

BMJ Best Practice

Blastomycosis

Straight to the point of care



Last updated: Jul 12, 2024

Table of Contents

Overview	3
Summary	3
Definition	3
Theory	6
Epidemiology	6
Etiology	6
Pathophysiology	6
Case history	7
Diagnosis	13
Approach	13
History and exam	23
Risk factors	27
Investigations	29
Differentials	35
Criteria	37
Management	39
Approach	39
Treatment algorithm overview	42
Treatment algorithm	44
Emerging	51
Primary prevention	51
Secondary prevention	51
Patient discussions	51
Follow up	52
Monitoring	52
Complications	52
Prognosis	52
Guidelines	54
Diagnostic guidelines	54
Treatment guidelines	54
Online resources	55
References	56
Images	61
Disclaimer	71

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

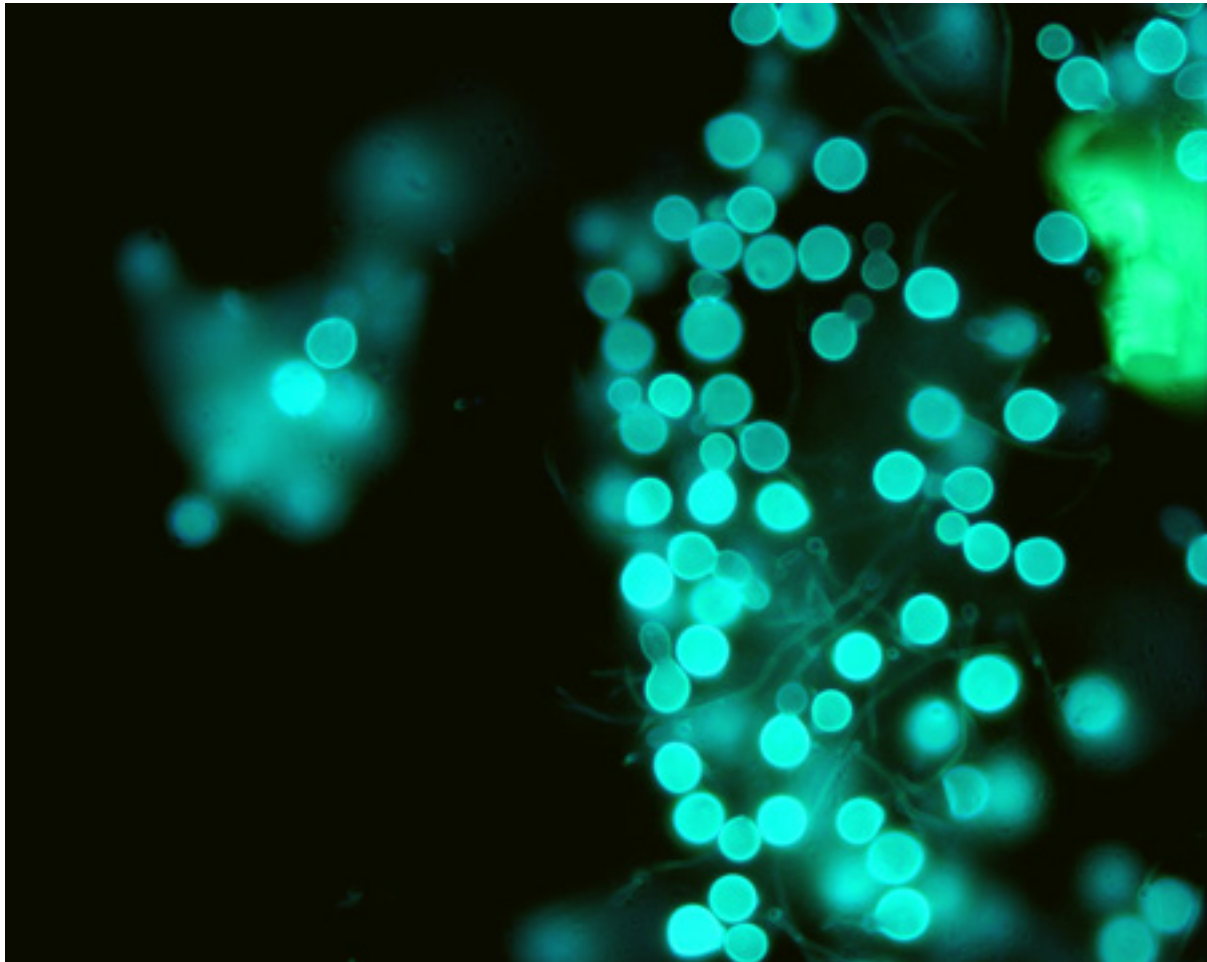
First-line treatment for ambulatory patients is a prolonged course of oral itraconazole. Amphotericin-B is reserved for patients with more severe disease or for patients in whom itraconazole is contraindicated.

