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Detection of Urinary Tract Infections by Rapid Methods

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INTRODUCTION

Infections of the urinary tract are second in frequency only to upper respiratory infections. However, the requests for detection of bacteriuria far exceed those for detection of respiratory pathogens. Most upper respiratory infections are only mildly symptomatic and have a viral etiology; therefore, medical intervention is not necessary. In contrast, urinary tract infections are usually caused by bacteria and require antimicrobial therapy for elimination of the infecting organisms. The infections may be symptomatic or asymptomatic, and either type of infection may cause serious sequelae if untreated. The infections range from a single acute symptomatic infection, with a susceptible organism such as *Escherichia coli* which may develop a spontaneous cure, to a more serious recurring infection such as chronic pyelonephritis which may be caused by resistant, and often difficult to treat, organisms.

EPIDEMIOLOGY OF URINARY TRACT INFECTION

All individuals are susceptible to urinary tract infections; however, the prevalence of infection differs with age, sex, and certain predisposing factors. Numerous urinary tract infection studies have been performed on different age groups including preschool, school age, young adults, and the elderly (1, 9, 17, 34, 42, 100). The studies show that infections occur as early as the first few days of life and can be contracted throughout life. The incidence of infection peaks at certain times during life and is associated with both age and sex. Throughout life, the incidence of infection is greater in females than in males with two exceptions, infants and catheter-related infections (Table 1). The ratio of infant male to female infection is 4:1, this changes to 1:15 to 1:>30 during adult life and finally decreases to 1:2 in the elderly population.

The first urinary tract infection peak occurs during the first few months of life, at which time bacteriuria is more common in males than in females. Also the incidence is higher in premature infants than in full-term babies. For this reason, a septic or febrile infant who fails to thrive should be screened for a possible urinary tract infection.

Symptomatic urinary tract infections in preschool children are not uncommon, and these infections are seen more frequently in girls than boys, a ratio of approximately 15:1 (42). This ratio increases to 30:1 among school age children. Approximately 5% of all girls will have at least one episode of urinary tract infection prior to completion of high school (42).

The prevalence of bacteriuria in nonpregnant females is approximately 1 to 3% and increases to 10 to 20% among elderly women (36). Interviews of women between the ages of 20 and 40 years have revealed that as many as 25 to 35% have had urinary tract infections (42). Approximately 25 to 40% of these individuals develop a spontaneous cure; however, as many as 50% may become reinfected within 1 year (36). The association between sexual intercourse and subsequent urinary tract infection contributes to the increased incidence of infection as well as to recurrence in young adult women (9).

The incidence of bacteriuria during pregnancy ranges from 2 to 5% and, if present, can result in serious infection of both the mother and the fetus. Undetected asymptomatic bacteriuria is of great concern because, if left untreated, it can lead to acute infection and symptomatic pyelonephritis, which usually occurs during the third trimester (35). Women who have had urinary tract infections as children have a much higher incidence of infection during pregnancy, as much as 26 times the attack rate of pyelonephritis (17). They deliver 1.7 times the number of low-birth-weight infants who

TABLE 1. Distribution of urinary tract infections by age and sex

Age group or condition	Male/female ratio
Newborns	4:1
Preschool	1:15
School age	1:30
Young adults	1:>30
Elderly	1:2
Catheter associated	1:1

are at 1.6 times greater risk of perinatal death (76). Pyelonephritis during pregnancy is the most frequent cause of hospitalization during this period and is associated with increased perinatal mortality, more frequent premature deliveries, and deficient development of the infant (35).

After infancy, bacteriuria in males is uncommon before the age of 50 years. Prostatic obstruction and instrumentation become the major causes of infection among middle-aged and older men (47). Inability to empty the bladder completely and seeding of the urinary stream with organisms from the prostate cause persistent or recurrent infection. Although sexual intercourse does not seem to be a common predisposing factor for urinary tract infection in men, an association has been made (98).

Bacteriuria in the elderly population occurs frequently in both men and women. The prevalence of infection in the elderly population ranges from 5 to 20% in men to 10 to 20% in women (100). Elderly patients with obstruction, poor bladder emptying, dementia, stroke, diabetes mellitus, and cardiovascular diseases are more likely to have bacteriuria than patients in the same age group without these abnormalities (100).

The risk of acquiring a urinary tract infection associated with catheterization ranges from 1 to 5% after a single brief catheterization to 100% in patients with an indwelling urethral catheter draining into an open system for longer than 4 days (34, 91). Use of a closed system decreases the incidence to 20% (21). Males and females are equally susceptible to these catheter-associated infections.

Certain diseases of the urinary tract also increase the incidence of infection. Acute pyelonephritis, a symptomatic infection of the upper urinary tract, is usually seen in women of childbearing age and in the elderly and may be associated with more serious diseases such as septicemia, shock, toxemias of pregnancy, diabetes mellitus, pregnancy, hypertension, and stone formation (35). The frequency of pyelonephritis increases with age and multiple births and is associated with urinary tract instrumentation and catheterization. The incidence of pyelonephritis is not known; however, the disease has been demonstrated in 10 to 20% of autopsied persons (51).

Symptomatic infections of the lower urinary tract involve the bladder (cystitis), urethra (urethritis), and prostate (prostatitis). Infections of the bladder usually contain $\geq 10^5$ colony-forming units (CFU)/ml, although as few as 10^2 CFU/ml have been isolated from young women with acute dysuria and lower urinary tract infection (83, 84).

Dysuria and frequency may be associated with infection of the urethra only; however, routine cultures may be "negative." These infections have been termed the acute urethral syndrome (20). Included in this group of patients with symptomatic lower tract infections are those that have no recognizable pathogen, but have acute dysuria and pyuria (dysuria-pyuria syndrome) (39). It is important for the physician to distinguish between urethritis and vaginitis, because in the case of vaginitis urine cultures are unnecessary. Patients with vaginitis have external dysuria compared with the internal dysuria and frequency experienced with urethritis. On the other hand, it is not necessary to distinguish between cystitis and the urethral syndrome. Patients with the acute urethral syndrome have been divided into four groups; those with $\geq 10^5$ CFU/ml, those with $<10^5$ CFU/ml, those with chlamydial infection or other microbial agents causing urethritis, and those with no recognized pathogen (84).

Asymptomatic (covert) bacteriuria refers to the presence of significant bacteriuria ($\geq 10^5$ CFU/ml) in the absence of symptoms (34). The prevalence varies depending on the patient population studied. It cannot be considered an infection unless there are invasion and an inflammatory response represented by the presence of pyuria (42). Although asymptomatic infections may occur in all ages, they pose a serious threat during pregnancy and to the elderly. Screening of these groups may help prevent the increased morbidity and mortality associated with undetected and untreated infections.

