URINARY TRACT INFECTIONS

BACKGROUND

Urinary tract infections (UTIs) are some of the most common infections seen in the primary care setting. Without appropriate treatment, acute cystitis has the potential to advance to more serious infections such as pyelonephritis and urosepsis. Because of this, treatment with standard antibiotics such as TMP-sulfa, nitrofurantoin, and ciprofloxacin should be strongly considered, especially in cases where a culture proves the infection positive for bacteria at >/= 100,000 CFU/mL. However, other strategies can be considered in those with recurrent infections or symptomatic colonization with lower concentrations of bacteria, or as adjuvants to antibiotic treatment.

MECHANICAL AND ANATOMIC CONSIDERATIONS

There are a number of anatomic and mechanical risk factors that increase the likelihood of colonization and infection of the urinary tract with pathogenic bacteria—most commonly, *E. coli*. Risk factors of this type include the following:[1]

- condom use
- · spermicide use
- diaphragm use
- delayed urination
- incomplete bladder emptying
- atrophic vulvo-vaginal changes
- lack of voiding after sex
- cystocele in females
- lack of circumcision in males
- penetrative anal sex
- prostatic hypertrophy

Simple, low risk interventions to reduce these risks include urination after intercourse, avoiding holding urine/waiting a long time to urinate after the urge arises, and, for women, wiping from front to back after urination (Natural Standard).[2] Cystoceles often respond well to regular completion of Kegel exercises. Vaginal estrogen can be considered in the postmenopausal woman with atrophic vulvo-vaginal changes and recurrent UTIs.

FOOD & DRINK

Diets high in fruits and vegetables promote good health in general and can boost proper functioning of the immune system. There seem to be some foods that may irritate the bladder. These include caffeine, simple sugars or starches, tobacco, alcohol, and some food additives. It is reasonable to consider an <u>Elimination Diet</u> that removes these substances for those with recurrent UTIs.[1]

GARLIC AND ONIONS

Garlic and onions contain the sulfur-containing compound allicin, as well as other antiinfective and anti-inflammatory components that have been found to be effective against urinary pathogens. They also have a wide range of other health benefits. Garlic seems to be more potent raw or crushed and lightly cooked.[1]

CRANBERRIES AND OTHER BERRIES

There has been some conflicting evidence around the efficacy of cranberry for adjunctive treatment or prevention of urinary tract infections. The sum total of the evidence appears favorable. Cranberry seems to work by preventing bacteria from attaching to the urinary tract lining.[3-8] Benefit may be particularly pronounced in those at some increased risk for recurrent UTIs. Dosing used for prevention is typically 500 mg daily of cranberry capsules or 30-300 mL of pure, unsweetened cranberry juice. Use of juice cocktails and sweetened juices adds extra calories and, especially in diabetics, can raise blood sugars.[9] At onset of symptoms, starting 500 mg twice daily is reasonable.

A study that compared lingonberry-cranberry juice to cranberry juice alone showed superiority of the former.[2] In general, inclusion of a variety of dark colored berries is part of a healthy diet—using these foods in higher amounts in those with recurrent or acute urinary infections is reasonable.

DIETARY SUPPLEMENTS

Note: Please refer to the <u>Passport to Whole Health</u>, Chapter 15 on Dietary Supplements for more information about how to determine whether or not a specific supplement is appropriate for a given individual. Supplements are not regulated with the same degree of oversight as medications, and it is important that clinicians keep this in mind. Products vary greatly in terms of accuracy of labeling, presence of adulterants, and the legitimacy of claims made by the manufacturer

UVA URSI (ARCTOSTAPHYLOS UVA-URSI)

Uva ursi is a small evergreen shrub with clusters of small white or pink bell-shaped flowers and dull orange berries.[10] It contains a potent urinary antiseptic called arbutin, which is hydrolyzed in alkaline urine to hydroquinone. Hydroquinone inhibits urinary tract pathogenic bacteria.[1] It is generally not recommended to take uva ursi longer than two weeks at a time, and it should be avoided in pregnant and lactating women, patients with renal disease, and children. Dosing is as follows:

- Tea: 1 tsp of dried leaf steeped in 1 cup of boiling water, 3-4 times daily.
- Capsule: 700-1000 mg of standardized extract, 3 times daily.
- Tincture: 1 tsp, 3 times daily.[11]

GOLDENSEAL (HYDRASTIS CANADENSIS)

The dried rhizome and root of goldenseal contain the alkaloid berberine, which has antibacterial, antifungal, and some antimycobacterial and antiprotozoal activity. Berberine from goldenseal seems to concentrate in the bladder and is thought to potentially prevent pathogenic bacteria, such as *E. coli*, from binding to the bladder wall. Traditional dose is as a tea taken three times daily. Add 0.5-1 gm of the dried root or rhizome to 150 mL of boiling water and simmer for 5-10 minutes then strain.[12] Berberine is generally not considered safe in pregnancy or for infants due to risk of kernicterus.[1]

HORSERADISH (ARMORACIA RUSTICANA)

