Optimized Urinary Microscopy for Assessment of Bacteriuria in Primary Care

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Microscopy of wet-stained urinary sediment as an indicator of bacteriuria was evaluated in 418 consecutive primary care visits in a small community. Delivery of morning urine was encouraged and contributed to bladder incubation times of 4 or more hours in 79% of the visits; the overall culture positivity was about 80%. Bacteria or leukocytes alone or together as minimal requirements were suboptimal microscopy criteria for bacteriuria, whereas a minimum of moderate amounts of bacteria or 5 leukocytes per high-power field (×400) as a cutoff point yielded the best diagnostic accuracy. Optimization of urinary sediment microscopy in this way resulted in a desirable high sensitivity (97%) and efficacy (86%) in acutely symptomatic patients, as well as reasonably high efficacy (79%) in other patients, independent of sex or bladder incubation time. The method's simplicity and speed recommend it for use in primary care, particularly in patients with acute symptoms of urinary tract infection.
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Patients seeking primary care for presumed urinary tract infection (UTI) represent a large and heterogeneous group.[1,2] The diagnosis of UTI is usually based on the concept of significant bacteriuria ($\geq 10^5$/mL).[3] Reportedly, only about one half of the patients presenting with acute dysuria and related micturition problems turn out to have significant bacteriuria.[4,5]

As unnecessary medication should be avoided because of the cost, risk of side effects, and ecological consequences, the primary care physician needs an accurate indicator of bacteriuria to target the therapy. In acutely symptomatic patients a rapid and sensitive diagnostic method is desired. On the other hand, in patients with vague symptoms, for post-treatment control, and for screening purposes, the specificity of the bacteriuria test is of particular importance to minimize the risk of false UTI diagnoses in populations of mainly abacteriuric individuals.

Microscopy of urine is commonly used for presumptive rapid diagnosis of UTI and has been extensively documented with respect to the presence of either bacteria or leukocytes. Six principal microscopy procedures for detection of bacteriuria have been reported: microscopy of unstained and uncentrifuged urine, or of unstained urine sediment in high-power field (HPF, usually ×400), or of stained uncentrifuged urine, or stained sediment using either HPF or oil-immersion field (usually ×1000). Furthermore, various interpretive criteria have been applied even within each method.[6] Pyuria as an indirect measure of host injury is most accurately indicated by the leukocyte excretion rate using uncentrifuged urine.[7,8] This method is, however, impractical for routine office use.[7] As an alternative, enumeration of leukocytes in uncentrifuged urine using a counting chamber has been found to correlate well with the leukocyte excretion rate.[8–11]

The method perhaps most commonly used in clinical practice to grade pyuria, the counting of leukocytes per HPF in stained or unstained urinary sediment, is sparsely documented. Also, there are considerable differences in the recommended pathological threshold values for pyuria, probably because of uncontrolled variables and technical errors,[12–14] including a poorly defined time and speed of centrifugation, inconsistent resuspension volume after centrifugation, a variable volume placed on the microscope slide, and different degrees of magnification used. If careful attention is paid to these details, however,

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the precision of the leukocyte sediment method is improved, making its correlation with leukocyte counts per microliters of urine satisfactory.[15]

Microscopy of both bacteria and leukocytes in urine for diagnosing UTI has rarely been studied. Nevertheless, HPF estimation of these components in urinary sediment is commonly used in primary care in Sweden and probably also elsewhere. As there is no consensus in regard to technique and diagnostic criteria, it was important to re-evaluate this method for diagnosis of UTI in office practice.

The aim of this study was to correlate quantitative urinary sediment microscopy findings of bacteria and leukocytes with the outcome of semiquantitative culturing of urine performed at a bacteriological laboratory. One important part was to evaluate the diagnostic efficacy of various combinations of different levels of these two components to optimize the sediment method.

METHODS

All patients consulting the primary health care center (PHCC) in Vännäs (population 8000) in northern Sweden for suspected UTI or post-treatment control during 12 months were studied (418 visits by 180 patients). The PHCC was the only outpatient facility in the community and also served the local nursing home. Patients with dominating symptoms or signs of prostatitis or gynecological disorder and 20 elderly patients with urinary incontinence requiring indwelling urethral catheter, diapers, or other aids were excluded. Also excluded were patients making 20 visits that lacked complete documentation of the microscopy findings. The UTI-related visits were categorized as follows: (1) lower symptomatic UTI, (2) upper symptomatic UTI (fever 38.5°C or above, tenderness by bimanual palpation or throbbing over one or both kidneys, specific urinary sediment findings), (3) post-treatment control, and (4) miscellaneous UTI (asymptomatic bacteriuria, foul-smelling urine, vague or uncharacteristic abdominal symptoms, systemic symptoms such as unexplained fever).

