Specialty Conference

Discussant
WALTER E. STAMM, MD

This discussion was selected from the weekly Grand Rounds in the Department of Medicine, University of Washington, Seattle. Taken from a transcription, it has been edited by Drs. Paul G. Ramsey, Assistant Professor of Medicine, and Philip J. Fialkow, Professor of Medicine and Chairman of the Department of Medicine.

Refer to: Stamm WE: Recent developments in the diagnosis and treatment of urinary tract infections—University of Washington (Specialty Conference). West J Med 1982 Sep; 137:213-220

Recent Developments in the Diagnosis and Treatment of Urinary Tract Infections

WALTER E. STAMM:* In the past few years, several well-established principles in the diagnosis and treatment of urinary tract infections (UTI) have been challenged. New diagnostic tests have emerged, the utility of older tests has been questioned, changing antibiotic sensitivity patterns of urinary pathogens have been documented, the role of *Chlamydia* and staphylococci in causing urinary infection has been better defined and recent data have given rise to debate over selection of antimicrobial agents and duration of therapy. In addition, the role of prophylactic antibiotic therapy in patients with recurrent urinary tract infections has been further studied, both with respect to cost considerations and clinical effectiveness. In light of these recent developments, a review of selected aspects of the care of patients with urinary tract infections seems warranted.

The Meaning of Significant Bacteriuria

To most physicians a culture of a clean-catch midstream urine specimen that grows more than 100,000 colonies per ml confirms a diagnosis of urinary tract infection, and a culture growing fewer than 100,000 colonies per ml makes the diagnosis unlikely. This diagnostic criterion arose from the classic studies of Kass[1,2] and Sanford.[3] They showed that over 95 percent of women with acute pyelonephritis have 100,000 or more bacteria per ml of urine and that this number of microorganisms, when found in two or more consecutive cultures, reliably distinguished infection from contamination in women who had asymptomatic bacteriuria. Most women seen by physicians for UTI, however, have acute symptomatic infection confined to the lower urinary tract, rather than acute pyelonephritis or asymptomatic bacteriuria. Using the 100,000 colonies per ml diagnostic criterion for infection in these patients has been less satisfactory. In one study of 130 women with an acute onset of dysuria and frequency, for example, only 56 actually had more than 100,000 colonies per ml on cultures of urine specimens, whereas 41 had sterile urine cultures and 33 had counts of fewer than 100,000.[4] Similar data in other studies[5-8] led to the concept that women whose midstream cultures grew fewer than 100,000 organisms per ml did not have UTI but suffered instead from the urethral syndrome. Because the pathogenesis of this syndrome was unclear, most women with urethral syndrome were not treated with antimicrobial drugs. Later, however, studies using suprapubic aspiration showed that nearly a third of symptomatic patients with low coliform counts in voided urine specimens also had coliform bacteria in their bladders.[9,10]

A recent Seattle study has provided information relevant to the interpretation of bacterial colony counts in midstream urine specimens obtained from symptomatic patients.[11] Of 181 women who came to an outpatient clinic with acute dysuria and frequency, 102 had counts of 100,000 per ml or more, but 79 had fewer than 100,000 colonies per ml. Women with evidence of upper urinary tract infection, vaginitis or herpes simplex virus infection were excluded from this study. In all, 56 of the 79 women with fewer than 100,000 colonies

*Associate Professor of Medicine, University of Washington, Seattle.

Reprint requests to: Department of Medicine, RG-20, University of Washington, Seattle, WA 98195.

ABBREVIATIONS USED IN TEXT

ACB = antibody-coated bacteria
IVP = intravenous pyelography
STD = sexually transmitted disease
UTI = urinary tract infections

per ml in a midstream urine specimen participated in the study and 27 had suprapubic aspirates that grew *Escherichia coli, Klebsiella* sp or staphylococci. In addition, cultures of urethral and vaginal specimens were obtained from all study patients, and the same high rates of *E coli* carriage in the urethra (78 percent to 84 percent) and vagina (79 percent to 92 percent) were found both in women with 100,000 or more organisms per ml and in those with low coliform counts in midstream urine specimens, but not in women without symptoms. These data suggested that the pathogenesis of infection in the group with low coliform counts in a midstream urine specimen may be similar to that in the group with 100,000 colonies per ml or more; that is, ascending infection probably occurs in both groups, ultimately resulting in cystitis. Indeed, the clinical presentation of patients with 100,000 or more colonies per ml in midstream urine specimens could not be distinguished from those with fewer than 100,000 colonies per ml. Approximately half of each group exhibited gross or microscopic hematuria (or both), essentially all women in both groups had pyuria and women in both groups typically described a sudden onset of illness that began three to four days before being seen in clinic.

