

Treatment and Prevention of Bladder Infections

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Ten (10) to 20 percent of all women have some kind of urinary discomfort or frank infection at least once per year. Acute uncomplicated cystitis (infection of the bladder) and recurrent cystitis are two important categories of urinary-tract infections (UTIs) in adults. Distinguishing between uncomplicated and complicated UTIs is important because they may require different evaluation tests and procedures, and different types and durations of treatment plans.

A complicated infection is associated with a condition that increases the risk for having UTIs or an increases the likelihood of treatment failure. Acute cystitis is generally uncomplicated but may be complicated if a patient has a catheter or also has an existing stone in the bladder. With the acute onset of urinary-tract symptoms, it is not always possible to classify the patient's UTI easily as being complicated or uncomplicated.

However, there are factors that can indicate the presence of an occult kidney infection or a complicated UTI in women. These include such risk factors as a patient being elderly, very young, or pregnant; having diabetes or immune deficiency; and/or being on antibiotics or immunosuppressive drugs. In addition, the patient may have:

- A nosocomial infection
- A urinary catheter
- A recent procedure involving urinary-tract instrumentation
- Symptoms that have lasted longer than 7 days.

Simple, short-duration therapies may not be appropriate for these situations.

It is reassuring that most acute UTIs are uncomplicated. One can generally assume that a premenopausal, sexually active woman who is not pregnant, has not been recently treated with antibiotics, and does not have a history of a genitourinary-tract abnormality has uncomplicated cystitis, if she presents with dysuria (painful or difficult urination), frequency, or urgency. It is even likely that most postmenopausal women who do not have genitourinary-tract abnormalities have uncomplicated UTIs.

Causes of UTIs

A narrow spectrum of microbes is responsible for the infections in young women with acute uncomplicated cystitis: *Escherichia coli* in 80 percent; *Staphylococcus saprophyticus* in 5–15 percent, and with the remainder being caused occasionally by *Klebsiella* spp., *Proteus mirabilis*, or other microorganisms.

Bacteriuria is more common in women who are sexually active, and certain forms of contraception are associated with UTIs. Sexual intercourse, diaphragm use with a spermicide, spermicides used alone, oral contraceptives, delayed postcoital urination, and a history of a recent UTI, all increase the risk of infection. Sexual intercourse is the strongest risk factor for UTIs, independent of contraception influences. As many as 30 percent of women who present with a cystitis-like syndrome may have subclinical upper urinary-tract involvement.

Young women who present with acute pain with urination or difficult urination usually have either acute cystitis or acute urethritis caused by *Chlamydia trachomatis*, *Neisseria gonorrhoea*, or *Herpes simplex virus*. Vaginitis caused by *Candida* spp. or trichomonas can also involve dysuria. These problems can usually be differentiated on the basis of presenting symptoms, physical examination, and urine analysis. A urine culture and vaginal cultures may also be needed.

Pregnancy is also a risk factor for UTIs. The American College of Obstetricians and Gynecologists recommends that all pregnant women be screened for bacteriuria, even if these women do not have UTI symptoms. However, not all major authorities recommend this.

When done, this screening involves an initial urine culture in all women who are pregnant. If a pregnant woman has classic symptoms of an acute and uncomplicated cystitis and no previous history of bacteria in the urine without symptoms, some clinicians would initiate treatment right away; others would do a urine culture before treating the patient.

Recurrence of UTIs

Recurrent infections occur in about 20 percent of young women who have experienced previous episodes of cystitis. More than 90 percent of recurrences in young women are episodes of reinfection from exogenous sources, typically months apart. Only occasionally are the recurrences the result of a persis-



Vaccinium macrocarpon (cranberry).

tent focus of infection or anatomical or functional abnormalities. One of the more common causes of recurrent infection is the use of diaphragms and spermicides. This is probably because the spermicide induces colonization of the vagina by *E. coli* and alters the overall vaginal flora. Cases of recurrent cystitis should be checked via a urine culture, and this information should be documented. Some women may need not only treatment, but also continuous prophylaxis (preventive measures) or postcoital prophylaxis.

Postmenopausal women may also have frequent reinfections, which often result from residual urine retention after voiding. A lack of estrogen can cause marked changes in the vaginal microflora, including loss of lactobacilli and increased colonization by *E. coli*. Vaginal estrogen treatments are a key to restoring normal vaginal and bladder flora, which can help prevent increased colonization by *E. coli*.

