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Editorial
Dr. Wright Does It Again: D-Mannose for UTI Prophylaxis Validated in a Clinical Trial
by Alan Gaby, MD

I have been privileged to have been associated with Jonathan Wright, MD, since 1978. At that time he was offering a "fellowship" for medical students, and I was given the opportunity to spend a month in his clinic, learning from him and from the large collection of medical journal articles on nutritional therapy that he had collected over the years. Five years later, we began coteaching seminars on how to incorporate nutritional therapy into medical practice, and we have continued to do so for 30 years.

One of the things that have impressed me about Dr. Wright is his ability to discover or develop or invent new therapies that turn out to be effective. He was the first doctor in the US to use bioidentical estrogen-replacement therapy (estrone, estradiol, and estriol), and one of the first to use DHEA in clinical practice. He also pioneered the use of selenium and vitamin E as a treatment for Osgood-Schlatter's disease.

Some 20 years ago, Dr. Wright began using D-mannose (a sugar structurally similar to glucose) to prevent and treat urinary tract infections, based on in vitro reports that it prevents uropathogenic *Escherichia coli* from adhering to the epithelial cells of the genitourinary tract. Since then he has administered D-mannose to more than 200 patients. In his experience, this treatment has an efficacy rate of 85% to 90%. Hes has found that in addition to being an effective treatment for UTIs, D-mannose can prevent postintercourse UTIs and is also effective for prophylaxis in women who are prone to recurrent UTIs. For treatment of UTIs, he recommends a dosage of 1 teaspoonful (about 2 g) for adults and ½ to 1 teaspoonful for children, dissolved in a glass of water or juice and repeated every 2 to 3 hours. Treatment should be continued for 2 to 3 days after symptoms have disappeared. For preventing recurrent infections, patients should start with the dosages listed above, and then reduce the dose if possible. For prevention of postintercourse UTIs, the recommended dosage is 1 tablespoonful 1 hour prior to intercourse and again immediately afterwards.[1] D-mannose is not effective for UTIs caused by organisms other than *E. coli.*

Hundreds of practitioners are now using D-mannose because of the writings and teachings of Dr. Wright, and informal surveys that I have conducted at medical conferences reveal that these practitioners generally concur with Wright's observations. D-mannose is now widely available in natural food stores and on the Internet. However, while it appears to be quite effective, the evidence supporting its use has been entirely anecdotal. Now, finally, a randomized controlled trial

has been published that confirms the efficacy of this treatment.

In the new study, 308 women with an acute UTI and a history of recurrent UTIs were treated with ciprofloxacin (500 mg twice a day for 1 week) and then randomly assigned to receive 2 g per day of D-mannose, 50 mg of nitrofurantoin once a day, or no prophylaxis for 6 months.[2] Women with urinary tract anomalies, interstitial cystitis, or diabetes, and those who were pregnant or taking hormone therapy or contraceptives were excluded. During the study, 98 women (32%) had a recurrent UTI. The recurrence rate was significantly lower in the groups that received D-mannose (15%) and nitrofurantoin (20%) than in the group that did not receive prophylaxis. The recurrence rate did not differ significantly between the D-mannose and nitrofurantoin groups. The incidence of side effects was significantly lower in the D-mannose group than in the nitrofurantoin group. Eight percent of patients receiving D-mannose experienced diarrhea, which did not require discontinuation of treatment.

The discovery of the D-mannose as a treatment for UTIs was an important medical advance, although its mechanism of action may be different than that initially hypothesized by Wright. D-mannose is absorbed intact into the blood, but there are no data indicating what proportion of an orally administered dose is excreted unchanged in the urine.[3] Even if 100% of the recommended oral dose of D-mannose were excreted in the urine, the average urinary mannose concentration would be less than half the concentration that decreased bacteriuria by 90% in rats. Moreover, once *E. coli* has adhered to the bladder wall, one could not necessarily expect that free mannose in the urine would successfully detach it from its cellular binding sites. Another possible explanation for the efficacy of D-mannose is its relationship to Tamm-Horsfall protein. This glycoprotein, produced by renal cells and excreted in the urine, plays a key role in the body's defense against UTIs. Tamm-Horsfall protein contains a large number of high-mannose structures, which appear to account for its infection-fighting activity.4 It is possible that orally administered D-mannose works primarily by facilitating the synthesis or promoting the activation of Tamm-Horsfall protein. Regardless of the mechanism, thousands of people are grateful to Dr. Wright for discovering the benefits of D-mannose and telling the world about it.

Alan R. Gaby, MD

Notes

1. Wright JV, Lenard L. *D-Mannose and Bladder Infection*. Auburn, WA: Dragon Art; 2001. Additional information regarding the use of D-mannose was obtained in a personal communication from Wright JV; September 10, 2008.
2. Altarac S, Papes D. Use of D-mannose in prophylaxis of recurrent urinary tract infections (UTIs) in women. *BJU Int*. 2014;113:9–10.
3. Alton G et al. Oral ingestion of mannose elevates blood mannose levels: a first step toward a potential therapy for carbohydrate-deficient glycoprotein syndrome type I. *Biochem Mol Med*. 1997;60:127–133.
4. Serafini-Cessi F et al. N-Glycans carried by Tamm-Horsfall glycoprotein have a crucial role in the defense against urinary tract diseases. *Glycoconj J*. 2005;22:383–394.

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