In summary, data now available suggest that symptomatic coliform infection of the bladder and urethra will not, in many women, be accompanied by midstream urine specimens that grow 100,000 colonies per ml or more on cultures. Clinicians and microbiologists must, therefore, reconsider the interpretation of culture results of midstream urine specimens. Further studies are urgently needed to more clearly define the sensitivity and specificity of quantitative criteria for infection in patients with lower urinary tract infection. Until these become available, clinicians and microbiologists must be aware that midstream urine specimens growing fewer than 100,000 bacteria per ml on culture can have diagnostic importance.

The Meaning of Pyuria

Although many experts have criticized using analysis of urine for diagnosing urinary tract infections, most physicians still place importance on the number of leukocytes in the urinary sediment. Unfortunately, measurement of pyuria by examination of the urinary sediment as practiced in most hospitals lacks precision. By this method, an unknown quantity of urine is centrifuged for an approximate period, and an unknown dilution of the sediment is then examined. In studies where pyuria has been more precisely measured, it has been found in nearly all women with acute UTI. Mabeck[12] showed that an elevated leukocyte excretion rate in the urine correlated with acute symptomatic UTI; most normal persons excrete less than 400,000 leukocytes an hour, while more than 95 percent of patients with acute symptomatic infection are well above this level.

A simpler and highly reproducible method of measuring pyuria has been described.[13] In this technique, leukocytes per cubic millimeter of urine are determined by examining a fresh, uncentrifuged specimen in a hemacytometer chamber. This method correlates well with the leukocyte excretion rate and can be done easily in a clinical setting. By hemacytometer determination, most asymptomatic women with sterile urine have fewer than eight leukocytes per cu mm in their midstream urine specimens. In contrast, nearly all patients with acute cystitis characterized by bacteriuria of 100,000 or more per ml have more than eight leukocytes per cu mm and most have more than 60 per cu mm. Patients with the acute urethral syndrome may be divided into those with or without eight or more leukocytes per cu mm of urine. In the Seattle study, 85 percent of patients with pyuria had a proved infection (coliform, staphylococcal, or chlamydial) and patients without pyuria usually had no demonstrable infection.[11] All patients positive for bacteria on suprapubic aspirate cultures and most patients positive for *Chlamydia* sp on cultures had pyuria with counts well above eight leukocytes per cu mm. Thus, careful measurement of pyuria in patients with urinary tract symptoms can be helpful in separating patients who will have proved infection from those who will not.

Antibody-Coated Bacteria Test

A relatively new diagnostic test, the antibody-coated bacteria (ACB) assay, has been proposed as a noninvasive, inexpensive and apparently accurate means of identifying the site of UTI. The ACB test uses a fluorescence assay to detect immunoglobulin on the surface of bacteria in the

TABLE 1.—*Studies Comparing the Antibody-Coated Bacteria (ACB) Test With Direct Localization Procedures*

Study	Patients	Method	Results of ACB	
			Sensitivity number (percent)	Specificity number (percent)
Jones et al, 1974[14]	26	Bladder washout	17/18(94)	8/8 (100)
Kohnle et al, 1975[18]	26	Bladder washout	18/18(100)	8/8 (100)
Hawthorne et al, 1978[20]	31	Ureteral catheterization	16/16(100)	10/15(67)
Riedasch et al, 1978[17]	134	Ureteral catheterization	36/50(72)	59/84(70)
Harding et al, 1978[19]	51	Bladder washout	31/37(84)	14/14(100)

urine. Early studies suggested that upper urinary tract infection was characterized by the presence of ACB in urinary sediment and lower urinary tract infection by its absence.[14,15] However, only a few studies have directly compared the ACB test with either ureteral catheterization or the bladder washout localization technique and, unfortunately, many of the patients in these studies were on urologic services and had chronic UTI (Table 1).[14,16-20] Further experience comparing the ACB test with direct localization procedures in acutely symptomatic younger women is still needed.

An interesting epidemiologic observation has been the variability in the percentage of women with positive ACB tests, depending on the population being studied. In a cooperative study involving Parkland Memorial Hospital in Dallas, the Kaiser-Permanente Hospital in Portland and the Massachusetts General Hospital in Boston, the percentage of women having only lower urinary tract symptoms but positive results on ACB assay ranged from 63 percent at Parkland to 8 percent at the Kaiser-Permanente Center.[21] The authors speculated that this difference might relate to health-care-seeking behavior, with some patients who had only mild symptoms obtaining care early in the course of infection, and others waiting until more severe symptoms develop before going to the hospital. Rates of positive findings on ACB test in Seattle range from 13 percent at the student health clinic at the University of Washington to nearly 50 percent at the sexually transmitted disease (STD) clinic at Harborview Medical Center. These data show a gradation similar to the findings of Rubin and colleagues[21] and may also be related to the availability of care.

