the wider range of treatments used in the United Kingdom versus the United States and the differences in approach when patients with heavy menstrual bleeding seek care from their primary care physician versus gynecologist. There is stronger evidence supporting nonsteroidal anti-inflammatory drugs than hormonal contraception for heavy menstrual bleeding; however, in the United States, practice patterns do not reflect the relative evidence. As compared with primary care physicians, we gynecologists tend not to use as exhaustive a list of medications before offering surgical treatments.

On the other hand, do you remember how your last patient expecting to be offered a hysterectomy responded when you offered her combined oral contraceptives years after her postpartum tubal sterilization because she developed heavy or painful periods? The process of Food and Drug Administration (FDA) approval for new indications can be equally confusing. Although some practicing physicians use medications “off label” in ways supported by evidence but not recognized by the FDA, the lack of FDA approval can be an important barrier for many physicians and nurse practitioners. As evidence strengthens on the noncontraceptive benefits of LNG-IUS, we will hopefully soon see heavy menstrual bleeding in noncontracepting women added to the list of indications.—LAL

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**Evaluation of a Therapeutic Vaccine for the Prevention of Recurrent Urinary Tract Infections Versus Prophylactic Treatment With Antibiotics**

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**ABSTRACT**

Urinary tract infections (UTIs) are common bacterial infections. Women are 8 to 30 times more likely to have this infection than men. The majority of women report at least 1 UTI in their lifetime. Within a year, about 25% or more of these patients will have a recurrence, and 22% will have recurrent UTIs (RUTIs). Continuous prophylaxis with antibiotics is commonly recommended as initial treatment for RUTIs. However, there is high risk for the development of multiresistance with their continuous use; in some regions of the world, more than 40% of the bacterial strains are already resistant to available antibiotics. Moreover, there is a high incidence of adverse reactions. To address these problems, preventive strategies such as vaccine use have been investigated that reinforce the natural mechanisms of pathogen defense. One such vaccine, Uromune, is an inactivated bacterial cell suspension composed of selected strains of *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus vulgaris*, and *Enterococcus faecalis*.

The aim of this multicenter retrospective observational study was to compare the clinical benefit of prophylactic use of Uromune with that of the currently accepted prophylactic treatment, sulfamethoxazole/trimethoprim (SMX/TMP) to prevent RUTIs. The authors reviewed the clinical history of 319 women who presented with RUTIs (defined as at least 2 episodes of UTI in the last 6 months or 3 in the last 12 months).
Data collected before the initiation of the corresponding treatment and after 3, 9, and 15 months included number of UTIs and time of evolution of RUTIs before initiation of treatment. Patients in group A (n = 159) received prophylactic treatment with Uromune for a period of 3 months, and patients in group B (n = 160) received oral doses of SMX/TMP (200/40 mg/d) as prophylactic treatment for a period of 6 months.

The data showed that patients in group A experienced a highly significant reduction in the mean number of infections in the first 3 months compared with patients in group B: 0.36 versus 1.60, \( P < 0.0001 \), respectively. There was also a significant reduction after 9 and 15 months (\( P < 0.0001 \)). Significantly more patients in group A than in group B did not suffer any UTI at 3, 9, and 15 months: 101, 77, and 55 patients in group A versus 9, 4, and 0 patients in group B (\( P < 0.000 \)).

These data show that the use of this bacterial-based therapeutic vaccine could be an effective strategy to reduce frequency, duration, severity, and costs of RUTIs.

EDITORIAL COMMENT

(Anyone who provides clinical care to female patients knows that the diagnosis and management of UTIs utilize a significant fraction of medical resources. Women are estimated to be 20 times more likely to be diagnosed with a UTI in their lifetime than men. Urinary tract infections account for 7 million office visits annually in the United States. Diagnosis and treatment costs in 2000 in the United States are estimated at $2.47 billion, not counting the expense of outpatient prescriptions [Heisler CA, J Pelvic Med Surg 2008;14(1)]. These facts are a compelling argument for finding a more effective therapy for women who suffer from RUTIs, defined in this article as 3 or more culture-proven UTIs per 12 months or 2 or more in 6 months. Recurrent UTIs represent a large minority of women with UTIs and are often associated with increasing drug resistance in bacterial isolates, as many as 40% of bacterial strains depending on geographic location. Many women with recurrent presentations to physicians’ offices with complaints of cystitis will be prescribed multiple courses of antibiotics with associated fungal vaginal infections and gastrointestinal disturbance. Daily low-dose antibiotic prophylaxis, although effective (Heisler), can be associated with toxicities such as irreversible pulmonary fibrosis from nitrofurantoin or acute renal insufficiency from SMX/TMP.