Presentation and Diagnosis

Symptoms of uncomplicated cystitis include painful and frequent urination, the urge to urinate even though the bladder may be nearly empty, and pressure and pain in the pelvic area.

Diagnosis of a bladder infection can be based on symptoms

and physical examination alone, a urine dipstick, urine analysis, and/or a urine culture. Basing the diagnosis on symptoms alone is considered reliable when the episodes are infrequent (less than 3 per year). A simple test used in the practitioner's office uses a dipstick of the urine. The dipstick is used to test for the presence of leukocyte esterase with or without urinary nitrite and pyuria (the presence of pus in the urine).

However, there are problems with the sensitivity and specificity of the test. Using a dipstick may produce a false-negative result if bladder bacteria have not had enough time to produce a sufficient amount of nitrite to be detected on the test. The accuracy of the test is also altered if the individual is eating a vegetable-free diet or is using a diuretic. Nitrite tests are also frequently negative, even in the presence of two bacteria, *S. saprophyticus* and *Enterococcus* spp. Thus, a more accurate assessment would rely on the results of the leukocyte esterase test than on the nitrite test.

A urine culture is often done after a history and physical examination suggests that something more than just a simple, acute uncomplicated UTI is occurring. If a recent UTI has just been treated and the symptoms are recurring, a culture would identify the possibility of a resistant pathogen. Symptoms that suggest that the infection has ascended the urinary tract also definitely indicate the need for a urine culture. These more-worrisome symptoms include fever, malaise, and back pain over the kidney area.

Other diagnostic evaluations of UTIs—such as cystourethroscopy, ultrasound, or intravenous pyelogram—should be considered in women who have recurrent UTIs (more than three infections in 6 months or six to seven infections in a year). Although these more sophisticated studies should be considered, it is also important to realize that some women may report symptoms that may appear to be infections but are actually symptoms of overactive bladder, interstitial cystitis, or pelvic-floor problems, such as cystocele or uterine prolapse.

Prevention

Simple practices, such as increasing the urinary flow, are easily accomplished by patients increasing liquid intake. Water, fluids, and herbal teas related to the treatment goals are the most logical choices. The common recommendation would be 64 ounces per day of cranberry juice and blueberry juice. Urinating after intercourse is also an important bladder-hygiene for patients to prevent recurring UTIs.

Intestinal bacteria have been long recognized as the reservoir for urinary infections caused by *E. coli*. In addition, studies have shown that women who have recurrent UTIs, have a preponderance of uropathogens on the introitus and in the vagina.¹ Vaginal ecology is dominated by lactobacilli species,² and these bacteria play a role in the defense against both UTIs and infectious vaginitis.

Lactobacilli adhere to the uroepithelial cells and inhibit the adherence of the pathogenic organisms, such as *E. coli*, to the cells. In this way, these pathogens are kept from proliferating. This is just one of the important mechanisms by which lactobacil-

li specifically are used to prevent and treat UTIs. In addition, carbon dioxide-producing lactobacilli, those most commonly found in the normal bladder flora (*Lactobacillus crispatus* and *Lactobacillus jensenii*), can help keep the bladder in its preferred acidic state.³

Other methods of prevention for patients include improving bathroom hygiene to minimize exposure of the urethra to *E. coli*; wearing cotton undergarments; avoiding the use of diaphragms for contraception if recurring UTIs are a problem; and reducing common bladder irritants, such as alcohol, chocolate, citrus fruits, coffee, black tea, tomatoes, vinegar, and sugar.

Nutrition

Because most UTIs are caused by *E. coli*, which resides predominantly in the gastrointestinal tract, it seems reasonable that the risk for infection might be altered by dietary influences and digestive health. In fact, it does appear to be the case that the risk for infection will change with dietary modifications.⁴

In a study of 139 women university students, those with diagnoses of acute UTI were compared with 185 age-matched women with no UTIs in the last 5 years. Information on the participants' dietary and lifestyle habits was collected. The researchers found that frequent consumption of fresh juices, especially berry juices, and fermented milk products containing probiotics was associated with a decreased risk of recurring UTIs. Consuming fermented milk products 3 or more times per week was more effective than less than one time per week. In this same study, frequency of intercourse was also associated with increased risk of UTI.

