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Current Comments®

Cystitis and Other Urinary Tract Infections. Part 2. Diagnosis and Treatment

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Last week, we discussed the etiology and epidemiology of cystitis and other urinary tract infections (UTIs).[1] UTIs are among the most common infections encountered by physicians around the world. They are caused primarily by bacteria from the bowels and most often affect women, especially elderly women. However, men and children are also victims. The onset and progression of UTIs are affected by numerous factors. As will be seen here, the diagnosis and treatment of these infections can also be complex.

Determining the cause of urinary symptoms is a formidable task. Diagnoses of lower- or upper-tract infections based solely on symptoms are frequently inaccurate.[2-4] According to a 1971 study of the sites of UTIs and of the patients' symptoms by K.F. Fairley and colleagues, then at the University Department of Medicine, Royal Melbourne Hospital, Australia, signs of lower-tract disorders were often the only symptoms exhibited by patients with proven renal infections.[2] Moreover, not all symptomatic patients have a UTI. They may be suffering instead from an inflammation of the vagina or vulva (vaginitis and vulvitis, respectively), or even from such sexually transmitted diseases (STDs) as candidiasis, trichomoniasis, gonorrhea, or genital herpes.[5] Indeed, it is estimated that 10 to 20 percent of women suffering from symptoms of UTIs have been infected by the sexually transmitted microorganism *Chlamydia trachomatis*.[6]

Many individuals with a UTI may suffer no symptoms at all.[7] In such cases, the key to an accurate diagnosis, according to Marvin Turck, University of Washington and Harborview Medical Center, Seattle, is detection of bacteriuria.[8] The simplest method is to examine a sample of freshly collected urine under an ordinary light microscope. A more accurate method is the urine culture. But a urine sample can be easily contaminated by bacteria from the vagina, perineum, or pubic hair, according to Walter E. Stamm, University of Washington and Harborview Medical Center.[9] So, in the 1950s, Edward H. Kass, then at the Department of Medicine, Harvard Medical School and Boston City Hospital, Massachusetts, established that a diagnosis of UTI should be made only if two consecutive urine cultures contain more than 100,000 microorganisms per milliliter.[10-12] This ruled out contaminated samples, which rarely contained so many microorganisms.

To reduce the risk of contamination, samples are sometimes collected by inserting a sterile catheter through the patient's urethra into the bladder, or by suprapubic aspiration, in which urine is collected through a large needle plunged through the patient's abdomen. Using the latter method, Stamm and colleagues, Department of Medicine, University of Washington School of Medicine, Seattle Public Health Center, and Harborview Medical Center, found that only 51 percent of the women whose

urine samples contained bacteria would have been diagnosed as having UTIs by Kass's criterion.[13] Thus, they recommended that the standard of 100 microorganisms per milliliter be used to diagnose lower-tract UTIs.[13]

But the urine cultures of 30 to 50 percent of all women with symptoms of lower-tract infections contain no evidence of bacteria.[14] Some of these women, when treatment repeatedly fails, may have to undergo a battery of tests, including urinalysis, excretory urography, cystography, urodynamic studies, and cystoscopic examination. Urinalysis consists of a microscopic examination of the urine's physical and chemical makeup.[15] For women whose predominant symptom is urgency or incontinence, urodynamics, the study of the urinary tract in action, may help identify functional irregularities.[15] Using specially designed catheters and recording equipment, the flow rate of the urine, the amount of urine left in the bladder after voiding, the pressure exerted by the urine in the urethra and the bladder, and the tension of the urethral sphincter and pelvic muscles are assessed.[16] In those instances in which abnormalities are found, UTIs are almost always secondary diseases.[15] It should be emphasized, however, that such extensive testing is rarely necessary.