This article describes a multicenter retrospective observational study of Spanish women with RUTI. The characteristics of the patients in this study seem fairly generalizable with an average age of about 48 years, and 79% of the women were regularly sexually active. The authors note that the most common pathogens associated with UTI in Spain are \( E. coli \), \( K. pneumonia \), \( P. vulgaris \), and \( E. faecalis \). (With the notable addition of \( Staphylococcus saprophyticus \), this list is very similar to the most common causes in US women.) To perform the study, the authors surveyed clinic records for 319 women who had presented to their sites with RUTI. This number was based on a power calculation, which anticipated an impressive 65% reduction in UTI during the 6-month treatment period. The agent potentially providing this superior treatment is an inactivated bacterial vaccine available commercially, called Uromune. Uromune is administered sublingually and contains equal amounts of strains of the above 4 most common pathogens for UTI in Spain. Bacterial vaccines to prevent UTIs are not a brand new concept; the authors discuss studies dating back to 1996 as well as a double-blind randomized controlled trial published in 2002, showing a significant decrease in UTIs in subjects receiving bacterial preparations. What is different about Uromune is that it is composed of inactivated whole, non-lysate bacteria, which elicits a more robust macrophage-driven immune response than earlier preparations of lysed bacteria. Furthermore, there is evidence that sublingual administration is superior to oral administration for stimulating a broad spectrum of mucosal and systemic immune response in the gastrointestinal as well as respiratory and genitourinary tracts. About one half of the women in the study received Uromune for 3 months, and one half received usual-care daily therapy with a single dose of SMX/TMP for 6 months. It is important to note that even though the women in these 2 study groups appear to have been similar in many
ways, this study is not a randomized trial. The women were identified retrospectively after the treatment had already been assigned or perhaps even completed. The authors do not present any information to help the reader understand how the treatments were assigned to each subject, or how potential sources of bias might have been minimized. Treatment outcomes included the number of UTIs and the number of positive urinary cultures during the 6-month treatment period. Unfortunately, further information about how these outcomes were defined is not available. How was a “UTI” defined as having occurred if not via a positive urine culture? The specific details of how these outcomes were defined and counted, particularly in a retrospective study where charts were being reviewed to determine how patients fared on the treatments, really should be included in the article. These limitations make it hard to know how to interpret the findings of the study.

Indeed, the women in the Uromune group seem to have done impressively well. Of 159 women receiving the vaccine, 101, 90, and 55 women at 3, 9, and 15 months, respectively, did not have any UTIs identified. In comparison, of the women receiving usual care with SMX/TMP, only 9, 4, and 0 women had no symptoms. These differences were highly statistically significant at each time point. The authors’ findings were similar for the other primary outcome of urine culture results. Overall, women receiving Uromune had a roughly 75% decrease in the frequency of UTIs maintained even after the study treatment period. The treatment appears to be safe, because no adverse events were reported associated with Uromune therapy, but this observation is also difficult to evaluate because adverse events were not defined or likely consistently reported in this retrospective study, and no data regarding safety for the women of the SMX/TMP group are given at all.

The authors recognize the limitations of their current study design in the discussion and allude to plans to perform a randomized trial of Uromune versus another treatment arm, possibly an antibiotic regimen similar to the one reported in this study. It would be difficult to randomize patients to Uromune versus placebo because antibiotic therapy remains effective. However, increasing prevalence of antibiotic resistance among bacterial strains is an indicator that we need better data on novel therapies such as Uromune if we are to effectively reduce the impact of RUTIs on our patients. Is Uromune effective with only a single formulation, or does it need to be tailored to the regional resistance patterns? Is it safe in all ages and in patients with comorbidities? Better designed prospective studies are needed to find these answers.—ACW)

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**Measuring Outcomes in Urogynecological Surgery: “Perspective Is Everything”**

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**ABSTRACT**

Although most pelvic floor disorders (PFDs) are not life-threatening, they are associated with significant morbidity and impairment in quality of life. Surgical intervention is usually planned and elective. It is difficult to compare results from