Common probiotic-containing fermented milk products include *Lactobacillus acidophilus* and kefir. Increasing garlic and onions in the diet—both of which produce antimicrobial activity against many organisms—may also be helpful. These two foods have been shown to inhibit the growth of *E. coli*, *Proteus* spp., *Klebsiella pneumoniae*, *Staphylococcus* spp., and *Streptococcus* spp.⁵⁻⁷

Other logical dietary considerations, especially for women who have recurring infections, are to assess and avoid food allergens as well as recommending avoidance of excess sugar and consumption of a diet that promotes healthy digestive function. This type of diet should have high levels of fiber and include complex carbohydrates; fermented dairy products; and good oils, such as olive oil, nuts, and seeds.

Supplements for Addressing UTIs

Cranberry

No natural approach to cystitis would be complete without mention of *Vaccinium macrocarpon* (cranberry). Women have used cranberry juice as a home remedy for decades. Several studies have shown that cranberries and cranberry juice are effective in women with active UTIs.⁸⁻¹⁰

In a large randomized controlled study, 300 mL of cranberry juice was given to 153 elderly women with confirmed bacteriuria.¹¹ The level of bacteria in the urine and the frequency

Tell Your Patients

Sample Treatment Plans for Urinary-Tract Infections

For acute infections

- Increase cranberry^a juice intake—to 16 oz per day.
- Increase water consumption—to 8 or more glasses per day.
- Take vitamin C—2000 mg every 2 hours for 2 days, then 2000 mg three times per day for 7–10 days.
- Take a combination herbal product^b—2 capsules every 2 hours for 2 days, then 2 capsules three times per day for 5–10 days.
- Take D-mannose—one-half to 1 tsp three times per day for 5–10 days.

For chronic recurring infections (3–6-month plan)

Pre-menopausal women

- Void upon urge and after intercourse.
- Use condoms during intercourse.
- Increase fluid intake.
- Take a combination herbal product^b—1–2 capsules per day.
- Take cranberry extract—400 mg two times per day.
Or drink cranberry juice—8–16 oz per day.
- Take oral probiotics—8–24 billion organisms per day.
- Take D-mannose—one-half to 1 tsp per day; more if needed.

Postmenopausal women

- Void upon urge and after intercourse.
- Use condoms during intercourse.
- Increase intake of fluids.
- Use a combination herbal product^b—1–2 capsules per day.
- Take cranberry extract—400 mg two times per day.
Or drink cranberry juice—400 mL per day.
- Take oral probiotics—8–24 billion organisms per day.
- Take D-mannose—one-half to 1 tsp daily; more if needed
- Use intravaginal estriol 1mg/g—insert 1 g two times per day for 2 weeks, then two times per week as a maintenance dose. Or use estriol suppositories—1 mg; insert 1 suppository per day for 2 weeks then two times per week as a maintenance dose.
- Discuss the possibility of oral hormone therapy with a physician.

^aLatin binomial is *Vaccinium macrocarpon*; ^bAn example of a combination herbal product would be one that contains cranberry, *Berberis aquifolium* (Oregon grape) root, *Barosma betulina* (bucchu), *Arctostaphylos uva-ursi* (uva ursi), *Chimaphilla umbellata* (pipsissewa), and *Althaea officinalis* (marshmallow).

of recurring infections was dramatically decreased. In another study, 0.5 liters/day of cranberry juice was shown to be helpful in 73 percent of the individuals with active UTIs.⁸

Cranberry has also been shown to reduce the ability of *E. coli* to adhere to the lining of the bladder and urethra.^{12,13} Many people still think that the action of cranberry juice results from its hippuric-acid content producing an antibacterial effect and acidifying the urine. However, recent studies have shown that components in cranberry juice reduce the ability of *E. coli* to adhere to the lining of the bladder and urethra.^{12,14} For this reason, the antibacterial effects of hippuric acid and any weak acidity effect are probably not the major mechanisms of cranberry against UTIs.

Often, women prefer cranberry extracts instead of cranberry juice. Cranberry juice can be problematic to drink. Unsweetened cranberry juice is not palatable to everyone, and cranberry juice that is typically sweetened with sugar or an artificial sweetener is more challenging to the immune system.



Plantago spp. (plantain).

