PEM GUIDE - UTI IN CHILDREN < 2 Years

INTRODUCTION

Urinary tract infection is the most common serious bacterial infection (SBI) in febrile infants and young children 2 months-2 years without an apparent source of the fever. In the past 2 decades the rate of UTI in this age group has remained unchanged at 5%, while other SBI such as bacteremia have decreased dramatically after the universal H Influenza immunization and are expected to further decrease following the universal pneumococcal immunization.

RISK FACTORS FOR UTI

The overall incidence of UTI in febrile children < 2 years of age is approximately 5%. UTI is also the most common serious bacterial infection in infants < 60-90 days of age. The overall SBI rate in this age group is reported to be 7-15%, and for UTI alone 6-13.6%. Within these age categories there is significant variation in risk of UTI based on gender, race and circumcision status.

AAP - RISK OF UTI – DEMOGRAPHIC CHARACTERISTICS		
AGE	FEMALE	MALE
< 12 mo	6.5 %	3.3 %
12-24 mo	8 %	2 %
Circumcised > 1 yr	NA	0.2 – 0.4 %

The 2 largest studies of prevalence of UTI in the US for this age group published by Hoberman in 1993 and Shaw in 1998 demonstrated clearly that white female infants had the highest incidence of UTI. In the study by Hoberman 17% of white infants with T>39°C had UTI, while black infants had only 3.6% incidence. Shaw found that up to 31% of febrile white female infants without a source had UTI, and among black female infants only 3% had UTI. She also demonstrated that uncircumcised males had 8 times higher likelihood of having UTI than the circumcised boys. Recent systematic review of the randomized and observational studies by Singh-Grewal on circumcision for prevention of UTI in boys also demonstrated significant decrease of the UTI rates among circumcised boys (OR 0.13; 0.08-0.2, p< 0.001).

PREDICTORS OF UTI			
DEMOGRAPHIC		CLINICAL	
1	White race	1	Fever without a source
2	Female	2	T > 39 C
3	< 12 months	3	Fever >+= 2 days
4	Uncircumcised Males	4	Ill appearance
		5	Suprapubic Tenderness
		6	Malodorous Urine
		7	Prior UTI

CLINICAL PREDICTION RULE – FEMALES < 24 mo	
VARIABLE	ADJUSTED ODDS RATIO
White Race	7.5
Age < 12 mo	3
T >= 39 C	2.6
No Source of Fever	2.4
Fever > = 2 days	2
Rule Performance - >= 2 predictors Sensitivity – 95% (85-99), Specificity 31 % (28-34)	

DIAGNOSTIC TESTING - COINCIDENCE OF VIRAL INFECTIONS

The presence of a documented viral infection with RSV, influenza, para-influenza, enteroviruses and other viruses lowers the risk for SBI and UTI, but the risk is not negligible. Levine and Byington consistently reported incidence of UTI in febrile infants < 60 days at 10% in the group without evidence of viral infection and at 5% in the group with viral infection. Levine found that febrile infants < 2 mos with clinical bronchiolitis irrespective of RSV status had significantly high UTI rate at 6.5%. This data suggests that febrile infants < 60 days should be evaluated for UTI even of the presence of a viral infection or bronchiolitis. Febrile children > 2 mos of age with bronchiolitis have very low incidence of UTI or bacteremia. Kupperman found that only 2% of febrile children 2mos-2years of age with bronchiolitis had UTI, while 12% of those without bronchiolitis had positive urine culture.

DIAGNOSTIC TESTING – URINE CULTURE

The diagnosis of UTI is confirmed with a positive urine culture growing a single pathogen at $\geq$10,000 CFU/mm^3 from a catheterized specimen or any number of CFU from a suprapubic aspirate. The best method for urine collection is sterile bladder catheterization with success rates up to 100%. Suprapubic aspiration (SPA) is least likely to produce specimen contamination, but it is perceived as more invasive and requires training in the proper techniques. Success rate of SPA is dependent on urine volume in the bladder, and the first attempt success rate is around 50%. Pre-hydration protocol and ultrasound guided SPA have increased success rates of SPA up to 87%. Bag urine specimens have high contamination rate up to 65% and should not be used for culture. If bag specimen was used for screening UA, catherized specimen should be obtained next for repeat UA and urine culture.

