BMJ Best Practice

Blastomycosis

Straight to the point of care

Last updated: Jul 12, 2024

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Summary

Blastomycosis is an invasive infection caused by the dimorphic fungus *Blastomyces dermatitidis* , endemic to the north central and southern US, Canada, and parts of Africa.

Most commonly involves the lungs. Dissemination can occur, with extrapulmonary infection often seen in the skin, bones, joints, central nervous system, and genitourinary system.

Although key epidemiological factors in the history are often suggestive of the diagnosis, histopathological or microbiological examination of clinical specimens with demonstration of *B dermatitidis* is necessary to establish the diagnosis.

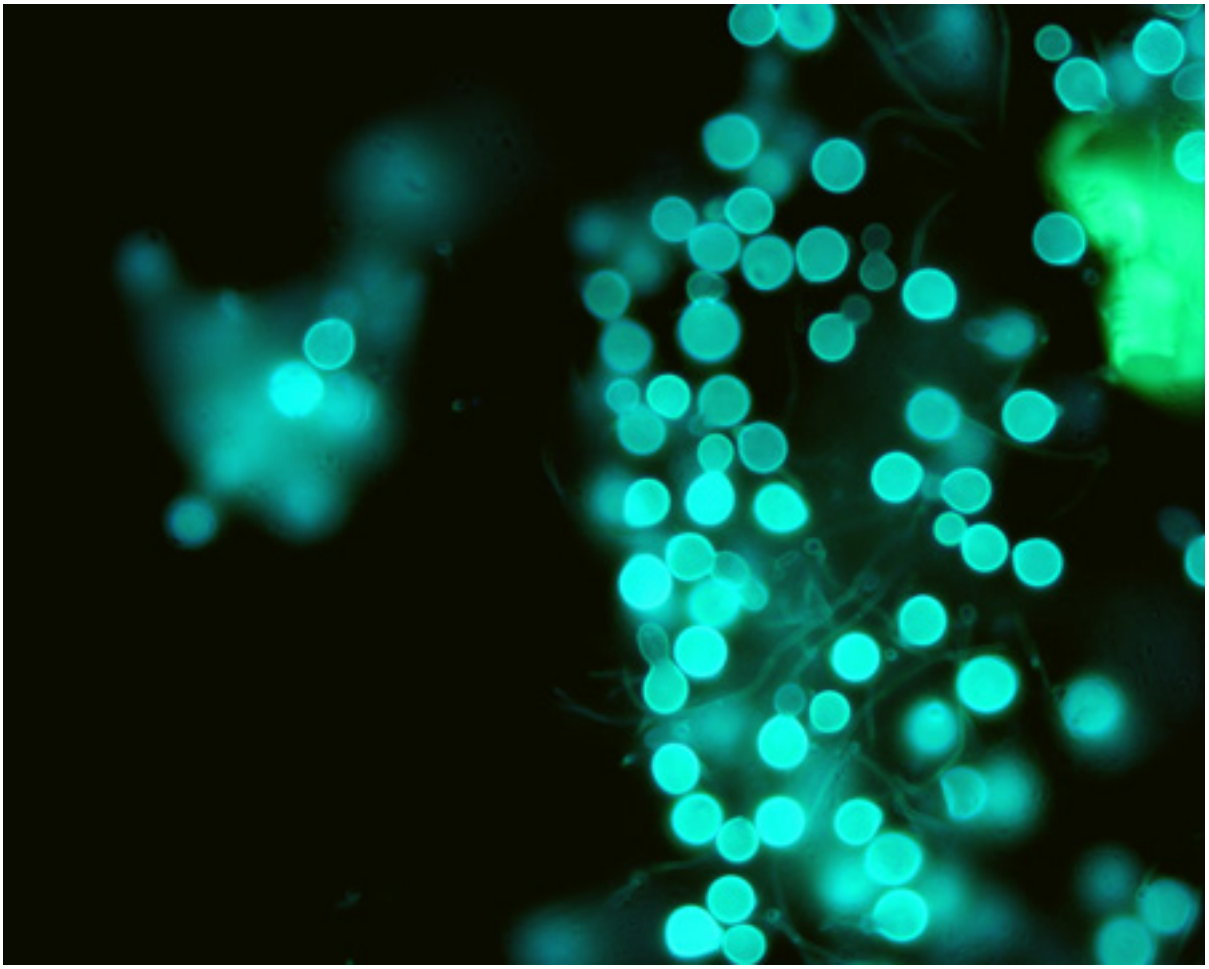
First-line treatment for ambulatory patients is a prolonged course of oral itraconazole. Amphotericin-B is reserved for patients with more severe disease or for patients in whom itraconazole is contraindicated.

No vaccine is available for disease prevention.

Definition

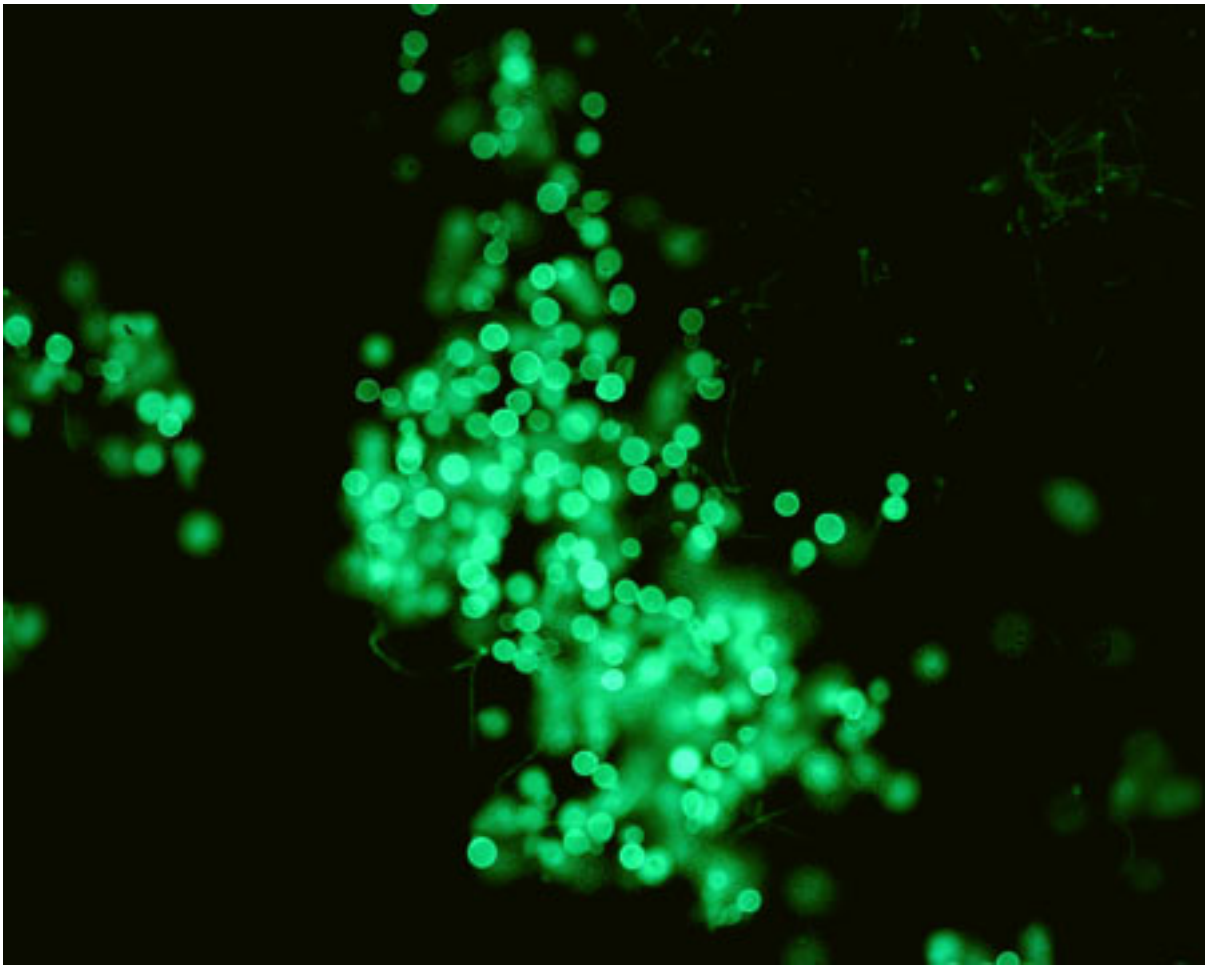
Blastomycosis is an invasive infection caused by the dimorphic fungus *B dermatitidis* , which is endemic to the upper and mid-Mississippi River valley in the US, Canada, the Mediterranean basin, and parts of Africa.[1] [2] Although pulmonary involvement is most common, skin, central nervous system, and osteoarticular involvement are frequently seen. Less commonly, infection can involve other sites, such as the genitourinary system, and patients can even have multiple sites of infection.

Diagnosis is usually based on either histopathological demonstration of the characteristic yeast form or culture of the mycelial form from clinical specimens.[3] There are no commonly accepted schematic classifications for blastomycosis, including formal criteria for severity of illness.



Direct potassium hydroxide preparation at 40x magnification of a sputum specimen

Nancy L. Wengenack, PhD, D(ABMM), Director of Mycology and Mycobacteriology Laboratories, Assistant Professor of Microbiology abd Lab Medicine, Mayo Clinic, Rochester, MN



Direct potassium hydroxide preparation at 20x magnification of a sputum specimen

Nancy L. Wengenack, PhD, D(ABMM), Director of Mycology and Mycobacteriology Laboratories, Assistant Professor of Microbiology and Lab Medicine, Mayo Clinic, Rochester, MN

Epidemiology

Blastomycosis occurs within geographically limited regions of the US, Canada, Mediterranean basin, and South Africa.[1] [2] Occasional cases are detected in Central and South America and the Middle East.[4] [6] [7] The incidence of blastomycosis in 2019 was 0.8 cases per 100,000 population in US states where it is a reportable condition, which include Arkansas, Louisiana, Michigan, Minnesota, and Wisconsin.[8] [9] A 2023 epidemiological study found that counties in 40 US states exceeded the clinically relevant threshold for blastomycosis.[10] Data suggest that blastomycosis may be endemic in the Northeastern region of the US.[11] [12]

In the Canadian provinces of Ontario and Manitoba, the annual incidence ranges from 0.29 cases per 100,000 population to as high as 7.11 cases per 100,000 in the Kenora, Ontario district.[13] [14] Epidemiological trends reveal a tendency for infection to occur in middle-aged men who have occupational or recreational exposure to soil, wooded areas, or waterways.[15] [16]

Blastomycosis has also been reported in all of South Africa.[17] Age and sex distribution are similar to the US, but the clinical manifestations are slightly different. South African patients tend to have more bone involvement and less central nervous system disease than patients in the US, and there is no apparent disease in dogs.[18] In the US, dogs and humans may simultaneously acquire the disease after exposure to the same environments, but a sick dog is a clue to exposure, rather than a vector for transmission of the disease to humans.

Aetiology

Blastomycosis is caused by *Blastomyces dermatitidis* .[4] It is a dimorphic fungus that grows as a white cottony mycelium that turns tan or brown at 25°C (77°F), and as a cream-to-tan, heaped, or wrinkled yeast at 37°C (98.6°F).[19] *B dermatitidis* exists as a saprophytic mould in the environment, and has been isolated from samples in such sites as a beaver pond and lodge, soil and organic debris from a fishing site along a river bank, and woodpiles.[15] [16] [20]

Other species within the *Blastomyces* genus have also been described, including *B helicus* , *B gilchristii* and *B percursus* .[21] [22] However, their relative importance as pathogens are yet to be defined.

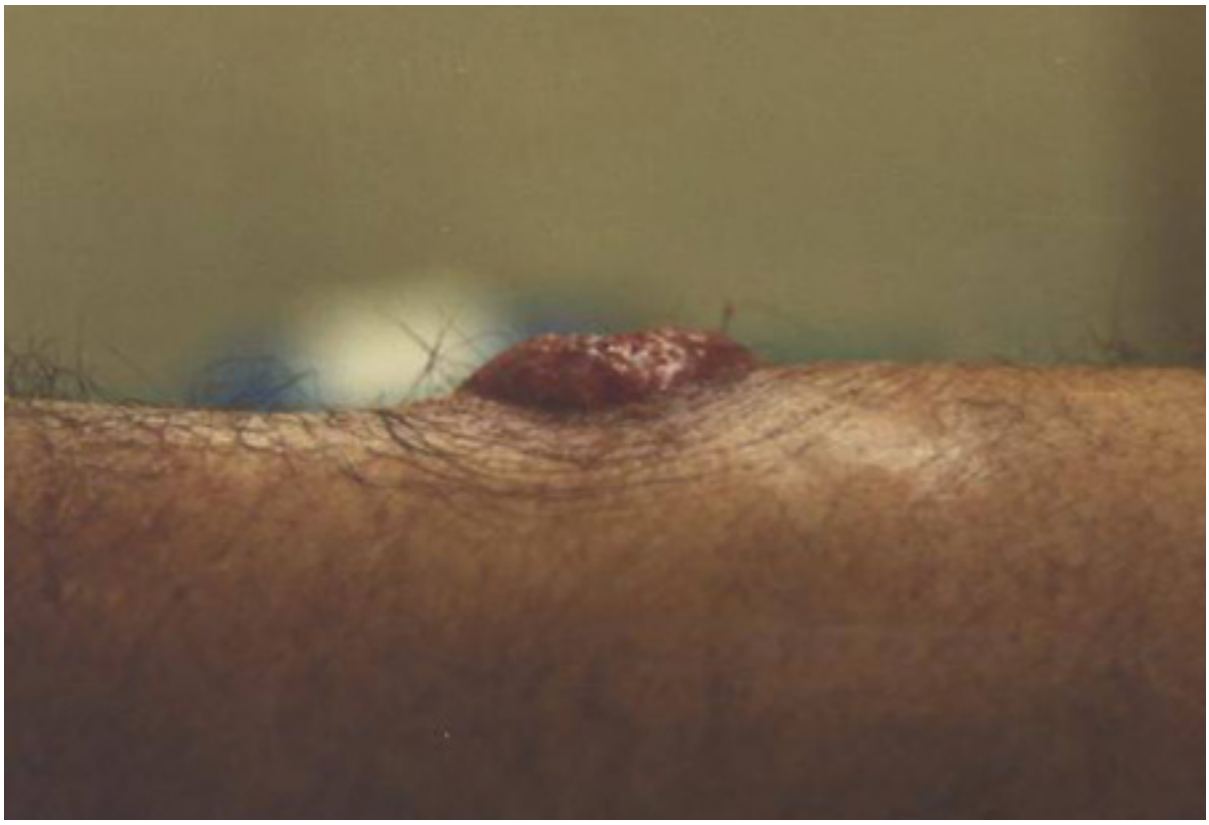
Pathophysiology

Infection with *B dermatitidis* usually occurs by inhalation.[4] In the lung, the conidia (spores) are either phagocytosed and eliminated by alveolar macrophages, neutrophils, or monocytes, or they convert to the yeast form, which is more resistant to phagocytosis.[23] This can lead to a self-limiting asymptomatic pulmonary infection or acute lobar pneumonia. From the lung, the yeast form can disseminate haematogenously, leading to extrapulmonary infection, most commonly in the skin and soft tissues, bones and joints, CNS, and urinary tract.[23] However, direct inoculation of the conidia into the skin can occur as well.[24]

Case history

Case history #1

A 57-year-old man presents with persistent cough and shortness of breath. He was recently treated for pneumonia with a 10-day course of oral levofloxacin. He also complains of multiple painless nodular skin lesions on his arms and legs. He has no significant past medical history and prior to the illness was taking no medicines. He enjoys hunting and fishing as hobbies. He notes that his hunting dog also has similar skin lesions. Physical examination is significant for multiple 1.5 to 2 cm erythematous nodules, some with central ulceration, on the extremities. He also has consolidative lung findings on pulmonary auscultation.

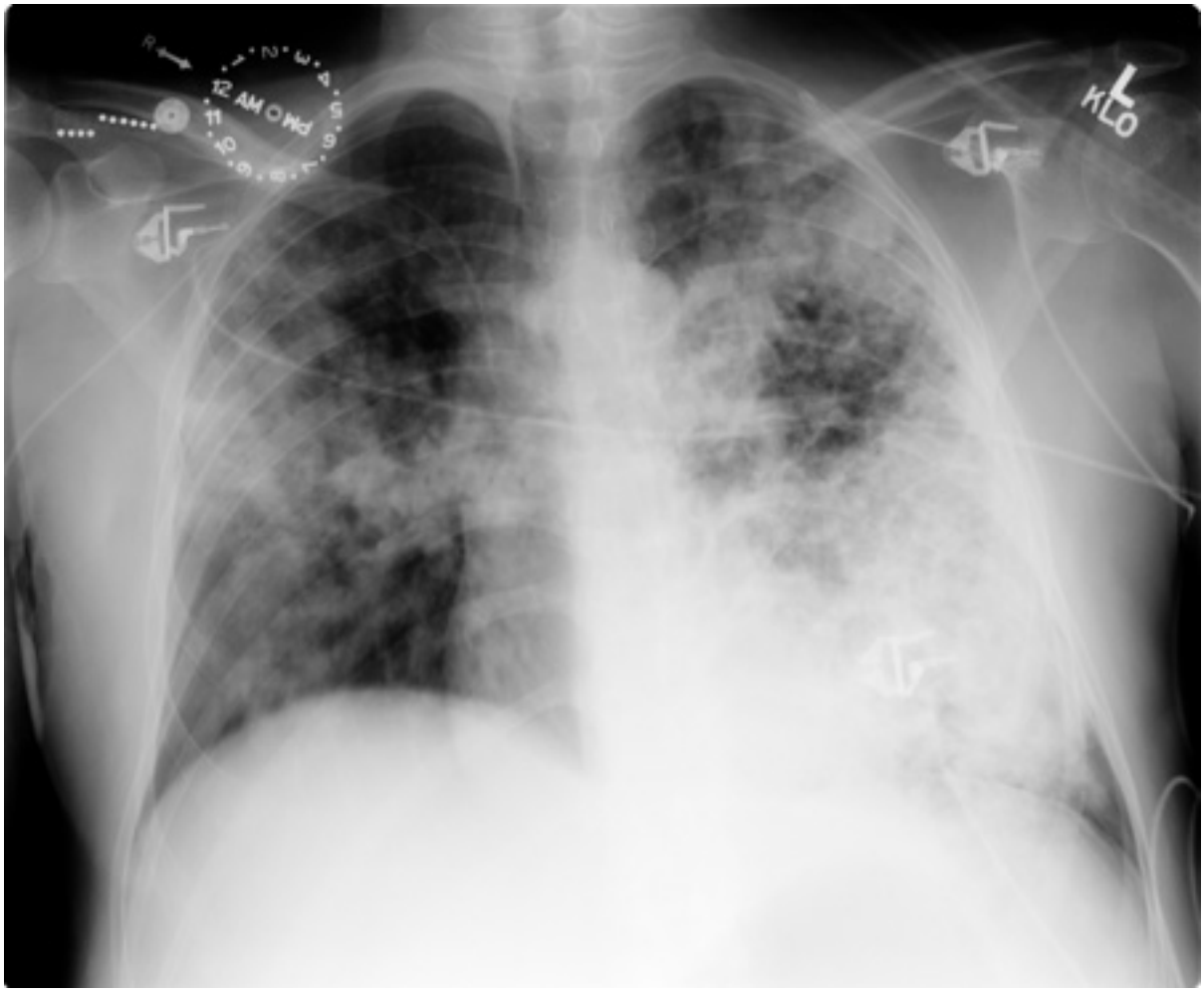


Cutaneous blastomycosis on the forearm

Personal files of Larry Baddour, MD

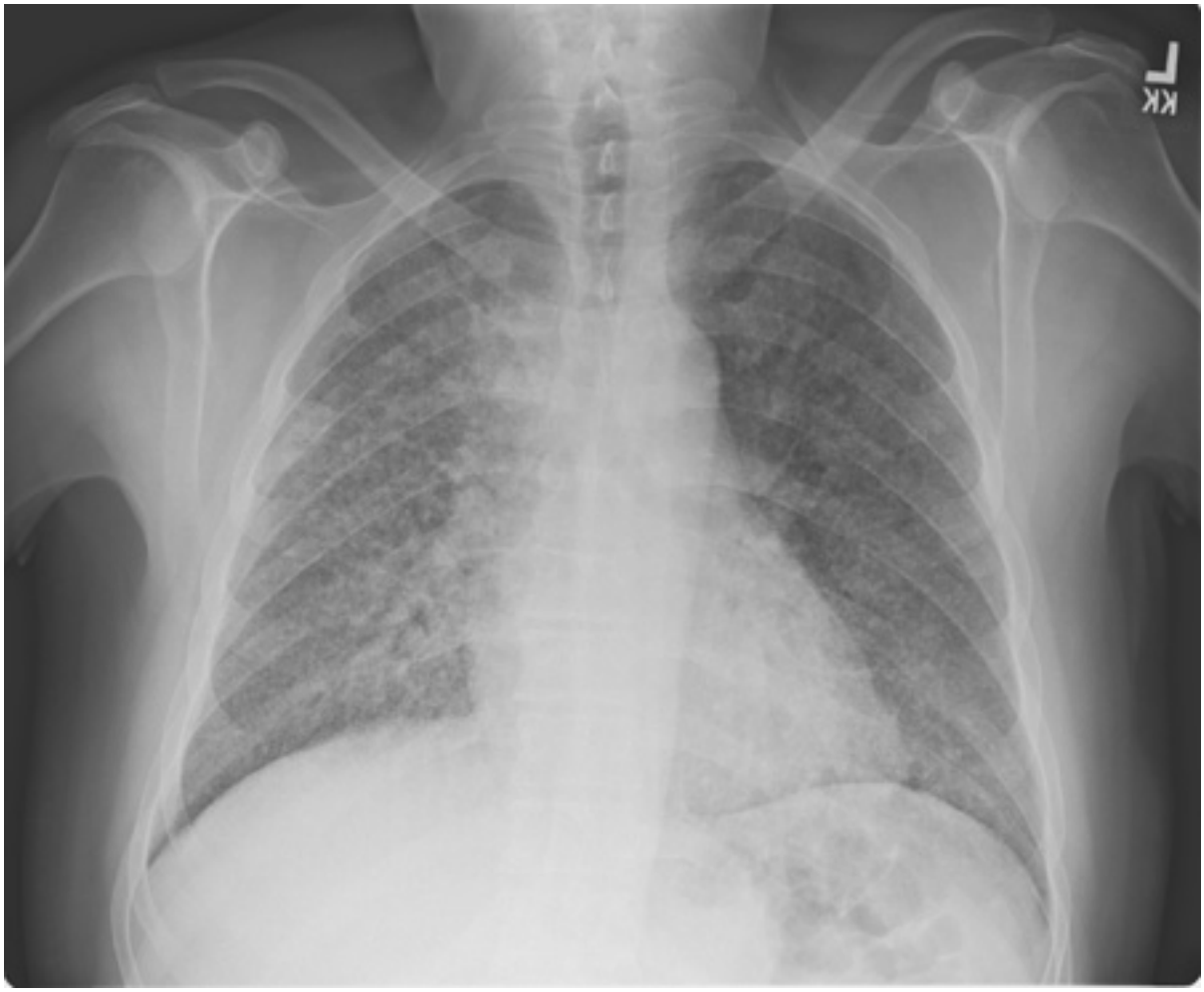
Other presentations

The majority of people acutely infected with *Blastomyces dermatitidis* develop asymptomatic, self-limiting pulmonary infections. The most common presentation is a mild-to-moderately severe community-acquired pneumonia that tends to involve the upper lobes. However, some patients can present with lung masses or progress to respiratory failure and adult respiratory distress syndrome.[4] Less common manifestations arise due to systemic spread of the infection.