SIGNIFICANT BACTERIURIA AND PYURIA

The presence of microorganisms alone in a urine specimen does not establish significance because bacteriuria can occur from colonization and contamination as well as infection. Often accompanied by significant bacteriuria is the presence of pyuria resulting from invasion of the urinary tract by the infecting microorganisms. Measurement of pyuria is the most readily available means of establishing the presence of host injury, thus differentiating colonization from infection (82). The criterion of a single organism at a concentration of $\geq 10^5$ CFU/ml in a voided urine specimen is the generally accepted definition of significant bacteriuria. However, it is important to note that this definition was established to distinguish contaminated specimens from true bacteriuria in asymptomatic patients and women with acute pyelonephritis (34). A majority of these patients, as well as those with acute cystitis, usually have $\geq 10^5$ CFU/ml in their urine specimens; however, only 56% of patients with the acute urethal syndrome fall into this category (84). For this reason, Stamm and associates attempted to establish a new definition of significant bacteriuria for this group of patients (83, 84).

Urine specimens from 59 young adult women with the acute urethral syndrome were collected by suprapubic aspiration, urethral catheterization, and midstream voiding (84). Approximately one-half of these cultures contained $<10^5$ CFU of gram-negative bacilli per ml and ≥ 8 leukocytes (WBC) per mm^3. In a subsequent study of 187 women with acute urinary symptoms, only 51% of infected patients were identified when 10^5 CFU/ml was used as the interpretive breakpoint; this increased to 95% when the breakpoint was dropped to 10^2 CFU/ml (83). Also, approximately 50% of these patients with coliform bladder infections had more than one organism in their midstream urine. Therefore, the criteria of 10^5 CFU/ml and a single organism could not be applied to this patient group.

However, the presence of pyuria together with $\geq 10^2$ coliforms per ml was a better predictor of bladder infection than either $\geq 10^5$ or $\geq 10^2$ CFU/ml without pyuria (83). Pyuria without bacteriuria raised suspicion that other more fastidious organisms which fail to grow on routine urine culture media might be the causative agents of infection. Significant pyuria has also been associated with pyelonephritis, prostatitis, and a number of noninfectious urinary tract disorders, including tumors and calculi.

Low-count bacteriuria and pyuria have been reported in females of all ages. Latham et al. studied 387 women ranging in age from 1 to 95 years old (44). Of these, 74 (19%) cultures were considered diagnostic of urinary tract infection, using the criteria of 10^5 CFU/ml alone or 10^2 CFU/ml plus symptoms. Using 10^5 CFU/ml as the definition of significant bacteriuria, they identified only 68% of the patients with infection; however, with 10^2 CFU/ml as the breakpoint, 100% were identified. In this study, only 73% of infected specimens and 20% of specimens without bacteriuria were found to have pyuria. Although the proportion of infected specimens with pyuria is lower than that reported by Stamm et al., collection, transport, and processing occurred in a routine laboratory setting rather than in a research setting.

Lipsky et al. also found that low-count bacteriuria better differentiated infected from noninfected urine of men (46). In their study, specimens of bladder urine were collected by suprapubic aspiration (10 ml) and urethral catheterization (10 ml). Collection of voided urine included an uncleansed first void (the first 10 ml voided without prior cleansing of the urethral meatus) and clean-catch midstream void (10 ml voided after cleansing the urethral meatus with povidone-iodine and voiding approximately 100 ml). Culture results of bladder specimens showed excellent agreement with voided specimens. The criterion which best differentiated sterile from infected bladder urine was a colony count of $\geq 10^3$ CFU/ml in this patient population; this definition had a sensitivity of 97%. Additional studies have shown that as few as 10^2 CFU/ml can reliably predict catheter-associated urinary tract infections (85; M. K. York and G. F. Brooks, Clin. Microbiol. Newsl. **9**:76–78, 1987).

Because bacteriuria can occur as a result of infection, colonization, or contamination, pyuria plays a major role in distinguishing between infected and noninfected patients. Bacteriuria occurs in noninfected patients as colonization or contamination. The term colonization usually applies to the transient occurrence of bacteriuria lasting 1 to many days followed by spontaneous resolution, and it is not associated with pyuria (82). Measurement of pyuria and its relation to bacteriuria and symptoms of urinary tract infection are most important in differentiating colonization from infection.

Contamination occurs when organisms from the external genitalia, urethra, or periurethral skin enter the specimen during collection. Contaminants include diphtheroids, lactobacilli, coagulase-negative staphylococci, and viridans streptococci (55). The presence of these organisms in urine is usually not significant. Also, the presence of any organism, at colony counts of $<10^5$ CFU/ml, from midstream voided urines of asymptomatic patients and women with acute pyelonephritis may represent contamination. The presence of squamous epithelial cells, but no WBC, will confirm contamination. However, similar bacterial findings on repeat culture of suprapubic bladder aspirates suggest infection.

These studies suggest that the microbiology laboratory must carefully consider the patient population served when determining the best diagnostic approach. The efforts to lower the criterion for significant bacteriuria refer primarily to women with the urethritis syndrome. These patients are symptomatic and a majority have pyuria. It would not be practical or cost-effective for the laboratory to consider bacterial counts of $\geq 10^2$ CFU/ml significant findings for all patients. Furthermore, low bacterial counts in an unselected patient population may represent contamination. Low bacterial counts may also be due to early infection, dilute urine due to forced fluids, rapid urine flow, low pH (<5), and the presence of antimicrobial agents. Results may be more meaningful if the culture is repeated when initial results are questionable or suggest a possible infection.

TABLE 2. Distribution of urinary isolates at University of California Irvine Medical Center, July 1985 to June 1987

Organisms	No. isolated (%)	
	July 1985–June 1986	July 1986–June 1987
Escherichia coli	1,305 (52.5)	1,398 (50.3)
Enterococci	217 (8.7)	281 (10.1)
Klebsiella spp.	203 (8.2)	260 (9.4)
Pseudomonas aeruginosa	141 (5.7)	141 (5.1)
Candida spp.	124 (5.0)	157 (5.3)
Proteus mirabilis	110 (4.4)	93 (3.3)
Enterobacter spp.	75 (3.0)	100 (3.6)
Group B streptococci	59 (2.4)	70 (2.5)
Citrobacter spp.	29 (1.2)	52 (1.9)
Staphylococcus aureus	34 (1.4)	27 (1.0)
Staphylococcus saprophyticus	28 (1.1)	34 (1.2)
Other	159 (6.4)	175 (6.3)

ETIOLOGY OF INFECTION

Bacteria are by far the most frequent cause of urinary tract infections, and aerobic gram-negative bacilli predominate (13). Although the majority of bacteria causing infections among all patient populations are gram-negative bacilli, gram-positive cocci contribute to large numbers of infections among hospitalized and institutionalized patients. Table 2 lists the prevalent bacterial pathogens isolated from urine specimens at the University of California Irvine Medical Center, an acute-care teaching hospital. These specimens were collected from hospitalized patients and outpatients for a period of 2 years. As expected, *E. coli* was the most common isolate. Enterococci, *Pseudomonas aeruginosa*, and *Candida* spp. were present most often in catheter-associated cystitis. Enterococci, common agents of nosocomial infections of the urinary tract, were isolated more frequently in men and have been associated with renal transplant rejection (10). *Proteus mirabilis* was also isolated more frequently in males at this institution, and similar findings have been reported by others (45, 46). *Streptococcus agalactiae* (group B streptococci), an uncommon cause of urinary tract infection, may account for 5% of infections in pregnant females (99). It represented approximately 2.5% of all isolates at the Irvine Medical Center, which serves a large prenatal clinic. Group B streptococcal infection in the mother predisposes the newborn infant to infection with the same organisms. In recent years, neonatal infections with group B streptococci have become more common than *E. coli* infections (63).