SCREENING FOR UTI – URINALYSIS

The performance of a variety of screening tests have been evaluated for the diagnosis of UTI in children. These include:

1. Standard urinalysis – dipstick and microscopy of spun urine
2. Gram stain of unspun urine
3. Hemocytometry of unspun urine
4. Enhanced urinalysis – hemocytometry and gram stain of unspun urine

Young infants may have absent pyuria in 20-25% of cases due to high urine flow rates and blunted inflammatory response. In addition, the high urine flow rates reduce the

time for production of nitrites by bacteria. Therefore, absence of pyuria or nitrites on a screening urinalysis does not exclude UTI in infants.

POSITIVE URINALYSIS
Dipstick urinalysis – any nitrite or ≥ 1+ Leucocyte esterase (LE)
Urinalysis microscopy ≥ 5 WBC/HPF
Gram stain – any bacteria present
Hemocytometry - ≥ 10WBC/mm^3
Enhanced Urinalysis - >10 WBC/mm^3 and/or >10 bacteria per field on Gram stain

Although the most sensitive screening test is the enhanced urinalysis, it is not widely available and it is time/resource intensive. The most cost effective and time saving approach would be to perform urine dipstick in the ED and send cultures for all specimens. Then if the dipstick is positive, empiric antibiotics for presumed UTI should be started, while those with negative dipstick can be expectantly managed until urine culture result is available.

AAP – DIAGNOSTIC ACCURACY OF UA COMPONENTS		
TEST	SN % (range)	SP % (range)
Nitrite	53 (15-82)	98 (90-100)
Leukocyte Esterase	83 (67-94)	78 (64-92)
>= 5 WBC/HPF	73 (32-100)	81 (58-91)
Bacteria	81 (16-99)	83 (11-100)

DIAGNOSTIC ACCURACY OF URINALYSIS			
TEST	SN	SP	PPV
+Nitrite *or* ≥trace LE	79	97	46
+Dipstick *or* + Microscopy	83	87	16
+Gram stain (any bacteria)	81	97	43
Any component of enhanced UA	94	84	13

ANCILLARY TESTING

Utility of Blood Culture - Bacteremia with UTI has been reported at rates between 4-9%. Several studies have demonstrated that bacteremia associated with UTI is most likely in the youngest infants, particularly < 6 mos of age with highest incidence in those < 2-3 months. The only reliable predictor for bacteremia is young age < 3 mos. Clinical parameters such as appearance, irritability, crying, vomiting, height or duration of fever as well as acute phase reactants such as WBC, ESR and CRP do not discriminate bacteremic from non-bacteremic infants. There is also no significant difference in the short-term and long-term outcomes of bacturia associated with bacteremia with exception of duration of fever, and high-grade vesico-ureteral reflux found on follow-up VCUG. Therefore, obtaining blood culture doesn't appear to have any significant impact on the ED management of these children, although it may be prudent to do it in infants < 6 mos of age.

Utility of WBC, ESR, CRP – Seventy percent of young febrile children with UTI will have pyelonephritis proven by DMSA renal scan. In general, WBC, ESR and CRP are likely to be elevated in most children with pyelonephritis, however normal values do not exclude it. As these tests do not carry any decision making power, their utility is questionable. As mentioned previously, they are also poor discriminators for bacteremic patients.

Utility of Eletrolytes - There is no data at this time to support or reject the need to obtain basic metabolic profile (BMP) in children with UTI. However, applying common sense would be reasonable. It is useful to check electrolytes and renal function in children with protracted vomiting and dehydration, ill or septic appearing patients, in a very young infant < 2-3 mos and those with known abnormality of the urinary tract.

Utility of Lumbar Puncture - Meningitis in infants with UTI is an extremely rare event. Bachur retrospectively studied 354 children < 2 years of age with UTI. Lumbar puncture was performed in 70%, to find only 14 infants with CSF pleocytosis. Of these, only 4 patients had positive CSF culture (all LP were done before administration of antibiotics) and all were < 1 month old. Based on this and other previous reports, it appears that LP is not indicated in infants with UTI > 1-2 mos of age.

