What are appropriate methods of urine collection in UTI?

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The World Health Organization has produced guidelines for the management of common illnesses in hospitals with limited resources. This series reviews the scientific evidence behind WHO's recommendations. The WHO guidelines, and more reviews are available at: http://www.who.int/child-adolescent-health/publications/CHILD_HEALTH/PB.htm

This review addresses the question: *What are appropriate methods of urine collection in UTI?*

The **WHO pocketbook of Hospital Care for Children**, in chapter 6.8 on p164, recommends that if possible, obtain a "clean-catch" urine sample for culture. In sick infants, supra-pubic aspiration may be required.

Introduction:

Urinary tract infection (UTI) is a common cause of fever in children <2 years of age. The prevalence of UTI is approximately 5% among febrile children in this age group[i], and may be as high as 9% in tropical regions[ii]. Invasive methods of urine collection are occasionally required to obtain urine samples from infants unable to void on command. Improper urine specimen collection can lead to contamination, and a clinical dilemma regarding which infants and children to treat, and how extensively to investigate them for suspected UTI. Under-resourced hospitals and clinics face the additional challenges related to limited means and expertise to adequately collect and process urine samples.

Methods currently available for urine collection, from most to least invasive, are: supra-pubic aspiration (SPA), catheter-specimen urine (CSU), bag-specimen urine (BSU), and clean-catch urine (CCU) or mid-stream urine (MSU). MSU was defined as a urine sample obtained from a child able to void on command, whereas a clean catch sample was defined as a urine sample obtained from a child unable to void on command. SPA is considered the "gold standard" method of urine collection.

The clinical dilemma when deciding which urine collection method to use in patients with suspected UTI involves using the least invasive method achievable using local means and expertise while minimising the risk of sample contamination.

Diagnosis of UTI in this review was based on positive urine culture as outlined in current AAP Subcommittee on UTI Clinical Practice Parameters[3]. Contaminated samples were defined as: growth of non-pathogenic organisms (Lactobacillus species, Coagulase-negative Staphylococcus, Corynebacterium species), growth of 2 or more organisms, and positive urine culture where a simultaneous "gold standard" specimen had no growth. Intermediate growth was defined as growth of a single pathogenic organism of insufficient quantity to be diagnostic of UTI. Sterile samples were defined as those with no growth.

Methodology

The Cochrane Database of Systematic Reviews, PubMed, and Medline were searched for original validation studies comparing rates of urine contamination in children when collected by CSU, BSU, or MSU. Only articles using SPA as a “gold standard” were included.

The Cochrane Database of Systematic Reviews was searched using the terms “urinary tract infection” AND “diagnosis” and “child”. Of the three articles identified, all were excluded.

PubMed Clinical Queries was searched through the “diagnosis” filter using the search terms (urinary tract infection OR UTI OR urine) AND (suprapubic OR catheter OR bag OR clean-catch OR mid-stream) and limited to children aged 0-18 and English language. Of 125 articles identified, 5 met inclusion criteria[3-6, 8].

Medline was searched using the terms “Urinary Tract Infections/di, ur” AND “(suprapubic OR catheter OR mid-stream OR clean-catch” AND “child/”. Of 32 articles identified, 1 additional article met inclusion criteria[7].

Results

Suprapubic aspirate

Studies validating SPA as the “gold standard” method of urine collection are limited. Pryles et al. performed SPA on 42 well children of both sexes, aged 3months to 10 years, undergoing elective surgery[iii]. Two positive samples were obtained, each demonstrating low level growth ($<10^3$CFU/ml) of gram positive bacteria (*Staphylococcus albus*) which were thought to be contaminants. Neither of these contaminated samples met AAP criteria for diagnosis of UTI. From this data, urine obtained by SPA has a rate of intermediate growth of 4.7% and a specificity of 100% in excluding UTI. No sensitivity for SPA in diagnosing UTI could be calculated from this study as it was performed in well children in whom no UTI was suspected.

Catheter specimen urine

Pryles et al. in the same study compared CSU with SPA urine specimens. No CSU samples grew sufficient bacteria to be diagnostic of UTI. However, 40.5% of samples obtained from the initial stream of urine had intermediate growth, compared with 19.5% of samples obtained from the latter stream. Using the AAP criteria for diagnosis if UTI (growth of $>10^5$CFU/ml of CSU urine), the specificity of CSU for excluding UTI is 100%. Again, the sensitivity of CSU for detecting UTI could not be determined based on the results of this study as it was conducted in well children in whom UTI was not suspected.

Bag specimen urine

Three papers were identified comparing urine contamination rates of bag specimens with those obtained concomitantly by SPA[iv,v,vi]. Hardy et al. performed SPA on all children admitted to a children’s ward with positive growth on BSU. Of 26 positive BSU samples, 22 (84.6%) were contaminated. A false positive rate of 50% and a false negative rate of 9% was reported. This corresponds well with a false positive and negative rate of 57% and 10%, respectively, found by Aronson et al.[5]. Sensitivity and specificity could not be calculated from either study as only patients with positive BSU were included; the total number of patients screened with BSU was unknown. Saccharow et al. performed SPA and BSU on a series of 154 children aged 6 months to 12 years attending a renal outpatient clinic for recurrent UTI[4]. The prevalence of UTI in these patients was 8.3%. 45 BSU samples (29%) had intermediate growth. The sensitivity of BSU in this series was 77% and the specificity 68%.