No vaccine is available for disease prevention.

Definition

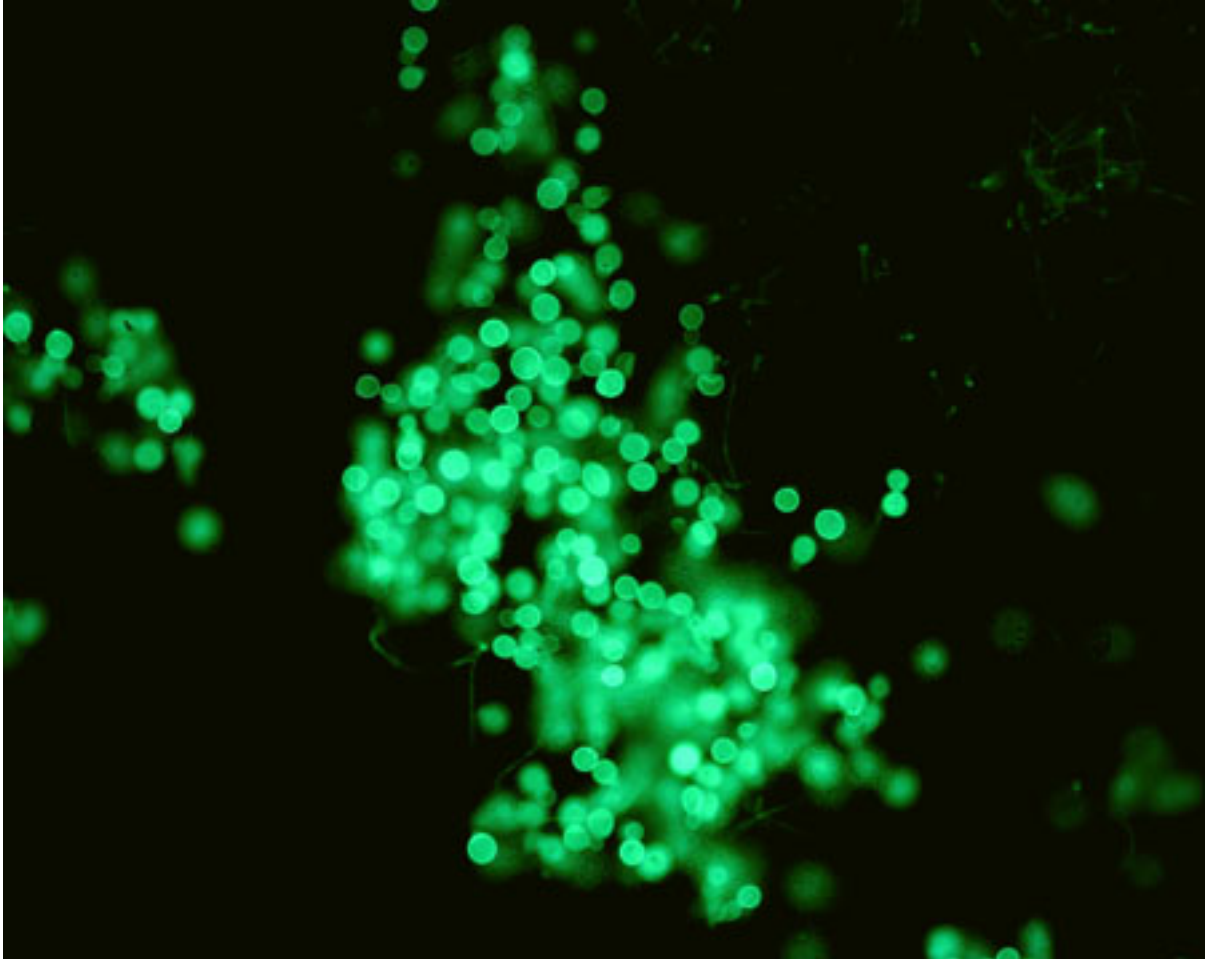
Blastomycosis is an invasive infection caused by the dimorphic fungus *B dermatitidis*, which is endemic to the upper and mid-Mississippi River valley in the US, Canada, the Mediterranean basin, and parts of Africa.[1] [2] Although pulmonary involvement is most common, skin, central nervous system, and 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 histopathologic 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

