosis a UTI in a child with symptoms and pyuria would result in few if any false positives and thus have minimal impact on specificity and a minimal impact on sensitivity.

Methods

Application of the stringent RIVUR primary outcome definition was standardized by an independent UTI classification committee². Specifically, a recurrent UTI required a cultureproven infection with a single organism 50 000 CFU/mL (catheterized or SPA urine) or 100 000 CFU/mL (cleanvoided); pyuria on microscopic urinalysis (5 wbc/mm in an uncentrifuged specimen or 10 wbc/hpf in a centrifuged specimen), or trace or greater leukocyte esterase on dipstick; and fever (38°C or greater) or symptoms (suprapubic, abdominal, or flank pain or tenderness; or urinary urgency, frequency, or hesitancy, or dysuria, or foul-smelling urine; or in infants aged 4 months or younger, failure to thrive, dehydration, or hypothermia) occurring within 24 hours of the urine collection. For the current analysis, data were first reanalyzed using the original RIVUR definition of a UTI but decreasing the colony count requirement to 50,000 CFU/mL for clean-voided specimens. Data were then reanalyzed using a colony count threshold of 10,000 colonies/CFU/ml for clean-voided, catheterized or SPA urines. Criteria for fever/symptoms and pyuria were unchanged.

Results

In the RIVUR trial 111 children of the enrolled 607 children had 171 recurrent UTIs that met the original protocol-specified criteria.^{1,2} (Table; available at www.jpeds.com) No additional children would have been diagnosed with a recurrent UTI if the culture criteria for a clean caught urine was dropped from >100,000 CFU/ml to 50,000 CFU/ml. One 8-month-old and 1 child older than 24 months, both of whom were receiving antibiotic prophylaxis, would have diagnosed with a recurrent UTI if the cut-off was decreased to 10,000 CFU/ml. Thus, lowering the colony count threshold to 10,000 colonies had little impact on the specificity of a recurrent UTI in the RIVUR study if both fever/symptoms and pyuria are present.

Discussion

Changing the colony count cut-off for diagnosis of a recurrent UTI in the RIVUR trial to 10,000 CFU/mL in children with symptoms and pyuria adds only two UTI diagnoses, has

minimal impact on specificity and makes no difference in the conclusions of the RIVUR study. This lower threshold is consistent with the European guidelines and suggests that serious consideration be given to decreasing the bacteriologic criterion for a UTI in the AAP and Canadian guidelines to 10,000 colonies of a single organism in a properly collected urine in children between 2 months and 2 years of age if symptoms and pyuria are present. As most of the urines in children >2 years of age were clean caught the lower colony count recommendation appears to be valid for children between 2 and 6 years of age as well as for those less than 2 years. As 6 years was the cutoff for the RIVUR study, no recommendation can be made for older children.

Use of the lower criterion is especially pertinent in pediatrics, as an infant or young child with urinary frequency or urgency from a UTI may be unlikely to hold urine long enough to allow bacterial growth to reach 50 or 100,000 CFU/mL, leading to a risk of underdiagnosis, and possible subsequent morbidity. Kass in his classic studies demonstrated that 1% of his adult women in urine obtained randomly during the day had colony counts between 10,000 and 100,000 CFU/mL.⁸ In these women UTI was confirmed by a 100,000 CFU/mL first morning urine, and the lower colony count obtained later in the day was attributed to hydration. Similarly, Pryles demonstrated the effect of hydration on colony count by subjecting several untreated children with UTI diagnosed by 10^7 CFU/mL on a first morning urine to serial catheterization during a 24-hour period and showed that the colony count during the day decreased by several orders of magnitude to as low as 10^3 to 10^4 CFU/mL.¹¹ Koskimies reported that 19% of his patients with bacterial growth on SPA had less than 10^5 CFU/mL.¹² Lubell et al in a multicenter emergency department study of 1870 infants 29–60 days of age diagnosed with UTI based on symptoms and either pyuria or a positive urine gram stain found that 6% had colony counts of 10,000–49,000 CFU/mL, 3% reported as 10,000 to 100,000 CFU/mL, and 20% reported as 50,000 to 100,000 CFU/mL.¹³ Thus potentially 9% of these infants might not have been diagnosed with a UTI unless the colony count cut-off is decreased to 10,000 CFU/mL. Similarly Schroeder et al report that 5% of their infants less than 3 months of age with a bacteremic UTI had colony counts between 10,000 and 49,000 CFU/mL.¹⁴ Also, as is noted in these reports, because some laboratories report colony counts as 10,000 to 100,000 CFU/mL, the 50,000 CFU/mL threshold sometimes cannot be ascertained. Thus infected urine properly collected from a child with a UTI during an office or emergency room visit may sometimes grow only 10,000 CFU/mL. Because prompt therapy is reported to decrease the incidence of renal scarring, delay in treatment awaiting a repeat urine culture may be deleterious.^{15–16}

