

Urine sampling and culture in the diagnosis of urinary tract infection

Urine collected in a normal individual by suprapubic aspiration of the bladder is sterile and does not contain leukocytes. This method represents the gold standard in the diagnosis of urinary tract infection (UTI) [1]. It is, however, not performed routinely in the clinical setting in which urine samples are generally obtained after natural micturition; in this setting, some degree of artifactual contamination with normal urethral organisms must be accepted.

In general, patients with symptoms suggestive of a UTI (dysuria and frequency) should have a clean-catch specimen sent for culture and for urinalysis. One suggested exception is a symptomatic young woman with pyuria (detected by urinalysis or dipstick) who has apparently uncomplicated cystitis. It has been proposed that this constellation of findings is sufficiently diagnostic that an empiric single-dose or three day course antimicrobial therapy can be initiated without performing a urine culture unless the patient does not respond. Some experts do not recommend this regimen, since a significant minority of such women will be infected with *Proteus* or *Staphylococcus saprophyticus*, organisms that may not respond to antimicrobial therapy directed against presumed *Escherichia coli*. (See "Overview of acute cystitis-I").

URINE SAMPLING – The likelihood of detecting a UTI by urine culture is highest if urine is collected on arising. This sample is likely to be most concentrated and bacteria in the bladder will have had time to multiply overnight. However, this ideal sample is not practical since most cultures are obtained at the time the patient is seeing the physician. In this setting, the combination of a more dilute urine and partial bacterial washout due to multiple voids may lower the colony count below the accepted definition for a UTI (see below).

Adults – The following steps should be performed to minimize the degree of bacterial contamination.

Local disinfection of the meatus and adjacent mucosa should be performed with a nonfoaming antiseptic solution; this region should then be dried with a sterile swab to avoid mixture of the antiseptic with urine.

Contact of the urinary stream with the mucosa should be minimized by spreading the labiae in females and by pulling back the foreskin in uncircumcised males.

The first voided specimen should be discarded since the initial urine flushes urethral contaminants. It is the second, midstream sample that should be sent to the laboratory.

Evaluation of the last few drops of urine is indicated after prostatic massage in men with suspected prostatitis. Firm prostatic massage per rectum, from lateral to midline on each side, causes the contents of the prostatic ducts to be expressed; vertical strokes in the midline will then project the secretions into the urethra and permit counting of leukocytes. (See "Prostatitis syndromes")

The urine sample should be sent immediately to the bacteriology laboratory since bacteria will continue to proliferate in the warm medium of freshly voided urine, leading to increased bacterial counts. (See "Microbiology specimen collection and transport"). If such immediate referral is not possible, the container should be transported in iced water and then stored in a refrigerator at 4°C. Cooling stops bacterial growth, but the following day the bacteria can still grow on culture medium. However, urinary leukocytes may be altered by refrigeration, possibly affecting interpretation of the urinalysis.

Considerations in children – Urine sampling is difficult to achieve and interpret in infants and young children. Collecting bags can be used, but contamination is almost inevitable [2–4]. As a result, suprapubic bladder aspiration or transurethral bladder catheterization should be performed when the physician in charge deems it

necessary to have reliable bacteriologic results [3,5,6]. This procedure should only be considered in a specialized pediatric setting. (See "Urine sampling techniques in children")

DEFINITION OF A POSITIVE CULTURE – Comparison of midstream voided specimens with urine obtained by suprapubic bladder aspiration or bladder catheterization has yielded the following results. If the above precautions are taken, normal values in a noninfected midstream, clean-catch sample are $<10(5)$ colony-forming units (CFU, primarily due to contaminating *Escherichia coli*) and $<10,000$ leukocytes per mL of urine [7–12]. Thus, the standard definition of a positive urine culture is $\geq 10(5)$ CFU/mL.

However, this definition does not apply to all patients. If fecal contamination has been ruled out, a lower colony count ($>10(2)$ /mL) may be indicative of urinary tract infection. This was best demonstrated in studies in women who had dysuria and frequency but a midstream culture contained less $10(5)$ CFU/mL [1,13,14]. This condition had been called the acute urethral syndrome [1]. In one study, for example, 42 such women (most of whom had $\geq 10(2)$ CFU/mL on culture of a midstream specimen) who also had pyuria underwent suprapubic bladder aspiration. Thirty seven had a positive aspirate culture: 24 *E. coli*, 3 *Staphylococcus saprophyticus*, and 10 *Chlamydia* [1]. All of these women responded to appropriate antimicrobial therapy. In comparison, a positive culture was very uncommon in women with similar symptoms but no pyuria.