The management of patients, routines for collection and transport of urine specimens, and their bacteriological analysis were as previously described.[1] Briefly, midstream voided specimens were collected, if possible, after 6 or more hours of bladder incubation (preferably morning urine) and were kept refrigerated until delivered at the PHCC. The bladder incubation time was recorded. On the day of collection, a portion of the urine specimen was transported to the laboratory at 4°C and cultured semiquantitatively, using a calibrated (10 μL) plastic loop. The definition of bacteriuria was a count of $\geq 10^5$/mL of urine, although 10^4/mL of urine was studied.

For sediment microscopy a 10-mL polystyrene tube with conical bottom (type 57462 Sarstedt, Nümbrecht-Rommelsdorf, FRG) was filled with urine, and centrifuged for 5 minutes at 3750 rpm (1250 G), followed by careful decanting of the urine. One drop of Sternheimer-Malbin wet stain[16] (SEDI-STAIN, Becton-Dickinson) was mixed with the sediment, a polypropylene drinking straw (inner diameter 2.5 mm) was used to apply 2 μL to 5 μL (average 3 μL) to a glass slide, and a 18×18-mm cover slip was placed on top. Samples were examined with a light microscope (Zeiss standard model) with a 40/0.65 achromatic objective and a ×10 wide angle ocular (CPL W ×10/18) giving a view field with a diameter of 450 μm and a depth of focus of 1.3 μm.

Three permanent physicians and three residents served at the PHCC during the study. The microscopy protocol was agreed upon, and the residents easily learned the procedures. The patient's physician classified the visit into the patient category and recorded the average quantity of leukocytes and bacteria per HPF after inspecting a minimum of five representative view fields. Leukocytes were counted up to 15/HPF and then approximated as 20, 25, or ≥30/HPF. Because of their movements and small size, bacteria could not be counted but were rapidly classified as no or a few bacteria per field (level 0), low (10 to 100, level 1), moderate (100 to 300, level 2) or high (innumerable, level 3) numbers of bacteria.

Statistical Analysis

Sensitivity, specificity, and predictive values were calculated using the predictive value theory.[17] Efficacy was defined as the percentage correct diagnoses, ie, 100 minus false (positive plus negative) results. It was postulated that the results of the reference method, urine culture, were correct.

RESULTS

Bladder incubation times of 4 hours or more were fulfilled in 79% of the visits, both in symptomatic (categories 1 and 2) and mainly asymptomatic (categories 3 and 4) patients, which contributed to relatively high culture positivity rates.

Urine Culture

Using a bacteria count of 10^5/mL as the cutoff point, the culture positivity rate was 82% in acutely symptomatic episodes (categories 1 and 2), but much lower in mainly asymptomatic patients (categories 3 and 4, 34%, Table 1). Of the bacteriuric patients, 87% were female, and *Esche-*

TABLE 1. URINE SPECIMENS STUDIED AND RESULTS OF CULTURE

Patient Category*	Description	Number of Specimens	Percent with Bacteriuria
1	Lower symptomatic UTI	170	82
2	Upper symptomatic UTI	31	84
3	Post-treatment control	181	33
4	Miscellaneous UTI	36	42
All visits		418†	57

UTI—urinary tract infection.
**See also Methods.*
†Contributed by 180 patients.

richia coli was the dominating pathogen (70% of episodes), followed by *Staphylococcus saprophyticus* (10%) as previously described.[1,18] The proportion of bacteriuric episodes was higher among men (77%) than among women (55%, Table 2). Lowering of the cutoff point to 10^4/mL resulted in culture positivity rates of 86% and 49% in acute and asymptomatic episodes, respectively (Table 2).

