

## ■ ORAL TREATMENT OF ONYCHOMYCOSIS

Epstein E. How often does oral treatment of toenail onychomycosis produce a disease-free nail? An analysis of published data. *Arch Dermatol* 1998; 134:1551-4.

**Clinical question** How effective are the newer oral antifungals for the treatment of toenail onychomycosis?

**Background** Standard topical antifungals are ineffective for the treatment of onychomycosis, and treatment with griseofulvin and ketoconazole is hampered by low cure rates, high relapse rates, high incidence of side effects, and the need for lengthy dosing schedules.<sup>1</sup> Newer oral agents such as itraconazole, terbinafine, and fluconazole have more favorable side-effect profiles and shorter dosing schedules. Although previous studies using these agents have reported high cure rates, there had been no recent systematic review to determine the relative efficacy of these agents in curing and preventing relapse of toenail onychomycosis.

**Population studied** This review included only studies enrolling 15 or more subjects with isolated toenail onychomycosis.

**Study design and validity** This is a systematic review rather than a meta-analysis, because it falls short of statistically combining data into a single estimate of efficacy. Studies from the MEDLINE database were identified using a title search for the key word "toenail," and medical subject heading searches combining "onychomycosis" and "therapy." Of these, only studies that used both clinical (morphologic) and mycologic (potassium hydroxide preparation and culture) cure as an end point were included in the analysis. The frequency with which treatment achieved disease-free nails was calculated for each study. Unfortunately, no study of fluconazole met the inclusion criteria for this review.

**Outcomes measured** The primary outcomes were the frequency of attaining a disease-free nail 1 year after the start of treatment and the relapse rate at 2 years. The former could be calculated for 3 studies of itraconazole and 8 studies of terbinafine. The 2-year relapse rate was calculated for 1 study of itraconazole; terbinafine studies lacked the data to allow relapse-rate calculation.

**Results** Except for 1 small study, the disease-free nail rates after 1 year of treatment were from 38% to 52% for terbinafine. Disease-free nail rates for itraconazole were 33% to 35%. The relapse rate in the 1 study of itraconazole was 17% at 2 years. No studies of terbinafine reported a relapse rate, and no studies of any oral agent reported relapse rates beyond 2 years.

A common weakness of the reviewed studies was the practice of considering "improved nail morphology" or a

"90% to 100%" normal nail as a successful outcome without requiring complete mycologic and morphologic cure. Other limitations included assessing a target nail to gauge cure rather than assessing all diseased nails, reporting relapse figures without supporting data, and estimating relapse by gross morphologic findings without mycologic findings.

**Recommendations for clinical practice** The cure rate for toenail onychomycosis appears to be higher with terbinafine than with itraconazole, and cure rates for either agent exceed those reported in most trials of griseofulvin.<sup>1</sup> However, given the lack of long-term relapse data and the flawed assessment of cure that characterized many of these studies, as well as the treatment's high cost and low clinical efficacy, we do not recommend the widespread use of these drugs. Until a well-designed randomized controlled clinical trial establishes improved and lasting efficacy of 1 or more of the oral agents, their use should be considered only on a case-by-case basis.

Mark R. Ellis, MD, MSPH

Kevin Y. Kane, MD

University of Missouri-Columbia

E-mail: ellismr@health.missouri.edu

## REFERENCES

1. Korting HC, Schafer-Korting M. Is tinea unguium still widely incurable? A review three decades after the introduction of griseofulvin. *Arch Dermatol* 1992; 128:243-8.

## ■ PROPHYLACTIC MASTECTOMY FOR PREVENTION OF BREAST CANCER

Hartmann LC, Schaid DJ, Woods JE, et al. Efficacy of bilateral prophylactic mastectomy in women with a family history of breast cancer. *N Engl J Med* 1999; 340:77-84.

**Clinical question** Does bilateral prophylactic mastectomy prevent breast cancer in women with a family history of breast cancer?

**Background** Breast cancer is the most common cancer in American women and will affect 1 in 9 in their lifetime.<sup>1</sup> Family history and genetic analysis can be used to predict individual risk levels. Women at high risk can be offered careful surveillance, chemopreventive therapy, or bilateral prophylactic mastectomy (BPM). The outcome data for women undergoing BPM are incomplete.

**Population studied** All women with a family history of breast cancer who underwent BPM at the Mayo clinic between 1960 and 1993 were included in the study. The median age at mastectomy was 42 years.

**Study design and validity** This was a retro-