The risks of underdiagnosis must be balanced against the risks of overdiagnosis, especially for the symptomatic child with bacteriuria without pyuria¹⁷. The likelihood of overdiagnosis in the RIVUR cohort was minimized because all the patients identified with a recurrent UTI had pyuria and symptoms or fever. In the RIVUR study, 29 children met the original criteria for a positive urine culture and fever/symptoms but did not demonstrate pyuria and thus were not diagnosed with a recurrent UTI. Lowering the culture criterion to 10,000 CFU/mL would add only one additional child for a total of 30. Half of these children grew organisms other than *E. coli*. Determining whether some of these children actually had a recurrent UTI is problematic. Shaikh¹⁸ found 13% of children with a UTI did not have pyuria, especially those infected with an organism other than *E. coli*. Similarly, Lubell found that the

sensitivity of pyuria was 75.9% for infants with an enterococcal UTI compared with 93.9% for those with an *E. coli* UTI.¹³ Perhaps when organisms other than *E. coli* are found in a urine without pyuria, physicians should have a higher index of suspicion for a UTI as these organisms may generate less of an inflammatory response.

Limitations of this post-hoc analysis of the RIVUR study data are that the recurrent UTI's were diagnosed by clinical and laboratory criteria and were not confirmed by contemporaneous radionuclide studies, the RIVUR trial was not designed to assess the bacteriologic criteria for diagnosing a UTI, and the relatively small number of patients studied. Also, since all the study subjects had vesicoureteral reflux and half were on prophylactic antibiotics, including the 2 additional cases (Table), data from this reanalysis may not be generalizable to the general pediatric population.

In summary, we suggest that decreasing the bacteriologic criterion for diagnosing a UTI in infants and children aged 2 months to 6 years with symptoms/fever and pyuria from 100,000 CFU/mL or 50,000 CFU/mL to 10,000 CFU/mL in a properly collected urine would not impact diagnostic specificity and would slightly increase sensitivity in concordance with the recently updated European guidelines.

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Abbreviations

SPA	suprapubic aspiration
RIVUR	Randomized Intervention for Children with Vesicoureteral Reflux
UTI	urinary tract infection
CFU	Colony forming units

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Table

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	Age			
Children	<= 6 months (N=147)	6 to <= 24 months (N=258)	> 24 months (N=202)	Overall (N=607)
Children with RIVUR UTI (% with UTI within age group)	21 (14%)	44 (17%)	46 (23%)	111
RIVUR UTI	33	61	77	171
C50+P+S	33	61	77	171
C10+P+S	33	62	78	173
RC+S (no P)	40	73	88	201
C50+S (no P)	40	72	89	201
C10+S (no P)	40	73	90	203

C10 is culture 10k or greater

P is pyuria based on RIVUR definition

S is symptoms based on RIVUR definition of fever or symptoms within 24 hours

RC is RIVUR culture cutpoints (50k for cath, 100K for clean catch)