A 31-year-old man from northern Ontario had acute swelling, purpura and pain in his left lateral forefoot region, which increased progressively over 10 weeks until he became bedridden. A clinical diagnosis of gout was made, but the pain did not improve with NSAIDs. One month later, a small pustule developed that progressed to an ulcer with purulent drainage. On presentation 1 month later, his left foot was swollen, and the lateral forefoot was exquisitely tender to palpation. A 2-cm ulcer, which probed to bone, was present on the lateral aspect of the foot (Fig. 1). The patient was afebrile, and findings on general medical and pulmonary examinations were unremarkable. A plain radiograph of the foot revealed dystrophic calcification in the soft tissues, with osteopenia and periosteal reaction along the fifth metatarsal bone consistent with active osteomyelitis (Fig. 2). The chest radiograph appeared normal.

Intravenous therapy with ciprofloxacin and clindamycin was started empirically. *Staphylococcus aureus* and *Streptococcus agalactiae* (group B streptococcus) were recovered from the deep wound swab. The patient’s condition did not improve after a week of parenteral antibacterial therapy. Surgical débridement revealed a pocket of grossly necrotic tissue that had replaced part of the fifth metatarsal. Histologic examination revealed broad-based budding yeast consistent with *Blastomyces dermatitidis* (Fig. 3). The antibiotic therapy was replaced by treatment with amphotericin B (40 mg intravenously once daily) for 1 week followed by itraconazole (400 mg orally once daily) to complete a 12-month course. The patient had prompt relief of pain, with healing of the wound and radiographic evidence of bone reconstitution occurring within 6 months.

**Foot ulcer and osteomyelitis**

Blastomycosis is an uncommon granulomatous systemic fungal infection caused by the thermally dimorphic fungus *B. dermatitidis.* Areas in North America in which this fungus is endemic include the Ohio and Mississippi River basins and the regions that border the Great Lakes. The annual incidence of blastomycosis is greater in the district of Kenora, Ont., than in all of Manitoba (7.1 v. 0.6 cases per 100 000 people).

*B. dermatitidis* exists in a mycelial form in the soil, but when disturbed, the released conidia are inhaled and converted to thick-walled budding yeasts that cause respiratory infection and hematogenous dissemination producing extrapulmonary disease. The median incubation period is 30–45 days. Pulmonary disease may be acute or chronic and can mimic infection from other fungi, malignant disease or infection from pyogenic bacteria or *Mycobacterium tuberculosis.* Extrapulmonary
In the Literature

Trastuzumab (Herceptin) and HER2-positive breast cancer

Piccart-Gebhart MJ, Procter M, Leyland-Jones B, et al. Trastuzumab after adjuvant chemotherapy in HER2-positive breast cancer. N Engl J Med 2005;353:1659-72.

Background: HER2 (human epidermal growth factor receptor 2) is present in 15%–25% of breast cancers. Women with HER2-positive breast cancer usually have more aggressive cancer, are at increased risk of recurrence and have a poorer survival than other women with breast cancer. Trastuzumab, a recombinant monoclonal antibody, acts against HER2 receptors.

Design: In this international randomized trial, women who had undergone surgical excision of a HER2-positive, early invasive breast cancer and who had completed 4 or more courses of chemotherapy were randomly assigned to receive trastuzumab every 3 weeks or observation alone (control group) for 1 or 2 years. Patients were included if they had adequate liver, kidney and bone marrow function and a normal left ventricular ejection fraction (LVEF). Women were excluded if they had metastases, prior invasive breast cancer, another neoplasm, or a cardiac condition such as angina pectoris requiring medication, uncontrolled hypertension or prior congestive heart failure or myocardial infarction. The primary outcome measure was disease-free survival; secondary end points were cardiac safety, overall survival, time to distant occurrence and site of first disease-free survival event.

Results: The results presented were from an interim analysis of data for women who had been followed for 1 year (1694 in the trastuzumab group, 1693 in the control group). Events (recurrences, new cancer [breast or other], death) were half as common in the treatment group as in the control group (hazard ratio 0.54, 95% confidence interval 0.43–0.67), although there was no improve-

Table 1: Outcomes of 4 trials of trastuzumab therapy for HER2-positive breast cancer

| Study                  | ARR, % | NNT | Absolute increased risk of CHF, % | No. needed to cause 1 case of CHF | Absolute increased survival |
|------------------------|--------|-----|-----------------------------------|----------------------------------|----------------------------|
| Piccart-Gebhart et al  | 5.5‡   | 18  | 1.7                               | 60                               | No significant improvement |
| Romond et al¹          | 11.8*  | 8.5 | 3†                                 | 30                               | 2.5% at 3 yr               |
| Marty et al²           | 5†     | 20  | 95                                | 11                               | 4% at cut-off (about 3 yr) |
| Slamon et al³          | 5¶     | 20  | 8                                 | 13                               | 11% at 1 yr                |

Note: HER2 = human epidermal growth factor receptor 2, ARR = absolute risk reduction, NNT = number needed to treat, CHF = congestive heart failure.

References:
1. Chapman SW. Blastomyces dermatitidis. In: Mandell GL, Bennett JE, Dolin R, editors. Principles and practice of infectious diseases. 6th ed. Philadelphia: Churchill Livingstone; 2005. p. 3027-40.
2. Crampton TL, Light RB, Berg GM, et al. Epidemiology and clinical spectrum of blastomycosis diagnosed at Manitoba hospitals. Clin Infect Dis 2002; 34:1310-6.
3. Chapman SW, Bradsher RW Jr, Campbell GD Jr, et al. Practice guidelines for the management of patients with blastomycosis. Infectious Diseases Society of America. Clin Infect Dis 2000; 30:679-83.