There is some evidence that horseradish, especially when mixed with nasturtium, can be as potent as standard antibiotic therapy.[13] The typical dose horseradish is 6-20 gm per day of the root or equivalent preparations. Large amounts can cause gastrointestinal upset, bloody vomiting and diarrhea, irritation of mucous membranes, and/or depression of thyroid function.[14]

TEAS

Teas and foods that are used for bladder health include asparagus ("spears," rhizome, root, and juice), goldenrod (above ground parts), java tea (leaf and stem tip), lovage (rhizome and root), parsley (leaf, seed, and root), and stinging nettle (above-ground parts and root). Data is lacking, but they appear to have anti-inflammatory and antioxidant properties and can increase urine flow. If used as part of a "urine flush," they should be used with copious fluids.[9] Peppermint tea has also been reported as a treatment for urinary tract infections but data is lacking.[2]

Betula Pendula (European White Birch) and Herniaria glabra (Smooth Rupturewort) have been found to have antimicrobial activity against urinary pathogenic *E. coli* strains *in vitro* and also to have mild diuretic effects.[15] Teas for these are prepared as follows:

- Birch: Steep 2-3 gm of finely cut dried leaf in 150 mL boiling water for 10-15 minutes and strain. Take several times daily. The tea should be taken with plenty of water.
- Rupturewort: Simmer 1.5 gm finely cut above ground parts in 150 mL boiling water for five minutes and strain. Take 2-3 times daily with plenty of water.[16]

Risks from the above are generally related to potential allergic reactions.

PROBIOTICS

The gut is lined with beneficial bacteria that aid in digestion and maintain a healthy gut. Most probiotics come from food sources such as yogurt, but they can also come as pills, beverages, and powders. While data on efficacy for prevention of UTIs is conflicting, the most efficacious strains in the literature appear to be *Lactobacillus rhamnosus* GR-1 and *Lactobacillus fermentum* RC-14.[1,17] The mechanism by which they act involves their

being a barrier in the vagina and on the perineum to prevent urinary tract colonization and by outcompeting and impairing adhesion of pathogenic bacterial strains. The typical dose used is 1 billion colony forming units (CFUs) once daily.[1,18] Oral and vaginal preparations of *Lactobacillus* species have shown decreased risk with few adverse effects in a small number of studies. Probiotics seem beneficial in the prevention of vulvo-vaginal candidiasis,[19] and, with the addition of the yeast *Saccharomyces boulardii*, diarrhea[20] that can result from antibiotic treatment of UTIs. A reasonable duration of treatment is one month. For more information, refer to "Promoting a Healthy Microbiome with Food and Probiotics" Whole Health overview.

VITAMIN C

There is some evidence that vitamin C can decrease a person's risk of developing urinary tract infections. Consider 100 mg daily for prevention.[1] Another regimen used, at first onset of symptoms, is 1,000 mg every 2 hours for 2 days, then 1,000 mg three times a day for 5-10 days.

D-MANNOSE

D-mannose is a simple sugar found in fruits. It concentrates in the urine, preventing bacterial adhesion to the bladder wall and thus increasing flushing of the bacteria through the urine.[3,6] Several studies have shown efficacy but additional studies are needed to confirm. The dose is d-mannose powder, three-fourths to 1 tsp. one to two times daily for prevention and three-fourths to 1 tsp three times daily to treat acute infection. High doses for prolonged periods of time may be toxic to the kidneys.[1]

OTHER THERAPIES

ACUPUNCTURE

There is some evidence that acupuncture can reduce recurrence rate of UTIs and reduced urine retained in the bladder after urination (Natural Standard).[2]

PHARMACEUTICALS

A full description of medications for UTIs is not within the scope of this document. However, many clinicians are not familiar with the potential for using methenamine for prophylaxis.

Methenamine hippurate exhibits antibacterial activity by the conversion of methenamine to formaldehyde in the presence of acidic urine, thus offering a nonantibiotic medication for prophylaxis in those at risk for recurrent UTIs. It is not to be used in those with urinary tract abnormalities. It should not be used long-term in those with neuropathic bladder. Methenamine should be avoided in those with renal impairment, severe hepatic impairment, dehydration, and with concomitant use of sulfonamides. Standard dosing is 1 gm orally twice daily.[21] The amount of methenamine hippurate that is converted to formaldehyde in the urine is dependent on the pH of the urine; much higher levels are seen

at pH below 6.[22] For this reason, checking a urine pH and, if necessary, supplementing with vitamin C and/or cranberry juice can offer a sense of methenamine's effectiveness.

RESOURCE LINKS

- "<u>Elimination Diet</u>": https://www.va.gov/WHOLEHEALTHLIBRARY/tools/elimination-diets.asp
- Passport to Whole Health: https://www.va.gov/WHOLEHEALTHLIBRARY/docs/Passport_to_WholeHealth_FY 2020_508.pdf
- "Promoting a Healthy Microbiome with Food and Probiotics": https://www.va.gov/WHOLEHEALTHLIBRARY/tools/promoting-healthy-microbiome-with-food-probiotics.asp

AUTHOR(S)

"Urinary Tract Infection" was written by Greta Kuphal, MD (2014, updated 2020).