The significance of urinary tract infection with staphylococci has been recognized in recent years. Although *Staphylococcus aureus* has been considered pathogenic, coagulase-negative staphylococci were often interpreted as genital or skin contaminants or colonizers. The incidence of infections in the urinary tract with the latter organisms is increasing, and their pathogenicity has been recognized (3). Patients at risk include males undergoing urologic procedures, those with underlying urinary tract pathology, and catheterized patients (80). During catheterization, the bladder becomes colonized, and if predisposing factors are present, infection with coagulase-negative staphylococci may occur. *Staphylococcus aureus* is not a common nosocomial pathogen; however, there is an increased incidence of infection with

this organism in association with urinary tract obstruction, neoplasm, and manipulation (18). Prior to antimicrobial therapy, *Staphylococcus aureus* was the leading cause of hematogenous infection of the kidney and perinephric abscesses. *Staphylococcus saprophyticus* is now recognized as a urinary tract pathogen, especially in young adult women (3, 93). The incidence of urinary tract infection with this organism may be as high as 30% in women between the ages of 16 and 25 years. There appears to be a seasonal association, with peaks in late summer and early fall. Anaerobes play a very minor role in urinary tract infection. The incidence of anaerobic bacteriuria has been reported to be 1.3% in patients with significant bacteriuria (79).

A negative culture or rapid screen does not exclude a urinary tract infection. Although uncommon, organisms such as *Chlamydia trachomatis*, *Mycoplasma hominis*, *Ureaplasma urealyticum*, *Mycobacterium* spp., *Haemophilus influenzae*, *Campylobacter* spp., *Legionella pneumophila*, *Salmonella* spp., *Shigella* spp., and *Gardnerella vaginalis* have been associated with urinary tract infection (42). *C. trachomatis* is the second most common infectious agent associated with the urethral syndrome in young adult women and has been established as a cause of nongonococcal urethritis in men (8, 84). This organism has also been isolated in a majority of patients with chronic prostatitis as well as from women with cystourethritis (6). *M. hominis* has been associated with pyelonephritis, and *U. urealyticum* has been associated with chronic prostatitis (8, 87). Although fungi are not common causes of urinary tract infections, they are associated with catheterization, pyelonephritis, and infections in symptomatic female patients (41). Funguria is usually caused by *Candida albicans*, *Torulopsis (Candida) glabrata*, and *Candida parapsilosis*.

Viruses and parasites are usually not considered urinary tract pathogens; however, cytomegalovirus and herpes simplex virus type 2 have been isolated from patients with the acute urethral syndrome in the absence of both WBC and bacteria. Cytomegalovirus may be shed in the urine of young females (<14 years old); however, this shedding stops by age 30 (40). The shedding of herpes simplex virus type 2 in women seems to increase with age.

Viruses also play a major role in the pathogenesis of hemorrhagic cystitis. These include varicella and herpes zoster virus, herpes simplex virus type 2, and adenovirus (42). Adenovirus types 11 and 21 have been associated with acute hemorrhagic cystitis in children, a self-limited benign disease (42). *Trichomonas vaginalis*, a protozoan associated with sexual transmission, has also been isolated from the urinary tract and has been indicated as a cause of nongonococcal urethritis (14, 28).

The etiology of the infection and the significance of pyuria must be considered when selecting a rapid urine screen. Many of the available screens do not detect fastidious organisms or pyuria. The advantages and limitations of these tests are discussed in a following section.

COLLECTION AND TRANSPORT

A microbiology examination is usually performed on urine specimens from patients with symptoms of urgency, frequency, or dysuria; on asymptomatic patients in a high-risk group (e.g., pregnancy), as a follow-up to antimicrobial therapy; on septic patients; and to monitor patients with urinary catheters. Proper collection and transportation are essential to ensure accurate results. Collection instructions should be provided to the patient, especially the female patient. For males, it has been reported that cleansing of the genital area may not significantly improve the detection of bacteriuria and may not be necessary (45). Collection instructions for all urine specimen types have been clearly outlined, and these guidelines should be practiced for hospital, physician office, or home collection (13, 42). A first voided morning specimen is preferred whenever possible to allow for growth of optimal numbers of organisms per milliliter of urine. Alternatively, urine should be allowed to remain in the bladder for as long as possible to allow multiplication of microorganisms for accurate test results. Testing of dilute urine may result in false-negative findings, especially with some of the rapid screens.

Microorganisms multiply rapidly in urine; therefore, specimen processing should be performed soon after collection. Since this is not always possible or practical, refrigeration is an acceptable alternative. For specimens collected offsite, refrigeration is not always a practical alternative. Use of a urine transport kit containing a preservative has been suggested to eliminate the need for refrigeration. Studies have shown that use of a preservative may have an inhibitory effect on some microorganisms, especially *E. coli*, and therefore jeopardize the urine screening method (24, 68, 77). However, the preservative boric acid-glycerol-sodium formate may be less inhibiting in a lyophilized form (95). To avoid an inhibitory effect, at least 3 ml of urine must be placed in the transport tube. For optimal results, urine should be processed within 24 h whether refrigerated or transported with a preservative (45). If urine is transported in a tube containing a preservative, the effect on test results must be considered.

LABORATORY ANALYSES

During the last decade, the literature has been filled with reports evaluating rapid urine screens. Manufacturers continue to introduce new test methods and systems, each more rapid and simple than before. The purpose of rapid bacteriuria screening is twofold: (i) to provide accurate information to the physician in a timely manner, which in turn leads to prompt care of the patients; and (ii) to eliminate negative specimens rapidly, allowing the microbiologist to spend more time on positive specimens which in turn leads to improved efficiency and cost-effectiveness.

