

# Current Comments®

## Cystitis and Other Urinary Tract Infections. Part 1. Etiology and Epidemiology

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In the past few years, we have published essays on numerous health problems, including herpes simplex virus infections<sup>1</sup> and trichomoniasis<sup>2</sup>—sexually transmitted diseases that are especially serious for women. This two-part essay reviews a family of closely linked disorders that primarily affect women: urinary tract infections (UTIs). UTIs are among the most common infections encountered by physicians around the world. Although UTIs occur most often in elderly women, they are common in sexually active women as well. Indeed, it is estimated that 10 to 20 percent of all women everywhere will experience at least one episode of UTI.<sup>3</sup>

Most UTIs involve only the lower urinary tract.<sup>4</sup> This consists of the bladder, which stores urine, and the urethra, which carries urine from the body. Lower-tract UTIs are designated by the terms cystitis (inflammation of the bladder) and urethritis (inflammation of the urethra—although some clinicians do not classify urethritis as a UTI). Indications of a lower-tract infection include: a frequent need to urinate, a burning sensation upon urination (dysuria), bacteria in the urine (bacteriuria), and occasional blood and pus in the urine (pyuria).

Occasionally, however, disease-causing bacteria may travel beyond the urethra and bladder to invade the upper urinary tract. The upper tract consists of the kidneys and ureters. The kidneys filter wastes from the blood and concentrate them in the form of urine. The ure-

ters are the fibrous, muscular tubes which carry urine from the kidneys to the bladder. An upper-tract infection, or pyelonephritis, is far more serious than its lower-tract counterpart. It generally combines the symptoms of lower-tract infections with fever, chills, nausea, vomiting, and pain in the lower back. And whereas lower-tract UTIs are virtually never life-threatening, pyelonephritis can cause massive kidney damage in a small percentage of cases. In rare instances, chronic pyelonephritis can lead to a systemic blood infection, which can cause death. One goal of lower-tract treatment is to prevent the spread of the disease to the upper urinary tract—not the mere relief of symptoms.<sup>4,5</sup>

In the past, lower-tract infections were thought to have a single cause, treatable with a few types of therapy.<sup>6</sup> Now, however, many causes have been identified. This has in turn resulted in an increase in the types of therapy available, and in controversies over the best treatment. The causes of lower-tract UTIs are discussed here. Diagnosis and treatment will be covered later.

According to Burke A. Cunha, Department of Medicine, State University of New York School of Medicine, Stony Brook, the most common bacteria responsible for lower-tract UTIs are Enterobacteriaceae, normally found in the intestines.<sup>6</sup> They account for 80 to 95 percent of such infections.<sup>7</sup> Of these, perhaps 80 percent are caused by *Escherichia coli*, which migrate from the

bowel to the vagina across the perineum, the fleshy bridge between the anal opening and the vulva. Other bacteria which often cause UTIs include *Proteus mirabilis*, *Klebsiella*, and *Enterobacter*.<sup>6,7</sup>

Marvin Turck, University of Washington, Seattle, and physician-in-chief, Harborview Medical Center, Seattle, suggests that the very structure of the female anatomy may predispose women to lower-tract UTIs.<sup>4</sup> The male urethra is eight to ten inches long—an arduous trip for bacteria trying to reach the bladder. Regular urination will wash them out before they attain their goal. Moreover, since the male urethra opens at the tip of the penis, it is far removed from the main reservoir of the bacteria that cause UTIs—the anus. Turck also speculates that an antimicrobial agent may be present in prostatic fluid, giving men added protection.<sup>4</sup> The female urethra, on the other hand, is a short, straight passage averaging only 1.5 inches. Situated in close proximity to the anus, it provides an easy avenue for bacterial invasion. Once in the urethra, they ascend rapidly into the bladder and begin to multiply.

Physical stress and injury to the urethra can also make it easier for bacteria to invade the urinary tract. Wayne C. Waltzer, Department of Surgery, State University of New York, Stony Brook, notes in a review that changes in the shape of the bladder and urethra during pregnancy and childbirth may prevent invading bacteria from being washed out by the flow of urine.<sup>8</sup> Structural degeneration of the pelvic organs, due to age and changes in hormonal levels, may also make women more susceptible to UTIs, according to urologist Patrick J.B. Smith, United Hospitals, Bath, England.<sup>9,10</sup> Smith found that the linings of both the vagina and the urethra tend to become atrophied, rigid, inelastic, and inflamed as estrogen levels fall in postmenopausal women. This provides bacteria with the opportunity to successfully colonize the tissue.