Excretory urography and cystography are used to identify structural abnormalities by outlining the urinary tract with a medium that is opaque to X rays. The routine use of these procedures is not justified, however, since about 90 percent of the patients who undergo these tests have no abnormalities.[15,17] Cystoscopy, the examination of cells scraped from the lining of the urinary tract under a local anesthetic, is also not recommended for routine use. But compared with the other procedures, it is relatively inexpensive, carries little risk for the patient, and occasionally reveals useful information.[15]

Once a UTI has been diagnosed, many practitioners recommend locating the site of the infection, since that, in part, determines how the disease will be treated. One method, the bladder-washout technique, developed by Fairley and colleagues, distinguishes upper- from lower-tract infections.[18] It involves collecting a urine sample through a catheter, emptying the bladder, and pumping back in a solution of sterile saline and antibiotic. After the bladder is again emptied and washed out with sterile water, urine is collected every 10 minutes and bacteria counts are made. If all specimens following the washout contain no microorganisms, then the site of the infection is the bladder itself. Bacteria in specimens immediately following the washout procedure indicate an infection in the ureters or kidneys.

Although highly reliable, the bladder-washout technique is expensive, cumbersome, and invasive. The patient may be catheterized for up to two hours or more.[19] Virginia Thomas, Alexis Shelokov, and Marvin Forland, Departments of Microbiology and Medicine, University of Texas Medical School, San Antonio, have developed a simple, risk-free method, using immunofluorescence, to detect the presence of bacteria coated with antibodies. They found that 34 of 35 patients known to have pyelonephritis had antibody-coated bacteria in their urine, while 19 of 20 patients with cystitis did not.[20] The results of the antibody-coated bacteria test, as it is known, correlate well with those of the bladder-washout technique.[4,21] However, according to Godfrey K.M. Harding and colleagues, University of Manitoba and the Health Sciences Center, Winnipeg, Canada, some women with upper-tract infections have bacteria in their urine that are not coated with antibodies.[4] They advise caution in interpreting negative results from the antibody-coated bacteria test.

In many cases of lower-tract UTIs, symptoms may disappear within 48 hours,[8] and 80 to 90 percent of patients rid their urine of bacteria within 72 hours to one week.[6,8] But symptoms and bacteriuria may not be gone for good, and, in any event, antibiotics will clear them

up much more quickly than simply allowing them to run their course.[9] So most clinicians prefer to treat all women with symptoms of UTIs. They also treat asymptomatic infections discovered during evaluations for other complaints, since many subsequently become symptomatic.[4] Since UTIs may be caused by one or more factors, and may be localized in the urethra or bladder or spread throughout the urinary tract, various therapies for UTIs have evolved, with varying degrees of success. The most commonly used treatments include courses of antibiotics. Dilatation of the urethra and surgery have also been common in the past and still have their adherents around the world, but many practitioners doubt their value. More will be said about this later.

Lower-tract UTIs in which the infecting bacteria can be identified usually respond to any broad-spectrum antibiotic, regardless of the patient's age or sex.[7] According to Burke A. Cunha, Department of Medicine, State University of New York School of Medicine, standard therapy consists of suitable dosages of a sulfanomide, ampicillin, trimethoprim, trimethoprim-sulfamethoxazole, or nitrofurantoin for 7 to 14 days.[6] Although symptoms may quickly disappear, Turck recommends a follow-up urine culture one to two weeks after therapy is completed.[8] A patient is said to be "cured" when the urine is sterile.[22] The cure rate immediately following an individual course of antibiotic therapy in uncomplicated UTIs ranges from 95 to nearly 100 percent. When a bacterial infection is secondary to an obstruction or other abnormality, these must be resolved first if the treatment for the UTI is to be successful.[7,8]

In recent years, however, the duration of antimicrobial therapy for uncomplicated, lower-tract UTIs has been reconsidered.[23] To improve patient compliance with therapy, contain costs, and reduce drug-related side effects—which may include rashes, yeast infections of the vagina, nausea, and vomiting—clinicians explored the feasibility of single-dose therapy. In 1978, Leslie S.T. Fang and colleagues, Department of Medicine, Harvard Medical School and the Renal and Infectious Disease Units, Massachusetts General Hospital, Boston, reported the results of the clinical trial of a single, three-gram dose of an antibiotic in each of 22 patients with lower-tract UTIs, as determined by the antibody-coated bacteria test.[24] All were symptom-free within 24 to 48 hours. Although single-dose therapies have proved to be about as effective as conventional therapy under certain circumstances,[25,26] they are by no means a panacea. In conventional therapy, a high concentration of medication builds in the urine, eradicating even antibiotic-resistant bacteria.[23] Preliminary data suggest, according to Stamm, that single-dose therapy is less effective against resistant bacteria than conventional therapy.[23] Stamm notes that using single-dose therapy in place of conventional therapy trades effectiveness for fewer side effects.[9]

