A 40-year-old man presented with an enlarging 3-cm verrucous nodule on the upper lip and three 1- to 2-cm crusted verrucous plaques on the right posterior thigh and bilateral posterior lower legs of 2 months’ duration. He was otherwise healthy. A biopsy of the lip nodule was performed.

H&E, original magnification ×600.

The best diagnosis is:

a. blastomycosis  
b. chromoblastomycosis  
c. coccidioidomycosis  
d. cryptococcosis  
e. histoplasmosis
Blastomycosis is caused by Blastomyces dermatitidis, which is endemic in the Midwestern and southeastern United States where it occurs environmentally in wood and soil. Unlike many fungal infections, blastomycosis most often develops in immunocompetent hosts. Infection is usually acquired via inhalation, and cutaneous disease typically is secondary to pulmonary infection. Although not common, traumatic inoculation also can cause cutaneous blastomycosis. Skin lesions include crusted verrucous nodules and plaques with elevated borders. Histologic features include pseudoepitheliomatous hyperplasia with intraepidermal neutrophilic microabscesses (Figure 1), and a neutrophilic and granulomatous dermal infiltrate. Organisms often are found within histiocytes (quiz image) or small abscesses. The yeasts usually are 8 to 15 µm in diameter with a thick cell wall and occasionally display broad-based budding.

Chromoblastomycosis is caused by dematiaceous (pigmented) fungi, including Fonseccae, Phialophora, Cladophialophora, and Rhinocladiella species, which are present in soil and vegetable debris in tropical and subtropical regions. Infection typically occurs in the foot or lower leg from traumatic inoculation, such as a thorn or splinter injury. Histologically, chromoblastomycosis is characterized by pseudoepitheliomatous hyperplasia; suppurative and granulomatous dermatitis; and sclerotic (Medlar) bodies, which are 5 to 12 µm in diameter, round, brown, sometimes septate cells resembling copper pennies (Figure 2).

Coccidioidomycosis is caused by Coccidioides immitis, which is found in soil in the southwestern United States. Infection most often occurs via inhalation of airborne arthrospores. Cutaneous lesions occasionally are observed following dissemination or rarely following primary inoculation injury. They may present as papules, nodules, pustules, plaques, and ulcers, with the face being the most commonly affected site. Histologically, coccidioidomycosis is characterized by pseudoepitheliomatous hyperplasia, suppurative and granulomatous dermatitis, and large spherules (up to 100 µm in diameter) containing numerous small endospores (Figure 3).

Cryptococcosis is caused by Cryptococcus neoformans, a fungus found in soil, fruit, and pigeon droppings throughout the world. The most common route of infection is via the respiratory tract. Systemic spread and central nervous system involvement may occur in immunocompromised hosts. Skin involvement is uncommon and may present on the head and neck with umbilicated papules, pustules, nodules, plaques, or ulcers. Histologically, Cryptococcus is a spherical yeast, often 4 to 20 µm in diameter. Replication is by narrow-based budding. A characteristic feature is a mucoid capsule,
which retracts during processing, leaving a clear space around the yeast (Figure 4). When present, the mucoid capsule can be highlighted on mucicarmine or Alcian blue staining. Histologic variants of cryptococcosis include granulomatous (high host immune response), gelatinous (low host immune response), and suppurative types.²

Histoplasmosis is caused by *Histoplasma capsulatum*, which occurs in soil and bird and bat droppings, with exposure primarily via inhalation. Cutaneous histoplasmosis is almost always a feature of disseminated disease, which occurs most commonly in immunosuppressed individuals.¹ Skin lesions may present as macules, papules, indurated plaques, ulcers, purpura, panniculitis, and subcutaneous nodules.² Histologically, there is a granulomatous and neutrophilic infiltrate within the dermis and subcutis. Yeasts are small (2–4 µm in diameter) and are observed within the cytoplasm of macrophages (Figure 5) where they appear as basophilic dots, sometimes surrounded by an artifactual clear space (pseudocapsule).²

**REFERENCES**