False-negative and false-positive results occur with the ACB test. False-negative tests usually result from a delayed or inadequate antibody response. In animal models, an infection must be established for 10 to 14 days to stimulate a sufficient immune response for the ACB test to become postive.[22] Most women with a first infection will receive treatment before the development of antibodies against their infecting strain. In a study by Rubin and co-workers,[21] the average duration of symptoms in ACB-negative patients was two days, compared with six days in ACB-positive patients. In a Scandinavian study,[23] the percentage of patients with positive ACB assays was greater among those with recurrent infections or with a long duration of illness than in patients with first infection. These studies, like the animal models, suggest that sufficient time for an immune response to develop is necessary before the ACB test becomes positive. False-negative results with the ACB test may also be seen in patients with infections characterized by fewer than 100,000 bacteria per ml. Presumably, there are insufficient bacteria to bind antibody, leading to a false-negative result in these patients.[24]

False-positive results on ACB tests occur for several reasons. Vaginal or fecal strains of *E coli* may be antibody coated and can contaminate urine specimens. Other tissue infections, primarily prostatitis and hemorrhagic cystitis, may result in antibody production and lead to a positive result. In addition, certain microorganisms (*Pseudomonas,* staphylococci and yeasts) often produce false-positive findings.[14]

Uncertainty concerning the specificity and sensitivity of the ACB test has led most investigators to recommend that it be reserved for epidemiologic and investigative purposes and not be used clinically at this time.

The Role of Cystoscopy and Intravenous Pyelography

Three recent studies have raised important questions about the routine use of intravenous pyelography (IVP) and cystoscopy in women with recurrent urinary tract infections (Table 2).[25-27] All three studies examined women with recurrent, acute lower urinary tract infections and excluded patients with known upper urinary tract surgical procedures, renal calculi, anatomic abnormalities

TABLE 2.—*Role of Intravenous Pyelography (IVP) in Women With Recurrent Urinary Tract Infection*

Method	*Fair et al, 1979*[25] *Questionnaire*	*Engel et al, 1980*[26] *Retrospective Record Review*	*Fowler & Pulaski, 1981*[27] *Prospective Study*
Women studied	164	153	104
IVP normal	144	136	87
Anatomic variant	11	9	6
IVP abnormal	9	8	11
Correctable	0	0	0

or relapsing infections. In the three studies, 80 percent to 85 percent of women had completely normal IVP's despite a history of two to three UTI's per year. Anatomic variants probably unrelated to infection were found in 6 percent to 8 percent. IVP abnormalities that could have been related to infection were found in 6 percent to 8 percent, but none of these abnormalities were considered correctable by the authors. Thus, none of the 421 patients had their treatment altered on the basis of an IVP. Similarly, cystoscopy rarely showed a correctable lesion: of 153 women studied, four had potentially correctable lesions (one patient with a colovesical fistula and three with urethral diverticula).[25-27]

Given the apparent low yield of IVP in women with recurrent UTI, the risks and benefits of the procedure should be carefully weighed. Important adverse reactions to IVP include minor skin reactions (1 in 100 patients), major vasomotor phenomena (1 in 1,000) and death (1 in 10,000 to 25,000). Furthermore, IVP's generally cost at least $110. An IVP appears to be most useful in patients with a history of childhood urinary tract infections, possible nephrolithiasis, relapsing infection or painless hematuria, but not in women with uncomplicated lower urinary tract infections.

Treatment of Urinary Tract Infection

Continuing emergence of antibiotic-resistant microorganisms has complicated the treatment of urinary tract infections. In Seattle microorganisms causing UTI in patients seen at the STD clinic at Harborview Medical Center, the student health clinic at the University of Washington and the Public Health Service Hospital frequently show in vitro resistance to ampicillin (20 percent to 25 percent), tetracycline (35 percent to 40 percent) and sulfa drugs (20 percent to 25 percent). Of the drugs routinely used for outpatient treatment of UTI, only trimethoprim-sulfamethoxazole was effective in vitro in over 95 percent of patients. In vitro resistance, however, does not necessarily imply that a drug cannot be successfully used to treat urinary infection. Urinary concentration of many antimicrobial medications may allow successful treatment of microorganisms judged resistant on the basis of in vitro testing.

In recent years, the duration of antibiotic therapy for urinary tract infection has been reconsidered. ACB testing, which may permit noninvasive identification of the site of infection in treatment studies, has been used to examine the feasibility of single-dose therapy of acute lower urinary tract infections.[28] The rationale for single-dose therapy stems from several considerations. First, histopathoiogic studies in which biopsy specimens of the bladder are taken show that acute cystitis is a superficial infection that does not extend beyond the mucosa in most cases.[29] Second, many clinicians have inadvertently seen single-dose therapy work when a patient with acute cystitis for whom ten days of antibiotic therapy was prescribed, feels better after one day of treatment and stops taking the medication. When seen for test of cure two weeks later, the patient has sterile urine. Third, physicians in STD clinics routinely use single-dose therapy for other genital mucosal infections, specifically gonococcal urethritis and cervicitis. Finally, the bladder washout procedure, which involves installation of antibiotics into the bladder, cures approximately 30 percent of patients with cystitis.[30]