This Whole Health tool was made possible through a collaborative effort between the University of Wisconsin Integrative Health Program, VA Office of Patient Centered Care and Cultural Transformation, and Pacific Institute for Research and Evaluation.

REFERENCES

- 1 Rakel D. *Integrative Medicine*. 3rd ed. Philadelphia: Elsevier Saunders; 2012.
- 2 Genitourinary disorders. Natural Medicines Comprehensive Database website; 2014. https://naturalmedicines.therapeuticresearch.com/.
- 3 Caretto M, Giannini A, Russo E, Simoncini T. Preventing urinary tract infections after menopause without antibiotics. *Maturitas*. 2017;99:43-46.
- 4 Liska DJ, Kern HJ, Maki KC. Cranberries and urinary tract infections: how can the same evidence lead to conflicting advice? *Adv Nutr.* 2016;7(3):498-506.
- Mantzorou M, Giaginis C. Cranberry consumption against urinary tract infections: clinical stateof- the-art and future perspectives. *Curr Pharm Biotechnol.* 2018;19(13):1049-1063.
- 6 Sihra N, Goodman A, Zakri R, Sahai A, Malde S. Nonantibiotic prevention and management of recurrent urinary tract infection. *Nat Rev Urol.* 2018;15(12):750-776.
- Luís Â, Domingues F, Pereira L. Can cranberries contribute to reduce the incidence of urinary tract infections? a systematic review with meta-analysis and trial sequential analysis of clinical trials. *J Urol.* 2017;198(3):614-621.
- Fortmann SP, Burda BU, Senger CA, Lin JS, Whitlock EP. Vitamin and mineral supplements in the primary prevention of cardiovascular disease and cancer: an updated systematic evidence review for the US Preventive Services Task Force. *Ann Intern Med.* 2013;159(12):824-834-834.
- 9 Natural Medicines in the Clinical Management of Urinary Tract Infections. Natural Medicines Comprehensive Database website.

- http://naturaldatabase.therapeuticresearch.com/ce/ceCourse.aspx?s=ND&cs=&pc=10%2D110&cec=1&pm=5. Accessed June 22, 2014.
- 10 Uva Ursi. Natural Standard website. https://naturalmedicines.therapeuticresearch.com/databases/food,-herbs-supplements/professional.aspx?productid=350. Accessed June 22, 2014.
- Johnson RL, Foster S, National Geographic Society. *National Geographic Guide to Medicinal Herbs: The World's Most Effective Healing Plants.* Washington, D.C.: National Geographic; 2012.
- Goldenseal. Natural Medicines Comprehensive Database website.

 http://naturaldatabase.therapeuticresearch.com/nd/Search.aspx?cs=NEWORDER&s=ND&pt=100&id=943&fs=ND&searchid=48372755. Accessed June 22, 2014.
- Fritz DJ, Carney RM, Steinmeyer B, Ditson G, Hill N, Zee-Cheng J. The efficacy of auriculotherapy for smoking cessation: a randomized, placebo-controlled trial. *J Am Board Fam Med.* 2013;26(1):61-70.
- 14 Horseradish. Natural Medicines Comprehensive Database website. https://naturalmedicines.therapeuticresearch.com/databases/food,-herbs-supplements/professional.aspx?productid=257. Accessed June 24, 2020.
- Wojnicz D, Kucharska AZ, Sokol-Letowska A, Kicia M, Tichaczek-Goska D. Medicinal plants extracts affect virulence factors expression and biofilm formation by the uropathogenic Escherichia coli. *Urol Res.* 2012;40(6):683-697.
- Fritz H, Kennedy D, Fergusson D, et al. Selenium and lung cancer: a systematic review and meta analysis. *PLoS One.* 2011;6(11):e26259.
- 17 Canales J, Rada G. Are probiotics effective in preventing urinary tract infection? *Medwave.* 2018;18(2):e7186.
- Probiotics. Natural Medicines Comprehensive Database website. https://naturalmedicines.therapeuticresearch.com/databases/health-wellness/professional.aspx?productid=1598. Accessed June 24, 2020.
- Borges S, Silva J, Teixeira P. The role of lactobacilli and probiotics in maintaining vaginal health. *Arch Gynecol Obstet.* 2014;289(3):479-489.
- Guandalini S. Probiotics for prevention and treatment of diarrhea. *J Clin Gastroenterol.* 2011;45 Suppl:S149-153.
- Lee BS, Bhuta T, Simpson JM, Craig JC. Methenamine hippurate for preventing urinary tract infections. *Cochrane Database Syst Rev.* 2012;10:Cd003265.
- Strom JG, Jr., Jun HW. Effect of urine pH and ascorbic acid on the rate of conversion of methenamine to formaldehyde. *Biopharm Drug Dispos.* 1993;14(1):61-69.