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

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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 epidemiologic study found that counties in 40 US states exceeded the clinically relevant threshold for blastomycosis.[10] Data also 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] Epidemiologic 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.

Etiology

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 77°F (25°C), and as a cream-to-tan, heaped, or wrinkled yeast at 98.6°F (37°C).[19] *B dermatitidis* exists as a saprophytic mold 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-limited asymptomatic pulmonary infection or acute lobar pneumonia. From the lung, the yeast form can disseminate hematogenously, leading to extrapulmonary infection, most commonly in the skin and soft tissues, bones and joints, central nervous system, and urinary tract.[23] However, direct inoculation of the conidia into the skin can occur as well.[24]

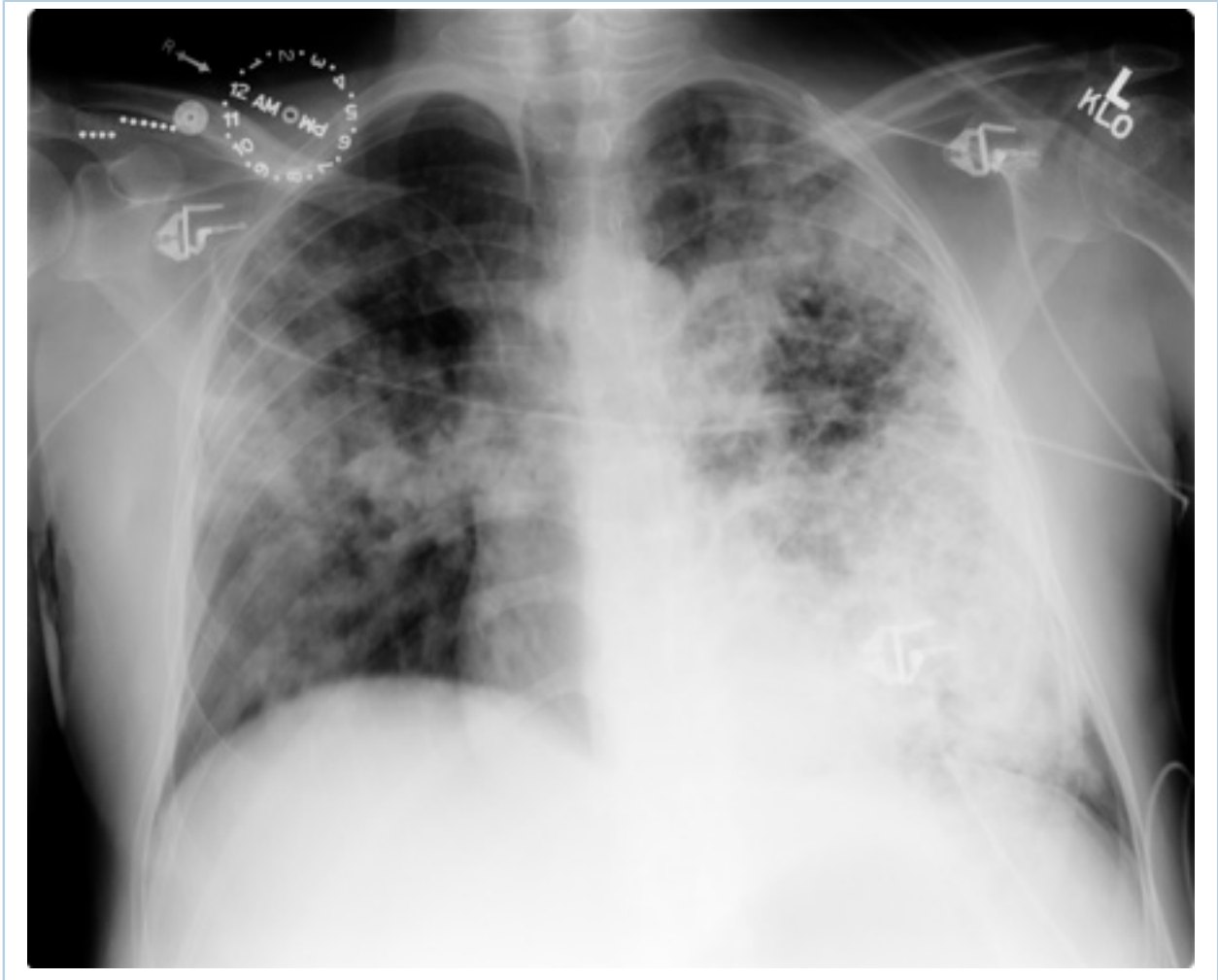
Case history

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 medications. He lives in Wisconsin and 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.

Other presentations

The majority of people acutely infected with *Blastomyces dermatitidis* develop asymptomatic, self-limited 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 radiograph

*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 radiograph

*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 nonhealing 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 hematogenous 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 neurologic 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]



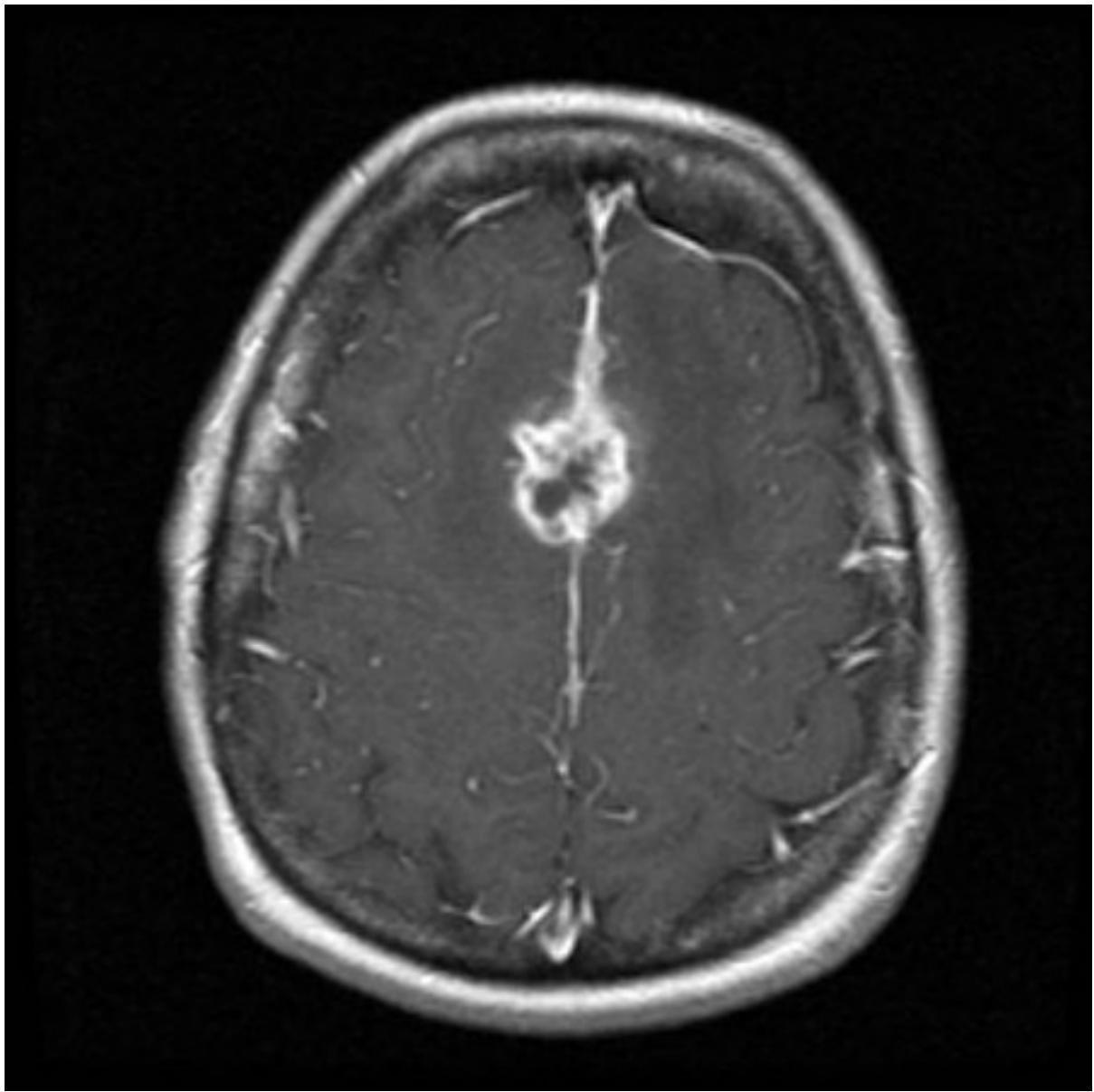
Cutaneous blastomycosis on the lower extremity