Pulmonary blastomycosis with focal infiltrates on chest x-ray

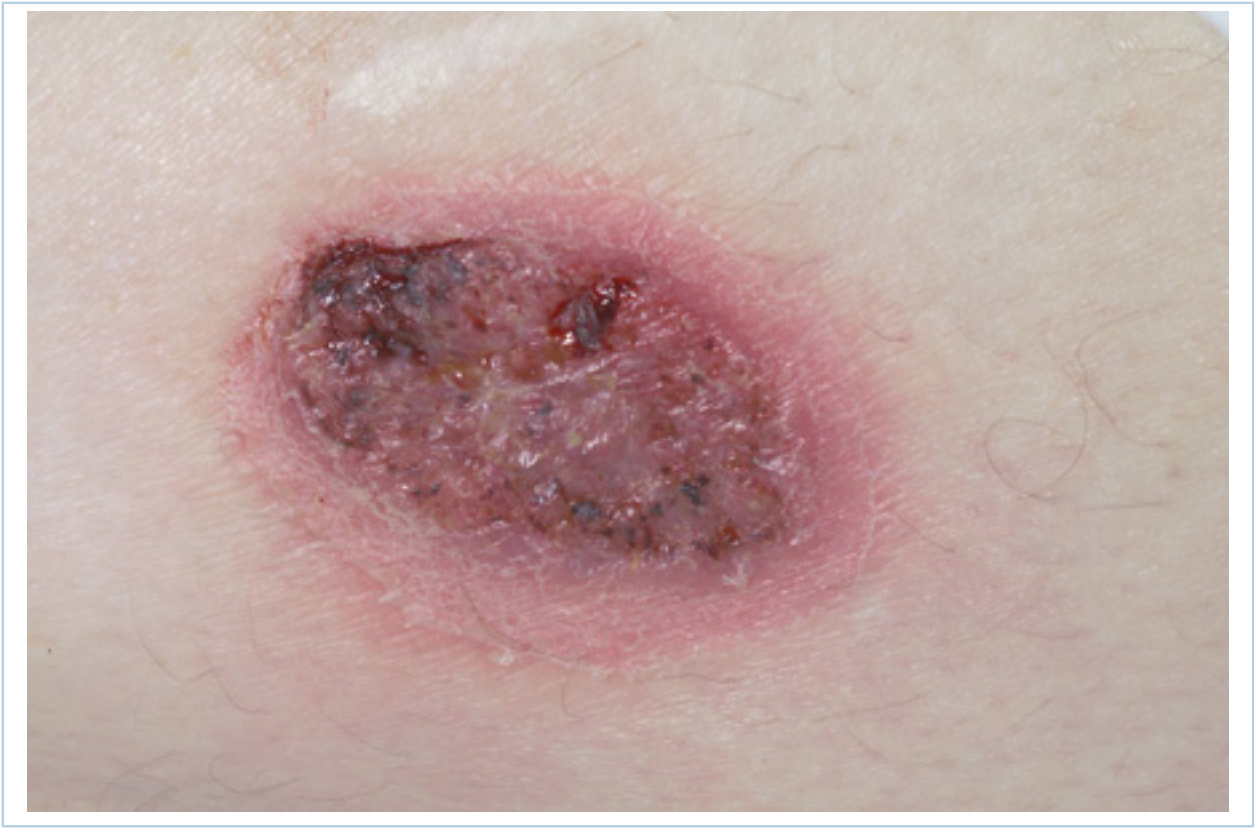
Dr Robert Orenstein, DO, Associate Professor of Medicine, Division of Infectious Diseases, Mayo Clinic, Scottsdale, AZ



Pulmonary blastomycosis presenting as a miliary pattern on chest x-ray

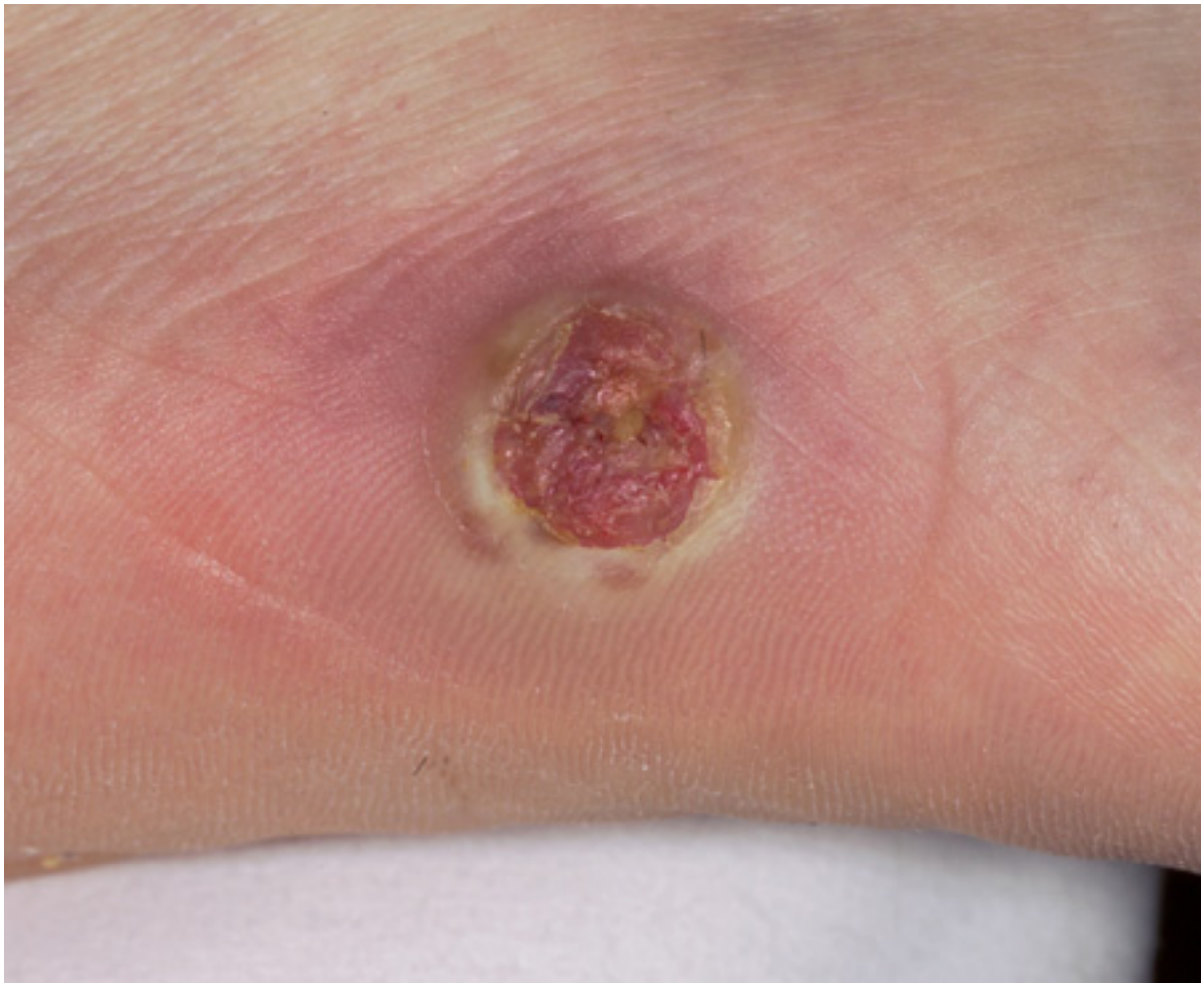
Dr Robert Orenstein, DO, Associate Professor of Medicine,
Division of Infectious Diseases, Mayo Clinic, Scottsdale, AZ

Cutaneous blastomycosis is the most common extrapulmonary presentation, and presents as painless nodules or non-healing ulcers mainly on the extremities. Cutaneous involvement usually results from disseminated disease.[4] Rarely, the skin is infected by direct inoculation via minor or major trauma. Primary osteoarticular involvement may result from haematogenous seeding, or secondary to direct bone invasion from overlying skin lesions, and patients can present with bone pain or septic arthritis. Central nervous system involvement can present either as acute or chronic aseptic meningitis or with space-occupying lesions on brain imaging with attendant neurological symptoms. Chronic prostatitis, which is always part of a disseminated process, is an unusual manifestation in men. Women can develop tubo-ovarian abscesses, endometritis, and salpingitis.[5]



Cutaneous blastomycosis on the lower extremity

LuAnn Ziemer, Office of Medical Photography, Mayo Clinic, Rochester, MN



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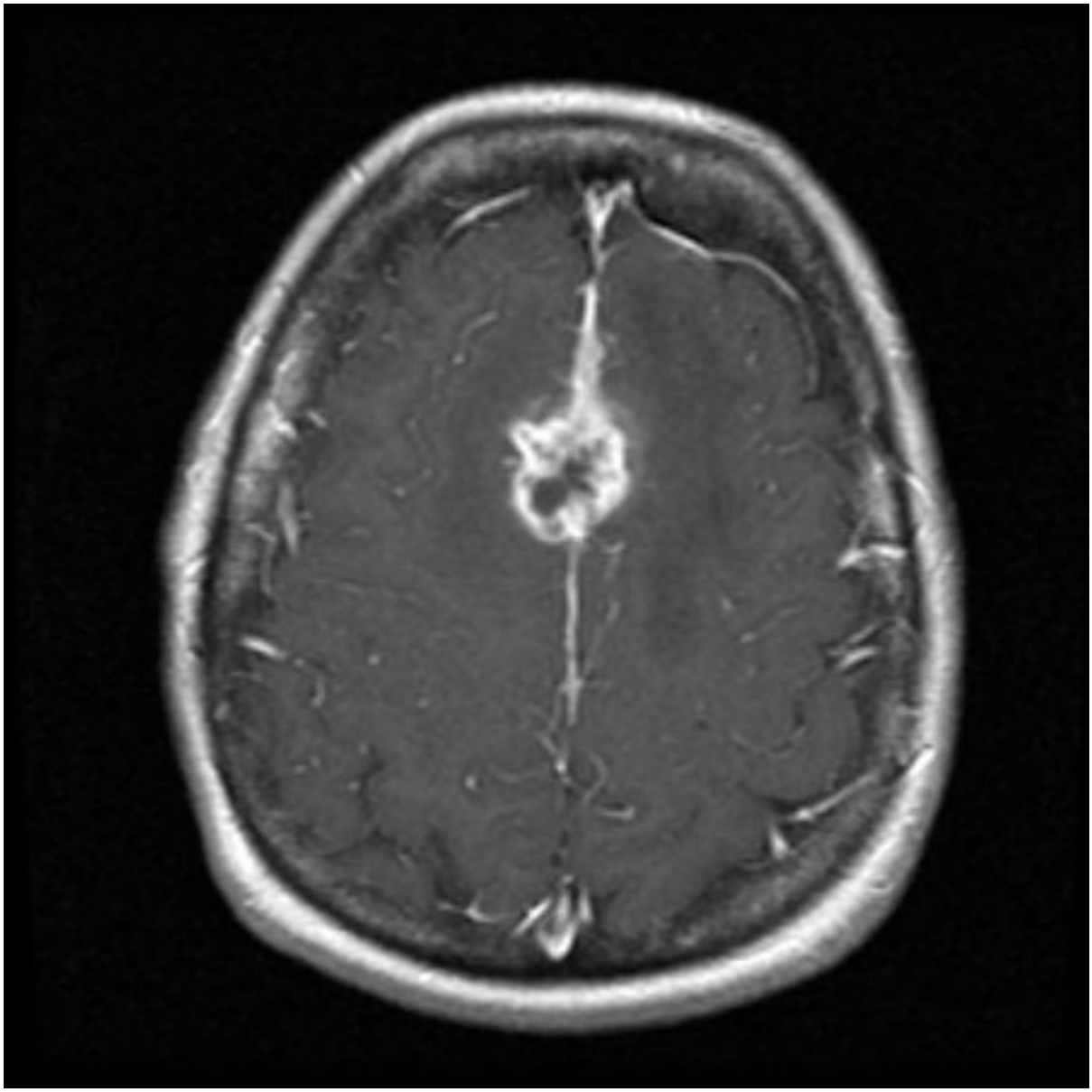


Axial T1 gadolinium-enhanced MRI image of cerebral blastomycosis

Dr William Marshall, MD, Assistant Professor of Medicine, Division of Infectious Diseases, Mayo Clinic, Rochester, MN

Approach

Residing in or travelling to areas of endemicity are important epidemiological clues. Men are infected more often than women, presumably due to increased outdoor environmental exposures. Detailing of potential employment or recreational exposures in the outdoors is important. Because blastomycosis is a common infection in dogs, disease to dogs in the endemic area can be a clue to the diagnosis. Otherwise, there are no pathognomonic features.

Symptoms

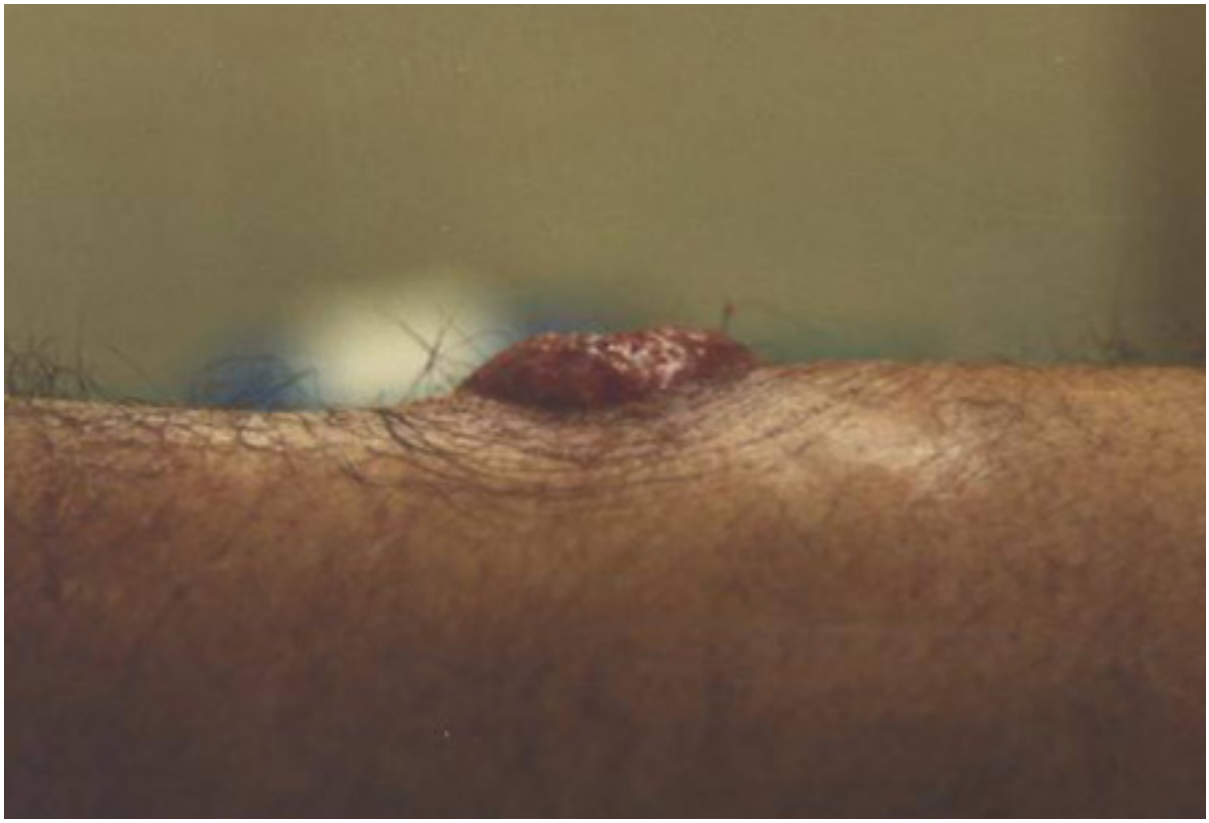
The majority of people acutely infected with *Blastomyces dermatitidis* develop asymptomatic, self-limiting pulmonary infections. Patients with overt disease may have cough or constitutional symptoms. The presentation is frequently as a community-acquired pneumonia with purulent sputum. A high level of clinical suspicion is needed as the diagnosis is often missed or delayed. Patients frequently undergo one or more courses of antibiotics before the disease is considered, after the patient has failed to improve or worsens. The course may be weeks or months. Other presentations may include:

- Acute monoarticular septic arthritis
- Skin lesions (nodular, ulcerated, or verrucous)
- Focal neurological symptoms or altered level of consciousness
- Dysuria or other symptoms of prostatitis.

In addition, many people have evidence of past asymptomatic disease according to serological or skin testing, but the specificity and sensitivity of these tests are not reliable.

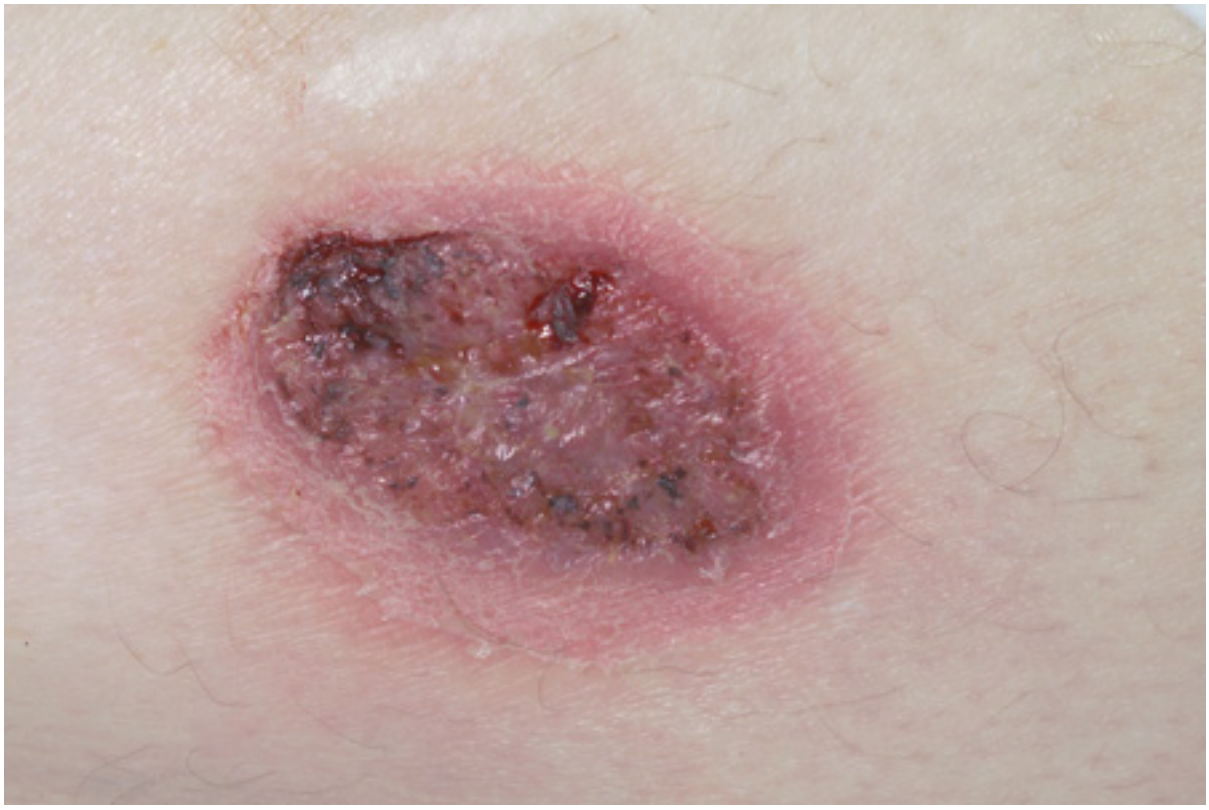
Physical examination

Rales may be heard on pulmonary auscultation. Complete examination of the skin is important to evaluate for cutaneous lesions, as well as careful examination of the joints to rule out osteoarticular involvement. Focal neurological deficits may be found. Men may have prostatic or testicular tenderness.