Bacteria or Leukocytes as Microscopy Criterion

As a single criterion of bacteriuria, using a bacteria count at level 1 or 2 as pathological threshold value offered the best compromise between sensitivity and specificity with an overall efficacy or 79% or 81%, respectively (Table 3). The use of leukocyte counts alone yielded a similar accuracy with cell counts of ≥3 or ≥5/HPF as optimal cutoff points (efficacy 77%). Using the latter cutoff point, the sensitivity was 88% in acute symptomatic and 63% in asymptomatic episodes. A lower leukocyte threshold value resulted in higher sensitivity and negative predictive value but lower specificity and positive predictive value, with the reverse being true for the higher threshold value.

Bacteria Plus Leukocytes as Microscopy Criterion

Various combinations of different levels of bacteria plus the optimal leukocyte threshold count (≥3 or ≥5/HPF) as an indicator of bacteriuria yielded high specificity (82% to 97%) but low sensitivity (40% to 77%) and at best modest efficacy (64% to 80%) in the total material. Thus, a compulsory presence of both bacteria and leukocytes in urinary sediment was unsatisfactory for diagnosing bacteriuria.

Bacteria or Leukocytes or Both as Microscopy Criterion

Bacteria and low numbers of leukocytes as optional indicators of bacteriuria yielded increased sensitivity but a dramatic loss of specificity (Figure 1). Raising the leukocyte threshold value resulted in only a slight decline of sensitivity, but markedly improved the specificity. This pattern was particularly evident in the asymptomatic episodes and was reflected also in the total material, with an apparent leukocyte cutoff point at ≥5/HPF. The level of bacteria used as optional indicator of bacteriuria had little influence on sensitivity, but higher bacterial levels improved the specificity. In acutely symptomatic episodes

TABLE 2. RESULTS OF URINE CULTURE IN DIFFERENT PATIENT GROUPS

	Number of Episodes per Level of Bacteriuria			
Patient group	$<10^4$/mL*	10^4/mL	$\geq 10^5$/mL	All Levels
Male	7	3	33	43
Female	138	38	219	395
Categories 1 and 2†	29	9	171	209
Categories 3 and 4†	116	32	81	229
All groups	145	41	252	438‡

**Classified as negative.*
†See Methods.
‡Of these visits 20 were excluded from further evaluation because of incomplete documentation of the microscopic findings.

TABLE 3. CORRELATION BETWEEN BACTERIURIA AS DEFINED BY URINE CULTURE AND LEVELS OF BACTERIA OR LEUKOCYTE COUNTS BY MICROSCOPY OF URINARY SEDIMENT IN THE TOTAL MATERIAL (N = 418)

Microscopy Criterion	Outcome of Urinary Sediment Microscopy (%)				
			Predictive Value		
	Sensitivity	Specificity	Positive	Negative	Efficacy
Bacteria*					
≥1	88	66	77	80	79
≥2	77	87	89	74	81
3	50	95	93	58	69
Leukocytes†					
≥1	90	43	68	77	70
≥3	81	70	78	74	77
≥5	72	82	85	69	77
≥7	62	84	84	62	72
≥10	58	86	85	61	71
≥15	52	92	89	59	69

*1 = low, 2 = moderate, 3 = high level of bacteria in high-power field (×400); see also Methods.
†Count per high-power field.

the sensitivity was far better than the specificity, whereas the opposite was true for asymptomatic episodes (Figure 1).

It is hardly realistic to aim at different urinary sediment microscopy criteria for different patient categories in routine clinical practice. The total material, therefore, was used to seek an optimal compromise between patient category, levels of leukocytes and bacteria, sensitivity and specificity, positive and negative predictive values, and efficacy (Figure 1). The minimum of a moderate level of bacteria or a leukocyte count of ≥5/HPF was found to represent the optimal choice as a general criterion for