As mentioned earlier, no infecting pathogen can be identified in many women with symptoms of lower-tract UTIs, so antibiotics are ineffective.[7] In some of these women, the symptoms may be due to renal tuberculosis,[14] although this is uncommon.[9] In others, highly spiced foods, alcohol, chocolate, and caffeine may irritate the bladder. Analgesics and antispasmodics are effective in such instances.[7] In a few cases, symptoms are due to inflammatory, ulcer-like lesions in the lining of the bladder—a condition called interstitial cystitis. Although its causes are unknown, it is treatable by repeatedly filling the bladder through a catheter with a solution of oxychlorosene sodium.[27] Often, however, the cause of symptoms falls into none of these categories. In such cases, some practitioners resort to surgery to correct a possible structural defect. However, Stamm notes that the overwhelming majority of women with lower-tract UTIs have no demonstrable abnormalities that need to be addressed through surgery.[9]

Almost 90 percent of the women who experience UTIs can expect another infection within 12 months.[28] Eighty percent of these recurrences are due to infections with microorganisms other than the type that caused the original UTI.[22] According to David A. Haase and Allan R. Ronald, Department of Medical Microbiology, University of Manitoba, the other 20 percent are due to numerous factors including: the emergence of an antibiotic-resistant strain of the original infecting organism, poor patient compliance, inadequate levels of medication in the patient's urine due to the kidneys' failure to concentrate the drug in the bladder, and the reemergence of the original infecting organism following successful therapy.[29]

Long-term antibiotic therapy, or prophylaxis, is an attempt to reduce or eliminate altogether the number of recurrences that infection-prone patients develop.[23] The treatment consists of various dosages taken at intervals of twice daily, thrice weekly, or after sexual intercourse for periods ranging from six months to two years.[23,30] Stamm and colleagues reported that 80 percent of infection-prone women given a placebo had another infection within six months of their original course of treatment, whereas women on antibiotics during that time experienced a recurrence rate near zero.[31] Although long-term therapy raises concerns about microbial resistance, its only drawback seems to be that its beneficial effects do not persist once the patient discontinues use of the drug. Still, long-term antibiotic therapy is far more cost-effective than treating each infection as it occurs. Stamm's group reported that the yearly cost of prophylaxis was $85 in 1981, compared with a cost of almost $400 for per-episode treatment.[32]

One of the most common methods of treating recurrent UTIs in the past has been urethral dilatation,[8] the enlarging of the urethral passage. It is still employed by some practitioners. Dilatation is usually performed under some kind of anesthesia. Dilatation is an attempt to reestablish normal urine flow in women whose urethras are thought to be so narrow that turbulence washes bacteria back into the bladder.[33] Its effectiveness, however, is questionable. A study by W.F. Hendry and colleagues, St. Peter's Hospitals and Institute of Urology, London, found that dilatation helps only when combined with antibiotic therapy.[33]

When UTIs are especially unresponsive to treatment, surgery may be an alternative among some practitioners. In a study of 40 women suffering from various combinations of symptoms, ranging from frequency of urination, dysuria, and incontinence to recurrent UTIs, urologist Patrick J.B. Smith, United Hospitals, Bath, England, and colleagues, found that removing one-third of the urethra (urethrectomy) helped 87 percent of those with urgency and dysuria.[34] In women also suffering from incontinence, however, only 14 percent benefited from the procedure. None of the women with recurrent UTIs experienced any improvement. Speculating on these results, Smith suggests that the women experiencing dysuria and urgency had "hypersensitive" urethras. Since the operation results in the partial denervation of the urethra, they felt less pain and experienced the urge to urinate less frequently. However, using a similar procedure, called urethrotomy, Richard D. Hart and Brent J. Murphy, Flint Osteopathic Hospital, Michigan, reported that 70 percent of their patients with recurrent UTIs had complete relief.[35] Twenty-two percent experienced some relief and only eight percent did not experience improvement in symptoms.