Fang and co-workers[28] described the first clinical trial of single-dose therapy in patients who had a negative ACB test. All 22 patients who had lower urinary tract infection as judged by the ACB test were cured by a single 3-gram dose of amoxicillin given by mouth. Patients with a positive ACB test were treated only with a conventional ten-day course of amoxicillin and 50 percent failed to improve on this therapy. Subsequently, other studies using several different antibiotic drugs have confirmed the efficacy of single-dose therapy in an ACB-negative patient (Table 3), achieving cure rates of 68 percent to 100 percent.[31-36]

It should be emphasized that most single-dose antibiotic studies have examined patients with a negative result on ACB test and an infecting microorganism that was sensitive to the antibiotic being used. Developing general recommendations for practicing clinicians based on these studies is complicated by their preselected nature. If an ACB test is not available and the sensitivity of the in-

TABLE 3.—*Recent Trials of Single-Dose Therapy Using Antibody-Coated Bacteria (ACB) Localization*

Study	*Drug*	*Dose*	*Efficacy**	*Relapse†*	*Reinfection†*
Fang et al, 1978[28]	Amoxicillin trihydrate	3 grams	22/22	0	2
Rubin et al, 1980[21] ...	Amoxicillin trihydrate	3 grams	34/38	0	1
Counts et al, 1982[33] ..	TMP-SMX	160 to 800 mg	36/38	3	6
Ludwig et al, 1980[31] ..	TMP-SMX	160 to 800 mg	18/19	0	1
	TMP-SMX	320 to 1,600 mg	19/20	0	2
	Sulfisoxazole	1 gram	17/20	0	1
	Sulfisoxazole	2 grams	15/17	0	2

TMP-SMX = trimethoprim-sulfamethoxazole.

*Eradication of infecting strain and symptoms at three to seven days' follow-up evaluation.
†At two to six weeks' follow-up evaluation.

fecting organism is unknown, as is usually the case in clinical practice, single-dose therapy poses several potential problems. Antimicrobial resistance may be more important when using single-dose therapy than with the conventional ten-day course. With conventional therapy, urinary tract infections can often be treated with antibiotics to which the organism is resistant in vitro, probably due to the high urine-to-serum concentration ratio (often 10:1) that many antibiotics achieve. As yet, the clinical efficacy of single-dose therapy in patients whose organism exhibits in vitro resistance has not been extensively studied. The effects of single-dose therapy on vaginal coliform colonization and long-term recurrence rates also deserve further study. Preliminary data suggest that single-dose therapy may be less efficacious than a ten-day course in eradicating vaginal coliforms[33]; failure to eliminate coliforms from the vaginal and urethral reservoir might result in more rapid recurrences. Finally, studies comparing different single-dose regimens and regimens of three to five days should be done in an effort to determine the optimal treatment for patients with dysuria and frequency.

Despite these uncertainties, single-dose therapy assures compliance, costs less than conventional therapy and causes fewer side effects. Even without the ACB test, physicians should consider single-dose therapy in adult women who have acute onset of lower urinary tract symptoms, no upper urinary tract signs, an illness of less than seven days' duration and where reasonable follow-up for a test-of-cure culture can be assured.[36] The clinical setting should not be a "high positive ACB population," such as a city hospital emergency room. Pregnant women and diabetic patients should not be treated with single-dose therapy until trials have been carried out on these types of patients.

Antimicrobial Prophylaxis for Recurrent UTI

Antimicrobial prophylaxis reduces the number of recurrences that develop in an infection-prone patient per year.[37] In Seattle studies 80 percent of infection-prone women given a placebo had a recurrent infection within six months, whereas administration of trimethoprim-sulfamethoxazole (half a tablet a day), nitrofurantoin (100 mg a day), or trimethoprim alone (100 mg a day) reduced the infection rate to near zero.[38] Unfortunately, the beneficial effect of antimicrobial prophylaxis does not continue after the patient stops taking the drug; as soon as prophylaxis is withdrawn, the infection rate returns to the baseline level. Studies to date have shown no significant emergence of resistant organisms in patients given long-term antimicrobial prophylaxis, and when recurrent infections have developed after stopping the antibiotic medication, the organisms identified have usually been sensitive to the agent previously used.

Who should receive antimicrobial prophylaxis and for how long? Our experience suggested that patients tend over many years to have a baseline pattern of recurrent infections that is predictable.[39] Most patients who have more than two infections per year appeared to benefit from long-term prophylaxis by reduced morbidity. In Seattle the cost of daily prophylaxis approximates $85 per patient per year, whereas the cost of three to four infections per patient-year exceeds $400.[40] Thus, prophylaxis appears cost effective in women with annual recurrence rates of three infections or more.