Little evidence supports the notion that lower-tract infections result primarily from sexual transmission, according to Walter E. Stamm, University of Washington and Harborview Medical Center.<sup>11</sup> Even so, the association between sexual activity and the incidence of lower-tract UTIs is strong enough to have fostered the term, “honeymoon cystitis.” A 1968 study by Calvin M. Kunin and Regina C. McCormack, then of the Departments of Preventive Medicine and Internal Medicine, respectively, University of Virginia School of Medicine, Charlottesville, is among the many investigations indirectly linking sexual activity and UTIs. Comparing the incidence of bacteriuria in nuns and married women, they found that in the urine of sexually active women, the bacteria count was almost triple that of nuns.<sup>12</sup> But is intercourse a direct cause of lower-tract infections, or does it merely provoke symptoms? Lindsay E. Nicolle and colleagues, Departments of Medical Microbiology and Medicine, University of Manitoba, Winnipeg, Canada, studied 15 sexually active women who had each experienced at least two lower-tract infections within a six-month interval. They found that most experienced an infection within 24 hours after intercourse. The authors speculate that bacteria from the perineum are massaged into the urethra during foreplay and intercourse.<sup>13</sup>

But to trigger the onset of symptoms and progression to a diseased state, it is not enough for bacteria to merely enter the urinary tract, according to urological surgeon Jack Lapidés, University of Michigan Medical Center, Ann Arbor.<sup>14</sup> The urinary tracts of normal, healthy men and women are constantly subjected to bacterial invasions, but the body's defenses and the wash of the urine stream remove the invaders. For infection to occur, Lapidés believes that some physical abnormality—whether permanent or transient, systemic or local—must allow the bacteria to remain there.

These abnormalities include outright structural damage, insufficient blood supply to the urinary tract tissues, and the presence of parasites, obstructions, and foreign bodies, including catheters.<sup>14</sup>

According to Lapidès, such abnormalities—particularly that of reduced blood supply—are linked to the victim's health and other habits. Lapidès theorizes that abnormally infrequent urination results in chronic overdistention of the bladder.<sup>14</sup> This, in turn, constricts the organ's blood vessels, restricting blood supply and increasing the likelihood of infection. To test this theory, Lapidès investigated 250 women and 71 girls with histories of recurrent UTIs.<sup>15</sup> Two-thirds were found to void only once in five to ten hours, and most had unusually large bladder capacities. However, Stamm notes that these ideas are not widely accepted and suggests that simply holding the urine for a long period of time—giving bacteria a chance to breed—goes further toward explaining some women's susceptibility to infection than notions about decreased blood supply.<sup>16</sup>

Other factors that may trigger the appearance of symptoms, but do not necessarily lead to UTIs, include the following: allergic reactions to bubble baths, vaginal douches, and aerosol deodorants; tight clothing, especially underwear made of synthetic fibers; lack of personal hygiene as well as excessive washing; the direction in which the perianal region is wiped after defecation; physical injury to the genitalia from frequent or clumsy sexual intercourse without adequate lubrication; and clumsy masturbation with foreign objects.<sup>17</sup>

In 1974, clinicians M. Takahashi, Kaiser-Permanente Contraceptive Drug Study, Walnut Creek, California, and D.B. Loveland, National Institute of Child Health and Human Development, Bethesda, Maryland, investigated the link between UTIs and the use of oral

contraceptives. They found that the prevalence of bacteriuria in women using the "pill" was one-and-a-half times the rate among both nonusers and those who had used the pill and stopped.<sup>18</sup> The authors speculate that the estrogen in oral contraceptives contributes to an excess of the hormone in the body, causing physical damage or anatomic changes in the urinary tract which increase susceptibility to infection.