Cutaneous blastomycosis on the forearm

Personal files of Larry Baddour, MD



Cutaneous blastomycosis on the lower extremity

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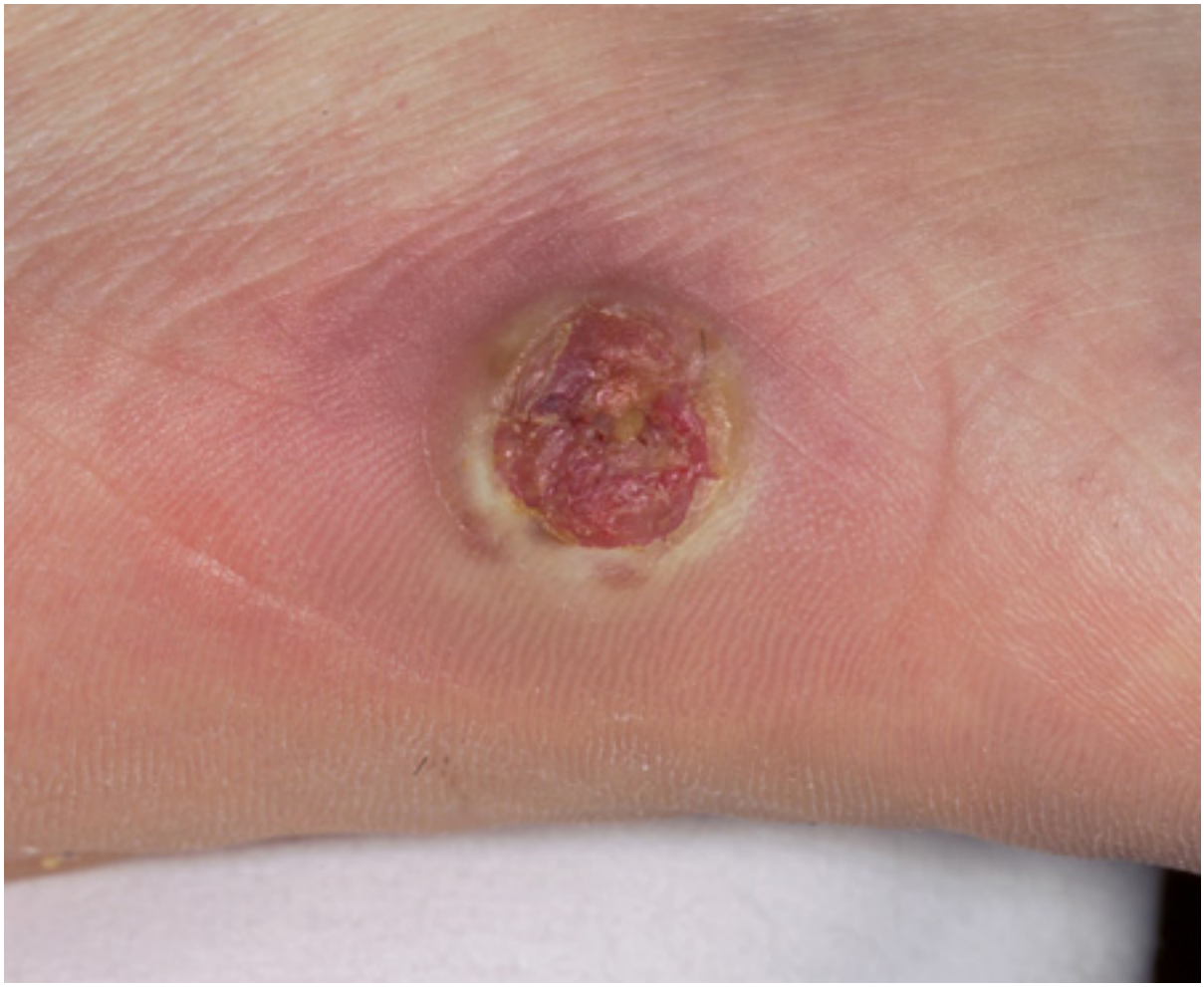

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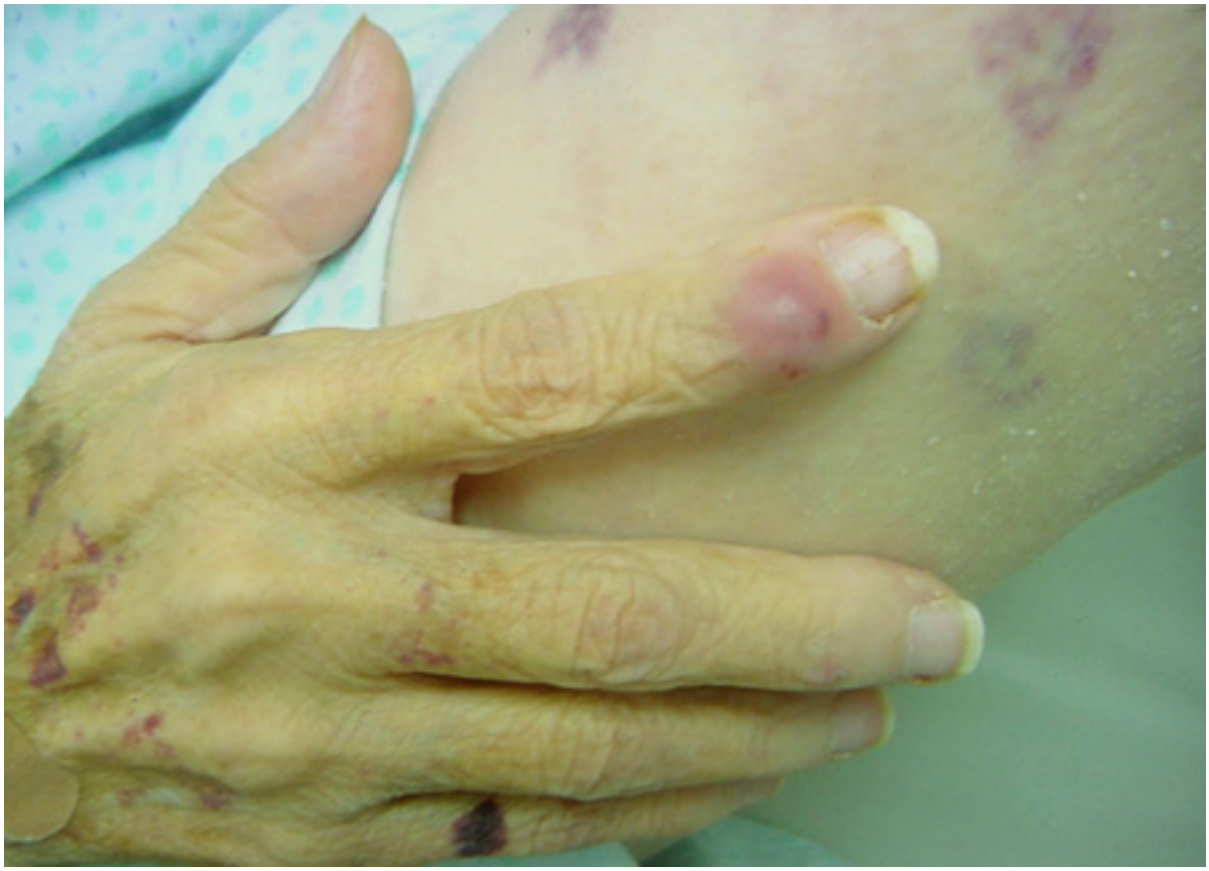


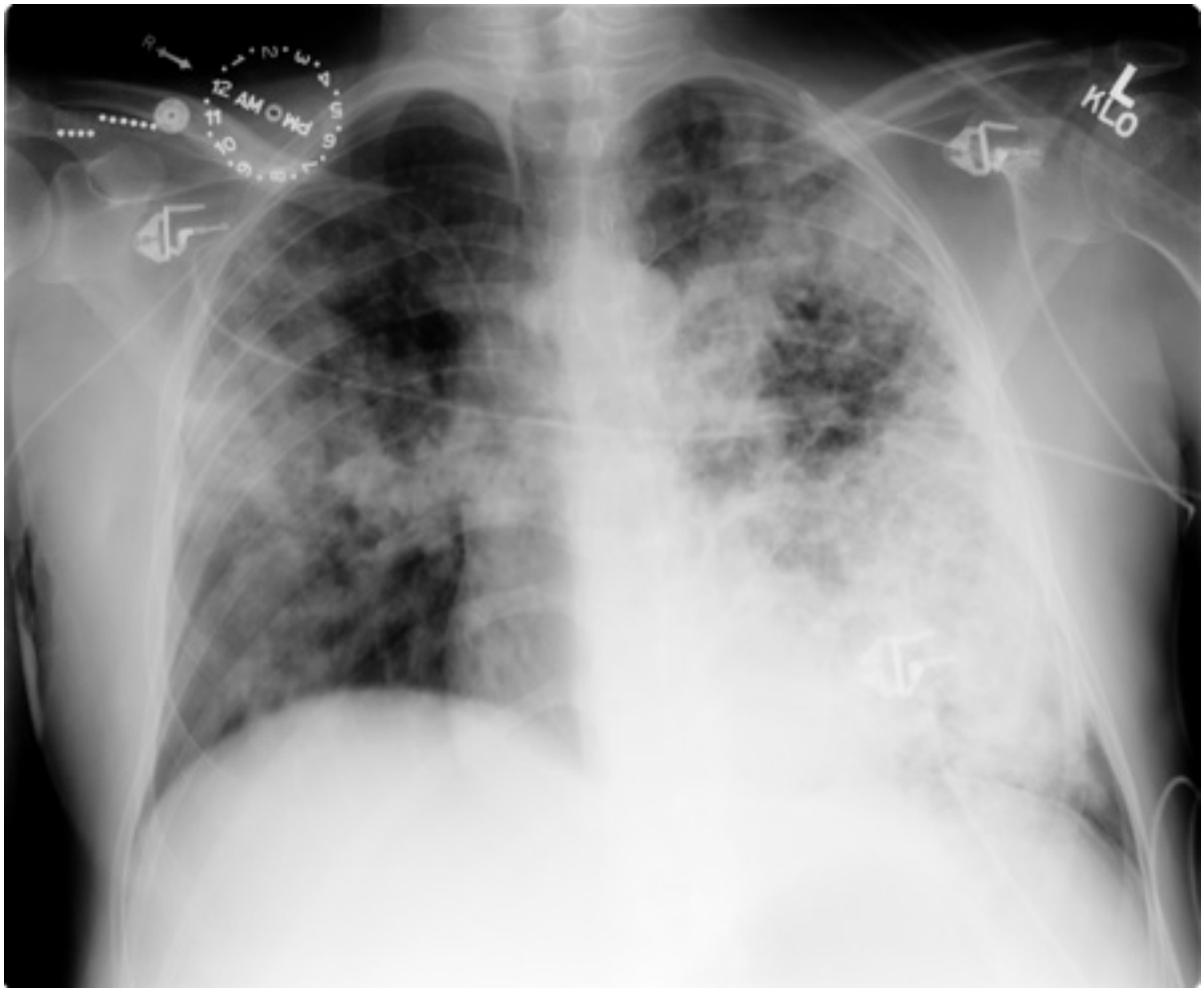
Cutaneous manifestation of disseminated blastomycosis

Personal files of Larry Baddour, MD

Diagnostic studies

Enzyme immunoassay (EIA) urine antigen testing should be considered in the first instance in patients presenting with community-acquired pneumonia of unknown aetiology who have not responded to one or more courses of antibiotics, and that have a relevant epidemiological history.[30] [31] EIA urine antigen tests have a quick turnaround time if available locally, and a positive result indicates probable acute pulmonary blastomycosis.[30] [31] While urine is preferred, the assay is also clinically available for use on serum, cerebrospinal fluid (CSF) or bronchoalveolar lavage samples.[2] [32]

Patients with pulmonary involvement should also have a chest x-ray and respiratory tract specimen smear and culture if possible. If expectorated sputum is unobtainable or non-revealing, bronchoscopy is performed. Patients with joint involvement undergo arthrocentesis with Gram stain and culture. Negative results are a clue to the diagnosis. Those with skin lesions undergo biopsy.



Pulmonary blastomycosis with focal infiltrates on chest x-ray

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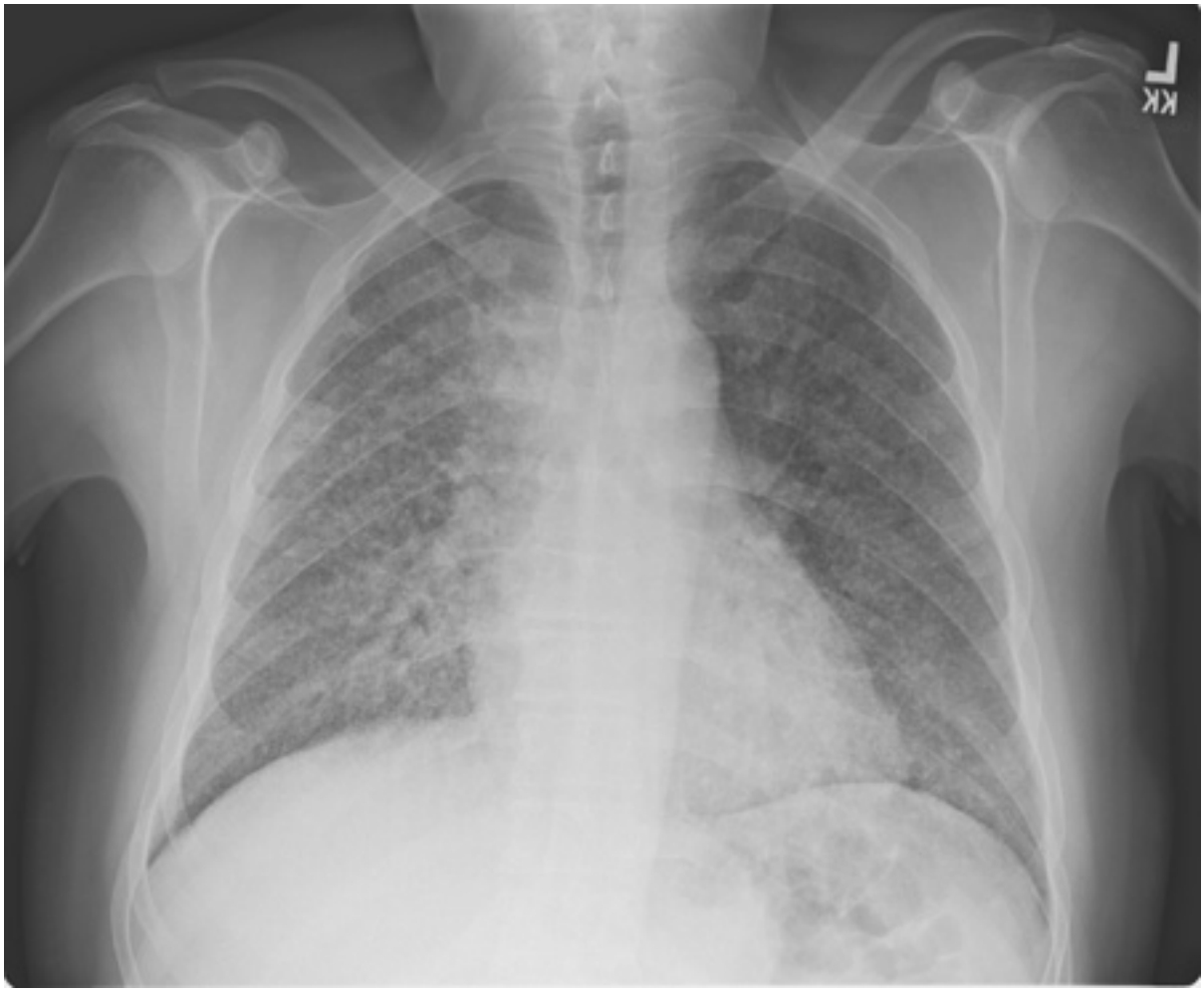

Pulmonary blastomycosis presenting as a miliary pattern on chest x-ray

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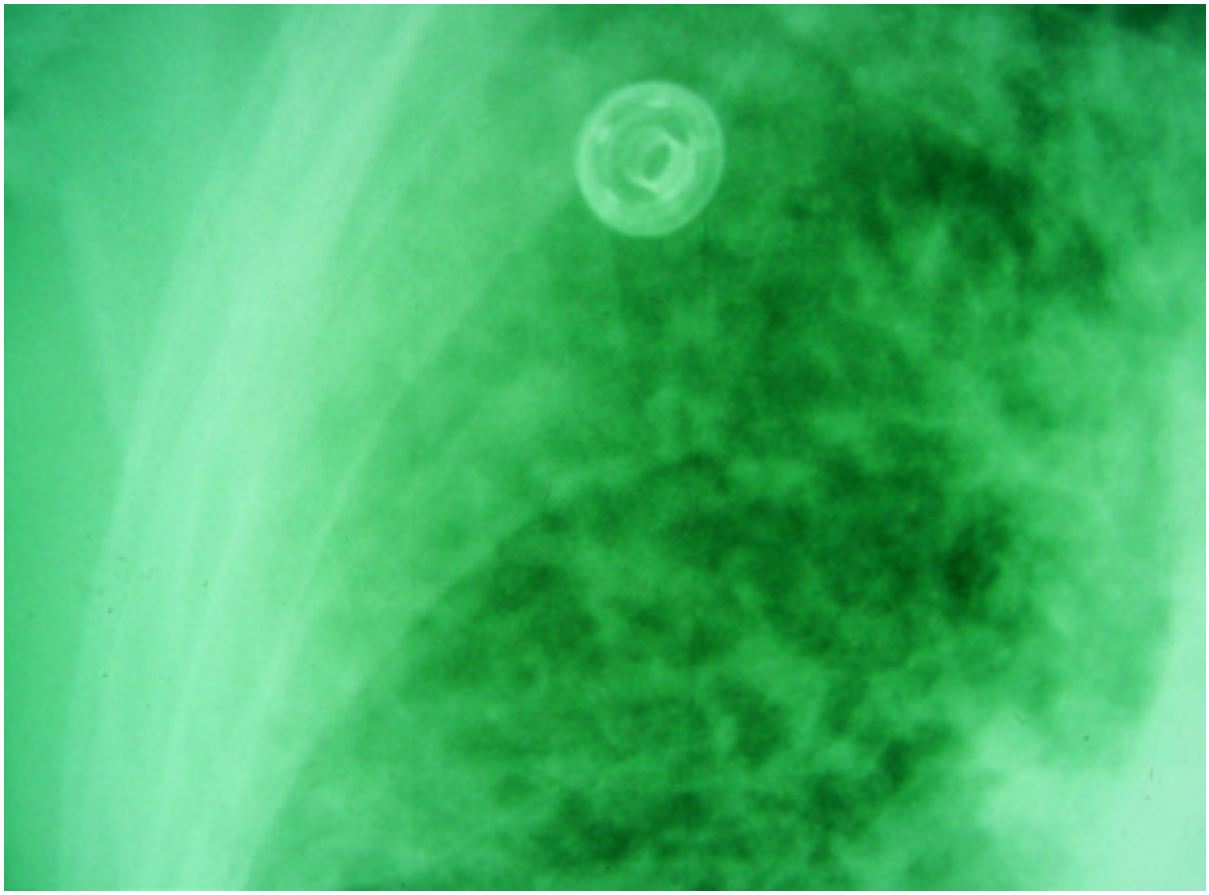
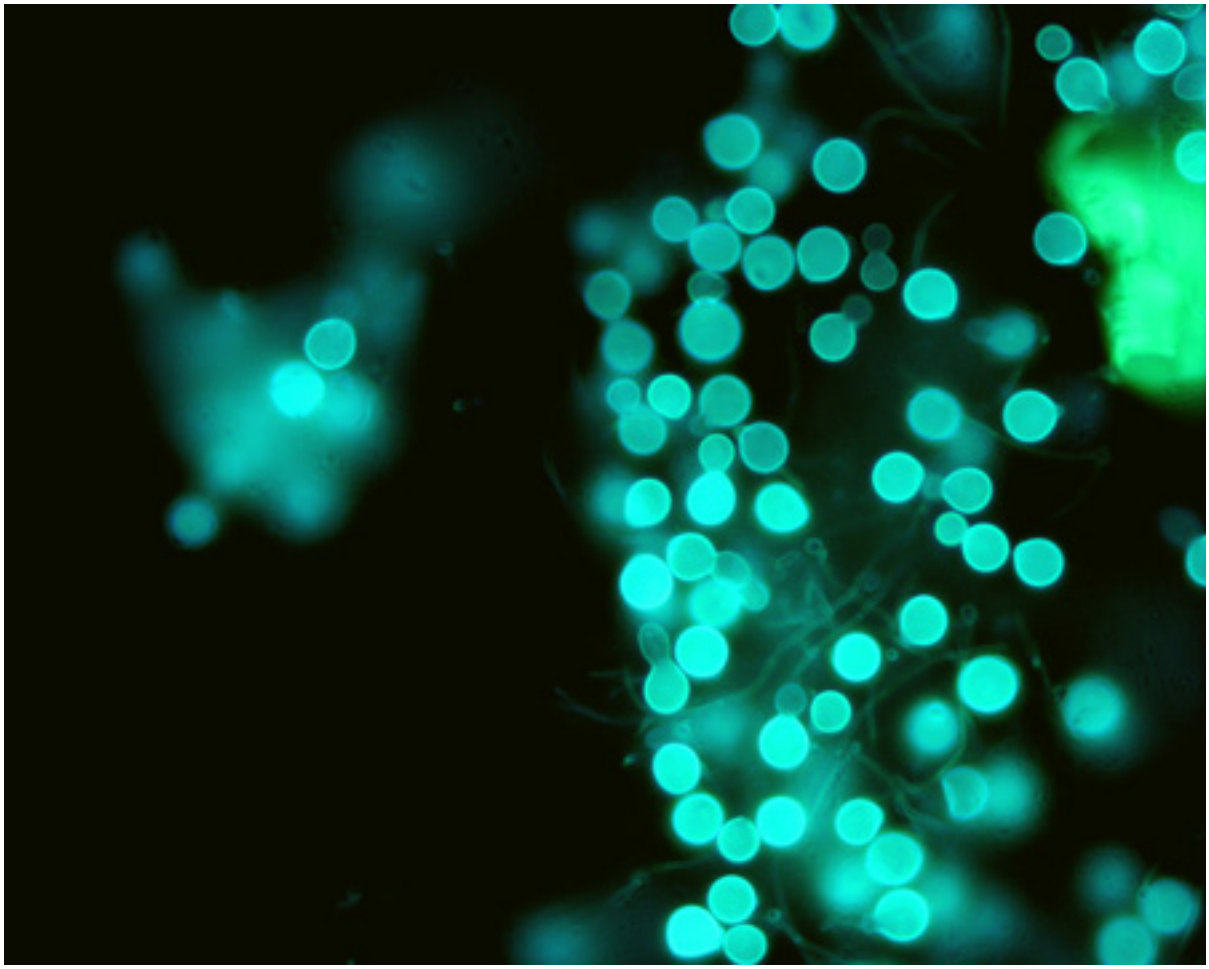