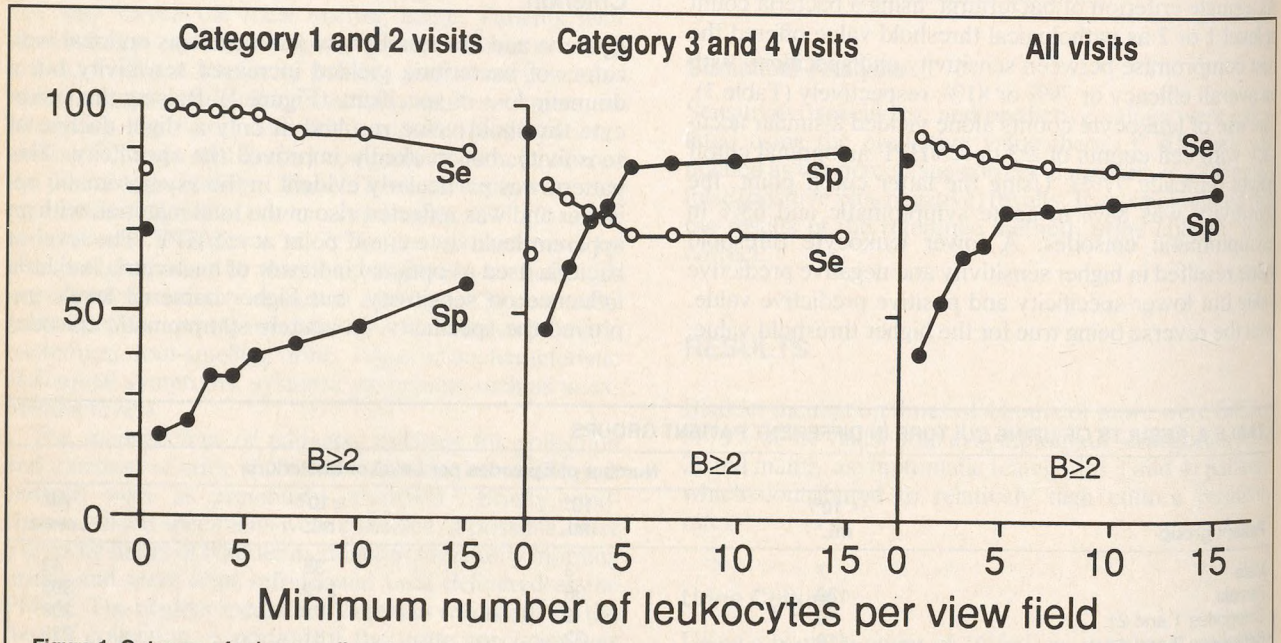

Figure 1. Outcome of urinary sediment microscopy in primary care patients based on an optional presence of bacteria (B) and/or leukocytes. Sensitivity (open circles) and specificity (closed circles) for minimum moderate levels of bacteria and/or various minimum levels of leukocytes are shown. The solitary symbols on the vertical axis represent sensitivities and specificities using bacteria as a single criterion and disregarding leukocytes. For patient categories 1 through 4, see Table 1 and Methods.

TABLE 4. CORRELATION BETWEEN BACTERIURIA AS DEFINED BY URINE CULTURE AND THE OPTIMAL COMBINATION OF LEUKOCYTE COUNT AND BACTERIAL LEVEL IN URINARY SEDIMENT*

	Outcome of Urinary Sediment Microscopy (%)						
			Predictive Value		False Results		
Patient Category†	Sensitivity	Specificity	Positive	Negative	Positive	Negative	Efficacy
Categories 1 and 2 (n = 201)	97	39	88	74	11	3	86
Categories 3 and 4 (n = 217)	70	84	69	84	10	11	79
All visits (n = 418)	88	75	82	83	11	6	83

*Minimum a moderate level of bacteria and/or ≥5 leukocytes per high-power field was used as the optimal cutoff point (see text).
†See Table 1 and Methods.

diagnosing bacteriuria—a conclusion reached after a thorough analysis of sensitivity, specificity, positive and negative predictive values, and efficacy for different levels of bacteriuria and leucocytes. In this paper, however, only the values of sensitivity and specificity can be shown in Figure 1.

Using these criteria, the outcome of sediment microscopy was the same in men and women. Outcome was also found to be almost identical in categories 1 and 2 and very similar in categories 3 and 4. The outcome, however, differed between symptomatic and asymptomatic episodes in a desirable way (Table 4). Although the specificity was low in symptomatic episodes (39%), high sensitivity (97%) and positive predictive value (88%) were emphasized, yielding an efficacy of 86% (11% false-positive, 3% false-negative results). Also, the sensitivity was independent of bladder incubation time in such episodes (95% to 100% for ≤1 hour to ≥6 hours, data not shown). In mainly asymptomatic episodes a higher specificity (84%) but modest sensitivity (70%) were obtained, resulting in an efficacy of 79% (11% false-negative, 10% false-positive results).