Prophylactic regimens of antibiotic medication taken daily, thrice weekly or after sexual intercourse all effectively prevent recurrent infections,[37] but deciding how long to give prophylaxis is difficult. An initial six months of prophylaxis should

be given to determine tolerance and effectiveness. Thereafter, knowledge of a woman's baseline rate of infection provides the best guide to need for longer prophylaxis. Many women with baseline infection rates of one to two a year may do well with three to six months of prophylaxis. Most women with three or more infections a year over many years will simply return to this baseline infection rate after discontinuation of prophylaxis and should be considered candidates for long-term prophylaxis.

Relationship of Sexual Activity to UTI

The epidemiologic observation that UTI's recur most frequently in young, sexually active women suggests a possible role of sexual activity in the pathogenesis of these infections. For *E coli* infection, however, there is little evidence supporting actual venereal passage of strains from a sexual partner. More likely, women in whom persistent coliform colonization of the periurethral area develops may be at increased risk of infection when they have regular sexual activity because urethral massage associated with intercourse facilitates entry of microorganisms into the bladder.[40-42] The successful use of postcoital prophylactic antibiotic therapy to prevent recurrent UTI supports this hypothesis.

Sexual transmission of urethral pathogens can produce dysuria and frequency, indistinguishable from coliform infection. Recent studies strongly suggest that among young, sexually active women, chlamydial infection causes the acute urethral syndrome.[11] Chlamydial infection in such women is characterized by dysuria, urinary frequency, sterile pyuria and response to treatment with tetracyclines.[11,43] *Staphylococcus saprophyticus,* a urinary pathogen responsible for about 10 percent of acute, symptomatic lower urinary tract infections in college women in Seattle, may also be sexually transmitted, but further study of this organism must be undertaken to substantiate this hypothesis.

Clinical Approach to Women With Acute Dysuria and Urinary Frequency

The newer concepts outlined can be incorporated into a revised clinical strategy for women with acute dysuria and urinary frequency (Figure 1). In a patient with lower urinary tract symptoms and signs, a diagnosis of vaginitis should be considered first. Factors favoring this diagnosis include an associated history of recently increased or changed vaginal discharge, vaginal odor, vaginal or labial itching or previous recurrent vaginitis. In most instances, women with vaginitis as the cause of dysuria have external symptoms, that is, burning as urine passes over the labia. They generally do not have associated symptoms of urinary urgency or frequency, suprapubic pain or hematuria. In sexually active women with dysuria and any of the historical factors noted above, a pelvic examination should be done and potential causes of vaginitis evaluated by physical examination, determination of vaginal fluid pH and wet smear (prepared with 0.9 percent sodium chloride solution) and potassium hydroxide (KOH) microscopy. Whether a vaginal examination should be done in all women with dysuria remains debatable. Komaroff and colleagues[44] suggested that in women with internal dysuria and none of the above-mentioned symptoms suggesting vaginitis, a pelvic examination was rarely helpful and could be omitted. However, because sexually transmitted pathogens such as *Chlamydia trachomatis* and *Neisseria gonorrhoeae* are prominent causes of dysuria, a strong argument can be made for doing a vaginal examination in all sexually active women with acute dysuria and urinary frequency.

After excluding vaginitis, a clinician should consider the two other causal categories, namely, urethritis-causing pathogens *(C trachomatis* and *N gonorrhoeae)* and urinary pathogens (coliforms and *S saprophyticus*). Although these two groups cannot be clearly distinguished on clinical grounds alone, suprapubic pain, gross hematuria or a history of UTI suggests the latter group.[11] In these women, abrupt onset of symptoms generally occurs and the patients have usually experienced symptoms for only one to four days before seeking medical care. Laboratory data consistent with coliform infection include the presence of pyuria on examination of a clean-voided, midstream, uncentrifuged urine specimen (more than eight leukocytes per cu mm when examined in a hemacytometer chamber), accompanied by hematuria in about 50 percent of cases.[11] When coliforms or staphylococci are present in bladder urine in quantities of more than 100,000 bacteria per ml, they can be readily seen in a Gram stain of unspun urine, confirming the diagnosis. However, if these agents are present in lesser quantities, the Gram stain will be negative and the organism identified only by culture.