Close-up of reticulonodular findings on chest x-ray in disseminated blastomycosis

Personal files of Larry Baddour, MD

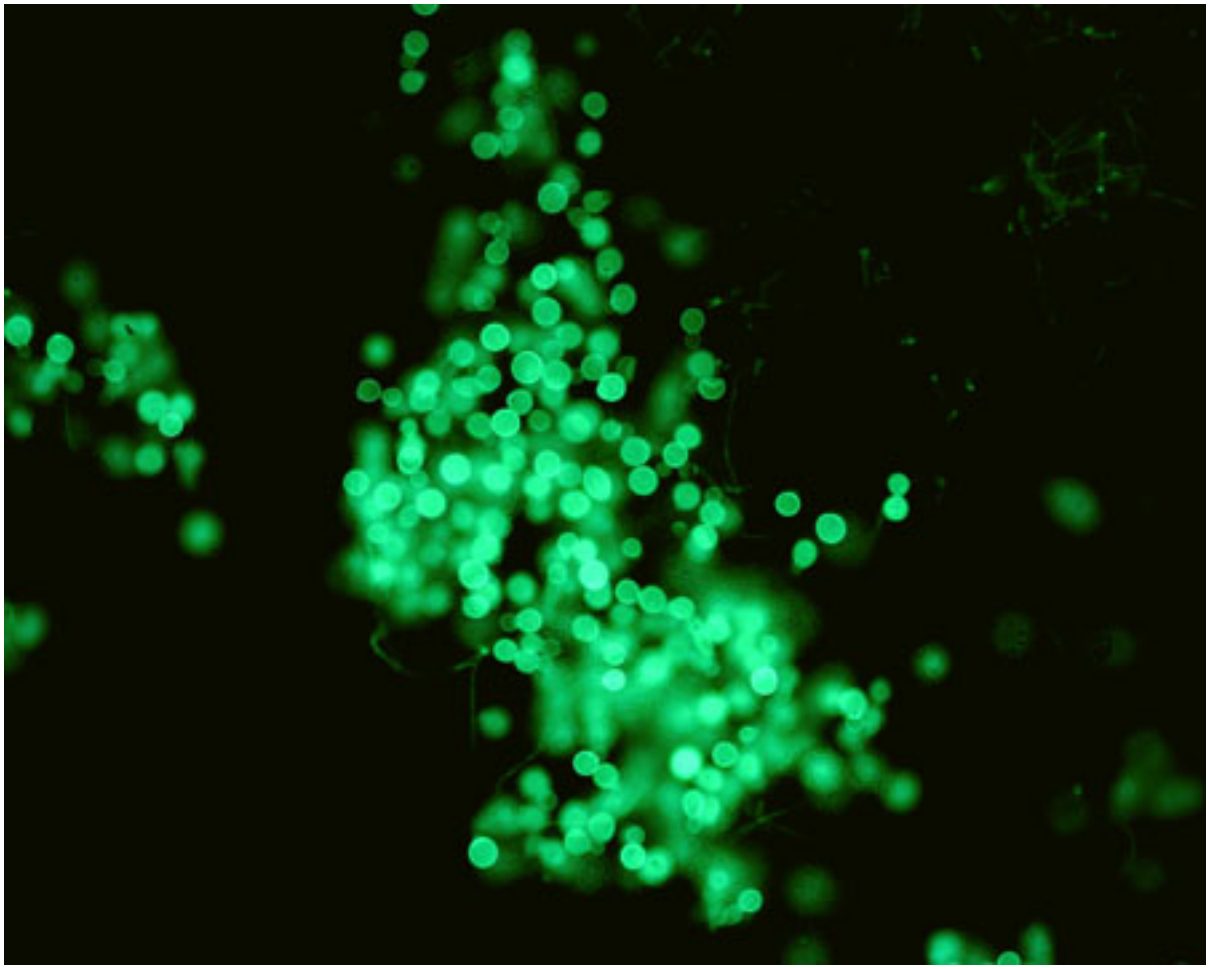
The direct pathological examination of clinical specimens such as sputum, bronchoalveolar washings, endoscopic lymph node needle aspiration, or cutaneous lesions is sufficient to provide quick diagnosis.[2] [33] The hallmark of the pathological diagnosis is the demonstration of the characteristic yeast form, usually 8 to 15 micrometres in diameter, with a thick refractile cell wall and typical single broad-based budding.[2] [34] [35] The yeast form can be seen on haematoxylin-and-eosin, Gomori-methenamine silver, or periodic acid-Schiff staining.[35]



Direct potassium hydroxide preparation at 40x magnification of a sputum specimen

Nancy L. Wengenack, PhD, D(ABMM), Director of Mycology and Mycobacteriology Laboratories, Assistant Professor of Microbiology abd Lab Medicine, Mayo Clinic, Rochester, MN

For definitive diagnosis, these specimens should also be sent for fungal culture to confirm *B dermatitidis* , as this remains the gold standard diagnostic method.[2] [36] Laboratory identification of *B dermatitidis* in culture historically depended on conversion from the mould to yeast form at 37°C (98.6°F). However, most laboratories use a commercially available DNA probe assay to confirm the mould form as *B dermatitidis* .[4][36][37]

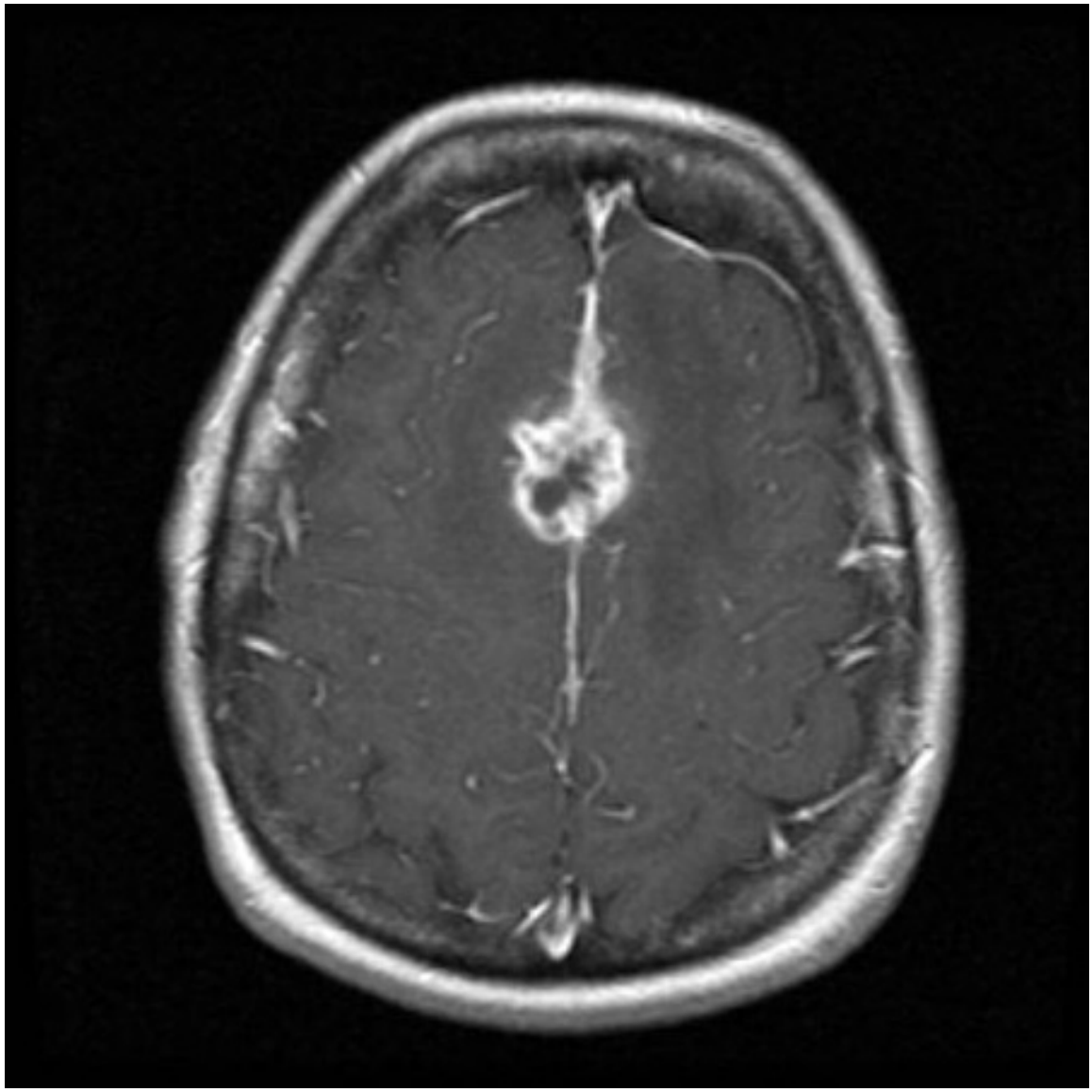


Direct potassium hydroxide preparation at 20x magnification of a sputum specimen

Nancy L. Wengenack, PhD, D(ABMM), Director of Mycology and Mycobacteriology Laboratories, Assistant Professor of Microbiology and Lab Medicine, Mayo Clinic, Rochester, MN

Other tests often follow more routine investigations once the diagnosis is considered:

- Although a fungal serological panel is available and often ordered, it is not of sufficient sensitivity to rule out the disease and useful only if positive.[2]
- Fungal blood cultures are done when disseminated disease is suspected, most usually in a patient who is immunocompromised.
- Pathological examination of lesions associated with blastomycosis generally reveals findings of acute inflammation with or without necrosis, granuloma formation, and multi-nucleated giant cells.[35]
- MRI may reveal evidence of intracranial blastomycosis.
- Polymerase chain reaction detection of fungal organisms in bronchoalveolar lavage or tissue specimens is available in some research laboratories, but is not US Food and Drug Administration (FDA) approved or widely available clinically.[38] [39]



Axial T1 gadolinium-enhanced MRI image of cerebral blastomycosis

Dr William Marshall, MD, Assistant Professor of Medicine, Division of Infectious Diseases, Mayo Clinic, Rochester, MN

History and exam

Key diagnostic factors

recreational or occupational exposures (common)

- Exposure through work or recreation to waterways with beaver ponds, dams, riverbanks, or wooded areas with decaying vegetation are important clues.[15] [16]

primary residence in or travel to endemic areas (common)

- Endemic areas include the Midwestern, South Central and Southeastern US and Mississippi River Valley, Canada, and South Africa.[13] [14] [17] [18] [26] [27] [28] [30] Data also suggest that blastomycosis may be endemic in the Northeastern region of the US.[11] [12]

Other diagnostic factors

male sex (common)

- Males outnumber females from 4:1 to 15:1.[23]

age 30 to 50 years (common)

- Most common age group.[15] [23]

constitutional symptoms (common)

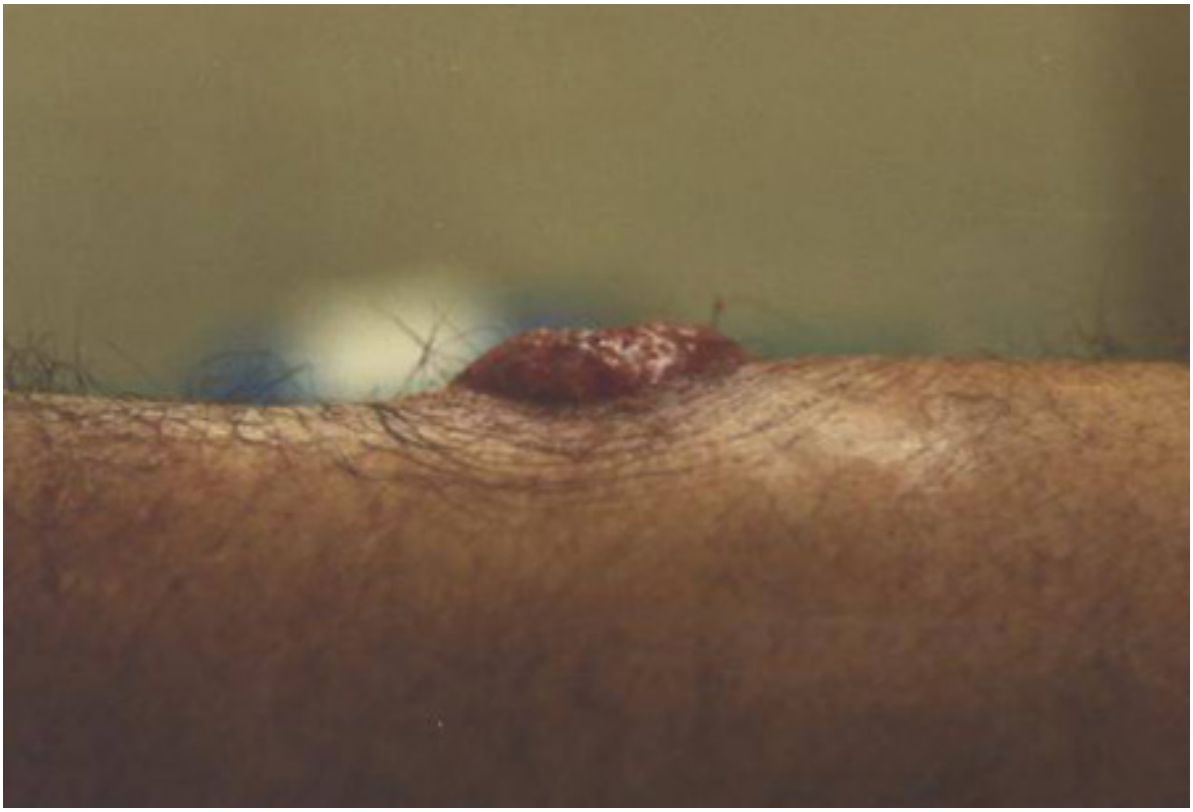
- Fever, weight loss, or fatigue may occur.

cough (common)

- Cough with purulent sputum is a common complaint in pulmonary disease caused by *Blastomycosis* . However, asymptomatic pulmonary involvement is frequently diagnosed by chest x-ray, and disseminated disease spread haematogenously may be the first clinical clue to disease.

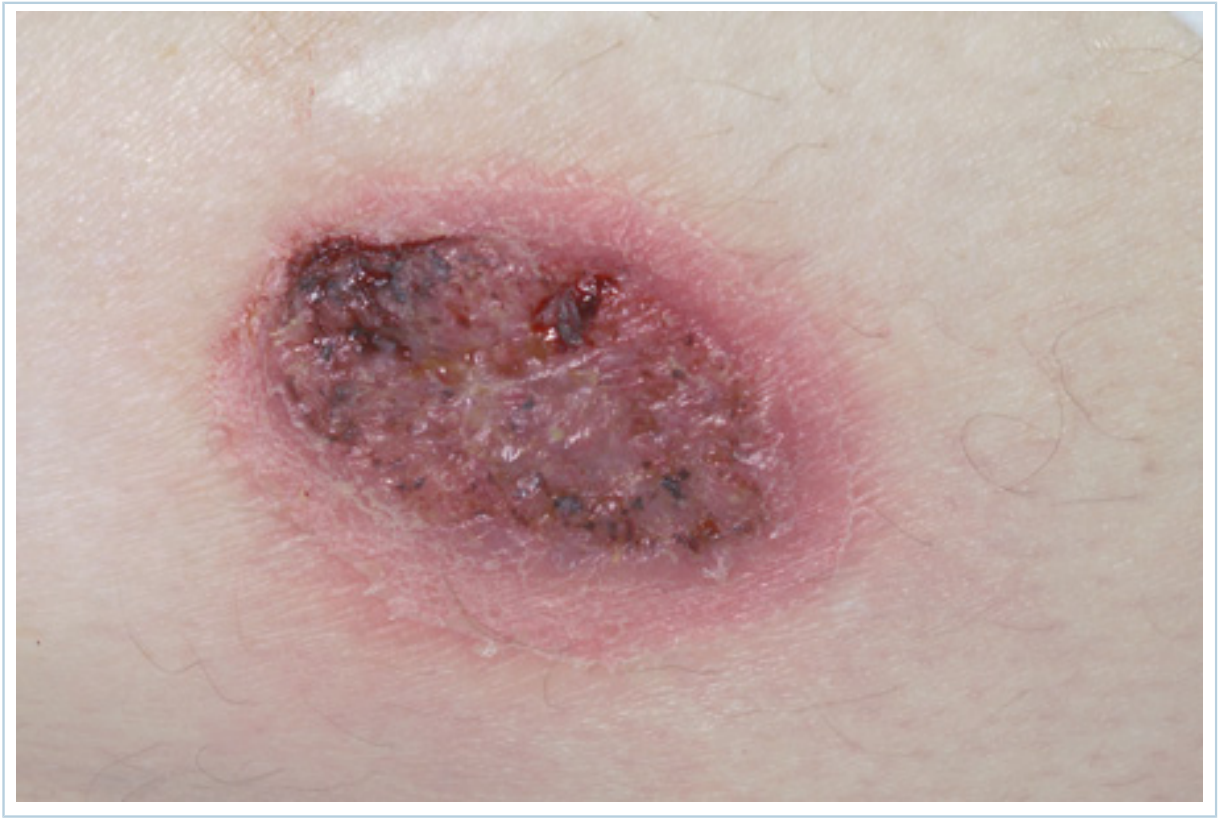
skin lesions (common)

- Skin lesions are usually chronic and can appear nodular, ulcerated, or verrucous. Typically have a raised irregular border. Skin lesions are the second most common manifestation of blastomycosis.