DISCUSSION

The purpose of this study was to reevaluate HPF microscopy of stained urinary sediment for diagnosis of UTI in primary care. A wide range of factors may greatly influence the outcome of UTI diagnostics, making published data difficult to interpret and apply. An attempt was made, therefore, to control the whole UTI analysis (bladder incubation time, urine sampling technique, further handling of the specimen by patient and staff, a standardized microscopy method) to a degree that is known to be practical in primary care.

Criteria for Significant Bacteriuria

As in most published evaluations of urinary microscopy, the criterion for bacteriuria was a count of $\geq 10^5$/mL of urine. This criterion was originally established for women with asymptomatic bacteriuria or acute pyelonephritis.[3] A lower limit for *S saprophyticus* ($\geq 10^4$/mL) has been suggested because of their slower growth[19] and pronounced tendency to clumping.[20] None of the 25 *S saprophyticus* episodes studied here, however, showed a count of 10^4/mL.

According to one interesting study, at least 30% of younger women presenting with symptoms of acute cystitis have low counts of bacteria (10^2 to 10^4/mL of urine) in samples obtained by suprapubic aspiration or urethral catheterization.[5] Thus, to improve the sensitivity of culture methods, lowering of the cutoff point to, eg, 10^2 to 10^4/mL in such patients has recently been suggested.[21–23] A lower cutoff point, however, has been disputed by other authorities because of the concomitant loss of specificity.[24] It has also been argued that different criteria for different patient groups would create practical problems in primary care and require altered culture methods and increased workloads in bacteriological laboratories,[25,26] and still more demanding methods would be required for the commonly occurring fastidious bacteria.[27] Thus, studies of the cost-effectiveness of traditional and new definitions of bacteriuria are needed.[21]

Prolonged bladder incubation was emphasized and usually also achieved, which apparently contributed to the high rates of positive cultures in acute episodes (82%). The scope of further positive diagnoses by lowering the cutoff point therefore became limited (eg, 86% positivity in categories 1 and 2 with $\geq 10^4$/mL of urine as threshold value, Table 2). Thus, the criterion $\geq 10^5$/mL may still remain acceptable for routine use in primary care, particularly if the patient population includes men and the elderly, and prolonged bladder incubation is achieved.

Microscopic Bacteriuria

In a recent comprehensive review of mircroscopy methods for rapid diagnosis of bacteriuria, differences in the outcome between methods, as well as large discrepancies between investigations, were noted.[6] Furthermore, high sensitivity was usually associated with low specificity, with the reverse being true, although one study using oil-immersion field was divergent with both a sensitivity and a specificity of 96%. Nevertheless, the author of the review considered oil-immersion field method to be "unsatisfactory" because of the difficult and ambiguous readings. The sensitivity and specificity of microscopic classification of bacteriuria in this study were 88% and 66% or 77% and 87% for low and moderate levels of bacteria, respectively, and comparable to those usually reported. Taken together, available data indicate that microscopic assessment of bacteriuria alone is not sufficient for office diagnosis of UTI.

Microscopic Pyuria

The indicator of pyuria most widely used (a leukocyte count of ≥5/HPF in sediment) yields highly variable sensitivity, both in acute and asymptomatic episodes.[3] Using this threshold, a somewhat higher sensitivity was obtained in the former patient group (80%) and higher specificity in the latter group (90%) than in other studies. Counting of leukocytes in uncentrifuged urine (≥10/μL) yielded higher sensitivity, but moderate specificity in symptomatic patients,[11,14,23,28] and opposite results in asymptomatic patients.[14] In conclusion, like microscopic assessment of bacteriuria, the determination of pyuria alone is only moderately efficacious as an indicator of true bacteriuria.

Bacteria and Leukocytes in Sediment

In an attempt to further improve the efficacy of urinary sediment microscopy in primary care, different combinations of various amounts of bacteria and leukocytes in HPF were studied. A presence of one or both of these components as a pathological threshold value proved to yield the best overall correlation with the results from urine cultures. The outcome was independent of both sex and bladder incubation time, and this criterion turned out to be suitable particularly in symptomatic patients with a desired high sensitivity (97%) and only a moderate risk of false-positive results (11%), and thus, an efficacy of 86%. Furthermore, as a bacteria count of ≥10^5/mL by urine culture was used as reference, part of the false-positive sediment readings could in fact represent true bacteriuria and false-negative culture results. In patients with vague or no symptoms, sediment analysis showed a rather low sensitivity, moderate specificity, and thus a somewhat lower total efficacy (79%).

