LETTERS TO THE EDITORS

Single Dose for Urinary Tract Infections

To the Editors: — Why are so many physicians who write about treatment of uncomplicated urinary tract infections in women so committed to single-dose antibiotic therapy? Dr. Fihn's editorial¹ claims that this therapeutic regimen is "effective, inexpensive, easy to comply with, causes fewer side effects, and may even be used to select out patients who require more intensive evaluation and treatment." I would like to take issue with each of these points:

1. *Effectiveness.* A recent methodologic review of all randomized controlled trials on the subject, using a rational data-pooling strategy, showed that amoxicillin in a single dose is clearly inferior to conventional therapy²; in addition, this review seriously questioned the effectiveness of trimethoprim-sulfisoxazole on the basis of a high likelihood of type II error. This suspicion was confirmed by the recent randomized trial of trimethoprim-sulfisoxazole that reported a cure rate of only 85% (58 of 68 patients) with single-dose therapy compared with 97% (66 of 68) with a standard multi-dose regimen ($p < 0.02$).³

2. *Expense.* True, single-dose therapy is cheap, but so is three-day or seven-day therapy. On the other hand, re-visits, re-cultures, and retreatment are expensive.

3. *Compliance.* Taking a single dose is easy. But what is so hard about taking two doses a day for a week?

4. *Side effects.* All randomized controlled trials to date that demonstrate side effects with single-dose therapy have major biases favoring this conclusion.² The one study that was truly double-blinded showed no difference in side effects.⁴

5. *Selection of patients.* Should we really evaluate further the 15–30% of patients who fail single-dose therapy? I prefer to give outpatients conventional therapy and have fewer treatment failures to worry about.

Dr. Fihn mentions the "skepticism of clinicians" towards using single-dose therapy. I would submit that it is because clinicians find that for "less antibiotic, the patient receives less effective treatment."² — John T. Philbrick, MD, Charlottesville, Virginia

On the other hand, single-dose trimethoprim/sulfamethoxazole (TMP/SMX), has not been shown to be less effective than longer treatment. The study by Schultz et al. cited by Dr. Philbrick, actually showed no significant

difference in overall rates of treatment failure between single- and multidose treatments.¹ The figures given by Dr. Philbrick are the numbers of relapses diagnosed but, unfortunately, the authors did not employ well-accepted microbiologic methods for identifying relapses (i.e., serotyping).²

I share Dr. Philbrick's concern about potential type II errors in published trials of single-dose SMX/TMP. In part for this reason, we compared single-dose and ten-day TMP/SMX in a double-blind, randomized trial involving 260 women.³ Our trial had a power of over 85% to detect a 25% difference (post hoc calculation) and yielded no significant difference in cure rates.

2. *Expense.* Since recurrence rates do not differ significantly, the frequency of office visits shouldn't either. More adverse reactions will, however, lead to more office visits (see below).

3. *Side effects.* Many studies, including ours and that by Schultz et al., have shown that single-dose therapy causes fewer adverse reactions than seven- to ten-day treatment.^{1,3}

4. *Compliance.* The problem with taking two doses a day for a week is that more than half of patients don't.^{4,5}

Seven to ten days of antibiotics for otherwise healthy women with uncomplicated UTIs is unnecessary. Personally, I favor the single-dose treatment, but to the skeptic I recommend therapy for three days, another approach shown to be efficacious.^{6,7}

Another issue raised in the editorial that deserves clarification is the use of single-dose treatment during pregnancy. Although some investigators have administered TMP/SMX without problem to pregnant women, recent animal data have raised concern about possible teratogenic effects of trimethoprim. It would, therefore, for the present be most prudent to avoid use of this drug during pregnancy. The use of single-dose therapy in this circumstance remains a reasonable approach provided that close follow-up is assured. — Stephan D. Fihn, MD, MPH, University of Washington, Seattle

REFERENCES

1. Fihn D. Single-dose antimicrobial therapy for urinary tract infections: "Less is more"? or "Reductio ad absurdum"? *J Gen Intern Med* 1986;1:62-5
2. Philbrick JT, Brackowski JP. Single-dose antibiotic treatment for uncomplicated urinary tract infections: less for less? *Arch Intern Med* 1985;145:1672-8
3. Schultz HJ, McCaffrey LA, Keys TI, et al. Acute cystitis: a prospective study of laboratory tests and duration of therapy. *Mayo Clin Proc* 1984;6:391-7
4. Hoover DO, Martin RW, Reynolds BH, et al. Rapid diagnosis and single-dose treatment of uncomplicated urinary tract infection. *J Am Coll Health* 1982;31:61-6

To the Editors: — In response to the issues raised by Dr. Philbrick I offer the following:

1. *Effectiveness.* As stated in my editorial I concur that single-dose amoxicillin is inferior to longer treatment.

1. Schultz HJ, McCaffrey LA, Keys TI, et al. Acute cystitis: a prospective study of laboratory tests and duration of therapy. *Mayo Clin Proc* 1984;6:391-7
2. Turck M, Ronald AR, Petersdorf RG. Relapse and reinfection in chronic bacteriuria. II. The correlation between site of infection and pattern of recurrence in chronic bacteriuria. *N Engl J Med* 1968;278:422-7.
3. Fihn SD, Johnson C, Running K, Roberts P, Stamm WE. Single-dose trimethoprim/sulfamethoxazole for women with acute dysuria. *Clin Res* (in press).
4. Andrews DA, Chuter PJ, Dawson MJ, et al. Trimethoprim and cotrimoxazole in the treatment of acute urinary tract infections: patient compliance and efficacy. *J Roy Coll Gen Pract* 1981;31:274-80.
5. Cartwright KA, Stanbridge TN, Cooper J. Comparison of once daily trimethoprim and standard co-trimoxazole in urinary infections. A trial in general practice. *Practitioner* 1982;226:152-6.
6. Charlton CAC, Crowther A, Davies JG, et al. Three-day and ten-day chemotherapy for urinary tract infections in general practice. *Br Med J* 1976;1:124-6.
7. Sigurdsson, Ahlmén J, Berglund L, et al. Three-day treatment of acute lower urinary tract infections in women. *Acta Med Scand* 1983;213:55-60.