Cranberry extracts are available in capsule form and have been studied for prevention of UTIs. Cranberry extracts were compared with cranberry juice in a 1-year randomized controlled trial in 150 sexually active younger and older women.¹⁵ In the trial, 1 tablet was given two times per day to one group of women and 250 mL of cranberry juice was given three times per day to another group of women.

Both forms of cranberry decreased the number of individuals who had at least one infection per year. Antibiotics were also used less in both the extract group and the juice group, compared with the placebo group. This study also demonstrated that the daily preventive dose of a cranberry-capsule extract was approximately half the cost of the daily cranberry juice. Another advantage of extracts in capsules versus in the juice is a concern that the oxalates in cranberry juice could contribute to kidney-stone formation. While this seems to be logical, no studies have yet demonstrated an increase in kidney stones after drinking cranberry juice.

Lactobacilli

The use of probiotics, especially lactobacilli, has been advocated by alternative providers for the prevention of UTIs. Lactobacilli species predominate in the vaginal and urinary tracts of healthy premenopausal women. This would suggest that women who have recurring UTIs have an imbalance of their flora, and if

the flora were restored, this could go a long way to prevent the infection-causing organisms from dominating.

A recent (2006) review was done of all studies on the role of lactobacilli and UTIs.¹⁶ Most of the laboratory and animal studies and clinical trials in women had encouraging findings, especially for some specific strains of lactobacilli. *Lactobacillus rhamnosus* and *Lactobacillus reuteri* (previously called *L. fermentum*) were the most effective. From the studies that are available, probiotics appear to be beneficial for preventing recurrent UTIs in women.

The hydrogen peroxide-producing lactobacilli are critical for keeping these areas acidic and are critical for inhibiting pathogenic bacteria from adhering to the vaginal and bladder walls. While a good prevention strategy is to consume fermented dairy products with lactobacilli, there are also other ways to administer lactobacilli including vaginal suppositories and oral supplementation. In a small study, women with recurrent UTIs were treated with a species called *Lactobacillus casei*, which was implanted in the vagina and swabbed onto the perineum and opening of the vagina two times per week.¹⁷ Each patient had infection-free periods ranging from 4 weeks to 6 months.

Vitamin C

Vitamin C is probably the most popular vitamin supplement. Its beneficial effects and functions are numerous and critical to optimal health. Vitamin C is involved in the manufacture of collagen, the main protein substance in the body, which results in its role in wound repair, connective-tissue structures, vascular-wall integrity, skin elasticity, healthy gums, and more.

Vitamin C is also critical to immune function, the absorption and utilization of other nutrients, the manufacture of numerous hormones and nerve-conduction substances, and as an antioxidant. While some of these functions help maintain normal tissue health of the bladder and urethra, vitamin C has some additional effects that are helpful for treating UTIs.

As early as in the 1960s, ascorbic acid (vitamin C) was shown to be an effective urinary-acidifying agent.¹⁸ As mentioned earlier, acidifying the urine is one of the avenues to success in treating infections of the urethra and bladder.

What is perhaps a bit more complex but important, is that nitrites may be generated by bacteria in the urine, during a UTI. If nitrite is acidified, nitric oxide (NO) is formed, along with other reactive nitrogen oxides, and these are toxic to a host of organisms.

A study was done to examine the effects of ascorbic acid on nitrite in the urine and growth of bacteria, to investigate this interaction more closely. Urine was collected from healthy individuals. Varying amounts of nitrite and/or ascorbic acid were added. What the researchers found was that acidifying the urine, even mildly, generated large amounts of NO, which was increased more, by larger amounts of ascorbic acid. As a result, the growth of three common bladder pathogens, *E. coli*, *Pseudomonas aeruginosa*, and *S. saprophyticus* were significantly inhibited by the addition of nitrite to acidified urine and, to an even greater extent, by the addition of ascorbic acid.¹⁹ These results provide a good rationale for the beneficial effects of acidifying the urine for preventing and treating UTIs.

D-Mannose

D-mannose is a naturally occurring simple sugar contained in cranberry juice. It might seem curious that a sugar would be helpful in treatment of UTIs. In this case, D-mannose adheres to the bladder epithelium and, in essence, interferes with the ability of the *E. coli* to adhere there.²⁰

The fimbriae of the *E. coli* are the bacterial surface appendages that agglutinate to the uroepithelium cell layer. These fimbriae projections are amino acid–sugar complexes, a glycoprotein called a lectin. However, the D-mannose adheres better to the *E. coli* lectins than the *E. coli* adheres to the bladder wall. A D-mannose–*E. coli* complex is formed, the *E. coli* do not adhere to the bladder wall and are simply rinsed away during urination.