In summary, optimized HPF analysis requiring at least a moderate level of bacteria or 5 or more leukocytes per view field in stained urinary sediment here proved to be a satisfactory method for diagnosing UTI in primary care patients. Centrifugation and staining also offers qualitative advantages, as detection of other elements of diagnostic importance is facilitated. Optimized sediment microscopy was found to be particularly useful in symptomatic episodes of UTI, ie, where the need for rapid diagnosis is greatest. This method, therefore, can be recommended for use in primary care.

References

1. Ferry S, Burman LG, Mattsson B: Urinary tract infection in primary health care in northern Sweden I. Epidemiology. Scand J Prim Health Care 1987; 5:123–128
2. Ferry S, Burman LG, Mattsson B: Urinary tract infection in primary health care in northern Sweden II. Clinical presentation. Scand J Prim Health Care 1987; 5:176–180
3. Kass EH: Asymptomatic infections of the urinary tract. Trans Assoc Am Physicians 1956; 69:56–64
4. Stamm WE, Wagner KF, Amsel R, et al: Causes of the acute urethral syndrome in women. N Engl J Med 1980; 303:409–415
5. Stamm WE, Counts GW, Running KR, et al: Diagnosis of coliform infection in acutely dysuric women. N Engl J Med 1982; 307: 463–468
6. Jenkins RD, Fenn JO, Matsen JM: Review of urine microscopy for bacteriuria. JAMA 1986; 255:3397–3403
7. Little PJ: Urinary white-cell excretion. Lancet 1962; 1:1149–1151
8. Little PJ: A comparison of the urinary white cell concentration with the white cell excretion rate. Br J Urol 1964; 36:360–363
9. Stansfeld JM: The measurement and meaning of pyuria. Arch Dis Child 1962; 37:257–262
10. Mabeck CE, Schiöttz-Christensen E: Kvantitativ bestemmelse af leucocytudskillelsen i urinen (Quantitation of urinary leukocyte excretion rate). Ugeskr Laeg 1968; 130:136–139 (in Danish, English summary)
11. Musher DM, Thorsteinsson SB, Aisola VM: Quantitative urinanalysis: Diagnosing urinary tract infection in men. JAMA 1976; 236: 2069–2072
12. Gadeholt H: Quantitative estimation of urinary sediment with special regard to sources of error. Br Med J 1964; 1:1547–1549
13. Gadeholt H: Cell counts in urine. Urology Dig 1976; 15:11–14
14. Stamm WE: Measurement of pyuria and its relation to bacteriuria. Am J Med 1983; 75 (1B):53–58
15. Alwall N: Pyuria: Deposit in high-power microscopic field—EBC/HPF—versus WBC/mm^3 in counting chamber. Acta Med Scand 1973; 194:537–540
16. Sternheimer R, Malbin B: Clinical recognition of pyelonephritis, with a new stain for urinary sediments. Am J Med 1951; 11:312–323
17. Ransohoff DF, Feinstein AR: Problems of spectrum and bias in evaluating the efficacy of diagnostic tests. N Engl J Med 1987; 299:926–930
18. Ferry S, Burman LG: Urinary tract infection in primary health care in northern Sweden III. Bacteriology in relation to clinical and epidemiological factors. Scand J Prim Health Care 1987; 5:233–240

19. Hovelius B, Mårdh PA, Bygren P: Urinary tract infections caused by *Staphylococcus saprophyticus:* Recurrences and complications. J Urol 1979; 122:645–647
20. Hovelius B, Mårdh PA: On the diagnosis of coagulase-negative staphylococci with emphasis on *Staphylococcus saprophyticus.* Acta Pathol Microbiol Scand [B] 1977; 85:427–434
21. Stamm WE: Quantitative urine cultures revisited. Eur J Clin Microbiol 1984; 3:279–281
22. Lipsky BA, Ireton RC, Fihn SD, et al: Diagnosis of bacteriuria in men: Specimen collection and culture interpretation. J Infect Dis 1987; 155:847–854
23. Pfaller M, Ringenberg B, Rames L, et al: The usefulness of screening tests for pyuria in combination with culture in the diagnosis of urinary tract infection. Diagn Microbiol Infect Dis 1987; 6:207–215
24. Smith GW, Brumfitt W, Hamilton-Miller J: Diagnosis of coliform infection in acutely dysuric women. N Engl J Med 1983; 309:1393
25. Hallander HO, Kallner A, Lundin A, Österberg E: Evaluation of rapid methods for the detection of bacteriuria (screening) in primary health care. Acta Pathol Microbiol Immunol Scand [B] 1986; 94:39–49
26. Latham RH, Wong ES, Larson A, et al: Laboratory diagnosis of urinary tract infection in ambulatory women. JAMA 1985; 254: 3333–3336
27. Fairley KF, Birch DF: Detection of bladder bacteria in patients with acute urinary symptoms. J Infect Dis 1989; 159:226–231
28. Mabeck CE, Schiöttz-Christensen E: Leukocyte-udskillelse ved urinvejsinfektioner (Leukocyte excretion rate in UTI). Ugeskr Laeger 1968; 130:140–143 (in Danish, English summary)