Rapid bacteriuria screens include a variety of methodologies that use microscopic, enzymatic, filtration, and automated procedures. These methods have been evaluated extensively, and most compare favorably when a culture method with $\geq 10^5$ CFU/ml is used as a reference. However, a comparison with lower colony counts provides less favorable results. It has been established that pyuria is also an important finding when evaluating urinary tract infections; however, many of the rapid screens lack the ability to detect WBC in urine. Lastly, cost is an important consideration. Initially, rapid bacteriuria screens were approximately one-third the cost of a culture method, and each provided an overall cost savings when only specimens with positive screens were plated (69). However, these screens required 1 to 13 h for detection of a positive specimen. More rapid screens for detection of urinary tract infection provide results within minutes, but are more expensive overall, due to higher reagent or consumable costs or both and increased "false-positive" rates. These rapid screens are reviewed with respect to methodology, detection time, sensitivity, specificity, and predictive values at various colony counts,

TABLE 3. Comparison of rapid urine screens[a]

Method	Detection time (min)	Sensitivity (%)			Predictive value negative (%)			Detects pyuria	Cost per test ($)[b]	Comment
		10^5 CFU/ml	10^4 CFU/ml	10^3 CFU/ml	10^5 CFU/ml	10^4 CFU/ml	10^3 CFU/ml			
Microscopic										
Gram strain	2	95	90	78	99	94	81	Yes	0.50	Many technical variations
Enzymatic										
Chemstrip LN	2	85		70	95		<90	Yes	0.44	Combination use recommended
RUS[c]	30				97			Yes	2.25	Requires 1 ml of urine
Filtration										
Bac-T-Screen	1	94	85	76	98	86	72	Yes	1.00	Requires instrumentation; requires 1 ml; sensitive for infection
FiltraCheck-UTI	1	95	89	84	97	84	67	Yes	1.25	Nonautomated; easy to batch
Bioluminescence										
Lumac[d]	30	98	>85		99	95		No	2.50	All require instrumentation and incubation step
Monoscreen[d]	10	97	>85		93			No	2.50	
UTIscreen[e]	10	96	86		98	89	72	No	0.97	
Photometry										
Autobac	1–6 h	97	90		99			No	0.53	All require instrumentation and incubation step; computer capabilities
AMS Vitek	4–13 h	96	91		99			No	1.00–3.00[f]	
Avantage	1–5 h	96	87		99			No	0.60	

[a] Data extracted from cited literature (see text).
[b] Includes technical time.
[c] RUS, Rapid-Urine-System; information from the manufacturer.
[d] No longer marketed for diagnostic use.
[e] Formerly Turner.
[f] Includes identification.

detection of pyuria, cost per test, and advantages and limitations of each method (Table 3).

Microscopic Methods

The Gram stain is one of the most rapid, reliable, and inexpensive methods for estimating bacteriuria at $\geq 10^5$ CFU/ml. Kass reported that the presence of one or more organisms per oil immersion field from uncentrifuged urine had a sensitivity of 85% when correlated with a colony count of $\geq 10^5$ CFU/ml (34). Other investigators have reported a sensitivity ranging from 94 to 97% and a negative predictive value of ≥99% (69, 90, 94). It has also been reported as the least expensive bacteriuria screen when compared with automated methods (69). Robbins et al. reported that, if uncentrifuged urine from an asymptomatic patient was negative by microscopy for bacteria and leukocytes, a culture could be eliminated (78). However, because of the decreased sensitivity at $\leq 10^5$ CFU/ml, most investigators have recommended the Gram stain as a screen only for those patients with predictably high colony counts, mainly asymptomatic patients and those with presumed pyelonephritis. Recently, the Gram stain has been reported to be an insensitive screening test for infection (59). Although it detected only 72% of patients with probable infection, 82% of asymptomatic infections were positive by Gram stain. The false-negatives may have been the result of infections with low colony counts.

A Gram-stained smear is accurate at $\geq 10^5$ CFU/ml and inexpensive; however, it is not the routine screening method in most laboratories, although it should be available at the request of the physician. Its decreased sensitivity at colony counts of $<10^5$ CFU/ml may be one reason for its limited use. Another, and perhaps equal, problem, in terms of practicality, is that because there may be very little difference between a positive and a negative urine, the procedure becomes tedious and time-consuming for the individual examining the specimen.

The acridine orange-stained smear has also been evaluated as a rapid microscopic bacteriuria screen (27, 47). Hoff et al. reported a sensitivity and negative predictive value of 98 and 99%, respectively, for cultures with $\geq 10^4$ CFU/ml and suggested that the acridine orange procedure may be a cost-effective method for eliminating the need for culture of urines having $<10^4$ CFU/ml (27). However, Lipsky et al. found no advantage of acridine orange when compared with results from Gram-stained smears (47). They demonstrated that the diagnostic accuracy was maintained when smears were read by either an expert microbiologist or a relatively inexperienced technician.

Lastly, Jenkins et al. reviewed approximately 40 publications relating to urine microscopy for bacteriuria and found a variety of approaches which included examination of stained and unstained, centrifuged and uncentrifuged specimens (31). As a result of their review, they suggested criteria for interpretation of urine microscopy for maximum sensitivity and specificity. They concluded that the least reliable method was examination of uncentrifuged unstained urine. On the other hand, the most sensitive method (98%) for detecting $\geq 10^5$ CFU/ml was the microscopic examination of stained centrifuged urine. However, this procedure is tedious and time-consuming because it requires centrifugation of 10 ml of urine for 5 min, followed by examination of 1 to 2 drops of Gram-stained sediment. Pezzlo et al. reported an 87% sensitivity for examination of stained uncentrifuged specimens when the urines contained $>10^5$ CFU/ml (69). This Gram stain sensitivity increased to 97% when the specimens contained pure pathogens alone.

Although the Gram stain has limitations as a bacteriuria screen and has many technical variations, it should be available for use in selected cases. When positive, it has the advantage of correlating with significant bacteriuria and provides specific information such as Gram stain characteristic and organism morphology which may be used to select initial antimicrobial therapy. It also has the advantage of being the least expensive rapid bacteriuria screen, with an estimated cost of <$0.50 (69).

The most commonly used method for detection of pyuria is the microscopic examination of urinary sediment; however, this method is not reliable unless the procedure is well defined and standardized. The method variables include the volumes of urine centrifuged, suspended, and examined, the speed and time of centrifugation, and observer bias (82). The method lacks precision and does not correlate with the leukocyte excretion rate. On the other hand, the leukocyte excretion rate method is a very tedious and time-consuming procedure and is not a practical test for use in the diagnostic microbiology laboratory.

A simpler and more reliable method of measuring pyuria has been described (7). By this method, WBC per cubic milliliter are determined by examining a fresh uncentrifuged specimen in a hemacytometer chamber. This method correlates with the leukocyte excretion rate and has been used by many investigators to determine the presence of significant pyuria (43, 50, 82–84).

Musher et al. described an even simpler method in which they examined uncentrifuged urine directly on a microscope slide and not in a hemacytometer (60). With this method, the finding of one WBC per low-powered field is equal to 3 WBC/mm^3. They estimated that infected urine contains approximately 30 WBC per low-powered field or 1 to 2 WBC per high-powered field. It is also possible to add a drop of stain to enhance the visualization of cellular elements.

Mabeck reported that a leukocyte excretion rate of ≥400,000 WBC per h correlated well with urinary tract infection; this corresponds to ≥10 WBC per mm^3 (50). Stamm reviewed this study and found that ≥10 WBC per mm^3 differentiated the infected from the noninfected patients; <1% of asymptomatic nonbacteriuric patients had ≥10 WBC per mm^3 compared with 96% of symptomatic men and women with significant bacteriuria (82). However, in a later study, Stamm and associates found that ≥8 WBC per mm^3 was slightly more accurate for detecting abnormal pyuria (84). There is no need for concern about cut-off points, because in actual practice the number of WBC per cubic centimeter may be considerably higher (42). If a microscopic method is used to measure pyuria, the test should be performed with uncentrifuged urine and results should be expressed as WBC per cubic millimeter.