Clean-catch urine

Ramage et al. performed a study comparing CCU and SPA in 49 infants <24months of age in a teaching hospital setting who were suspected of having UTI[8]. The prevalence of UTI in this study was 32%. They demonstrated a sensitivity and specificity of 89% and 95%, respectively. It should be noted that the two false-positive results in this study would have been considered contaminated, and not diagnostic of UTI, using AAP guidelines (heavy mixed growth). This would increase the sensitivity of MSU to 100%. Amir et al. compared CCU and SPA in 60 circumcised males aged less than 21 weeks[vii]. All were having urine cultures taken as part of a septic screen. The prevalence of UTI in the study population was 26%. In 9 infants no SPA sample could be obtained, in the remainder a sensitivity of 97% and specificity of 100% was demonstrated (one sterile SPA sample had intermediate growth on CCU).

Mid-stream urine

One study was identified comparing contamination rates of urine obtained by MSU using SPA as a gold standard[viii,ix]. Morton et al. performed SPA and concomitant MSU in 51 children aged <10 years in an outpatient setting in Nigeria[7]. The prevalence of UTI in the study population was 10%, the proportion of children younger than 2 years of age was unpublished. 90% of MSU samples demonstrated intermediate growth. These were collected by mothers who were instructed but unsupervised in cleaning the external genitalia and collecting specimens. MSU had a sensitivity of 100% and a specificity of 100%, though growth of $>10^5$CFU/ml was used as a cut-off for diagnosing UTI (AAP guidelines suggest using 10^4CFU/ml).

Discussion

SPA is considered the “gold standard” method of urine collection; the least likely to be contaminated (level 1b evidence, Oxford grading system). SPA samples have less than a 5% chance of having intermediate growth[3], and using AAP guidelines for interpreting urine culture results, have close to 100% specificity for excluding UTI’s. The major drawbacks of using SPA as a method of urine collection include the invasiveness of the test, and possible failure to obtain a sample using this technique. Success rates for obtaining SPA samples range from 25-98%, though many of these studies included children greater than 2 years of age who would no longer be considered for SPA and in whom a higher failure rate might be expected[2,5]. Increased success has been reported using bladder ultrasound and waiting 60 minutes after an infants last void prior to attempting SPA[x,13]. The invasiveness of SPA may be of concern to parents, though few adverse sequelae have been reported following this procedure. Transient microscopic haematuria is the most common complication of SPA, and is of no clinical significance[xi]. Macroscopic haematuria and bowel perforation have been reported, with an incidence of 0.5-2.0% and o.2% respectively[4,7,12]. One case of macroscopic haematuria has been reported as requiring blood transfusion, no sequelae following bowel puncture have been reported [7,10,xii]. Lack of local expertise with collection of urine by SPA may limit it’s use in some circumstances, though guidelines on SPA technique have been published[xiii].

CSU samples have a negligible false positive rate when growth of $>10^5$ CFU/ml is used as a cut-off point for diagnosing UTI (level 1b evidence). The specificity of CSU in excluding UTI thus approaches 100%. Sensitivity of CSU has been reported as 95%, though this has not been validated[xiv]. Higher rates of intermediate growth in CSU samples occur if the initial few mL of urine are not discarded, though not to such a degree as to falsely diagnose UTI on culture[2]. The success rate when using CSU as a means of urine collection approaches 100%[xv]. Potential complications of CSU include microscopic haematuria, catheter-induced UTI, and urethral stricture formation. Transient microscopic haematuria has been reported in 17% of infants having in-out catheterisation[xvi]. The risk of iatrogenic UTI and stricture formation has yet to be quantified, but is thought to be negligible[2,3].

BSU samples have a high rate of contamination (level of evidence 1a). They have a high false-positive rate (50-57%), and a substantial false-negative rate (9%)[6].

Sensitivity and specificity have been reported as 77% and 68%, respectively[5].

CCU as a means of collecting urine in infants has a sensitivity of 90-97% and a specificity approaching 100% in diagnosing UTI (level 1b evidence). CCU can be collected by parents in young children who are not sufficiently unwell to require immediate administration of antibiotics. This method of obtaining urine samples is preferred by parents, and is one which they can easily be taught to perform[xvii]. Close to 100% success rates for obtaining MSU samples within 5 minutes of a feed in infants has been described by Boehm et al. using the Perez reflex[xviii]. This involves holding the infant prone over a sterile urine container and gently stroking the back.

MSU samples have both a sensitivity and specificity approaching 100% in diagnosing UTI on culture (level 1b evidence). MSU samples demonstrate high levels of intermediate growth, which can be reduced by parental supervision during collection[9]. MSU samples can easily be collected in children able to void on command.

Summary

SPA and CSU are rapid and accurate methods of obtaining urine samples from infants who are unable to void on command. Lack of expertise and parental concerns regarding complications from these relatively invasive methods may limit their use. They should, however, be considered in all infants unwell enough to require immediate antibiotic treatment (Grade A recommendation). In older children and infants who do not require immediate antibiotic treatment, CCU or MSU are the methods of choice for obtaining a urine sample (Grade A recommendation). Care should be taken to obtain a true mid-stream sample to increase the accuracy of the sample collected in diagnosing UTI. BSU samples cannot be recommended in diagnosing UTI (Grade A recommendation)[20] .

ABBREVIATIONS

CEBM LOE	Centre for Evidence-Based Medicine Levels of Evidence
MIC	Minimum Inhibitory Concentration
RCT	Randomised Controlled Trial
SR	Systematic Review
WHO	World Health Organisation

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