Another procedure, called urethroplasty, is sometimes used to treat women whose symptoms are associated with sexual activity. It involves severing the lowest portion of the urethra, including its opening, from its vaginal attachments, and moving it farther away from the vagina. Smith found that of 41 women treated with urethroplasty, 21 had no

further symptoms, seven had significant relief, but 13 showed no improvement.[36] And of 40 women between the ages of 40 and 50 who had symptoms of frequency of urination, an interrupted urine stream, and a need to strain when urinating, A.J. Splatt and D. Weedon, Departments of Surgery and Pathology, respectively, Royal Brisbane Hospital, Australia, reported that 38 showed improvement following urethroplasty.[37] The remaining two showed improvement after further surgery.

However, Stamm emphasizes that neither dilatation nor surgery is a common or recommended procedure, and that neither can be justified by any reliable evidence.[9] No substantive evidence supports the idea that a "tight urethra" plays a role in the development of recurrent UTIs.[8] Indeed, according to Ross R. Bailey, Department of Renal Medicine, Christchurch Hospital and Clinical School, New Zealand, "The popular urological practice of dilating the female urethra is unnecessary and unjustified."[38] Joseph N. Corriere, Department of Surgery, University of Texas Medical School, Houston, asserts that most women with UTIs "merely need the cheapest effective antibiotic available."[39] In a comparison of urethrotomy with antibotic therapy in the treatment of recurrent UTIs, N.R. Netto and R. Pimenta da Silva, Department of Urology, Hospital Beneficencia Portuguesa, São Paulo, Brazil, found that two-thirds of the 41 women they treated with antibiotics had relief from their symptoms, whereas only one-third of the other 30 they treated surgically had similar relief.[40] They concluded that antibi-

Table 1: A selected list of organizations that are concerned with urinary tract infections.

American Association of Clinical Urologists (AACU)
21510 South Main Street
Carson, CA 90745

American Association of Genito-Urinary Surgeons (AAGUS)
Mayo Clinic
Rochester, MN 55905

American Urological Association (AUA)
1120 North Charles Street
Baltimore, MD 21201

Association Française d'Urologie
60 Blvd. de Latour-Maubourg
F-75327 Paris, France

Berufsverband der Deutschen Urologen e.V.
c/o Dr. Dieter Heck
Tullastrasse 3
D-6800 Mannheim 1, FRG

British Association of Urological Surgeons (BAUS)
Royal College of Surgeons
35-43 Lincoln's Inn Fields
London WC2A 3PN, UK

Clinical Society of Genito-Urinary Surgeons (CSGUS)
c/o Dr. Jay Gillenwater
Box 422
University of Virginia Hospital
Charlottesville, VA 22908

National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases (NIADDKD)
c/o Dr. George Brooks
Westwood Bldg., Room 637
Bethesda, MD 20205

National Kidney Foundation (NKF)
Two Park Avenue
New York, NY 10016

Nippon Hinyoki-ka Gakkai
c/o Dr. Tadao Niijima
Taisei Bldg.
3-14-10 Hongo, Bunkyo-ku
Tokyo, Japan

Società Italiana di Urologia (SIU)
c/o Dr. Luciano Giuliani
Viale Cortina d'Ampezzo 49
I-00135 Rome, Italy

Société Française d'Urologie
6 Ave. Constant Coquelin
F-75007 Paris, France

Société Internationale d'Urologie (SIU)
63 Ave. Niel
F-75017 Paris, France

Society for Pediatric Urology (SPU)
c/o Dr. John Woodard
School of Medicine, Division of Urology
Emory University
Atlanta, GA 30322

Society of University Urologists (SUU)
Box 403, Section of Urology
University of Chicago
950 East 59th Street
Chicago, IL 60637

otic treatment was superior to surgery. Moreover, since surgery is always accompanied by antibiotic therapy, any favorable results are actually due to the medication, rather than to the procedure itself.[40]

Although the topic of preventing UTIs is limited, in the scientific literature, to discussions of long-term antibiotic therapy, popular articles in "women's magazines" contain numerous suggestions. Most encourage women to drink at least six glasses of fluid a day and to void regularly and frequently. But there are no systematic studies that demonstrate that anyone is really cured through such measures.[41] A high fluid intake can produce a decreased bacteria count in the urine.[42] Many popular articles go a step further, however, and recommend that drinking large quantities of cranberry or grapefruit juice or taking vitamin C can acidify the urine and thus make it less hospitable to bacteria.[43-46] No evidence exists to support this claim. Yet some of the advice given in these articles is practical: a woman should always wipe from front to back after using the toilet, and both she and her sex partner should be clean before engaging in intercourse.