Recently, microscopic examination of urine has been automated. The Yellow IRIS (International Remote Imaging Systems, Inc., Chatsworth, Calif.) incorporates a flow microscope in which an uncentrifuged urine specimen is presented to a video camera. Aliquots of the flowing specimens are taken as stop-motion pictures by the video camera. The resulting pictures are digitized and delivered to the image-processing computer which recognizes the individual particle images by size (2 to 100 μm). These particles are examined under low- and high-powered magnifications. Analysis of a single specimen varies from 1 to 4 min. This instrument recognizes many different cellular elements including bacteria and WBC. One major advantage of this new technology is that the urinalysis procedure is standardized. The cost of the instrumentation is approximately $100,000.

Enzymatic Methods

The most common enzymatic tests for the detection of bacteriuria or pyuria include catalase, glucose oxidase, nitrate reductase (Greiss test), and leukocyte esterase. These tests have been used primarily in the urinalysis section of the laboratory, in the physician's office, at the bedside, and, more recently, in home testing. They have been developed to detect the presence of enzymes resulting from urinary tract infection. The tests are easy to perform, rapid, and inexpensive. However, some of these tests, especially the dipstick method, have low sensitivities (<90%) and, therefore, should not be used alone as a screen for urinary tract infection.

The factors that contribute to these low sensitivities include low concentration of enzyme in the urine specimen, presence of interfering substances, and misinterpretation of borderline results by the observer (30). The limited sensitivity of dipstick testing probably contributes to the large number of erroneous results obtained, especially when tests are performed outside of the diagnostic laboratory.

Catalase test. Many organisms causing urinary tract infection contain the enzyme catalase. A positive reaction occurs when urine is mixed with hydrogen peroxide, causing the release of oxygen. The presence of catalase may be due to bacteria, but also to erythrocytes, WBC, or kidney cells. Therefore, this test is not specific for bacteria; however, the presence of these other cells may also indicate abnormal findings.

Glucose oxidase. Bacteria metabolize glucose normally present in urine (2 to 10 mg/100 ml). Therefore, a positive glucose oxidase test is indicated by the absence of glucose. Bladder incubation time is needed, and a first morning specimen is required for reliable results. High sensitivity of this method results in false-positives; false-negative results occur when the test is performed on urine samples collected from diabetic patients, because the concentration of glucose is much higher than in normal individuals. Bacteria present in the urine of these patients will metabolize some glucose but not enough to give a positive test reaction.

Nitrate reductase (Greiss) test. Urinary nitrite has been used as an indicator of urinary tract infections for many years. Nitrate is reduced to nitrite by the enzyme nitrate reductase, which is present in gram-negative bacilli causing urinary tract infection. Therefore, the test, an enzyme dipstick method, should be an excellent indicator of gram-negative bacteriuria. However, this test has a very poor sensitivity when performed on randomly selected urine specimens (30). James et al. reported sensitivities of 29.2 and 44.9% when testing 790 urine specimens for nitrite reductase, using dipsticks from two manufacturers (30). However, the specificity for each of the dipstick tests was 98%. The test is highly specific but not ideally sensitive.

The presence of abnormal amounts of urobilinogen and ascorbic acid in urine as well as a urinary pH of <6 account for some of the false-negative results (30). Performing the test on dilute urine also contributes to false-negative findings. It has been suggested that testing be performed only on urine that has remained in the bladder overnight or for at least 4 h to allow for a higher concentration of urinary nitrite (58). This is not always possible or practical and, although sensitivity is slightly improved, urinary nitrite alone is not a dependable indicator of a urinary tract infection.

Leukocyte esterase. A simple, rapid, inexpensive dipstick method for the detection of pyuria is the measurement of the enzyme leukocyte esterase (64). Studies have demonstrated

a correlation between leukocyte esterase activity and the chamber count (43, 71). The sensitivity for leukocyte esterase with a cutoff of >10 WBC per mm^3 ranged from 88 to 94%. Although the leukocyte esterase test has been shown to be a sensitive test for pyuria, vitamin C, phenazopyridine, or high levels of protein may interfere with results; therefore, tests must be interpreted with caution (22, 37).

The Chemstrip LN (Bio-Dynamics, Div. of Boehringer Mannheim Diagnostics, Indianapolis, Ind.) is a 2-min enzyme dipstick test combining the leukocyte esterase and nitrite reactions. Ten clinical evaluations of 13,443 urine specimens reported test sensitivities ranging from 79 to 90% (5, 11, 25, 32, 53, 56, 59, 71, 75, 81). When results of this test were compared with clinical findings rather than culture results and presence of WBC, the sensitivity was 84% (59). Although the sensitivity of this combination strip is higher than the leukocyte esterase and nitrite tests when performed alone, it still remains too low to be used alone as a rapid urine screen. Use of this strip in combination with another urine screen may help to decrease the number of false-negative results (71). The results obtained from combination testing may be used to "minimize" the number of urine specimens cultured and provide rapid reports of negative results.

Another rapid enzymatic test, Lyfo Kwik (Rapid-Urine-System; Micro-Bio-Logics, St. Cloud, Minn.) differs from the other enzyme tests in detecting many enzymes rather than just one. The substrate complex detects two categories of enzymes, including those produced by viable infection-causing microorganisms and those produced by the phagocytic neutrophils responding to the site of infection. Thus, the enzymes detected by this test are unique to phagocytic function and to the disease process rather than to the presence of bacteria or WBC. Although the manufacturer states that the system can detect $>10^5$ CFU/ml and >8 WBC per high-powered field in urine, its purpose is to rapidly (30 min) detect infection. If bacteriuria occurs as a result of colonization or contamination of the urinary tract, the test will be negative. Therefore, the culture method alone cannot be used as the reference to evaluate this system. Published evaluations of the product are currently not available.

Colorimetric Filtration

Use of filtration for the rapid determination of bacteriuria was first described by Wallis and associates (92). A sample of urine is passed through a filter, and if cells are present, they are trapped on the surface of the filter. Safranin O dye is used to stain the trapped cells. Acetic acid is used as both the urine diluent and the decolorizer to remove the dye from the filter fibers. This procedure has been adapted for use with a semiautomated instrument, the Bac-T-Screen (Vitek Systems, Inc., Hazlewood, Mo.). Clinical evaluations have been reported on this rapid, 1-min urine screen and include accuracy, ability to detect pyuria along with bacteriuria, and cost (12, 15, 16, 29, 70, 72, 73). The average test sensitivity reported from these seven evaluations when compared with $\geq 10^5$ CFU/ml was 93.9%, with a range of 88.2 to 98%. The average negative predictive value was 97.5%, with a range of 94 to 99.7%. Many of these evaluations report a high (>25%) false-positive rate; however, it is now known that these results are due to specimens that yield low colony counts and contain WBC (59, 71). The initial problem of specimens clogging the filter has been solved by increasing the vacuum force which causes the entire specimen to be pulled through the filter card. The Bac-T-Screen is a sensitive screening test (98%) for detecting clinically significant bacteriuria (49). When compared with the clinical classification of infection rather than quantitative urine cultures, the sensitivity of the Bac-T-Screen was higher than that of the culture method at $\geq 10^5$ CFU/ml, 98 and 45%, respectively. However, the sensitivity of the culture method increased to 95% when $\geq 10^2$ CFU/ml was considered positive.