Commentary

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There are many pitfalls for the clinician in balancing the historical, physical examination, and laboratory data that are processed in patient care. For example, M.G., a patient of mine, is a frail 89-year-old woman with many chronic medical problems. During a recent visit she commented, "By the way, I have been having some of that right-sided pain just like when I had my last kidney infection." Her examination revealed no costovertebral angle tenderness, and urine microscopy showed neither bacteriuria nor pyuria. With this information in hand, I reassured her that her "kidney was not infected." Four days later she called me late in the evening complaining of dysuria, nausea, fever of 102°F, and "that same back pain that I told you was a kidney infection." She was appropriately treated for pyelonephritis at that time.

The article by Ferry et al[1] provides some guidance for the use of microscopy to detect urinary tract infections. In this day of sophisticated, rapid enzyme-linked immunosorbent assay tests to detect group A streptococci, chlamydia, and other organisms, it is important to remember urine microscopy was one of the first "rapid" microbiology tests. The study concludes that the presence of moderate bacteriuria and a few leukocytes (5 or more per high-power field [HPF] on spun sediment) is a pretty good indicator of a urinary tract infection. This finding is true for patients suspected of having such infections and those being followed up after antibiotic treatment, as well as for a group of miscellaneous patients in whom a urinary tract infection (UTI) was a possibility but not the principal diagnostic consideration (ie, vague abdominal pain).

The subjects for this study were recruited from a primary care site in a small town in Sweden. The findings are therefore likely to be generalizable to many family practice sites in the United States. The most common organisms that were isolated were *Escherichia coli* and *Staphylococcus saprophyticus*. These organisms are the same as those reported in other studies of outpatient populations.[2] There are, however, two distinguishing characteristics about the study population. The first is that 10% of the patients were male. Such specimens represent a smaller percentage of all urine cultures in our own laboratory. Second, the largest group of samples (n = 181) came from patients who had been treated and were being followed up as test of cure. Given the great success of empiric therapy for urinary tract infections, many US clinicians do not routinely order follow-up cultures after appropriate antibiotic treatment.

The microscopy and culture methods that were used in this study are standard and are easily done in office laboratories. One aspect of the specimen collection, however, should be emphasized. The specimens were collected at home after a long bladder incubation period (4 to 6 hours). This is in contrast to common practice in the US where symptomatic patients present to the office and then are asked to collect a random specimen for testing. The specimen collection method used in the study is obviously in part responsible for the very high prevalence of UTIs in this population (80%). Longer bladder incubation times should produce higher levels of bacteriuria. Also, any delay in refrigeration of the specimen can lead to bacterial

overgrowth. It is very likely that some of the positive cultures in this study had initially very low colony counts (less than would be considered infected), but developed bacterial overgrowth because of improper storage of the specimen in the patient's home or during transport to the laboratory.

The authors of this study found that either pyuria without bacteriuria or bacteriuria without pyuria is an unreliable predictor of a UTI. How can this be so? Leukocytes often appear in the urine in female patients with vaginitis or cervicitis because of contamination from vaginal secretions during specimen collection. An important clue to this problem is the presence of squamous epithelial cells. This microscopic finding is consistent with vaginal contamination. When such contamination exists, it is impossible to interpret reliably the urine microscopy findings. It is important to remember that about one half of women who present with dysuria have vaginitis as a cause of their symptom.[3]

Bacteriuria can also occur in the absence of pyuria and does not always indicate a urinary tract infection. When this microscopic finding is seen, consider the possibility of bacterial overgrowth because of improper specimen storage. Another possibility is an error in microscopic interpretation. Small amorphous crystals are easy to confuse with bacteria. Some laboratorians believe that the two can be distinguished because of the nonrandom movement of bacteria. This distinguishing characteristic is difficult for even experienced microscopists.