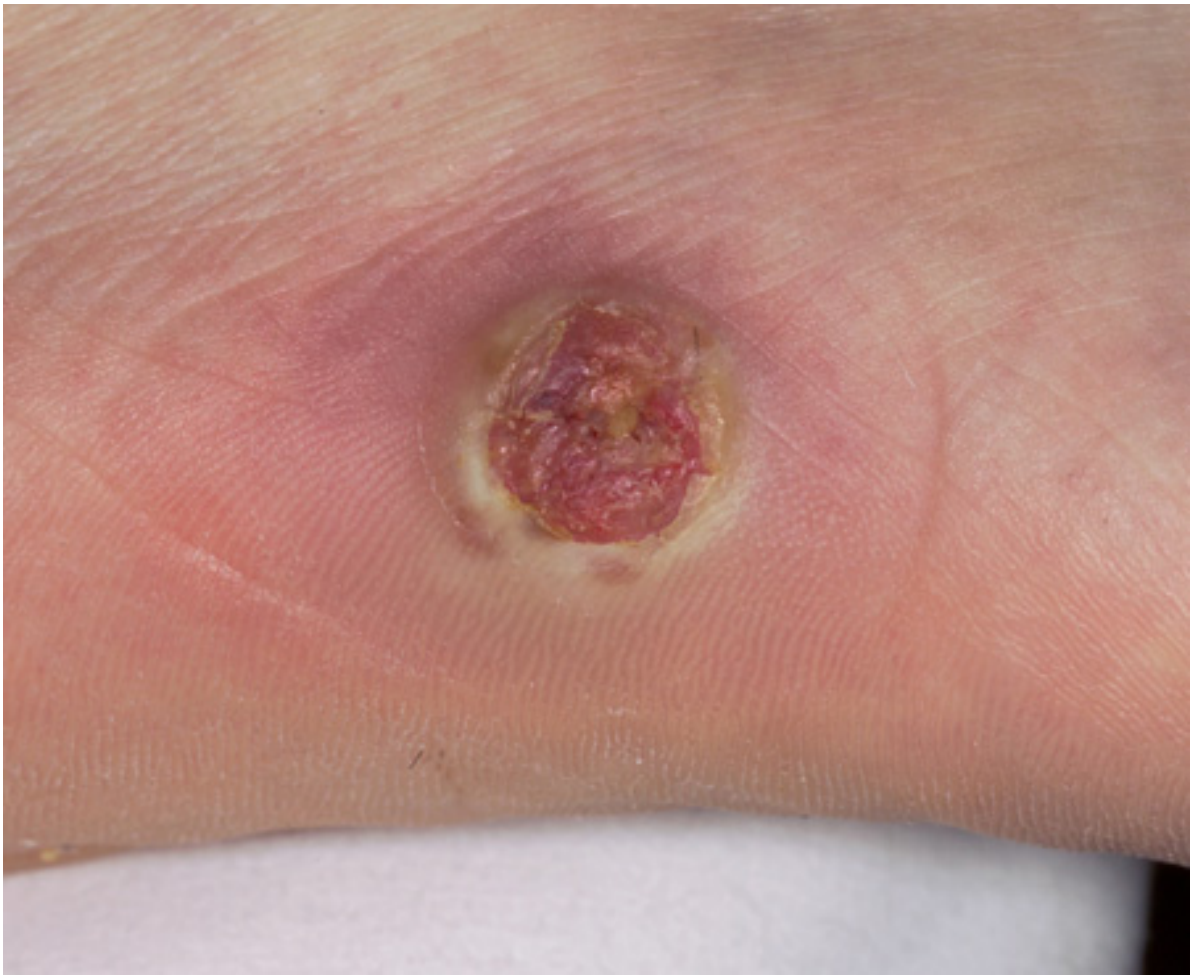
Cutaneous blastomycosis on the forearm

Personal files of Larry Baddour, MD



Cutaneous blastomycosis on the lower extremity

LuAnn Ziemer, Office of Medical Photography, Mayo Clinic, Rochester, MN



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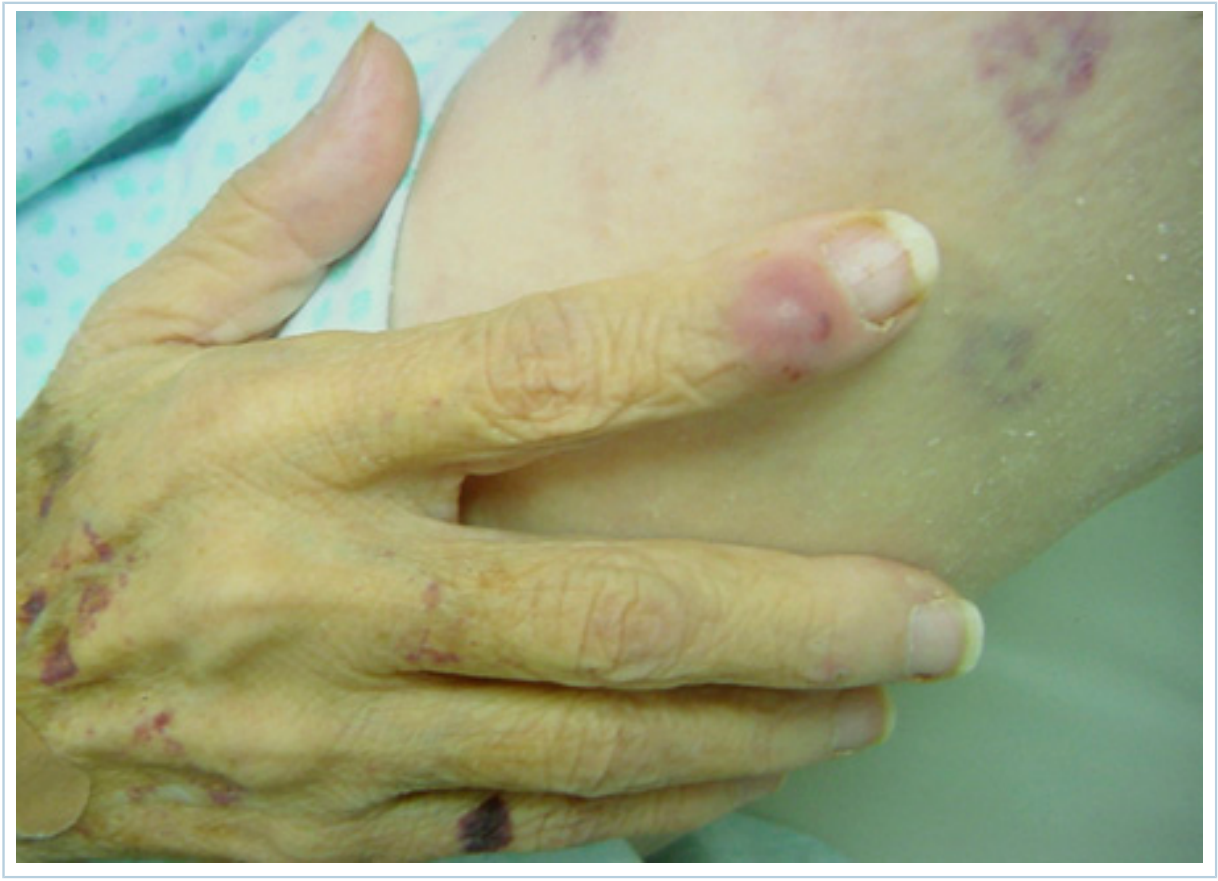


Cutaneous manifestation of disseminated blastomycosis

Personal files of Larry Baddour, MD

animal exposure (uncommon)

- A previous or co-incident infection in a pet dog is a clue to environmental exposure of the fungus rather than a mode of transmission.

bone or joint pain (uncommon)

- Bone or joint pain may be a clue to osteoarticular involvement with blastomycosis.
- Presentation most frequently mimics a monoarticular, septic arthritis.

genitourinary#symptoms (uncommon)

- In men, blastomycosis can present with prostatitis, epididymo-orchitis, or infection of other genitourinary (GU) sites. Women can develop tubo-ovarian abscesses, endometritis and salpingitis.[5]
- Always a manifestation of disseminated disease, but not all people with disseminated disease have GU involvement.

headache or focal neurological complaints (uncommon)

- Central nervous system involvement occurs in 5% to 10% of cases of blastomycosis and can manifest as meningitis or as a space-occupying lesion.[23]

Risk factors

Strong

recreational or occupational exposures

- Important exposures include to waterways with beaver dams or ponds, wooded areas, or river banks with rotting vegetation.[15] [16]
- One study using a lymphocyte stimulation assay found that 30% of forestry workers in Northern Minnesota and Wisconsin had been exposed to *Blastomyces dermatitidis* in the past.[25] Direct inoculation of the skin has occurred with various types of outdoor and occupational activities.[24]

travel to or residence in an area of endemicity

- Although occasional sporadic cases have a worldwide distribution, areas of high endemic rates include the Midwestern, South Central and Southeastern US along the Mississippi river valley, Canada, and South Africa.[13] [14] [17] [18] [26] [27] [28] Data also suggest that blastomycosis may be endemic in the Northeastern region of the US.[11] [12]

Weak

male sex

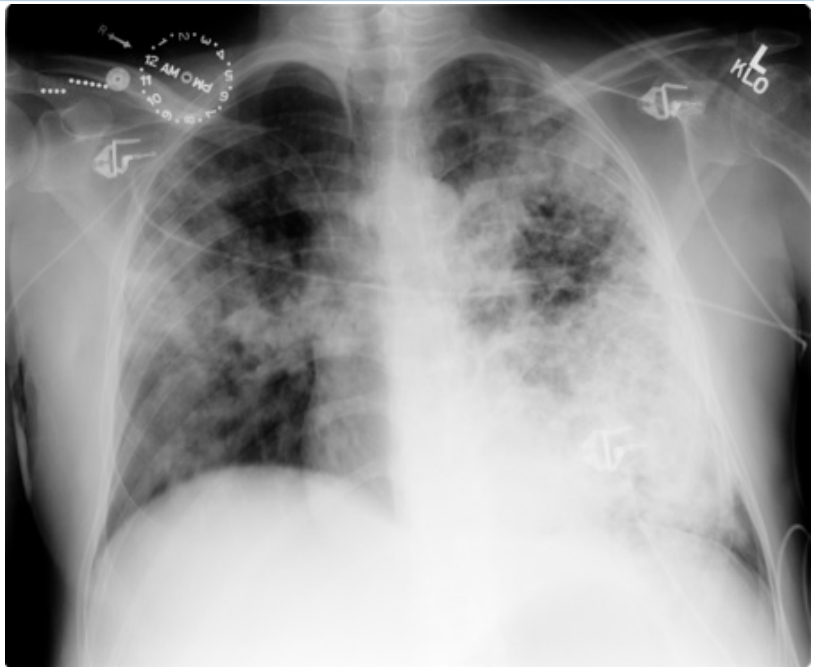
- Cases in men typically outnumber those in women, with a ratio between 4:1 and 15:1 depending on the series. However, this is generally thought to be secondary to increased environmental exposure in men as opposed to an actual sex predilection.[15]

immunocompromise

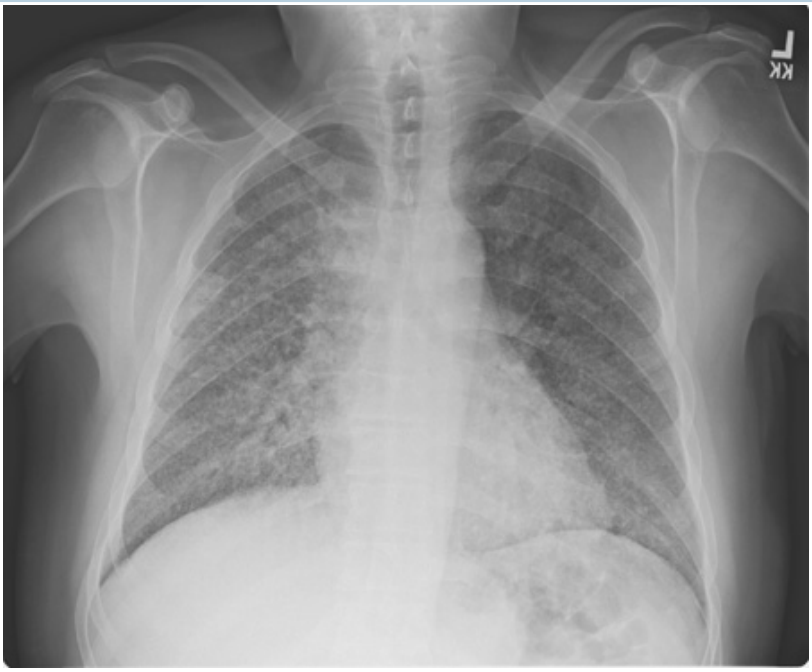
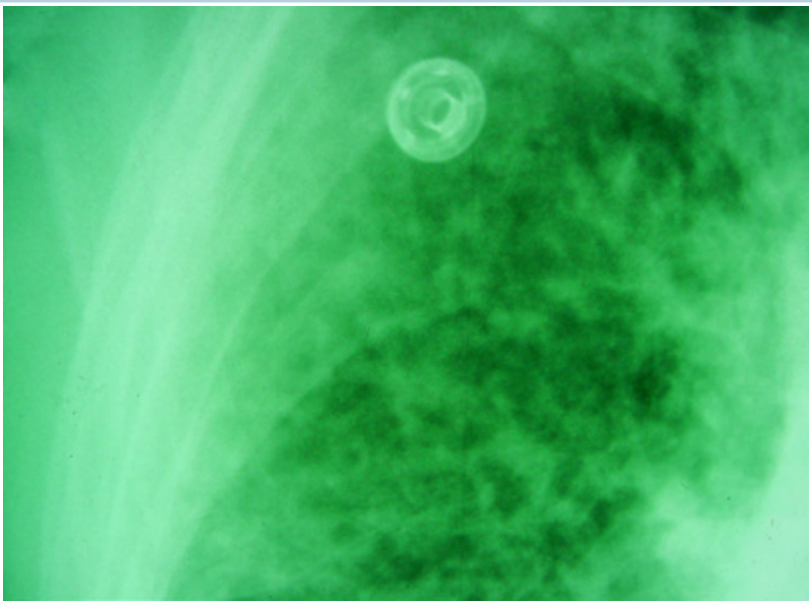
- Blastomycosis does not appear to be more common in people who are immunocompromised. However, infection in a compromised host is more frequently complicated with adult respiratory distress syndrome or extrapulmonary dissemination.[29]
- Very few patients with HIV/AIDS develop disseminated disease. This is because neutrophils are important for the host defence of blastomycosis, and patients with HIV/AIDS generally have T-cell defects but intact neutrophil function.

Investigations

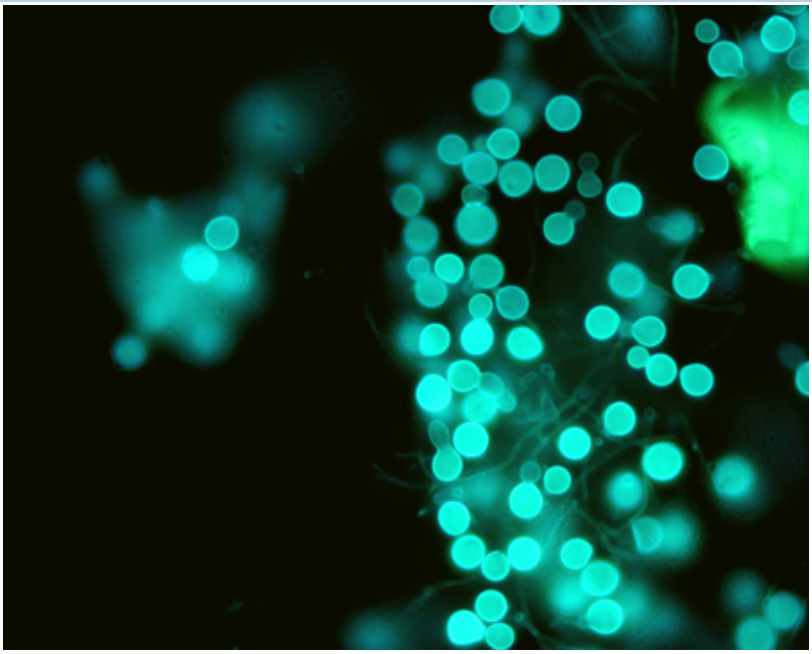
1st test to order

Test	Result
Blastomyces dermatitidis enzyme immunoassay (EIA) urine antigen testing • EIA urine antigen testing is indicated in the first instance, with reported sensitivity varying from 76% to 90%.[32] • Although urine samples are preferred, the assay is also clinically available for use on serum, cerebrospinal fluid (CSF) or bronchoalveolar lavage samples.[2] [32] Sensitivity ranges from 80% to 93% depending on the sample and clinical manifestation of disease, although sensitivity may be as low as 55% in routine clinical settings.[2] [40] False positive rates of 2% in the healthy population and less than 5% in other invasive fungal infections lead to a higher specificity than serology.[3] • False-positive results due to cross-reactivity can occur in patients with Histoplasma infection, however cross-reactivity is unlikely to change therapy.[30] [31] [32]	**positive for *B dermatitidis* galactomannan antigen**
chest x-ray • Posteroanterior and lateral chest x-ray should be obtained in all patients suspected of having blastomycosis to document pulmonary involvement and to guide invasive diagnostic strategies.[2] However, there are no imaging findings that are specific enough to blastomycosis to establish the diagnosis.  *Pulmonary blastomycosis with focal infiltrates on chest x-ray* *Dr Robert Orenstein, DO, Associate Professor of Medicine, Division of Infectious Diseases, Mayo Clinic, Scottsdale, AZ*	**lobar pneumonia, mass-like or cavitary lesions, diffuse interstitial infiltrates, or signs of adult respiratory distress syndrome**

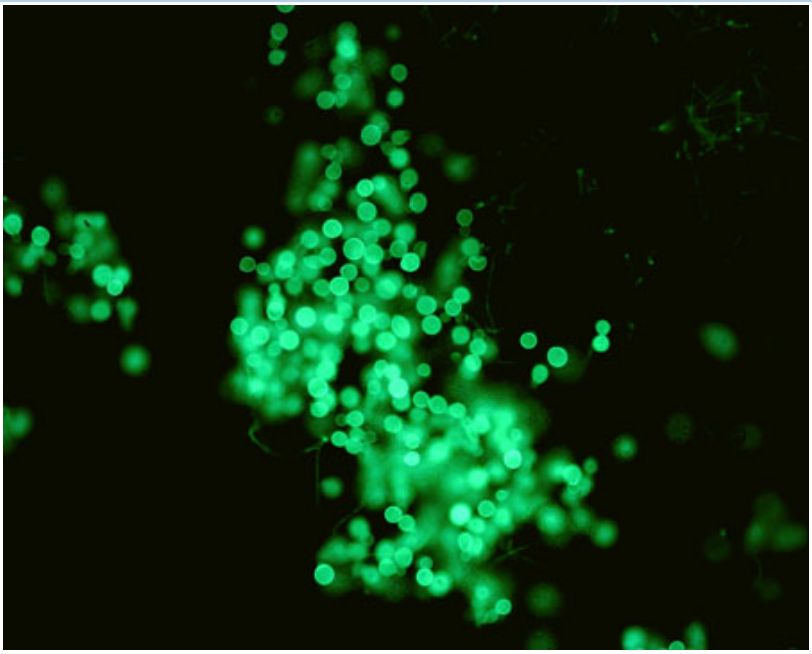
DIAGNOSIS

Test	Result
 *Pulmonary blastomycosis presenting as a miliary pattern on chest x-ray* *Dr Robert Orenstein, DO, Associate Professor of Medicine, Division of Infectious Diseases, Mayo Clinic, Scottsdale, AZ*  *Close-up of reticulonodular findings on chest x-ray in disseminated blastomycosis* *Personal files of Larry Baddour, MD*	
respiratory tract specimen smear and culture • Confirmatory of the diagnosis and can be performed with potassium hydroxide preparations or special fungal stains.[2] [35]	**large, oval, broad-based budding yeast; or positive DNA probe assay result**

Test	Result



Direct potassium hydroxide preparation at 40x magnification of a sputum specimen
Nancy L. Wengenack, PhD, D(ABMM), Director of Mycology and Mycobacteriology Laboratories, Assistant Professor of Microbiology abd Lab Medicine, Mayo Clinic, Rochester, MN



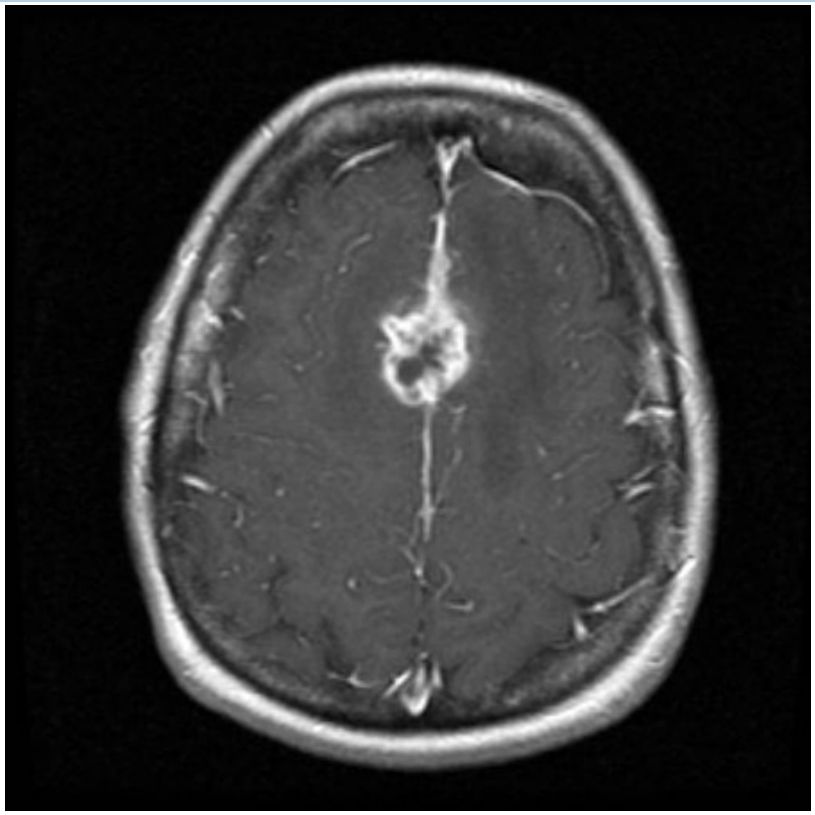
Direct potassium hydroxide preparation at 20x magnification of a sputum specimen
Nancy L. Wengenack, PhD, D(ABMM), Director of Mycology and Mycobacteriology Laboratories, Assistant Professor of Microbiology and Lab Medicine, Mayo Clinic, Rochester, MN

- From expectorated specimen or bronchoalveolar lavage.
- Demonstration of typical yeast in fluid or tissue specimens is usually sufficient to start treatment for blastomycosis. However, definitive

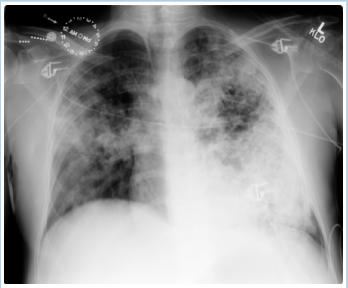
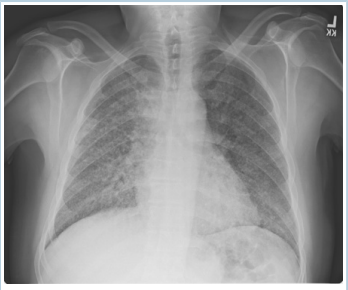
Test	Result
diagnosis usually requires culture confirmation, which can take 2 to 4 weeks. • Culture on Sabouraud dextrose agar or potato dextrose agar with and without cycloheximide should be incubated at 25 to 30°C for up to 6 weeks.[2] The off-white mould form should be tested for *Blastomyces dermatitidis* with a commercially available DNA probe assay.	