Recently, a nonautomated filtration device has been described (48). The FiltraCheck-UTI (Vitek Systems) is also a colormetric filtration test which uses a disposable filter disk and does not require instrumentation, and test results are available within 1 min. The disposable filter disk consists of a conical well with 0.254-cm-diameter orifice at its base where the WBC and bacterial cells concentrate. Reagents are similar to those used with the Bac-T-Screen except that dilute solutions of hydrochloric acid instead of acetic acid are used as the diluent and decolorizer. if bacteria or WBC are present in urine, they are strongly bound to the electronegatively charged filter pad. Of the 1,198 randomly selected clean-voided urine specimens tested, the FiltraCheck-UTI had a sensitivity of 96.5% for probable pathogens at $\geq 10^5$ CFU/ml and 91.2% at $\geq 10^4$ CFU/ml; the specificity was 81% at both $\geq 10^5$ and $\geq 10^4$ CFU/ml; and the negative predictive values were 99.1 and 97.4%, respectively (92). Similar results have been reported for all species at 10^5 CFU/ml; also, the sensitivity at $\geq 10^3$ CFU/ml was 84.1% (M. Pezzlo, S. Choi, A. Woolard, E. Peterson, and L. de la Maza, Program Abstr. 27th Intersci. Conf. Antimicrob. Agents Chemother., abstr. no. 210, 1987). In this study, results compared favorably to those with the Bac-T-Screen and the Gram stain. The high number of false-positive results was due to low levels of bacteria or increased WBC, erythrocytes, and squamous epithelial cells; however, the presence of large numbers of WBC and erythrocytes is an abnormal finding in urine and therefore these results should be investigated.

The major difference between the two filtration methods is that the FiltraCheck-UTI is manual and the Bac-T-Screen is semiautomated. The FiltraCheck-UTI allows for batching of specimens more readily than the Bac-T-Screen. Clinical evaluations have shown that each system has the ability to detect significant bacteriuria accurately and the tests are simple to perform. Analysis of false-positive reactions suggests that these methods have the ability to detect pyuria as well as bacteriuria.

Bioluminescence

Use of bioluminescence as a urine screen was first described in 1944; however, the technology was not used in the clinical diagnostic laboratory until the last decade (57). The method is based on the enzymatic bioluminescent reaction of adenosine 5′-triphosphate (ATP) with luciferin and luciferase, which is measured by a luminometer. Measurements may include both somatic and bacterial ATP or bacterial ATP alone after the removal of nonbacterial ATP.

Three bioluminescent systems have been used in the diagnostic laboratory for detection of bacteriuria: Lumac Bacteriuria Screening Kit (formerly marketed by 3M, St. Paul, Minn.), the Monoscreen system (formerly marketed by Analytical Luminescence Laboratory, San Diego, Calif.), and the UTIscreen Bacterial ATP test (Los Alamos Diagnostics, Los Alamos, N.M.). The test procedure for each of these systems is similar; however, Lumac requires a 30-min incubation step versus 10 min with the other systems. Clinical evaluations of the systems reported sensitivities of >92% at $\geq 10^5$ CFU/ml and >85% at $\geq 10^4$ CFU/ml (2, 19, 26,

52, 54, 61, 62, 74, 86, 88, 89, 96, 97). The total cost per test for Lumac and the Monoscreen systems, which includes reagent cost, technical time, and cost of plating true and false-positives, was estimated at $2.50 or $1.77 for reagents or consumables alone, compared with $0.97 for the UTI screen.

Bioluminescence assays have the advantage of providing rapid results, although an incubation step is required. Earlier studies reported high false-positive findings (2, 52, 61, 86, 88, 89). However, by changing the interpretive breakpoint, it is possible to decrease the number of false-positive results without appreciably increasing the false-negative results. Low levels of bacteria may be detected by these assays. If bacteria are present, the specimen should contain bacterial ATP; this ATP is then measured by the assay. It has been reported that the average ATP per CFU is considerably higher in specimens with low CFU per milliliter than those with heavy bacterial growth (89). False-positive findings may also result from the inability of the culture method to detect growth because the appropriate nutritional or atmospheric requirements of the infecting organism are absent (89). Also, if large numbers of WBC are present, nonbacterial ATP may not be completely inactivated (19). Lastly, the presence of antimicrobial agents may inhibit the growth of the microorganisms but may not inhibit their detection by bioluminescence.

Photometric Detection of Growth

Automated photometry has also been applied to detection of bacteriuria. These systems, the Autobac (Organon Teknika Corp., Durham, N.C.), the Vitek (AMS, Vitek Systems, Inc.), and the Avantage (Abbott Laboratories, Irving, Tex.), differ from previously described colorimetric filtration and bioluminescence methods in that growth is required prior to detection and, as a result, detection times are somewhat delayed (30 min to 13 h). The methodology is similar for each of the systems. Urine is diluted in a broth medium and incubated at 35 to 37°C, allowing any bacteria present to grow in the medium. The resulting turbidity is detected by changes in light transmission that are measured photometrically. Growth occurs within 2 to 3 h because most aerobic gram-negative bacilli causing urinary tract infections are rapid growers. Agitation of the diluted urine during incubation speeds growth, allowing turbidity to occur more rapidly. Only the Autobac system takes advantage of this agitation step.

Evaluation of the three commercially available systems have been reviewed in detail (65–67). Each of the systems has a sensitivity of >95% at $\geq 10^5$ CFU/ml and a negative predictive value of 99%. The cost per test for each system is slightly lower than that for the colorimetric filtration and bioluminescence methods. The instrument cost for each of the photometric systems exceeds $30,000 compared with <$10,000 for colorimetric and bioluminescent instrumentation. However, these growth-dependent systems have the additional capacity for organism identification and antimicrobial susceptibility testing. These systems also have the advantage of computer capabilities, allowing results to be reported as soon as they are available, especially if the instrument is interfaced with a laboratory or hospital information system. The Vitek system has an advantage over the others in that it can simultaneously identify and detect isolates in positive urine specimens. One disadvantage of the growth-dependent systems is the need for incubation, which may limit their use in some laboratories. Positive results may be available in 1 h, but negative results cannot be reported before 5 to 13 h. These systems detect only bacteriuria, not pyuria.