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



Cutaneous blastomycosis on the lower extremity

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



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 traveling to areas of endemicity are important epidemiologic 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-limited 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 neurologic symptoms or altered level of consciousness
- Dysuria or other symptoms of prostatitis.

In addition, many people have evidence of past asymptomatic disease according to serologic 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 neurologic deficits may be found. Men may have prostatic or testicular tenderness.



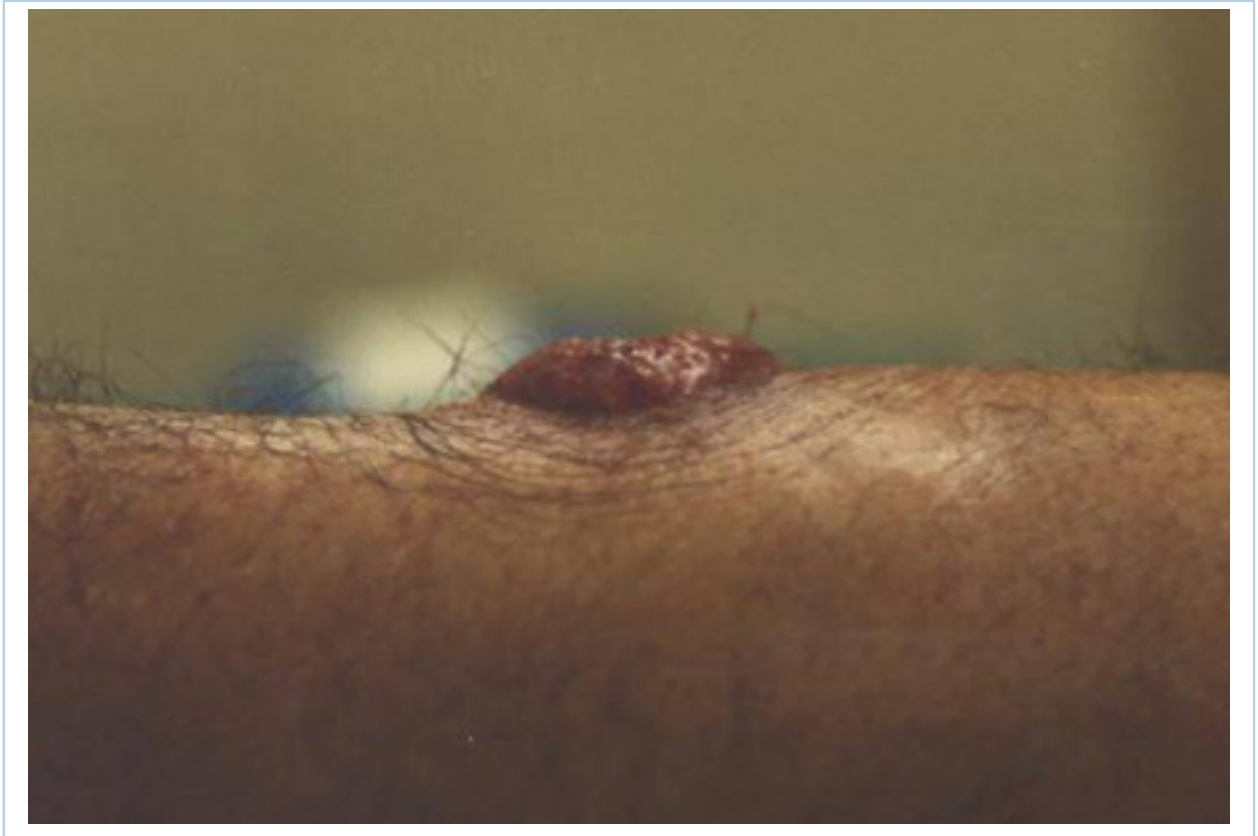
Cutaneous blastomycosis on the lower extremity