Psychological factors may also contribute to the development of symptoms. Urologist John B. Graham, Northwestern University Medical School, Chicago, and Evanston Hospital, Illinois, speculates that many women may suffer from a "nervous bladder" akin to a host of other, better-known psychosomatic disorders, such as the nervous bowel and the nervous stomach.<sup>19</sup> And in fact, urologists Richard A. Schmidt and Emil A. Tanagho, University of California School of Medicine, San Francisco, found that some women may turn feelings of stress and anxiety inward. This results in muscular spasms of the sphincter controlling the flow of urine, and, thus, more painful and frequent urination.<sup>20</sup>

Although UTIs are primarily a disease of women, men and children can also be victims. The appearance of symptoms and bacteriuria in men, according to Turck, are secondary effects of an obstruction of the urinary tract or of prostatitis (inflammation of the prostate gland).<sup>4</sup> However, clinicians Linda Pead and Rosalind Maskell, Public Health Laboratory, St. Mary's General Hospital, Portsmouth, England, found that UTIs are perhaps not as rare among men as has previously been thought. During a 14-month study of 999 men between the ages of 15 and 50, 223 had bacteriuria and 63 had pyuria—even though most (65 percent) had anatomically normal urinary tracts.<sup>21</sup> They speculate that the site of infection in these men may have been the prostate. Prostate infections

seem to be associated with far fewer bacteria in the urine than are infections of the bladder. This may partially account for the lower level of reported incidence of UTIs in men.

In children, the incidence of symptomatic UTIs occurring between the ages of one month and 11 years is approximately 0.7 percent for boys and 2.8 percent for girls.<sup>22</sup> According to Kunin, UTIs in children are commonly associated with vesicoureteral reflux, a condition in which urine backs up from the bladder into the ureters and kidneys.<sup>23</sup> This can cause renal scarring and tissue damage. Obstructions are also commonly found in male children with UTIs. And in a study of 100 infants aged five days to eight months who were hospitalized for acute UTIs, pediatricians Charles M. Ginsburg and George H. McCracken, University of Texas, Southwestern Medical School, Dallas, found that uncircumcised males accounted for 75 percent of those aged three months or less.<sup>24</sup> The immature immune system, the relatively short length of the urethra, and a reservoir of bacteria trapped by the foreskin close to the urethral opening may predispose the male infant to UTIs. Ginsburg and McCracken also found that 45 percent of infant girls with UTIs had unsuspected congenital or other defects of the urinary tract, making them more susceptible to infection.

As mentioned earlier, UTIs are most common among the elderly—especially women. However, the prevalence varies according to whether they live at home, in a nursing care facility, or are under extended care in a hospital. In a review of UTIs in the elderly, Donald Kaye, chairman, Department of Medicine, Medical College of Pennsylvania, Philadelphia, notes that in men aged 65 and older, the incidence of UTIs among those at home was 6 to 13 percent; in nursing homes or extended care facilities, 17 to 26 percent; and among those in the hospital, 30 to 34 percent.<sup>25</sup> For women aged 65 and older, UTIs oc-

curred in 17 to 33 percent of those living at home; 23 to 27 percent of those in extended care facilities; and 32 to 50 percent of those in the hospital.<sup>25</sup> The higher incidence of UTIs among those in hospitals and extended care facilities is due mainly to the bacteria introduced into the urinary tract by catheters.

Other causes of UTIs in the elderly include obstructions, loss of blood flow to the tissues of the urinary tract, and neglected care of invalid patients.<sup>25,26</sup> Prostate disease and the surgery resulting from the disorder, as well as the loss of the bactericidal secretions of the prostate, may predispose elderly men to UTIs.<sup>25</sup> Both elderly men and women have trouble emptying their bladders completely. The residual urine provides a fertile environment for the growth of bacteria. In elderly women, fecal incontinence and the soiling of the perineum may play a role in the development of UTIs. Finally, an increase in UTIs in the elderly is associated with such conditions as cerebrovascular disease, senile brain syndrome, and cardiovascular disease and with those in whom illness or infirmity enforces prolonged bed rest.<sup>25</sup>

The pathogens responsible for UTIs have been identified. But the reason some people seem more susceptible to one or more occurrences of the disease remains elusive. As we have seen, there are a variety of factors and conditions that seem to be associated with either symptoms of UTIs or true bacterial infections. Together with the differences of opinion concerning the etiology and epidemiology of UTIs, this suggests that there is considerably more work to be done in this area. Much the same can be said of the diagnosis and treatment of UTIs. These aspects of cystitis and UTIs will be covered in the second part of this review.

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