TABLE 4. Guidelines for assessment of urine cultures

CFU/ml	WBC	Patient population or clinical condition
$\geq 10^5$	+	Acute cystitis
	+	Acute pyelonephritis
	+	Asymptomatic bacteriuria
$\geq 10^3$	+/−	Symptomatic infections in men
$\geq 10^2$	+	Acute dysuria and frequency in women
	+/−	Catheter-associated infections

Limulus Amoebocyte Lysate Endotoxin Test

The *Limulus* amoebocyte lysate endotoxin test is a rapid method for detecting gram-negative bacteria or their endotoxin. This test has been used to detect meningitis, septicemia, and genitourinary tract infections. In a study of 1,077 urine specimens, it detected 98.8% of urine samples with gram-negative bacilli at $\geq 10^5$ CFU/ml (33). The overall sensitivity was 87% because gram-positive pathogens were not detected. In addition to its inability to detect gram-positive organisms, the *Limulus* amoebocyte lysate test does not provide useful information on low-level bacteriuria (10^2 to 10^4 CFU/ml) because endotoxin from normal urethral and vaginal flora is usually present in voided specimens (33).

LABORATORY APPROACH TO SCREENING

Several guidelines have been suggested for the microbiological assessment of urine specimens from a variety of patient populations. The patient population served by the laboratory must be considered prior to selection of any one approach. Numerous studies reviewed in this article and elsewhere have established certain criteria which should be applied to this decision-making process. Existing data strongly support the following criteria (Table 4): (i) $\geq 10^5$ CFU/ml as the criterion for diagnosis of pyelonephritis, acute cystitis, and asymptomatic bacteriuria; (ii) bacterial colony counts of 10^2 to 10^4 CFU/ml for evaluation of specimens associated with catheter-related infections; (iii) $\geq 10^2$ CFU/ml for assessment of urine cultures from women with acute dysuria and frequency; and (iv) $\geq 10^3$ CFU/ml to identify infections in symptomatic males. Measurement of pyuria is important in differentiating infected from noninfected patients when bacteria are present. Demonstration of pyuria in the presence of symptoms and the absence of bacterial growth on routine laboratory media is also a significant finding. This information will assist the physician in the diagnosis of urinary tract disease.

The efforts of Stamm and his associates to establish a better definition of a urinary tract infection for a select patient population have caused confusion among microbiologists. Studies by Stamm, by Latham, and by Komaroff and their associates were intended to define more accurately the criteria for diagnosing infection in symptomatic women, thereby providing diagnostic laboratories with guidelines for interpreting urine test results from these patients (39, 44, 83, 84). Lipsky, Musher, and associates established a similar

TABLE 5. Comparison of laboratory approaches by Latham, Pfaller, and associates for screening urine specimens (44, 74)

Screening test	Infections detected (no.)[a]		Uninfected specimens correctly identified (no.)[a]	
	Latham (n = 74)	Pfaller (n = 100)	Latham (n = 313)	Pfaller (n = 240)
Standard culture (SC)	50 (68)	64 (64)	313 (100)	240 (100)
Dual-plating method (DPM)/low-count culture (LCC)	74 (100)	100 (100)	287 (92)	235 (98)
Pyuria determination				
LE		84 (84)		199 (83)
Hemacytometer	54 (73)	95 (95)	250 (80)	172 (72)
Pyuria-guided SC				
LE		56 (56)		240 (100)
Hemacytometer	36 (49)	60 (60)	313 (100)	240 (100)
Pyuria-guided DPM/LCC				
LE		84 (84)		239 (99)
Hemacytometer	54 (73)	95 (95)	307 (98)	238 (99)
Pyuria-guided DPM/LCC or SC without pyuria				
LE		92 (92)		239 (99)
Hemacytometer	68 (92)	99 (99)	307 (98)	238 (99)

[a] Percentages are given in parentheses.

definition for urinary tract infections in men and recommended that $\geq 10^3$ CFU/ml be used when evaluating voided urine (47, 60). Stark and Maki found that $\geq 10^2$ CFU/ml was a more valid index of infection when patients were catheterized and had urinary tract symptoms or were immunosuppressed; however, these colony counts usually increased to $\geq 10^5$ CFU/ml within a few days (85).

The selection of an accurate efficient criterion must be based on the prevalence of the disease in the patient population served by the diagnostic laboratory (4). It may be necessary for the laboratory to use more than one criterion to evaluate urine specimens. Other factors to consider when selecting a rapid urine screening test include accuracy, reproducibility, detection time, ease of test performance, cost, and detection of bacteriuria, pyuria, and/or infection.

Studies by Latham, Murray, Pfaller, and associates have attempted to correlate urinary tract infection with the laboratory findings (44, 59, 74). Latham, Pfaller, and associates evaluated similar laboratory procedures to determine which screening test or combination would most accurately and efficiently identify urine specimens from infected patients (44, 74). They evaluated six approaches; (i) the standard culture ($\geq 10^5$ CFU/ml); (ii) low-count culture ($\geq 10^3$ CFU/ml) or dual-plating method ($\geq 10^5$ and $\geq 10^2$ CFU/ml); (iii) pyuria determination, using a hemacytometer chamber or the Chemstrip LN; (iv) pyuria-guided standard culture; (v) pyuria-guided low-count culture or dual-plating method; and (vi) a combination of pyuria-guided low-count culture or dual-plating method and a standard culture in the absence of pyuria. There were two minor differences in their approaches: Latham and associates used the dual-plating method, whereas Pfaller's group used either a low-count or a high-count culture; and Latham's group used the hemacytometer chamber alone to determine pyuria, while Pfaller's group used both the chamber method and the Chemstrip LN (Table 5).

The two best approaches in terms of detecting infection and minimizing false-positive outcomes in Latham's study of 74 infected and 313 noninfected patients were the dual-plating method and the pyuria-guided dual cultures coupled with the standard culture without pyuria detection (approaches ii and vi). The dual-plating method detected 100% of infected patients with only 8% false-positive results; the second approach detected 92% of infected patients and there were only 2% false-positive results. However, they found that performing dual cultures on all urine specimens increased their workload by approximately 40%. Both the workload and cost could be reduced if standard cultures ($\geq 10^5$ CFU/ml) were performed on patients without pyuria and dual cultures were done on those with pyuria. Pfaller et al. obtained the most accurate results for the 100 infected and 240 uninfected patients with approaches ii and vi also (74). In their study, they identified only 64% of infected patients by using $\geq 10^5$ CFU/ml alone as the interpretive breakpoint compared with 68% in Latham's study. Although the results from these studies are similar, the patient populations differed; Pfaller's group studied a random patient population, whereas Latham's worked with a patient population of ambulatory women.

Murray et al. evaluated 500 randomly selected urine specimens by using three screening tests, Bac-T-Screen, Chemstrip LN, and Gram stain, and correlated their results with the clinical classification of urinary tract infection (59). The Bac-T-Screen detected 98, 93, and 100% of infections classified as probable, possible, and asymptomatic, respectively. The Gram stain and Chemstrip LN were both insensitive screening tests for infection in this study. Also, if $\geq 10^5$ CFU/ml was used as the interpretive breakpoint, only 45% of patients with probable infections would have been identified. These three well-performed evaluations suggest that quantitative urine cultures cannot be used to determine urinary tract infections unless small numbers of organisms are identified and pyuria is measured. Both Latham and Pfaller measured pyuria microscopically; however, Murray et al. used a rapid screen for this determination.