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



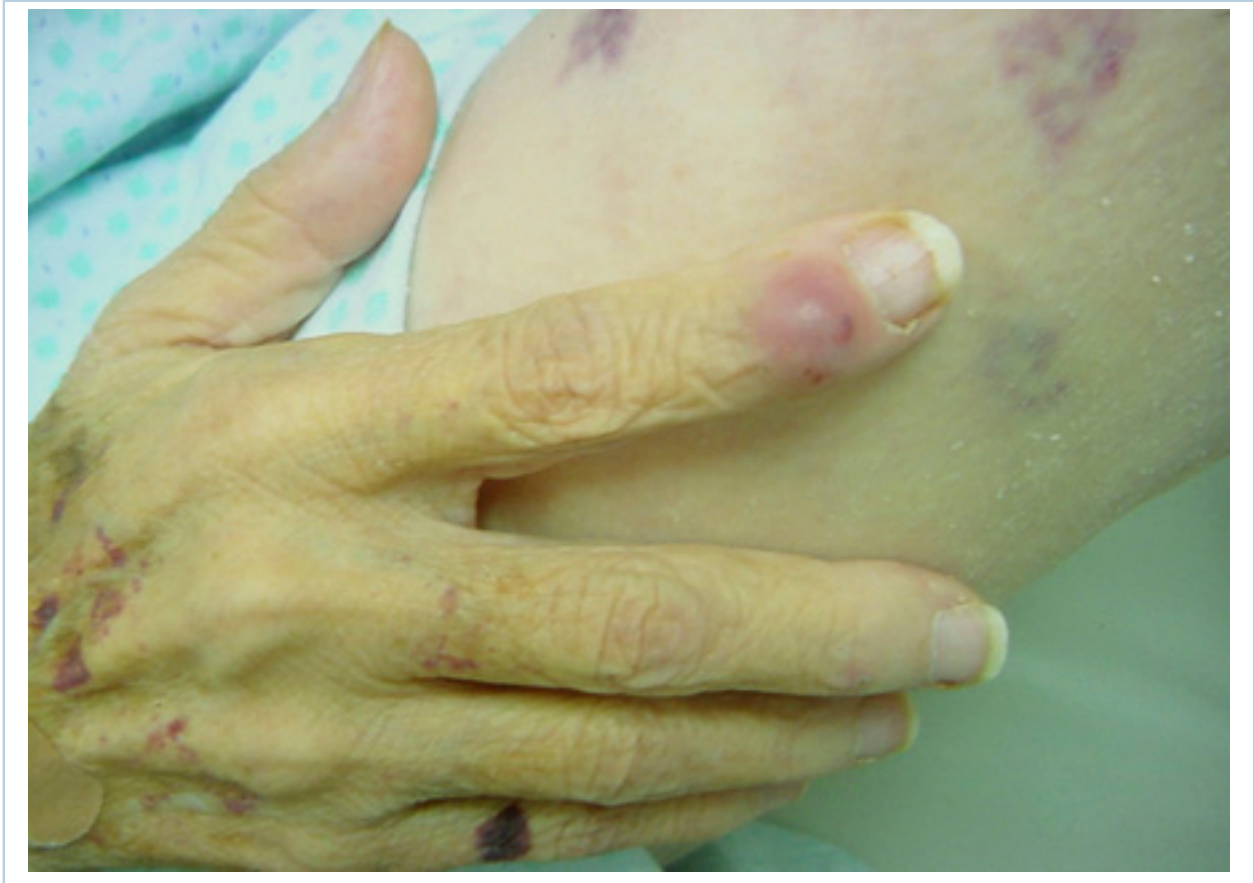
Cutaneous blastomycosis on the lower extremity