Similar findings have been reported by others. In a Gynecology clinic at a student health center, for example, 33 percent of women with urinary tract symptoms had $\geq 10(5)$ CFU/mL while another 46 percent had CFU counts between $10(2)$ and $10(4)$ /mL [15]. When asymptomatic patients were included, there was a stepwise relation between the colony count and the likelihood of symptoms.

On the basis of these findings, it has been suggested that a CFU count $\geq 10(2)$ /mL be considered positive on a midstream urine specimen in women with acute symptoms and pyuria. It has been estimated that 88 percent of such women have a UTI [13]. If symptoms persist and the standard bacterial culture is negative, a pelvic examination should be performed with culture of a cervical swab for *Chlamydia*.

It is not well understood why some infected women have low colony counts. Two possibilities are that low counts reflect an earlier stage of infection and that low counts reflect the efficacy of bladder washout during urination to eliminate the organisms.

There are also several other settings in which a colony count of $< \geq 10(5)$ /mL often represents true infection rather than contamination:

In patients already being treated with antimicrobials.

In men in whom contamination is a much lesser problem.

When organisms other than *E. coli* and *Proteus* are present. Included in this group are *Pseudomonas*, *Klebsiella-Enterobacter-Serratia*, and *Moraxella* species, particularly in symptomatic patients with an indwelling bladder catheter. (See "Urinary tract infection associated with indwelling bladder catheters").

DEFINITION OF PYURIA – Given the very high association between infection and pyuria, a careful examination of the urine sediment is indicated in all patients with suspected UTI. However, assessment of pyuria is subject to some technical pitfalls [14]. Two important variables are contamination with vaginal secretions in women and the volume of supernatant in which the centrifuged pellet is resuspended, which will affect the leukocyte count. Stamm has defined pyuria as the presence of at least eight thousand leukocytes per mL of uncentrifuged urine, which corresponds to two to five leukocytes per high-power field in a centrifuged sediment [1]. Others have defined pyuria as $>20,000$ leukocytes/mL (by hemocytometry) in women with low count bacteriuria.

These observations indicate that the customary determination of leukocyte counts per high-power field is not sufficiently accurate and that the use of white cell counting is preferred in the diagnosis of UTI. A significant number of leukocytes ($>10/\mu\text{L}$ or $10,000/\text{mL}$) should be presented in truly infected patients. The presence of bacteria in the absence of pyuria, especially when various strains are found, is usually due to contamination during sampling.

Sterile pyuria – Whereas true infection without pyuria is unusual, pyuria can occur in the absence of apparent bacterial infection, particularly in patients who have already taken antimicrobials (often due to self-medication). Patients with dysuria and frequency should be tested for atypical organisms such as Chlamydia, Ureaplasma urealyticum, or tuberculosis [1,16]. (See "Renal disease in tuberculosis"). Other causes of sterile pyuria include:

Contamination of the urine sample by sterilizing solution

Contamination of the urine sample with vaginal leukocytes

Chronic interstitial nephritis (such as analgesic abuse nephropathy)

Uroepithelial tumor

Nephrolithiasis

DIPSTICK DIAGNOSIS OF URINARY TRACT INFECTION – Dipsticks are commercially available that detect the presence of leukocyte esterase and nitrite; the former corresponding to significant pyuria and the latter to enterobacteriaceae which convert urinary nitrate to nitrite [17,18]. The dipstick has a sensitivity of 95 percent and a specificity of 75 percent [19]. The positive predictive value is 30 to 40 percent (when tested in patients suspected of possible UTI) and the negative predictive value is 99 percent.

We recommend use of the dipstick for rapid and easy screening for UTI, even when laboratory facilities are available. There are very few false negative results; as a result, a negative dipstick test is usually sufficient to exclude true infection unless the symptoms are very suggestive. On the other hand, a positive test should always be followed by urinalysis in the bacteriology laboratory in order to carry out antibiotic sensitivity tests.