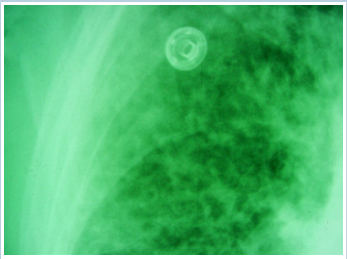
Other tests to consider

Test	Result
bronchoscopy • Performed when sputum samples are unobtainable or non-revealing in patients with pulmonary involvement.	**washings with large, oval, broad-based budding yeast; or tissue specimen with granuloma**
tissue biopsy or cytology (lung, skin, or bone) • Transbronchial biopsy of lung lesions, or biopsy of suspicious skin or bone lesions.	**acute inflammation with or without necrosis, granuloma formation, and multi-nucleated giant cells**
arthrocentesis • A negative Gram stain and culture may be a clue to the disease.	**large, oval, broad-based budding yeast in joint fluid**
fungal serology panel • Including complement fixation, immunodiffusion, and enzyme immunoassay, this measures antibodies to *Blastomyces dermatitidis* . • Frequently ordered, but notoriously low sensitivity (9% to 64%) and specificity (50% to 67%) and generally not useful in making the diagnosis.[2] [3] • Useful only if positive. • Repeat testing is not recommended regardless of the initial test result.	**may be positive**
fungal blood cultures • Positive fungal blood cultures can be seen in disseminated disease and offer a non-invasive diagnostic strategy. A negative fungal blood culture does not rule out disseminated disease. • Can take up to 2 weeks for results.	**positive**
MRI brain • Central nervous system involvement occurs in 5% to 10% of cases of blastomycosis and can manifest as meningitis or as a space-occupying lesion.[23] • MRI may reveal evidence of intracranial blastomycosis.	**positive**

Test	Result
 *Axial T1 gadolinium-enhanced MRI image of cerebral blastomycosis* *Dr William Marshall, MD, Assistant Professor of Medicine, Division of Infectious Diseases, Mayo Clinic, Rochester, MN*	
B dermatitidis# polymerase chain reaction • Polymerase chain reaction detection of fungal organisms in bronchoalveolar lavage or tissue specimens is available in some research laboratories, but is not US Food and Drug Administration (FDA) approved or widely available clinically.[38] [39]	**presence of *Blastomyces dermatitidis***

Differentials

Condition	Differentiating signs / symptoms	Differentiating tests
Community-acquired pneumonia	• Acute pulmonary blastomycosis is commonly mistaken for community-acquired pneumonia. Failure to respond to antibacterial therapy and extrapulmonary manifestations are clues to the aetiology.[30]	• Findings of blastomycosis on chest x-ray can be atypical for community-acquired pneumonia, and include mass-like or cavitary lesions or diffuse interstitial infiltrates.  *Pulmonary blastomycosis with focal infiltrates on chest x-ray* *Dr Robert Orenstein, DO, Associate Professor of Medicine, Division of Infectious Diseases, Mayo Clinic, Scottsdale, AZ*  *Pulmonary blastomycosis presenting as a miliary pattern on chest x-ray* *Dr Robert Orenstein, DO, Associate Professor of Medicine, Division of Infectious Diseases, Mayo Clinic, Scottsdale, AZ*

Condition	Differentiating signs / symptoms	Differentiating tests
		 *Close-up of reticulonodular findings on chest x-ray in disseminated blastomycosis* *Personal files of Larry Baddour, MD* • A positive *Blastomyces dermatitidis* enzyme immunoassay (EIA) urine antigen test indicates probable acute pulmonary blastomycosis, though this may not be available in some centres.[30] [31]
Histoplasmosis	• Histoplasmosis and blastomycosis share many of the same clinical manifestations, and the endemic areas overlap to a great extent. • However, sputum in blastomycosis is generally purulent, in contrast to histoplasmosis.	• Differentiation between these 2 diseases often relies on culture data. *Histoplasma* yeast are typically smaller, have narrow-based budding, and are found intracellularly within macrophages in clinical specimens. There is some cross-reactivity with serological and antigen assays for these 2 organisms.
Coccidioidomycosis	• Coccidioidomycosis and blastomycosis share many of the same clinical manifestations. However, the endemic area of *Coccidioides* is the desert region of the south-western US.	• Serological testing for coccidioidomycosis is of higher sensitivity than for blastomycosis, and the yeast in pathological specimens appears as the characteristic spherule.
Paracoccidioidomycosis	• Acute/sub-acute paracoccidioidomycosis more often presents with lymphadenopathy, hepatosplenomegaly, and bone marrow dysfunction, while chronic paracoccidioidomycosis	• *Paracoccidioides* yeast are typically smaller than *Blastomyces dermatitidis* with thinner cell walls, and can be found in the mariner wheel formation, with multiple small budding yeast circumferentially surrounding the parent cell.[35]

Condition	Differentiating signs / symptoms	Differentiating tests
	generally presents with dry cough and dyspnoea. • Paracoccidioidomycosis is also endemic to Central and South America.	
Sporotrichosis	• The cutaneous lesions of sporotrichosis are similar in appearance to blastomycosis. However, lymphadenitis (generally nodular and subacute to chronic) is pathognomonic in sporotrichosis.	• Microbiological and pathological examination of skin biopsies will yield the diagnosis.
Tuberculosis	• Cutaneous disease is less common in tuberculosis than in blastomycosis.	• Acid fast smear and mycobacterial culture of clinical specimens generally lead to the diagnosis of tuberculosis. Tuberculin skin testing and the in vitro interferon gamma release assays of sensitised lymphocytes are also helpful in diagnosis of tuberculosis.
Nocardiosis	• Nocardiosis and blastomycosis share many of the same clinical features. *Nocardia* is more common in people who are immunocompromised and has a worldwide distribution.	• Microbiological examination of clinical specimens in nocardiosis reveals thin, branching gram-positive bacilli that stain positively by the modified acid fast stain. Culture of *Nocardia* species is confirmatory of that diagnosis.
Malignancy	• The pulmonary, cutaneous, osteoarticular, and central nervous system manifestations of blastomycosis can all be mistaken for primary or metastatic neoplasms.	• Pathological examination of tissue specimens can confirm or rule out malignancy.

Criteria

Stratification by disease severity

There are no commonly accepted schematic classifications for blastomycosis, including formal criteria for severity of illness. The general approach to treatment is based upon the severity of disease and clinical manifestations. The most severe manifestation of the disease determines the treatment choice. Infectious diseases consultation should be considered in the management of moderate-to-severe disease or in complicated cases.

- Mild-to-moderate disease generally refers to pulmonary, cutaneous, or genitourinary disease amenable to ambulatory care management with itraconazole.
- Moderate-to-severe disease generally refers to disease that requires hospitalisation: more severe pulmonary disease, central nervous system or bone disease, or disease in pregnant or immunosuppressed patients. However, clinical judgement is involved in making treatment decisions.

Approach

The main goals of treatment of blastomycosis are resolution of the symptoms and signs of the disease and microbiological eradication of the fungus. Eradication is sometimes not achievable, particularly in patients who are immunosuppressed, and can be difficult to prove. The treatment options are limited to a select few antifungal medicines with activity against *Blastomyces dermatitidis* . These include amphotericin-B preparations and azole antifungals.[2] Of the available azoles that have been studied in small randomised trials, the most effective is itraconazole, followed by fluconazole and lastly ketoconazole.[2] [41] [42] [43] Ketoconazole is not used routinely due to its associated toxicities; however, it may be all that is available in resource-limited settings. Echinocandins (e.g., caspofungin) do not have activity against this organism. Surgical therapy is rarely performed except occasionally in a solitary pulmonary nodule or skin lesion resected to rule out malignancy.

Treatment duration is generally at least 6 months in immunocompetent patients and can be longer in severe disease or in immunocompromised patients.[2] Clinical judgement is involved in treatment decisions, and infectious diseases consultation should be considered in the management of hospitalised or complicated cases. The most severe manifestation of the disease determines the treatment choice, and pregnancy supersedes other considerations.

Although the diagnosis of blastomycosis is sometimes made during an inpatient work-up of an acutely ill patient, the decision on whether to hospitalise a patient with an outpatient diagnosis of blastomycosis must be individualised. There are no formal guidelines that outline criteria for hospitalisation of patients. The treating clinician should take into account several factors, including the severity of the illness, the need for initiation of intravenous therapy, risk of potential complications, and availability of close outpatient follow-up.

Immunocompetent non-pregnant ambulatory adults

- Outpatients with cutaneous, milder genitourinary (GU), or milder pulmonary disease are treated with full-dose itraconazole for 6 to 12 months.[2]

Choice of amphotericin-B preparation in hospitalised patients

A lipid formulation (liposomal or lipid complex) or the deoxycholate formulation can be used, depending on the particular patient group:

- Most patients are treated with a lipid formulation.[2] In particular, it has good nervous system penetration for patients with central nervous system (CNS) disease, and it is amenable to dose escalation.
- Children and infants are treated with the deoxycholate formulation, unless they have CNS disease. It is better tolerated in children than in adults, and is the least expensive formulation.

Hospitalised immunocompetent non-pregnant adults

CNS disease:

- Treated with 4 to 6 weeks of intravenous amphotericin-B followed by 12 months of azole antifungal therapy, regardless of the immune status of the host or whether other sites are involved with infection.[2]

- Azole therapy includes itraconazole, voriconazole, or high-dose fluconazole.[2] There are no head-to-head studies and no preferences. Itraconazole may have best overall effectiveness, but voriconazole has good blood-brain penetrability.

Pulmonary, osteoarticular, or GU disease:

- Treated initially with 1 to 2 weeks of amphotericin-B until there is evidence of clinical improvement in symptoms or signs of the disease.[2]
- This is then followed by itraconazole therapy. Pulmonary or GU disease requires 6 to 12 months of itraconazole; osteoarticular no less than 12 months.[2]
- Corticosteroids are sometimes used for blastomycosis-associated acute respiratory distress syndrome in some centres. However, there is no evidence or expert consensus supporting this.[2]

Immunosuppressed non-pregnant adults

- Immunosuppressed patients should be treated initially with 1 to 2 weeks of amphotericin-B.[2]
- However, full-dose itraconazole therapy should be continued for 1 year, and consideration should be given to subsequent lifelong secondary prophylaxis with low-dose itraconazole therapy if the underlying immunosuppression cannot be reversed.

Pregnant patients

- Pregnant patients should be treated with amphotericin-B. Azole antifungals are contraindicated in pregnancy due to teratogenicity.
- Duration of treatment depends on the severity of the disease. Pregnancy always supersedes other treatment considerations.
- Itraconazole is given post-delivery if not breastfeeding. There is not a recommended therapy for breastfeeding women, as there are insufficient data in this population. Risks of treatment should be reviewed with an infectious disease consultant in these circumstances.

Newborns and children

- Ambulatory children can be treated with itraconazole with weight-based dosing for 6 to 12 months.
- Children with more severe disease should receive amphotericin-B initially, followed by itraconazole for at least 12 months. All children with CNS involvement require amphotericin-B.
- Neonates (<30 days old) should also be treated with amphotericin-B.

Antifungal therapy adverse effects

Amphotericin-B is associated with nephrotoxicity, hypokalaemia, and hypomagnesaemia. These are generally reversible and occur early in the course of therapy. Use of liposomal preparations when indicated decreases the risk of nephrotoxicity. If nephrotoxicity develops, and the patient is clinically improving, an early switch to oral antifungal therapy should be considered. If the patient's clinical condition warrants continued amphotericin-B therapy, aggressive pre-infusional hydration with normal saline and electrolyte replacement can be helpful.

Treatment with any azole antifungal is associated with a low risk of hepatotoxicity, usually manifested as asymptomatic elevated aminotransferase levels. Discontinuation of the medicine should only be considered if aminotransferase levels are greater than 2.5 times the upper limit of normal. Serum itraconazole and voriconazole levels can be measured and dose adjusted accordingly. Otherwise, re-

challenge with the same medicine after liver enzymes return to normal is recommended to complete a treatment course.

Itraconazole has been associated with CNS depression, cardiovascular effects (e.g., new or worsening hypertension, new or worsening heart failure, prolonged QT interval [obtain a baseline ECG before starting treatment], torsades de pointes), transient or permanent hearing loss, pseudoaldosteronism, hypokalaemia, and peripheral neuropathy. Discontinuation of the drug may be required in some circumstances.

Fluconazole has also been associated with cardiovascular effects such as prolonged QT interval and torsades de pointes. Serious dermatological reactions have also been reported.

Azole antifungals undergo many significant drug-drug interactions.

Treatment algorithm overview

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: see disclaimer

Ongoing (summary)		
ambulatory immunocompetent non-pregnant adults		
	1st	itraconazole maintenance
hospitalised immunocompetent non-pregnant adults		
■ with CNS disease	1st	amphotericin-B
	plus	azole antifungal maintenance therapy
■ with pulmonary, osteoarticular, or genitourinary disease	1st	amphotericin-B
	plus	itraconazole maintenance therapy
immunosuppressed non-pregnant adults with or without CNS disease		
	1st	amphotericin-B
	plus	prolonged itraconazole maintenance therapy
pregnant		
	1st	amphotericin-B
	plus	post-delivery itraconazole maintenance therapy
neonates <30 days old		
■ without CNS disease	1st	amphotericin-B deoxycholate
■ with CNS disease	1st	amphotericin-B lipid formulation
infants/children ≥30 days old		
■ immunocompetent ambulatory	1st	itraconazole
■ immunosuppressed or hospitalised: without CNS involvement	1st	amphotericin-B deoxycholate
	plus	itraconazole maintenance therapy

Ongoing			(summary)
	immunosuppressed or hospitalised: with CNS involvement	1st	amphotericin-B lipid formulation
		plus	itraconazole maintenance therapy

Treatment algorithm

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: see disclaimer

Ongoing

ambulatory immunocompetent non-pregnant adults

1st **itraconazole maintenance**

Primary options

» itraconazole: 200 mg orally three times daily for 3 days, followed by 200 mg orally twice daily

» Outpatients with cutaneous, milder genitourinary, or milder pulmonary disease are treated with full-dose itraconazole for 6 to 12 months.[2]

» Itraconazole has been associated with hepatotoxicity, CNS depression, cardiovascular effects, transient or permanent hearing loss, pseudoaldosteronism, hypokalaemia, and peripheral neuropathy. Azole antifungals undergo many significant drug-drug interactions.

hospitalised immunocompetent non-pregnant adults

with CNS disease

1st **amphotericin-B**

Primary options

» amphotericin B lipid complex: 5 mg/kg/day intravenously

OR

» amphotericin B liposomal: 3-5 mg/kg/day intravenously

» CNS disease is treated regardless of the immune status of the host or whether other sites are involved with infection.[2]

» Amphotericin-B should be continued for 4 to 6 weeks before switching to an oral agent for maintenance.

» Amphotericin-B is associated with nephrotoxicity, hypokalaemia, and hypomagnesaemia.

plus **azole antifungal maintenance therapy**

Ongoing

Treatment recommended for ALL patients in selected patient group

Primary options

» itraconazole: 200 mg orally two to three times daily

Secondary options

» fluconazole: 800 mg orally once daily

» Maintenance treatment, after 4 to 6 weeks of amphotericin-B.

» Duration of treatment is at least 12 months.

» Itraconazole has been associated with hepatotoxicity, CNS depression, cardiovascular effects, transient or permanent hearing loss, pseudoaldosteronism, hypokalaemia, and peripheral neuropathy.

» Fluconazole has also been associated with cardiovascular effects, as well as serious dermatological reactions. Azole antifungals undergo many significant drug-drug interactions.

with pulmonary, osteoarticular, or genitourinary disease

1st **amphotericin-B**

Primary options

» amphotericin B lipid complex: 5 mg/kg/day intravenously

OR

» amphotericin B liposomal: 3-5 mg/kg/day intravenously

Secondary options

» amphotericin B deoxycholate: 0.7 to 1 mg/kg/day intravenously

» Amphotericin-B is given for 1 to 2 weeks, followed by oral itraconazole maintenance.[2]

» Amphotericin-B is associated with nephrotoxicity, hypokalaemia, and hypomagnesaemia. Use of liposomal preparations when indicated decreases the risk of nephrotoxicity.

plus **itraconazole maintenance therapy**

Treatment recommended for ALL patients in selected patient group

Primary options

MANAGEMENT

Ongoing

» itraconazole: 200 mg orally three times daily for 3 days, followed by 200 mg orally twice daily

» Duration for pulmonary or genitourinary disease is 6 to 12 months.[2]

» For osteoarticular disease it is no less than 12 months.[2]

» Itraconazole has been associated with hepatotoxicity, CNS depression, cardiovascular effects, transient or permanent hearing loss, pseudoaldosteronism, hypokalaemia, and peripheral neuropathy. Azole antifungals undergo many significant drug-drug interactions.

immunosuppressed non-pregnant adults with or without CNS disease

1st **amphotericin-B**

Primary options

» amphotericin B lipid complex: 5 mg/kg/day intravenously

OR

» amphotericin B liposomal: 3-5 mg/kg/day intravenously

Secondary options

» amphotericin B deoxycholate: 0.7 to 1 mg/kg/day intravenously

» Amphotericin-B is given for 1 to 2 weeks and then oral itraconazole maintenance is given.[2]

» Amphotericin-B is associated with nephrotoxicity, hypokalaemia, and hypomagnesaemia. Use of liposomal preparations when indicated decreases the risk of nephrotoxicity.

plus **prolonged itraconazole maintenance therapy**

Treatment recommended for ALL patients in selected patient group

Primary options

» itraconazole: 200 mg orally three times daily for 3 days, followed by 200 mg orally twice daily

Ongoing

» Duration is 6 to 12 months, but some immunocompromised patients may require lifelong suppressive therapy.[2]

» Itraconazole has been associated with hepatotoxicity, CNS depression, cardiovascular effects, transient or permanent hearing loss, pseudoaldosteronism, hypokalaemia, and peripheral neuropathy. Azole antifungals undergo many significant drug-drug interactions.

pregnant

1st **amphotericin-B**

Primary options

» amphotericin B lipid complex: 5 mg/kg/day intravenously

OR

» amphotericin B liposomal: 3-5 mg/kg/day intravenously

» Should be continued for the entire duration of treatment or the duration of pregnancy, whichever ends first.

» Amphotericin-B is associated with nephrotoxicity, hypokalaemia, and hypomagnesaemia.

» If treatment is required after delivery, oral itraconazole can be used. However, there are insufficient data to support the safety of itraconazole during breastfeeding.

plus **post-delivery itraconazole maintenance therapy**

Treatment recommended for ALL patients in selected patient group

Primary options

» itraconazole: 200 mg orally three times daily for 3 days, followed by 200 mg orally twice daily

» Provided the patient is not breastfeeding. There is not a recommended therapy for breastfeeding women, as there are insufficient data in this population. Risks of treatment should be reviewed with an infectious disease consultant in these circumstances.

» Some immunocompromised patients may require lifelong suppressive therapy with 200 mg once daily.

Ongoing

» Itraconazole has been associated with hepatotoxicity, CNS depression, cardiovascular effects, transient or permanent hearing loss, pseudoaldosteronism, hypokalaemia, and peripheral neuropathy. Azole antifungals undergo many significant drug-drug interactions.

neonates <30 days old

without CNS disease — 1st — **amphotericin-B deoxycholate**

Primary options

» amphotericin B deoxycholate: refer to consultant for guidance on dosage

» The duration of treatment is not well defined.

» Amphotericin-B is associated with nephrotoxicity, hypokalaemia, and hypomagnesaemia.

with CNS disease — 1st — **amphotericin-B lipid formulation**

Primary options

» amphotericin B lipid complex: refer to consultant for guidance on dosage

OR

» amphotericin B liposomal: refer to consultant for guidance on dosage

» CNS disease involvement requires the lipid formulation as it crosses the blood-brain barrier better and the increased safety factor allows higher doses into the brain.

» Amphotericin-B is associated with nephrotoxicity, hypokalaemia, and hypomagnesaemia.

infants/children ≥30 days old

immunocompetent ambulatory — 1st — **itraconazole**

Primary options

» itraconazole: 10 mg/kg/day orally, maximum 400 mg/day

» Duration is 6 to 12 months.

» Itraconazole has been associated with hepatotoxicity, CNS depression, cardiovascular effects, transient or permanent hearing loss, pseudoaldosteronism, hypokalaemia, and

Ongoing

peripheral neuropathy. Azole antifungals undergo many significant drug-drug interactions.

immunosuppressed or hospitalised: without CNS involvement

1st **amphotericin-B deoxycholate**

Primary options

» amphotericin B deoxycholate: refer to consultant for guidance on dosage

» Amphotericin-B is associated with nephrotoxicity, hypokalaemia, and hypomagnesaemia.

plus **itraconazole maintenance therapy**

Treatment recommended for ALL patients in selected patient group

Primary options

» itraconazole: 10 mg/kg/day orally, maximum 400 mg/day

» Duration of treatment is 12 months.

» Itraconazole has been associated with hepatotoxicity, CNS depression, cardiovascular effects, transient or permanent hearing loss, pseudoaldosteronism, hypokalaemia, and peripheral neuropathy. Azole antifungals undergo many significant drug-drug interactions.

immunosuppressed or hospitalised: with CNS involvement

1st **amphotericin-B lipid formulation**

Primary options

» amphotericin B lipid complex: refer to consultant for guidance on dosage

OR

» amphotericin B liposomal: refer to consultant for guidance on dosage

» CNS disease involvement requires the lipid formulation as it crosses the blood-brain barrier better and the increased safety factor allows higher doses into the brain.

» Amphotericin-B is associated with nephrotoxicity, hypokalaemia, and hypomagnesaemia.

plus **itraconazole maintenance therapy**

Treatment recommended for ALL patients in selected patient group

Primary options

» itraconazole: 10 mg/kg/day orally, maximum 400 mg/day

Ongoing

» Itraconazole has been associated with hepatotoxicity, CNS depression, cardiovascular effects, transient or permanent hearing loss, pseudoaldosteronism, hypokalaemia, and peripheral neuropathy. Azole antifungals undergo many significant drug-drug interactions.

» Consult specialist for duration.

Emerging

Other azole antifungals

There are increasing clinical experience and case reports of successful treatment of blastomycosis with other azole antifungals (e.g., voriconazole, posaconazole).[2] [4] [44] [45] [46] However, large prospective trials have not been completed. Isavuconazole has demonstrated in vitro activity against *Blastomyces dermatitidis*, but reported clinical use in this setting is limited.[47] [48] [49] Isavuconazole is approved in some countries for the treatment of adults with invasive aspergillosis and mucormycosis.