Infection with *C trachomatis* or *N gonorrhoeae* occurs most commonly in young, sexually active

women who have had a recent sex partner change. A history of a partner with recent gonococcal or nongonococcal urethritis may also be obtained. Women with acute dysuria and urinary frequency due to chlamydial infection usually do not have symptoms of urgency, hematuria or suprapubic pain and give a history of a gradual onset of illness and 7 to 21 days of symptoms before seeking medical attention.[11] Pelvic examination may show mucopurulent cervicitis and many polymorphonuclear leukocytes but no gonococci on Gram stain of a cervical smear. Urine analysis shows pyuria (defined above), no hematuria and no bacteria on Gram stain of an unspun urine specimen. A Gram stain of a urethral smear will frequently show leukocytes. Women with gonococcal urethritis or cervicitis, or both, also tend not to have suprapubic pain or hematuria but may exhibit an illness of more abrupt onset. A Gram stain of a cervical smear will show intracellular Gram-negative diplococci in about 50 percent of women and, as with a chlamydial infection, pyuria should be seen. However, it must be emphasized that laboratory values for the diagnosis of urethritis due to *Chlamydia* or gonococci in women have not been as well studied as in men. The less precise measurement of pyuria in a centrifuged urine specimen examined under a coverslip, as done in most routine hospital laboratories, may be less useful in separating infected and uninfected patients. Gram stain of urethral smears in women needs further evaluation.

In cases not due to vaginitis, final diagnostic confirmation usually requires culture. The urine will reveal coliforms or staphylococci in quantities greater than 100,000 bacteria per ml in women with acute cystitis. Care should be taken to be certain the laboratory does not disregard *S saprophyticus,* a coagulase-negative *Staphylococcus,* as a contaminant. In women with a clinical presentation typical of cystitis but with 100 to 10,000 coliforms or staphylococci in a midstream urine

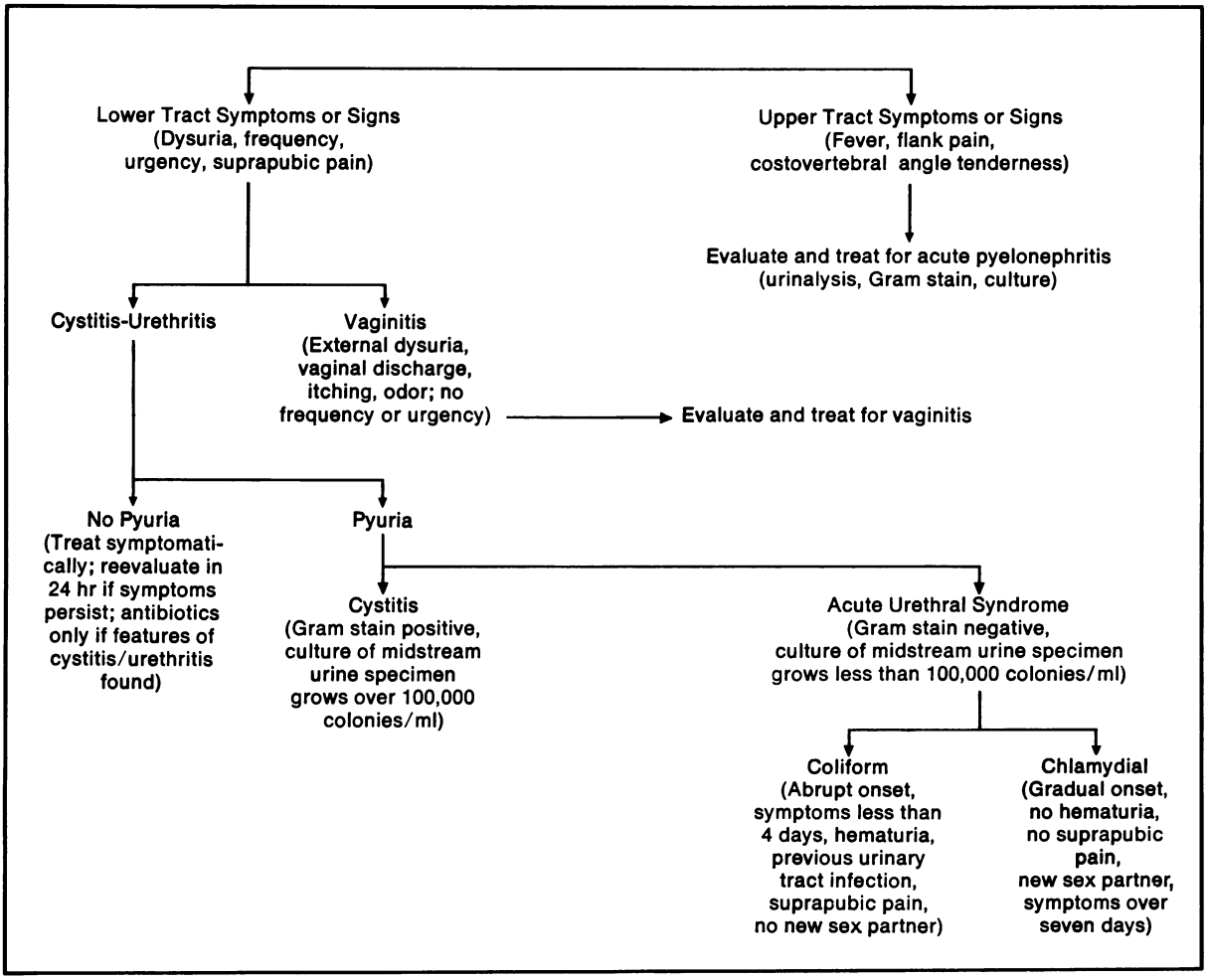

Figure 1.—Approach to the diagnosis of dysuria and urinary frequency.