The authors present their results using the concepts of sensitivity, specificity, and predictive value. These terms have become common in the clinical literature during the past decade. The concepts permit quantification of how good a test really is. The sensitivity of the test is the rate of positive results in people known to have the disease (ie, the percentage of individuals with urinary tract infections who have pyuria). Specificity is the rate of negative results obtained when a test is applied to patients known to be free of the disease (ie, the percentage of cases with negative urine cultures that also have negative microscopy findings). Predictive value takes the disease prevalence into account. It is defined as the percentage of patients with a positive test who are diseased (ie, those with microscopic findings who will have positive urine cultures). Predictive value is the most useful of these concepts from a clinical perspective.

To calculate both sensitivity and specificity, it is necessary to have a "gold standard" test to determine whether a person either has, or is free of, the disease in question. This issue is not trivial; however, it is often ignored in the testing literature. An objective and widely accepted gold standard is, in fact, not available for most common diseases (eg, bronchitis, alcoholism, tension headaches). One recent study has shown that coronary angiography is in fact an inadequate gold standard for coronary artery disease, since it frequently misclassifies the presence or absence of significant coronary artery stenosis.[4] If the gold standard misclassifies individuals, then both sensitivity and specificity of a second test will be artificially altered.

Choice of a gold standard is a special problem with urinary tract infections. The colony count that has traditionally been accepted as indicating a urinary tract infection is 10^5 colonies per milliliter of urine. As indicated by Ferry et al,[1] this standard was derived from studies of pyelonephritis. More recent work has indicated that colony counts as low as 100 may indicate infection in women with dysuria.[2] Women with cystitis urinate frequently and drink large volumes of liquids in an attempt to "wash out" their infection. This practice results in high urine volumes and short bladder incubation times, both of which reduce the colony count. Ferry et al have indicated that their results were relatively insensitive to changing the cutoff colony count to 10^4/mL. Would the same be true for 10^3/mL or 10^2/mL? Probably not. There is unfortunately no precise way to adjust for the errors of an imperfect reference test. Clinicians must rely on their common sense.

I must disagree with the authors when they say, "It is hardly realistic to aim at different urinary sediment microscopy criteria for different patient categories in routine clinical practice." It is probably true that this degree of information makes predictive value calculations hopelessly complex. It is, however, exactly this level of complex judgment that physicians use every day. Three to five leukocytes per HPF in a woman with urinary frequency, pain, and urgency is just not the same as encountering these same microscopic findings in a routine urinalysis for a patient hospitalized for elective surgery. Clinicians are required to weigh and balance many types of data. All too often the data conflict.

Finally, the literature has for too long ignored the assumptions that clinicians bring to the diagnostic process. These assumptions interact with predictive value calculations. DeNeef has very elegantly described this interaction for the treatment of pharyngitis.[5] In the case of urinary tract infections, do clinicians want to avoid missing even a single urinary tract infection, or avoid the use of antibiotics in those with a low likelihood of infection, or minimize total health care costs? These therapeutic goals directly determine which qualities of a test are desirable (ie, high sensitivity, high specificity, short turn-around time, low test cost, etc). Most of the controversies over appropriate test use can be traced to differences in the assumptions about the natural history of disease or the benefits of treatment. Few are due to honest disagreements about how well a test really works.

References

1. Ferry S, Andersson S-O, Burman LG, Westman G: Optimized urinary microscopy for assessment of bacteriuria in primary care. J Fam Pract 1990; 31:00–00
2. Stamm WE, Counts GW, Runnings KR, et al: Diagnostics of coliform infection in acutely dysuric women. N Engl J Med 1982; 307:463–468
3. Komaroff AL: Acute dysuria in women. N Engl J Med 1984; 310: 368–374
4. Boyko EJ, Alderman BW, Barron AE: Reference test errors bias the evaluation of diagnostic tests for ischemic heart disease. J Gen Intern Med 1988; 3:476–481
5. DeNeff P: Selective testing for streptococcal pharyngitis in adults. J Fam Pract 1987; 25:347–351

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