Other Botanicals

In addition to cranberry, there are other botanicals that are useful for addressing UTIs.

Uva Ursi

One of the most useful herbs for treating a bladder infection is *Arctostaphylos uva-ursi* (uva ursi; also known as bearberry or upland cranberry). The antiseptic, antibacterial, and astringent activity of uva ursi is largely the result of its arbutin content. Uva ursi is especially active against *E. coli* as well as having diuretic properties.

Uva ursi has also been used with recurrent bladder infections and was shown to be effective in a double-blinded study of 57 women.²¹ After 1 year, 5 of 27 women in the placebo group had recurrences of cystitis, while none of 30 women in the uva ursi group had recurrences.

Historically, many herbalists have taught that herbs with arbutin work best in an alkaline environment. That would appear to present a problem given that acidifying the urine is a fundamental concept in the successful treatment of UTIs. While it is not certain, it may be true that herbs with arbutin could work even better in an alkaline environment. This has not been a factor in the great success I have witnessed in treating UTIs by acidifying the urine with vitamin C and using uva ursi and other botanicals.

Pipsissewa

Chimaphilla umbellata (pipsissewa; also known as chimaphila, bitter wintergreen, or ground holly), a Native American remedy of the Pacific Northwest, has been used traditionally to treat urinary infections. Its antiseptic, mildly antimicrobial effects have also been attributed to its arbutin content. This herb has mildly diuretic, astringent, and antispasmodic properties, all of which are important for treating UTIs. As a result of its arbutin content, this herb is best for shorter-term or occasional use (up to 4–5 times per year).

Oregon grape root and goldenseal

Berberis aquifolium (Oregon grape) root and *Hydrastis canadensis* (goldenseal) are two of the most important herbs for treating UTIs because of the herbs' antimicrobial properties. Berberine alkaloid constituents found in the rhizomes and roots of these



Apium petroselinum (parsley).

plants, has produced antibacterial activity against *E. coli* species, *Klebsiella* spp., *Staphylococcus* spp., and *Pseudomonas* spp.^{22,23} Berberine is effective against many bacteria and is also able to fight infections by inhibiting the bacteria from adhering to the host cell.²⁴

Additional Ways to Address UTIs

Yet more botanicals have been traditionally used for treating bladder infections with positive effects. The water-soluble mucilage herbs are known to be soothing to the irritated uroepithelium and to reduce inflammation. These include *Zea mays* (corn silk), which produces a soothing and cooling effect on the urinary tract; *Althaea officinalis* (marshmallow) root, which contains mucilage that can form a protective layer on the lining of the bladder; and even *Plantago* spp. (plantain) leaf, which has a high percentage of mucilage and allantoin.

Additional antimicrobials for the bladder include bee pollen (propolis) and several herbs such as *Barosma betulina* (bucchu), *Commiphora molmol* (myrrh), and *Juniperus communis* (juniper) berry.

Numerous immune stimulants may be helpful including *Echinacea* spp. (echinacea), *Ligusticum porteri* (osha), and *Baptisia tinctoria* (wild indigo) root. Bladder tonics stimulate the flow of blood and nutrients to the urinary tract and may be useful as adjunct herbs. These herbs include *Urtica dioica* (nettle) leaves, *Solidago* spp. (goldenrod), *Piper methysticum* (kava

kava), and *Equisetum arvense* (horsetail). *Taraxacum officinale* (dandelion) leaf, buchu, and *Apium petroselinum* (parsley) root have diuretic effects and increase the flow of urine to help flush the bacteria.

Conclusions

Other influences are important to consider in postmenopausal women who have chronic recurring UTIs. Lower estrogen states result in lower amounts of lactobacilli in the vagina and bladder. Fortunately, we have very safe and effective solutions in the form of vaginal estrogens. Intravaginal estriol has been shown to be an effective treatment for recurring UTIs in postmenopausal women.²⁶ Vaginal estrogen has been shown to restore the normal vaginal flora and reduce the risk of vaginal *E. coli* colonization. Other more commercially available vaginal estrogens are also used for this purpose. □

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