specimen, there is a strong indication of a diagnosis of acute urethral syndrome. Particular care should be exercised to obtain clean-voided specimens in these patients to minimize contamination of the cultured urine with low quantities of perineal or fecal coliforms. In some patients, specimens obtained by urethral catheterization or suprapubic aspiration may be the only means of accurately distinguishing "low count" coliform infection from a contaminated specimen.

If available, chlamydial cultures of both urethral and cervical specimens should be obtained in women with sterile pyuria. A thin, calcium-alginate swab should be used for the former and a plastic-shafted swab for the latter, with care taken in both cases to obtain many epithelial cells. In instances where chlamydial cultures are not available, a tentative diagnosis of *C trachomatis* infection can be made by finding sterile pyuria (that is, pyuria associated with neither coliforms nor *S saprophyticus*), a culture negative for gonococci and clinical features of chlamydial infection, including dysuria and urinary frequency. Chlamydial infection can be effectively treated with a 10- to 14-day course of tetracycline, erythromycin or trimethoprim-sulfamethoxazole.[43] It should be emphasized, however, that simultaneous infection with more than one agent may occur, and all appropriate cultures should be obtained if possible.

In women without demonstrable pyuria, an infectious agent responsible for acute dysuria and frequency usually has not been found.

REFERENCES

1. Kass EH: Chemotherapeutic and antibiotic drugs in the management of infections of the urinary tract. Am J Med 1955; 18:764-781

2. Kass EH: Asymptomatic infections of the urinary tract. Trans Assoc Am Physicians 1956; 69:56-63

3. Sanford JP, Favour CD, Mayo FH, et al: Evaluation of the "positive" urine culture: An approach to the differentiation of significant bacteria from contaminants. Am J Med 1956; 20:88-93

4. Gallagher DJ, Montgomerie JZ, North JDK: Acute infections of the urinary tract and the urethral syndrome in general practice. Br Med J 1965; 1:622-626

5. Brooks D, Mandar A: Pathogenesis of the urethral syndrome in women and its diagnosis in general practice. Lancet 1972; 2: 893-898

6. Mond NC, Percival A, Williams JD, et al: Presentation, diagnosis and treatment of urinary-tract infections in general practice. Lancet 1965; 1:514-516

7. Tapsall JW, Taylor RC, Bell SM, et al: Relevance of "significant bacteriuria" to aetiology and diagnosis of urinary-tract infection. Lancet 1975; 1:637-644

8. O'Grady FW, Richards B, McSherry MA, et al: Introital enterobacteria, urinary infection, and the urethral syndrome. Lancet 1970; 2:1208-1210

9. Stamey TA, Govan DE, Palmer JM: The localization and treatment of urinary tract infections: The role of bactericidal urine levels as opposed to serum levels. Medicine (Baltimore) 1965; 44:1-36

10. Mabeck CE: Studies in urinary tract infections—I. The diagnosis of bacteriuria in women. Acta Med Scand 1969 Jul-Aug; 186:35-39

11. Stamm WE, Wagner KF, Amsel R, et al: Causes of the acute urethral syndrome in women. N Engl J Med 1980; 303:409-415

12. Mabeck CE: Studies in urinary tract infections—IV. Urinary leucocyte excretion in bacteriuria. Acta Med Scand 1969; 186: 193-198

13. Brumfitt W: Urinary cell counts and their value. J Clin Pathol 1965; 18:550-553

14. Jones SR, Smith JW, Sanford JP: Localization of urinary tract infections by detection of antibody-coated bacteria in urine sediment. N Engl J Med 1974 Mar 14; 290:591-593

15. Thomas V, Shelokov A, Forland M: Antibody-coated bacteria in the urine and the site of urinary-tract infection. N Engl J Med 1974 Mar 14; 290:588-590

16. Mundt KA, Polk BF: Identification of site of urinary-tract infections by antibody-coated bacteria assay. Lancet 1979 Dec 1; 2:1172-1175

17. Riedasch G, Ritz E, Möhring K, et al: Antibody coating of urinary bacteria: Relation to site of infection and invasion of uroepithelium. Clin Nephrol 1978 Dec; 10:239-240

18. Kohnle W, Vanek E, Federlin K, et al: Lokalisation eines Harnwegsinfektes durch Nachweis von antikörperbesetzten Bakterien im Urin. Dtsch Med Wochenschr 1975 Dec 19; 100:2598-2602 (Eng. Abstr.)