Primary prevention

There are no effective primary preventative measures for blastomycosis. There is no vaccine available for clinical use.

Secondary prevention

- The only secondary preventative measure for blastomycosis is to decrease exposure to the environmental source of the infection, if the source is known. For some patients, due to occupational requirements or recreational preferences, this is not possible. In these instances, patients should be instructed to monitor carefully for signs or symptoms of recurrent disease and to seek medical attention early if symptoms recur.
- If the patient is immunocompromised, and the cause of the immunocompromise is reversible, the risk of recurrent disease can be decreased. Full-dose itraconazole therapy should be continued for 1 year, and consideration should be given to subsequent lifelong secondary prophylaxis with low-dose itraconazole therapy if the underlying immunosuppression cannot be corrected.

Patient discussions

- Patients should be instructed to monitor for medicine-related side effects, particularly the development of signs or symptoms of hepatotoxicity such as jaundice or stool colour changes associated with azole antifungal therapy.
- Women of childbearing age on azole therapy should be cautioned to avoid becoming pregnant during this therapy. Patients should be questioned about the possibility of pregnancy.
- Patients should be evaluated in follow-up, initially on a monthly basis and then every 3 months until resolution of disease and discontinuation of antifungal therapy.

Monitoring

Monitoring

- Liver function tests should be followed on a monthly basis while on azole therapy.
- A serum itraconazole level should be checked 2 to 3 weeks after starting therapy to ensure adequate absorption. A serum concentration of more than 1 microgram/mL is considered therapeutic. Repeat levels are generally not needed unless failure of therapy or symptomatic toxicity. Similarly, in patients with central nervous system disease being treated with voriconazole, it is advisable to check a trough level 1 to 2 weeks after starting therapy. Although there are no trials evaluating voriconazole therapeutic drug monitoring in blastomycosis, a serum trough concentration between 1 microgram/mL and 5 to 6 micrograms/mL is likely to be optimal to balance therapeutic efficacy and risk of toxicity.[51]
- While on amphotericin-B therapy, serum potassium, magnesium, and creatinine should be monitored at least twice weekly.
- If a urine, serum, cerebrospinal fluid (CSF) or bronchoalveolar lavage *Blastomyces dermatitidis* antigen was measured and positive at diagnosis, repeating levels every 1 to 3 months can be used to monitor response to therapy. Ideally the antigen is eliminated.
- Radiographical abnormalities should be followed up with repeat examinations every 1 to 3 months until resolution.
- It is important to monitor for drug interactions between the azole antifungals and other medicines metabolised by the cytochrome P450 system, particularly warfarin (using INR) or statins (symptoms of rhabdomyolysis). However, routine laboratory monitoring for rhabdomyolysis is not warranted.

[Centers for Disease Control and Prevention: fungal diseases - blastomycosis] (http://www.cdc.gov/fungal/diseases/blastomycosis/index.html)

Complications

Complications	Timeframe	Likelihood
acute respiratory distress syndrome	**short term**	**low**
Immunosuppression or a very heavy inoculum of fungus may predispose.		

Prognosis

Prognosis

Although unrecognised and untreated blastomycosis can be a fatal disease, the prognosis for treated blastomycosis is quite good, with most symptoms and radiological manifestations responding quickly to appropriate antifungal therapy. Overall mortality associated with blastomycosis is 6.6%, although the risk is increased in patients who develop acute respiratory distress syndrome, have disseminated disease, or are immunosuppressed.[50]

Relapse

If undertreated, blastomycosis has a high rate of relapse, which is the primary factor in the prolonged treatment courses lasting 6 to 12 months. Infection with *Blastomyces dermatitidis* does lead to the

development of lasting specific cell-mediated and humoral immunity, as evidenced by the ability to perform serological and skin antigen testing. However, this specific immunity is not necessarily protective, and re-infection can occur in the face of repeated exposure.

Diagnostic guidelines

Europe

Global guideline for the diagnosis and management of the endemic mycoses (https://pubmed.ncbi.nlm.nih.gov/34364529/)

Published by: European Confederation of Medical Mycology; International Society for Human and Animal Mycology **Last published:** 2021

North America

Clinical testing guidance for coccidioidomycosis, histoplasmosis, and blastomycosis in patients with community-acquired pneumonia for primary and urgent care providers (https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciad619/7295325)

Published by: The Centers for Disease Control and Prevention, Mycoses Study Group and Coccidioidomycosis Study Group **Last published:** 2023

Microbiological laboratory testing in the diagnosis of fungal infections in pulmonary and critical care practice (https://pubmed.ncbi.nlm.nih.gov/31469325/le-of-contents)

Published by: American Thoracic Society Clinical Practice Guideline **Last published:** 2019

Treatment guidelines

Europe

Global guideline for the diagnosis and management of the endemic mycoses (https://pubmed.ncbi.nlm.nih.gov/34364529/)

Published by: European Confederation of Medical Mycology; International Society for Human and Animal Mycology **Last published:** 2021

North America

Endemic fungal infections in solid organ transplant recipients (https://pubmed.ncbi.nlm.nih.gov/30924967)

Published by: American Society of Transplantation Infectious Diseases Community of Practice **Last published:** 2019

Treatment of fungal infections in adult pulmonary and critical care patients (http://www.thoracic.org/statements)

Published by: American Thoracic Society **Last published:** 2011

Online resources

1. Centers for Disease Control and Prevention: fungal diseases - blastomycosis (http://www.cdc.gov/fungal/diseases/blastomycosis/index.html) *(external link)*

Key articles

- Thompson GR 3rd, Le T, Chindamporn A, et al. Global guideline for the diagnosis and management of the endemic mycoses: an initiative of the European Confederation of Medical Mycology in cooperation with the International Society for Human and Animal Mycology. Lancet Infect Dis. 2021 Dec;21(12):e364-e374. Abstract (http://www.ncbi.nlm.nih.gov/pubmed/34364529?tool=bestpractice.bmj.com)

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Images

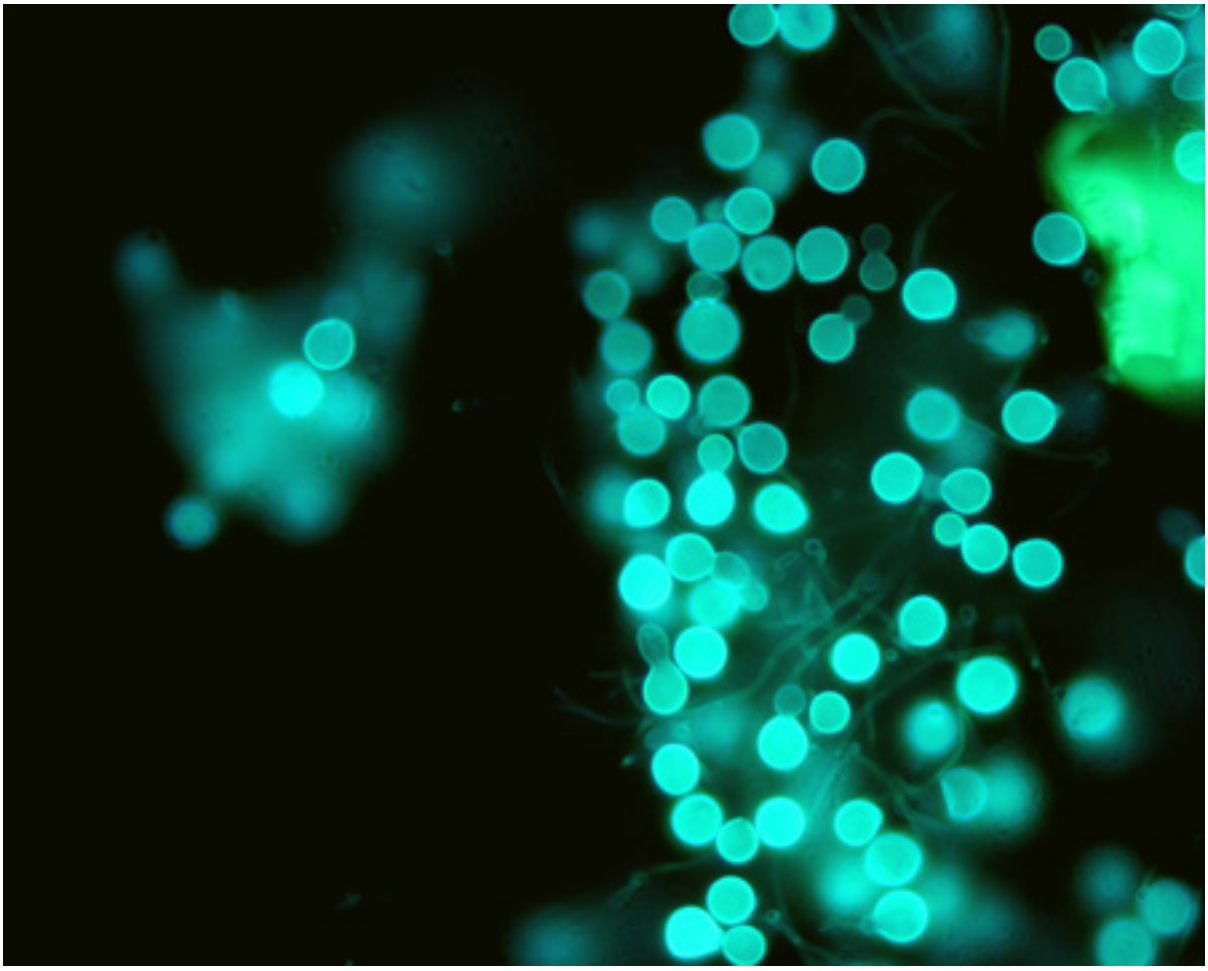

Figure 1: Direct potassium hydroxide preparation at 40x magnification of a sputum specimen

Nancy L. Wengenack, PhD, D(ABMM), Director of Mycology and Mycobacteriology Laboratories, Assistant Professor of Microbiology abd Lab Medicine, Mayo Clinic, Rochester, MN

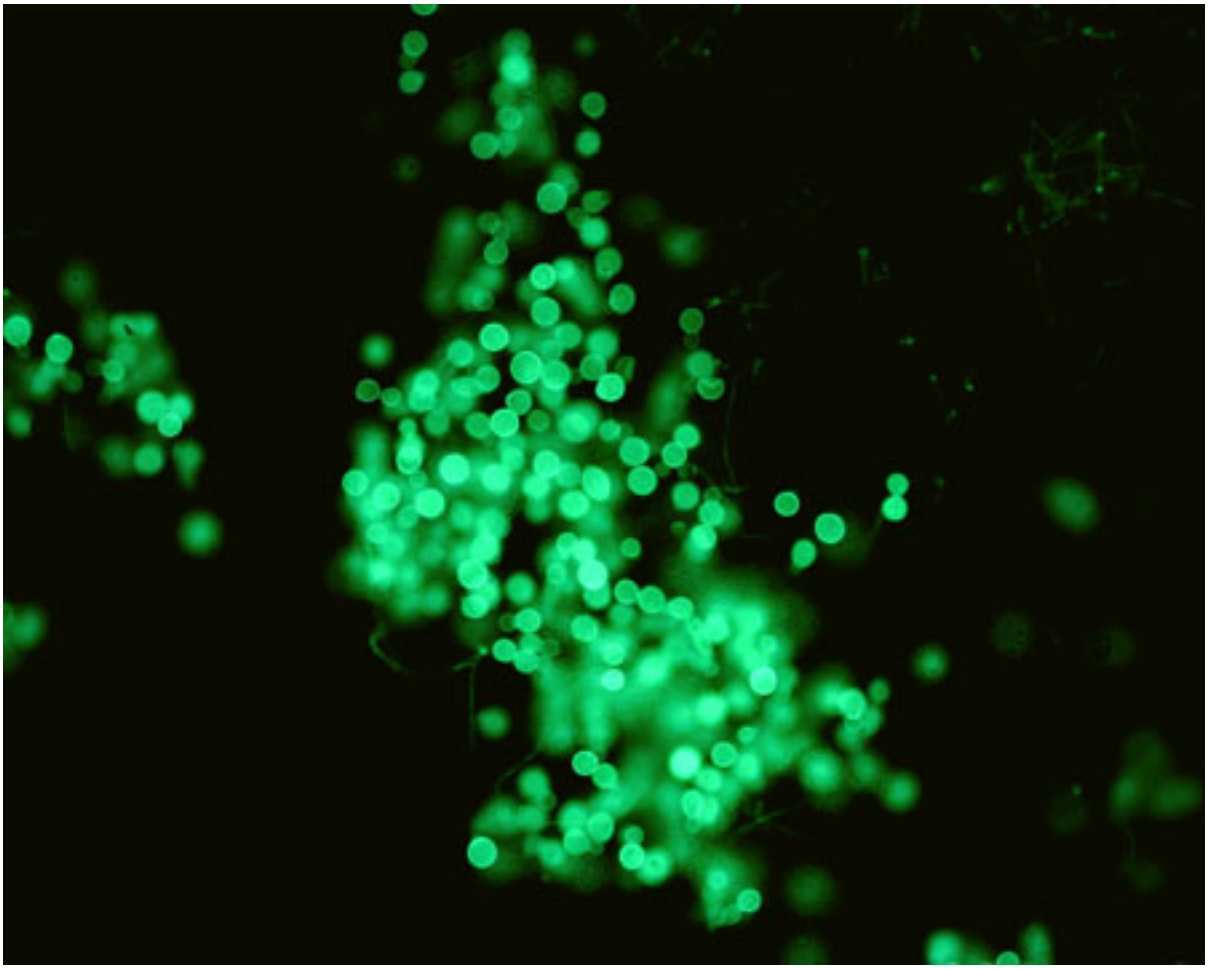

Figure 2: Direct potassium hydroxide preparation at 20x magnification of a sputum specimen

Nancy L. Wengenack, PhD, D(ABMM), Director of Mycology and Mycobacteriology Laboratories, Assistant Professor of Microbiology and Lab Medicine, Mayo Clinic, Rochester, MN

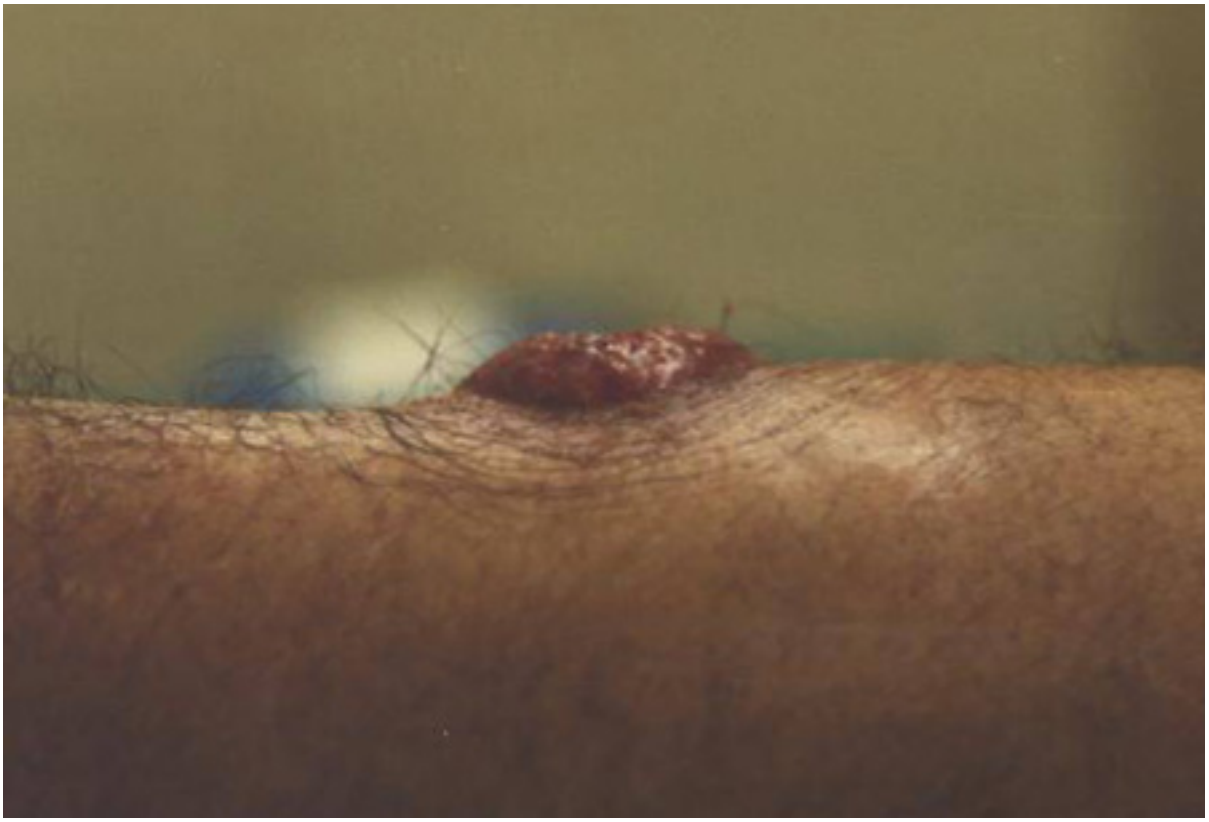

Figure 3: Cutaneous blastomycosis on the forearm

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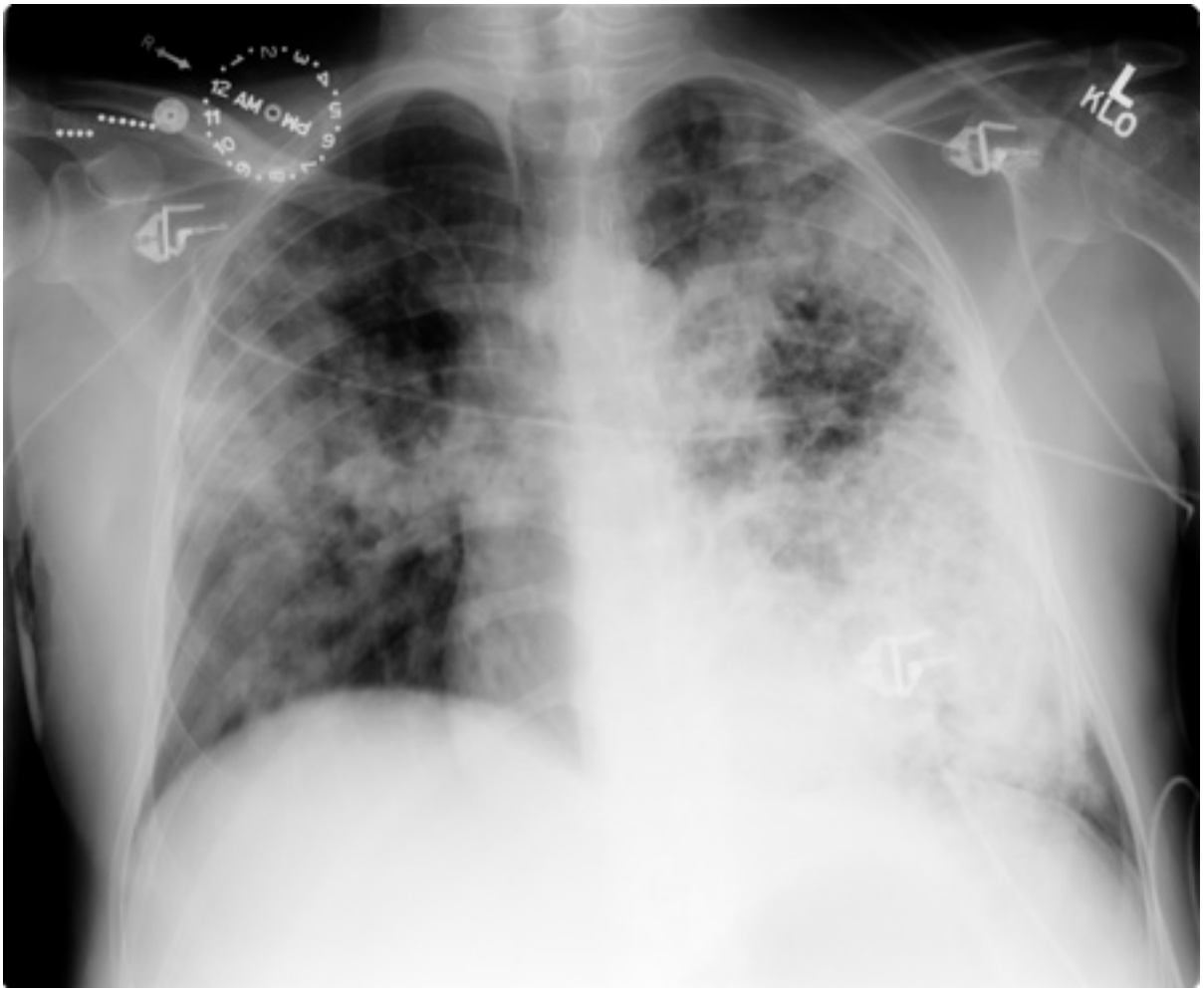

Figure 4: Pulmonary blastomycosis with focal infiltrates on chest x-ray

Dr Robert Orenstein, DO, Associate Professor of Medicine, Division of Infectious Diseases, Mayo Clinic, Scottsdale, AZ