Cumitech 2A presents guidelines for interpretation of urine specimens (13). These guidelines are based on the principle that four factors (number of isolates, density of isolates, type of specimen, and clinical information) must be considered to assess the significance of an isolate(s) and to

determine the amount of time and effort and the cost that should be expended. These guidelines suggest that as many as two organisms should be identified, especially if the specimen was collected by suprapubic aspiration, from a straight in-and-out catheterization, or by cystoscopy. These guidelines can be used to develop flow diagrams (algorithms) to assist with specimen interpretation.

Komaroff and Loo and associates have presented a different approach, using a urinalysis test strategy (38, 49). Komaroff restricts his recommendations to use of urinalysis and urine culture results from specimens from women with different suspected etiology of acute dysuria (38). Urine cultures are necessary for those patients with suspected causes and clinical findings of acute and subclinical pyelonephritis. He recommends that urinalysis results be used to begin therapy in the patient suspected of having lower urinary tract infection. The presence of pyuria justifies giving immediate therapy, whereas the absence of pyuria justifies withholding therapy (38).

Loo and associates used the Chemstrip-9 (Bio-Dynamics) to determine the urine specimen workup (49). If the urine had an abnormal color and appearance or if leukocyte esterase, nitrite, blood, or protein were positive, a urinalysis sediment microscopy was performed. If $\geq$5 WBC or >10 bacteria per high-powered field or yeast cells were observed, a culture was performed. This approach decreased sediment microscopy by approximately 50%. They also used a Gram stain of uncentrifuged urine and found it to be of value in cases of suspected acute pyelonephritis when rapid diagnosis may be critical; $\geq$95% of patients with a positive Gram stain result had $\geq 10^5$ CFU/ml. There was a substantial savings to the laboratory because unnecessary urine sediment microscopy was eliminated. This urinalysis approach would be limited to microbiology laboratories with readily available urinalysis results. Many of the rapid urine screens, previously discussed, provide similar data generated by the urinalysis test and can easily be incorporated into the routine workflow of the diagnostic microbiology section of the laboratory.

COST ANALYSIS

One additional factor to consider prior to the selection of a rapid urine screen is cost. An analysis of cost should include urine screen supply costs, technical time, and supply costs for plating positive specimens. Examples of time and cost analysis determinations have been reported (44, 69). Pezzlo et al. estimated the cost for screening urine cultures by three automated methods (69). In that study, there was a \$0.50 per specimen cost savings over routine plating by using one of the photometric systems previously described. Although the initial cost of the instruments is high, this is recovered by eliminating the plating of negative urine specimens.

Latham et al. described workload calculations and cost comparisons of six approaches to screening urine specimens for infection (44). The cost per infection ranged from \$41.93 to \$77.01. Surprisingly, the cost per infection was higher for the standard culture ($\geq 10^5$ CFU/ml) than for the dual-plating method ($\geq 10^2$ CFU/ml), which produced more accurate results; the costs were \$55.54 and \$52.04, respectively.

Combination testing has been recommended to improve the sensitivity of detection of positive specimens (5, 75). However, this can be a very expensive approach because additional reagents and technical time are required. Some of the more sensitive urine screens have a high false-positive rate that eliminates any cost savings from screening. The least expensive screening tests with respect to supply costs and technical time are the urine dipstick tests (Table 3); however, these tests have the highest false-negative rates. Results from these tests may have a negative and expensive impact on patient care.

Some investigators have demonstrated a cost savings by using the Chemstrip LN to determine the need for culturing urine specimens (5, 49, 56). With this approach, Marsik and associates evaluated urine specimens from pediatric and adolescent patients and estimated a \$5,000/year savings to the laboratory and a \$10,000/year savings to the patient (56). Bartlett et al. reported an 18% reduction in total cost and a 19% reduction in labor cost when specimens were screened by the Chemstrip LN and cultured only when LN screens were positive (5). Loo and associates reported a cost savings to the laboratory of approximately \$32,000 when they used the urinalysis test strategy, i.e., a screening dipstick analysis with sediment microscopy performed on urine samples positive for leukocyte esterase, nitrite, protein, or blood (49). This cost savings has also been reported with a similar approach used to test urine samples in a population of veterans (25).

Pezzlo et al. reported a supply cost of \$0.67 for the culture method compared with \$0.90 for the Bac-T-Screen and \$0.17 for the Chemstrip LN (71). The cost per test for a negative screen was \$1.34 for the culture method, \$1.15 for the Bac-T-Screen, and \$0.34 for the Chemstrip LN. For a positive screen, the cost was increased by \$1.34 for the Bac-T-Screen and the Chemstrip LN since each positive result required a culture. The average cost per specimen in that study, including both positive and negative specimens, was calculated at \$1.34, \$1.88, and \$0.97 for the culture method, Bac-T-Screen, and Chemstrip LN, respectively. These data demonstrate that, although screening by the Bac-T-Screen is a more sensitive method than Chemstrip LN, the cost was 40% higher than the culture method and approximately 100% higher than Chemstrip LN.

The purpose of urine screening should be to rapidly eliminate those specimens which do not warrant a culture. Rapid screening tests have the advantage of providing same-day results, which is usually a more efficient approach for the laboratory. Based on currently available data, rapid accurate urine screening tests do not provide a major cost savings to the laboratory. However, same-day reporting may influence the behavior of the clinician, resulting in earlier treatment of the infection. This, in turn, may contribute to a more rapid recovery from the infection, less sequelae, and, for some patients, a shortened hospital stay, resulting in an appreciable cost savings to the medical care system.

SUMMARY

A review of rapid urine screens for detection of bacteriuria and pyuria demonstrates a number of available alternatives to the culture method. Selection of one or more of these systems for routine use is dependent upon the laboratory and the patient population being tested. The laboratory approach to the diagnosis of urinary tract infection should consider the clinical diagnosis of the patient whenever possible. Keeping in mind that quantitative urine cultures alone cannot be used to detect infection in some patient populations unless lower colony counts are considered, a rapid screen may be a more practical approach. It has become accepted that 10^5 CFU/ml can no longer be used as the standard for all patient groups, that pyuria often is important in making the diagnosis of a

urinary tract infection, and that most of the rapid screens are more sensitive than the culture method at 10^5 CFU/ml.

Presently, no one approach can be recommended for all laboratories and all patient groups. However, each diagnostic laboratory should select one approach which is best for its situation. It is not practical, efficient, or cost effective to define a protocol for each possible clinical condition; however, all should be considered when developing a protocol. This protocol should be compatible with the patient population and communicated to the physicians. Use of a rapid screen should be beneficial to the patient, the physician, and the laboratory.

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