19. Harding GKM, Marrie TJ, Ronald AR, et al: Urinary tract infection localization in women. JAMA 1978 Sep 8; 240:1147-1151

20. Hawthorne NJ, Kurtz SB, Anhalt JP, et al: Accuracy of antibody-coated-bacteria test in recurrent urinary tract infections. Mayo Clin Proc 1978 Oct; 53:651-654

21. Rubin RH, Fang LST, Jones SR, et al: Single-dose amoxicillin therapy for urinary tract infection—Multicenter trial using antibody-coated bacteria localization technique. JAMA 1980 Aug 8; 244:561-564

22. Smith JW, Jones SR, Kaijser B: Significance of antibody-coated bacteria in urinary sediment in experimental pyelonephritis. J Infect Dis 1977 Apr; 135:577-581

23. Pylkkänen J: Antibody-coated bacteria in the urine of infants and children with their first two urinary tract infections. Acta Paediatr Scand 1978 May; 67:275-279

24. Stamm WE, Cutter BE, Grootes-Reuvecamp GA: Enzyme immunoassay for detection of antibody-coated bacteria. J Clin Microbiol 1981 Jan; 13:42-45

25. Fair WR, McClennan BL, Jost RG: Are excretory urograms necessary in evaluating women with urinary tract infection? J Urol 1979 Mar; 121:313-315

26. Engel G, Schaeffer AJ, Grayhack JT, et al: The role of excretory urography and cystoscopy in the evaluation and management of women with recurrent urinary tract infection. J Urol 1980 Feb; 123:190-191

27. Fowler JE, Pulaski ET: Excretory urography, cystography, and cystoscopy in the evaluation of women with urinary-tract infection. N Engl J Med 1981; 304:462-465

28. Fang LST, Tolkoff-Rubin NE, Rubin RH: Efficacy of single-dose and conventional amoxicillin therapy in urinary-tract infections localized by the antibody-coated bacteria technique. N Engl J Med 1978; 298:413-416

29. Marsh FP, Banerjee R, Panchamia P: The relationship between urinary infection, cystoscopic appearance and pathology of the bladder in man. J Clin Pathol 1974 Apr; 27:297-307

30. Ronald AR, Boutros P, Mourtada H: Bacteriuria localization and response to single-dose therapy in women. JAMA 1976 Apr 26; 235:1854-1856

31. Buckwold FJ, Ludwig P, Harding GK, et al: Therapy for acute cystitis in adult women. JAMA 1982; 247:1839-1842

32. Anderson JD, Aird MY, Johnson AM, et al: The use of a single large dose of amoxycillin for the treatment of acute urinary tract infections. J Antimicrob Chemother 1979 Jul; 5:481-483

33. Counts GW, Stamm WE, McKevitt M, et al: Treatment of cystitis in women with a single dose of trimethoprim-sulfamethoxazole. Rev Infect Dis 1982; 4:484-490

34. Bailey RR, Abbott GD: Treatment of urinary tract infection with a single dose of amoxycillin. Nephron 1977; 18(6): 316-320

35. Bailey RR, Abbott GD: Treatment of urinary tract infection with a single dose of trimethoprim-sulfamethoxazole. Can Med Assoc J 1978 Mar 4; 118:551-552

36. Stamm WE: Single-dose treatment of cystitis. JAMA 1980 Aug 8; 244:591-592

37. Ronald AR, Harding GK: Urinary infection prophylaxis in women (Editorial). Ann Intern Med 1981 Feb; 94:268-270

38. Stamm WE, Counts GW, Wagner KF, et al: Antimicrobial prophylaxis of recurrent urinary tract infections: A double-blind, placebo-controlled trial. Ann Intern Med 1980; 92:770-775

39. Stamm WE, Counts GW, McKevitt M, et al: Urinary prophylaxis with trimethoprim and trimethoprim-sulfamethoxazole—Efficacy, influence on the natural history of recurrent bacteriuria and cost control. Rev Infect Dis 1982; 4:450-455

40. Stamm WE, McKevitt M, Counts GW, et al: Is antimicrobial prophylaxis of urinary tract infections cost effective? Ann Intern Med 1981 Feb; 94:251-255

41. Kunin CM: Sexual intercourse and urinary infections (Editorial). N Engl J Med 1978 Feb 9; 298:336-337

42. Buckley RM Jr, McGuckin MB, MacGregor RR: Urine bacterial counts after sexual intercouse. N Engl J Med 1978 Feb 9; 298:321-324

43. Stamm WE, Running K, McKevitt M, et al: Treatment of the acute urethral syndrome. N Engl J Med 1981 Apr 16; 304: 956-958

44. Komaroff AL, Pass TM, McCue JD, et al: Management strategies for urinary and vaginal infections. Arch Intern Med 1978 Jul; 138:1069-1073