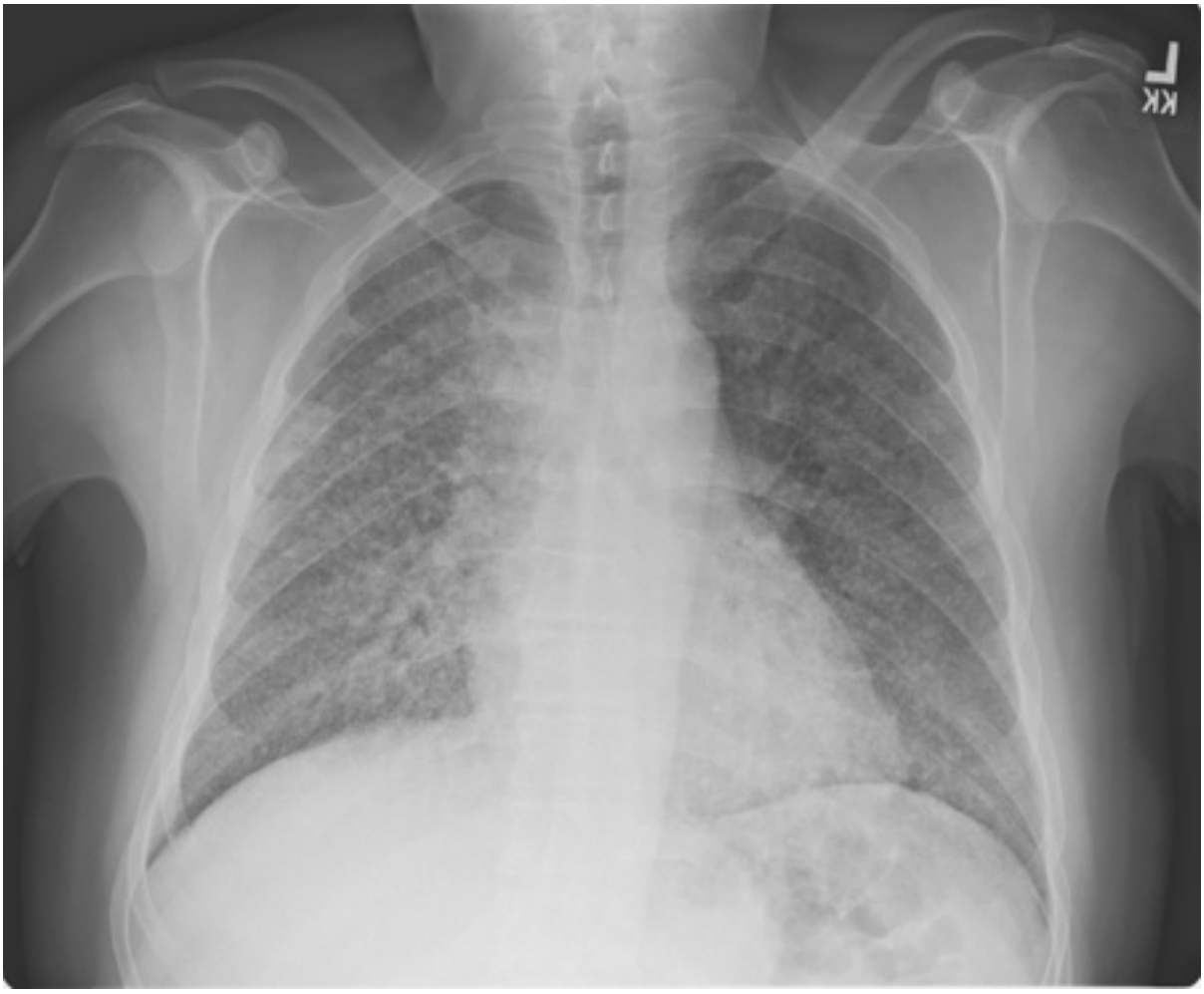

Figure 5: Pulmonary blastomycosis presenting as a miliary pattern on chest x-ray

Dr Robert Orenstein, DO, Associate Professor of Medicine, Division of Infectious Diseases, Mayo Clinic, Scottsdale, AZ

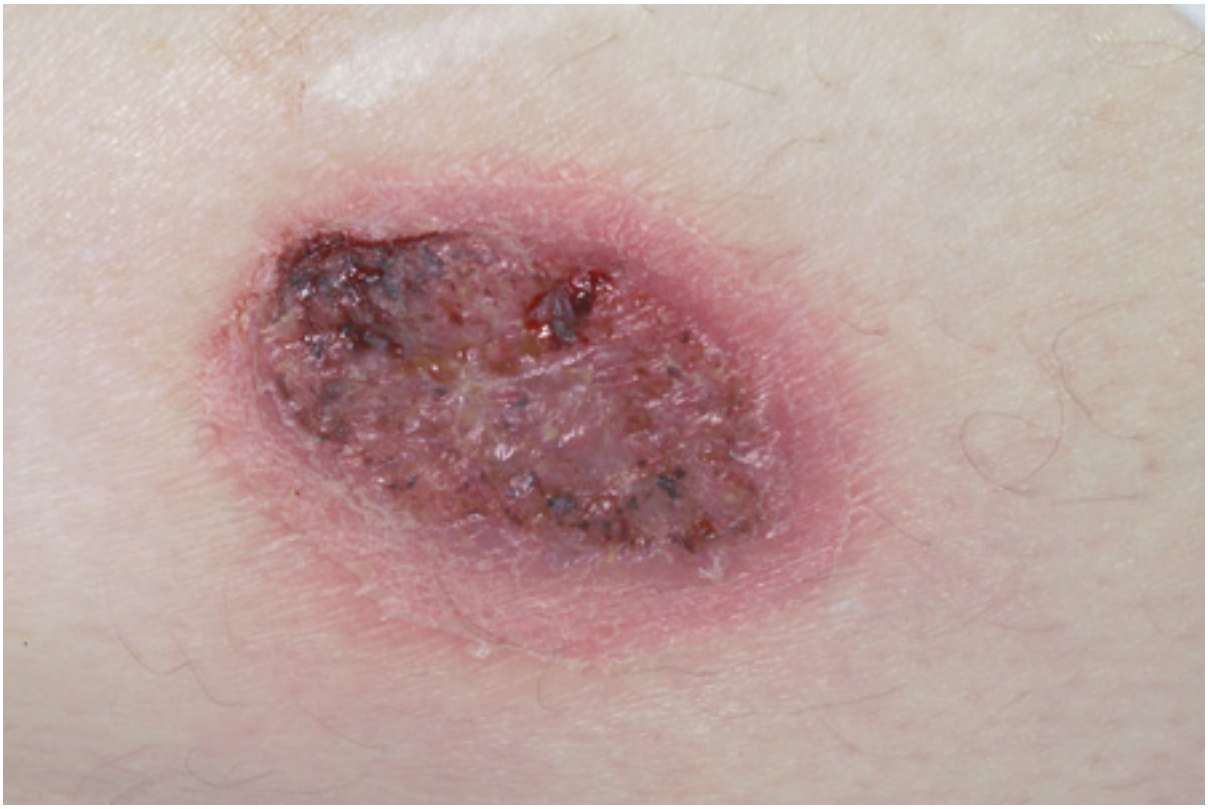

Figure 6: Cutaneous blastomycosis on the lower extremity

LuAnn Ziemer, Office of Medical Photography, Mayo Clinic, Rochester, MN

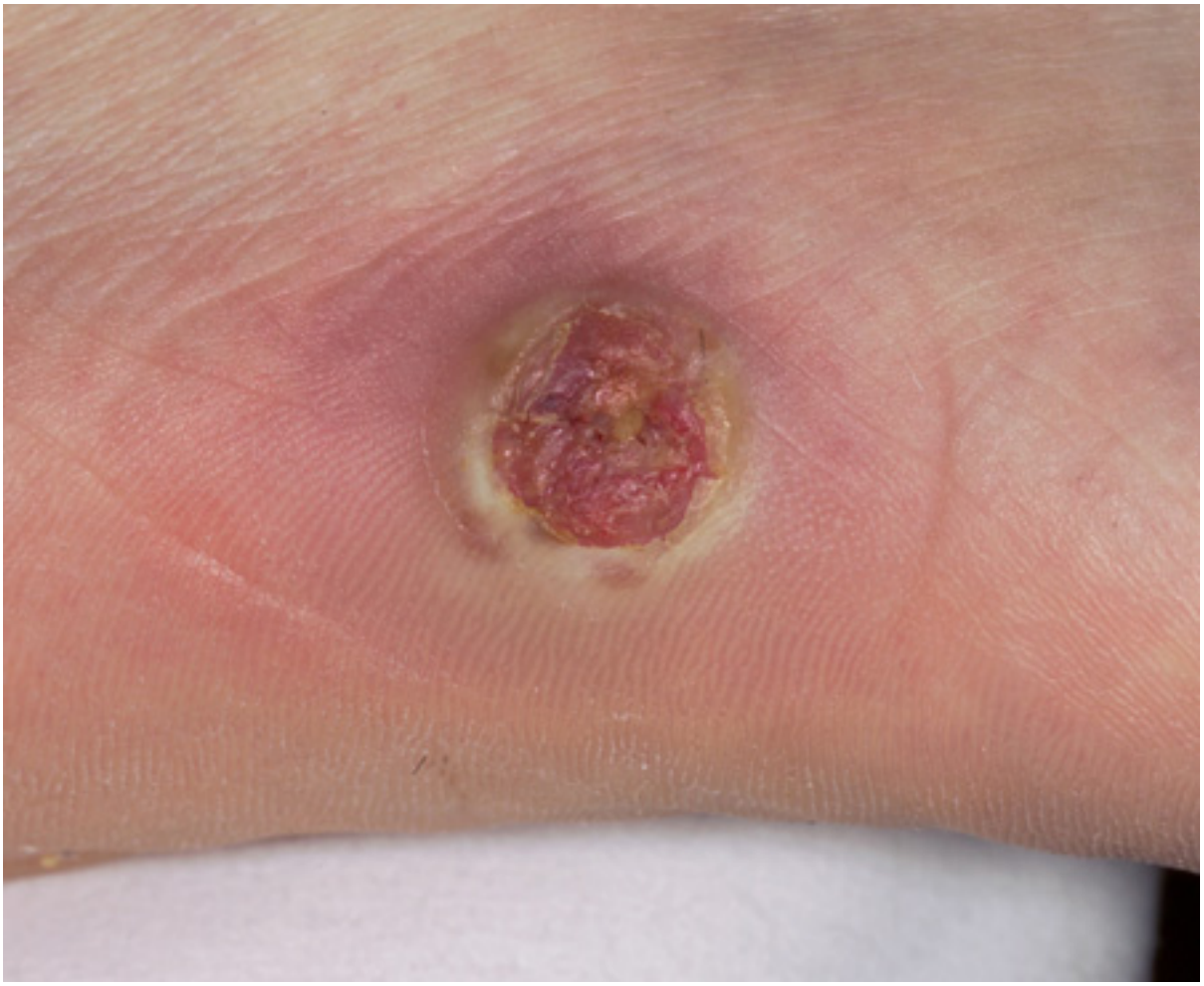

Figure 7: Cutaneous blastomycosis on the lower extremity

LuAnn Ziemer, Office of Medical Photography, Mayo Clinic, Rochester, MN

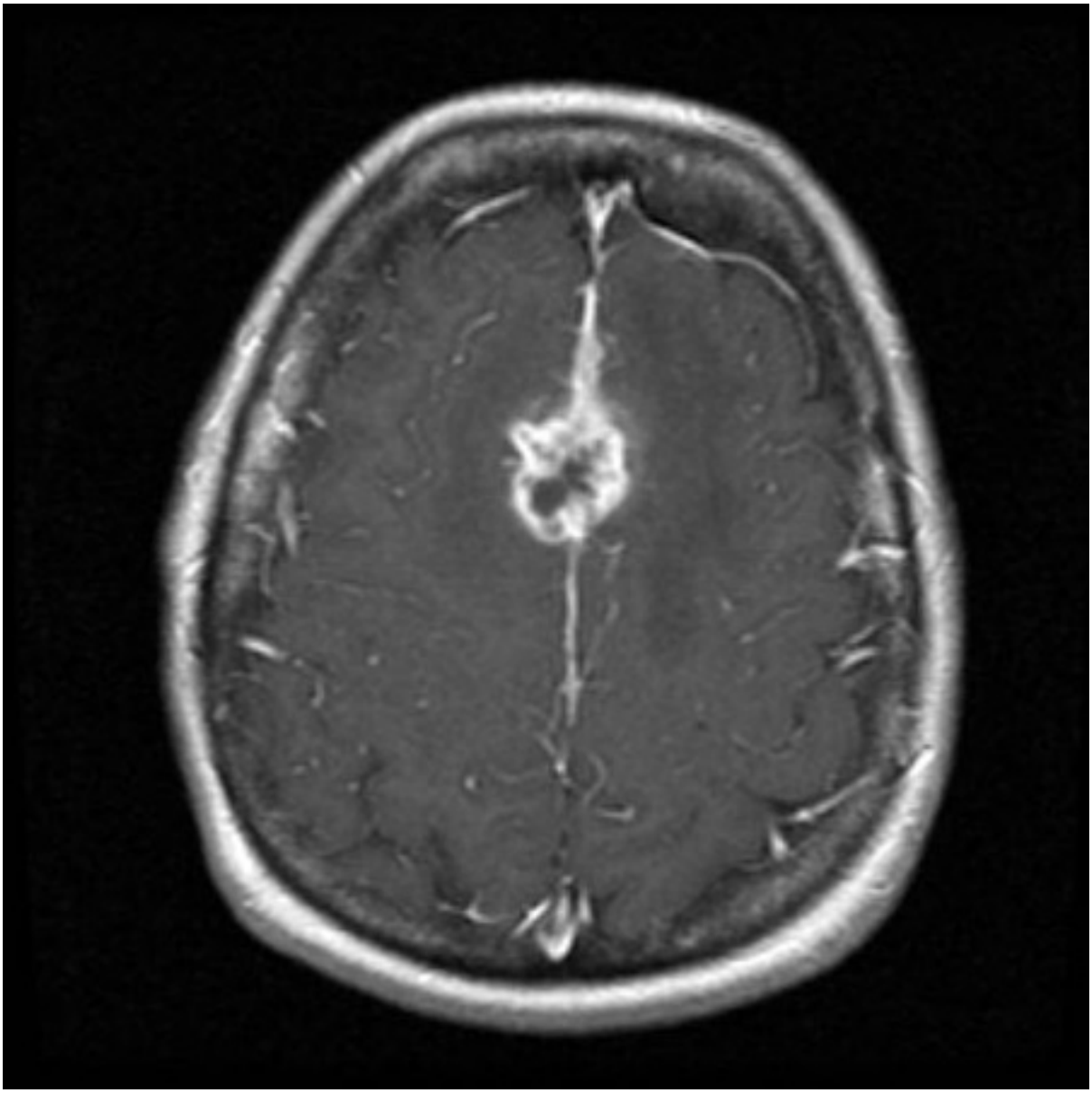

Figure 8: Axial T1 gadolinium-enhanced MRI image of cerebral blastomycosis

Dr William Marshall, MD, Assistant Professor of Medicine, Division of Infectious Diseases, Mayo Clinic, Rochester, MN

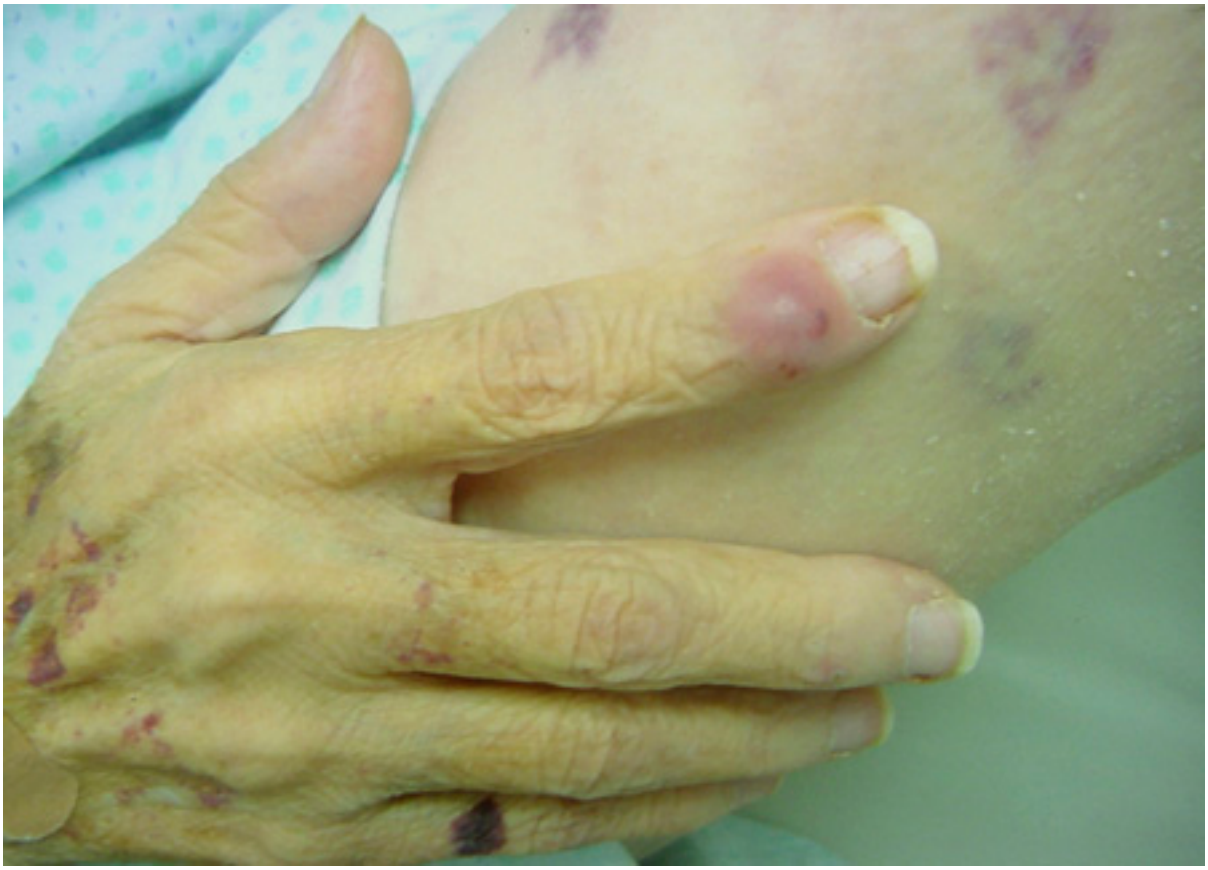

Figure 9: Cutaneous manifestation of disseminated blastomycosis

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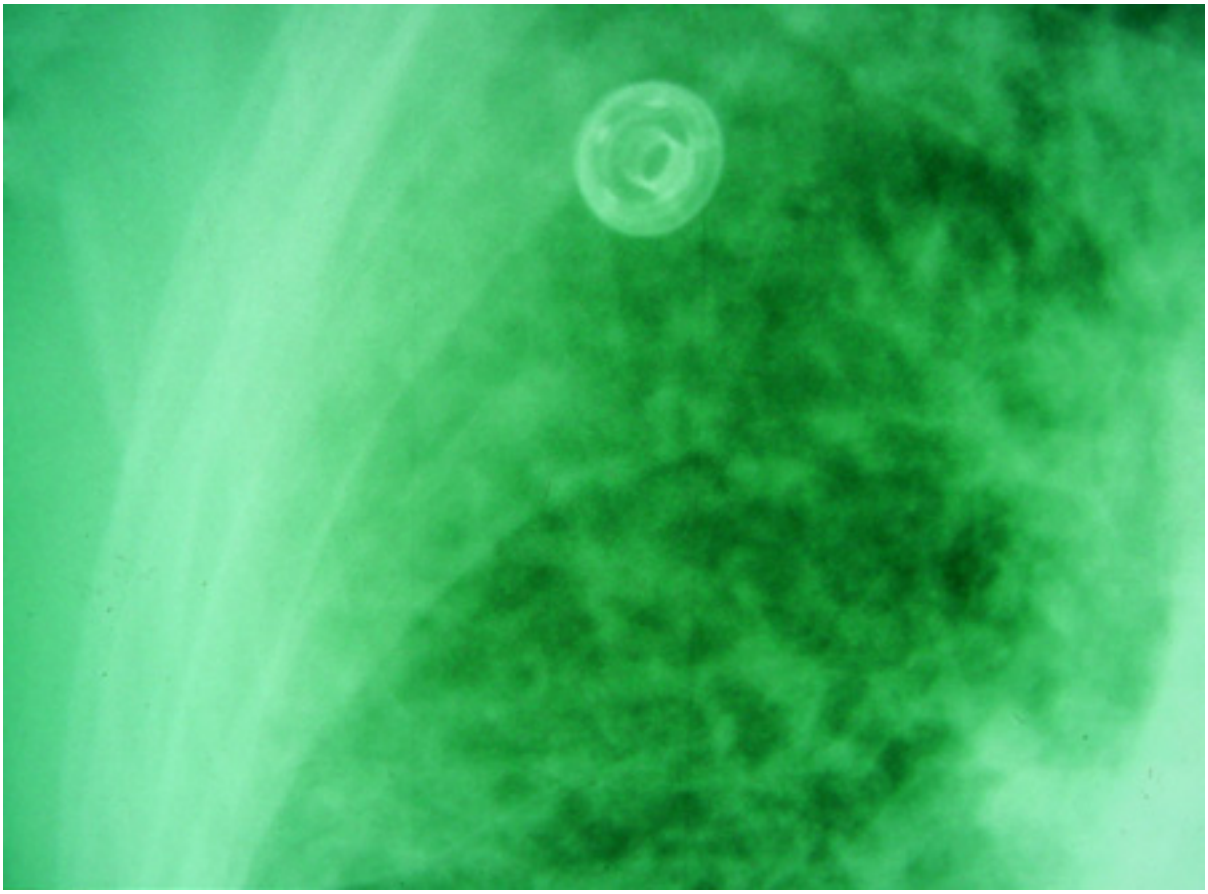

Figure 10: Close-up of reticulonodular findings on chest x-ray in disseminated blastomycosis

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