Table 1 lists the associations in which physicians concerned with the diagnosis and treatment of UTIs may hold membership. These organizations hold annual meetings and continuing education seminars and some sponsor a journal reflecting the society's interests. For example, the American Urological Association sponsors the *Journal of Urology*.

Journals covered in *Current Contents*® (*CC*®) and *Science Citation Index*® (*SCI*®) that include most of the articles on urinary tract infection are in fact urological journals. These are listed in Table 2 with their associated 1983 impact values. Impact indicates how often, on average, an article published by a certain journal in a given two-year period was cited during a particular year. The impacts given in Table 2 were arrived at by dividing the number of citations received in 1983 by the number of articles published in 1981 and 1982.

Table 2: Some of the main journals publishing research on urinary tract infections. The 1983 impact factor of each is listed.

Journal	Impact Factor
Annales d'Urologie	.17
British Journal of Urology	.66
European Urology	.55
Investigative Urology	1.36
Journal d'Urologie	.13
Journal of Urology	1.32
Kidney International	4.19
Scandinavian Journal of Urology and Nephrology	.71
Urologe-Ausgabe A	.37
Urologic Clinics of North America	1.04
Urologic Radiology	.79
Urological Research	.63
Urology	.72

Table 3: *SCI*® research fronts on urinary tract infections. A = research front number. B = research front name. C = number of core papers in the research front.

A	B	C
83-0493	Use of trimethoprim and other drugs in the treatment of urinary tract infections in women	34
82-0722	Antimicrobial therapy for urinary tract infection	4
82-1305	Clinical and pharmacological comparison of use of trimethoprim alone or in combination as co-trimoxazole in treatment of urinary tract infections and other infections	2
82-2616	Chemical and clinical studies on the role of adherence of *E. coli* to host glycolipid receptors in the pathogenesis of urinary tract infection	2
81-0652	Treatment of urinary tract infection	3
81-1465	Interstitial cystitis and secondary dysfunctions associated with systemic lupus erythematosus	2
81-1953	Diagnosis of urinary tract infections	2
81-2387	Urinary tract infections	2

A number of the papers mentioned in this essay are core documents in several *SCI* research fronts. The titles of these research fronts are listed in Table 3. As I have explained previously, a research front is determined by identifying a group of current papers that collectively cite a cluster of older "core" papers.[47] Papers by Fairley and colleagues,[2,18] Harding and colleagues,[4] Stamm's group,[13] Thomas and colleagues,[20] and Kunin[22] are included in the core literature of the 1983 research front entitled "Use of trimethoprim and other drugs in the treatment of urinary tract infections in women." The papers by Thomas and colleagues,[20] Fang and colleagues,[24] and Bailey and Abbott[25] appear in the core literature of the 1982 front entitled "Antimicrobial therapy for urinary tract infection." Thomas's paper[20] is also among the core articles of the 1981 front on "Diagnosis of urinary tract infections." The papers by Fang,[24] Bailey and Abbott,[25] and A.R. Ronald and colleagues[3] make up the core of the 1981 research front, "Treatment of urinary tract infection."

Although literature on UTIs is abundant, a consensus among clinicians and practitioners on its causes and treatment in women who experience chronic recurrences is elusive. For instance, whereas some physicians believe surgery to be a viable treatment for women suffering from chronic cystitis, others react with horror and disbelief that any competent practitioner would even consider such a course of action. And while comparisons of the efficacy of various treatments are useful, endless debate on such matters may result in the neglect of other promising avenues of research.

Indeed, it is difficult to decide whether cystitis and other UTIs constitute another of the neglected areas of medicine, simply because they are almost never fatal. As such, they will not produce a significant lobby, as do diseases such as lung cancer and heart disease. It is absurd to hope that genetic engineering may provide the desired result.

* * * * *

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