MANAGEMENT

Approximately 90% of all pediatric UTI's are caused by E. coli. The remainder is comprised by Klebsiella, Proteus, Enterobacter, Pseudomonas, Enterococcus, Staph. aureus, and group B streptococcus. Initial empiric antibiotic treatment is directed to cover these pathogens, and primarily E. coli.

The choice of initial empiric antibiotic treatment depends on the local sensitivities of E. coli. In the recent 10 years, resistance to commonly used antibiotics has dramatically increased. It appears that the best empiric antibiotic choice is a 3rd generation cephalosporin.

ANTIBIOTIC RESISTANCE			
	1999 LA, CA	1997-2002 Bellevue	2004 Bellevue
Ampicilin	40 %	54 %	47 %
Amoxicillin-Clavulanate	40 %	27 %	NA
Bactrim	28 %	28 %	30 %
Cefazolin	18 %	14 %	7 %
Ceftriaxone	1 %	2.5 %	2 %

Children on prophylactic Antibiotics for urinary tract abnormalities are at risk for having higher resistance rates to 3rd generation cephalosporins and but relatively low rates for Aminoglycoside resistance. Data from a recent study by Lutter demonstrated that isolates from hospitalized children receiving prophylactic antibiotics had 27% resistance to Cefotaxime and 5% to aminoglycosides, while those from children not on prophylaxis were resistant in 3% and 1% respectively.

DISPOSITION

In the past, the standard of care for children with UTI was hospitalization for intravenous antibiotics for at least 3-7 days or until 24 hours after defervescence, followed by oral antibiotics to complete a 14 days course. Recent data suggest that shorter intravenous antibiotic courses with 1-3 days of parenteral antibiotics followed by oral antibiotic are comparable.

Hoberman published a large, well designed randomized clinical trial for treatment of children 1 mos – 2 years of age with UTI, comparing oral 3rd generation cephalosporin (Cefixime) for 14 days and parenteral 3rd generation cephalosporin Cefotaxime for 3 days or until defervescence followed by oral Cefixime to complete 14 days. Both short-term (time to defervescence, sterilization of urine at 24 hours) and long term outcomes (recurrent UTI, renal scarring on DMSA scan at 1 month and 6 mos) were comparable between the groups. Based on this study, outpatient treatment of well-appearing infants and young children with UTI appears to be a viable option.

There is still insufficient data as to the optimal duration of treatment. Current AAP recommendations are for 10-14 days of antibiotic treatment of pyelonephritis. Two meta-analyses looked at shorter duration of antibiotics uncomplicated UTI (cystitis) in all pediatric age groups and found that single or very short course $\leq$ 3 days of antibiotics were inadequate for eradication of the infection, while 7-10 day courses were sufficient.

Following the treatment course, all children with UTI should be maintained on prophylactic antibiotic until radiologic evaluation of the urinary tract.

ADMISSION CRITERIA
Ill or septic appearing child
Dehydration
Inability to tolerate oral liquids
Compliance concerns / social reasons
Oral treatment failure at 48 hours
Clinical deterioration

FOLLOW-UP

Children should follow up with their primary care provider within 24-48 hours. If still febrile or no clinical improvement at 48 hours, the child needs to be re-evaluated with repeat urine culture, urgent renal ultrasound to look for hydronephrosis/obstruction, and admission for parenteral antibiotics.

RADIOGRAPHIC EVALUATION OF FIRST FEBRILE UTI

The AAP recommends that all children < 2 years of age undergo radiographic evaluation for abnormality of their urinary tract following the first episode of UTI. This is routinely accomplished with renal ultrasound to detect hydronephrosis and a voiding cystourethrogram (VCUG) to evaluate for vesico-ureteral reflux (VUR). Approximately 50% of children < 1 year of age with UTI have VUR. Children with VUR $\geq$ grade 3 have 4-6 times higher risk of renal scarring than those with VUR $\leq$ grade 2 and 8-10 times higher than those without VUR.

Diagnosis and Management of the Febrile Infant and Child at Risk for UTI