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Cutaneous blastomycosis on the forearm

Personal files of Larry Baddour, MD



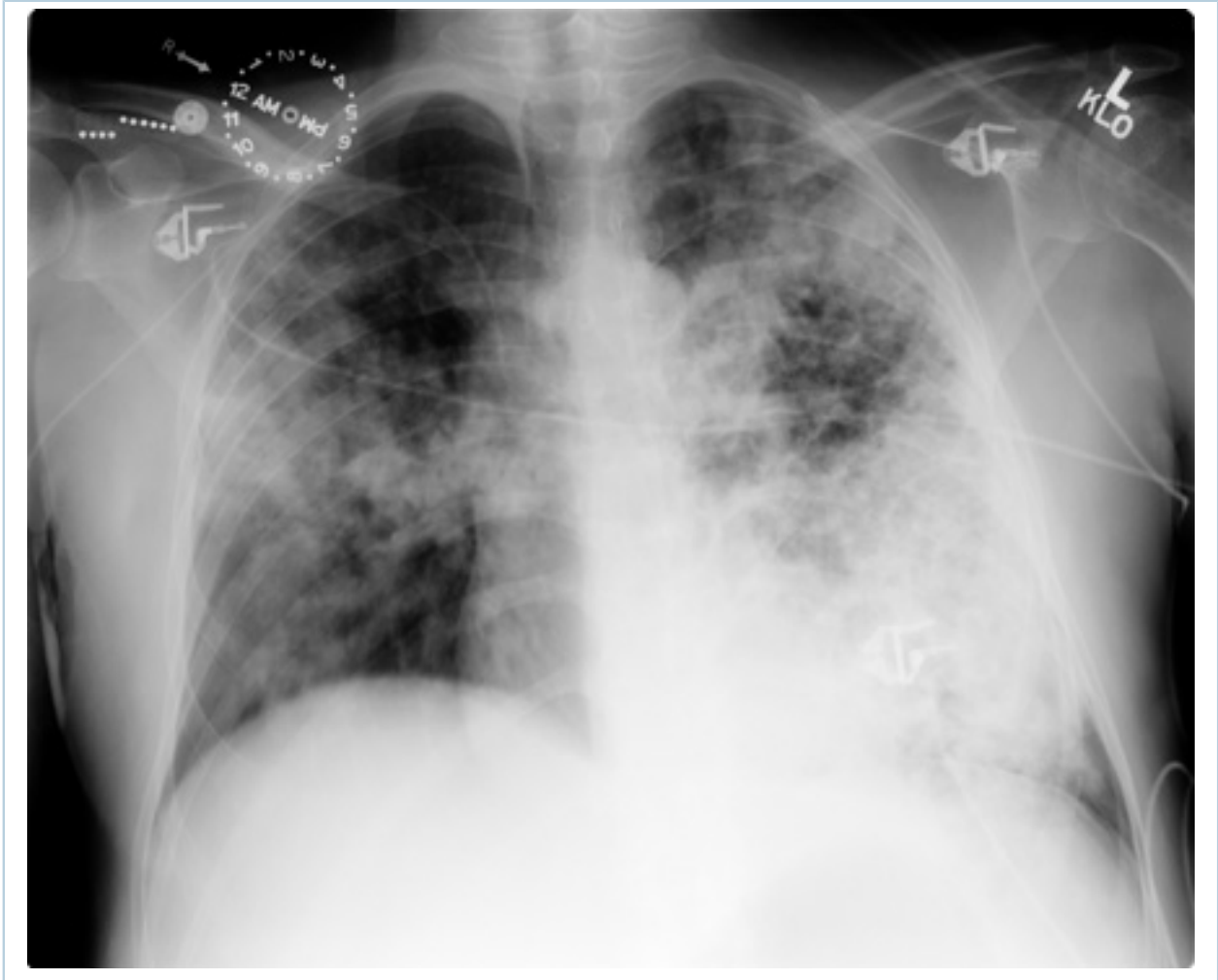
Cutaneous manifestation of disseminated blastomycosis

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 etiology who have not responded to one or more courses of antibiotics, and that have a relevant epidemiologic 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 nonrevealing, 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.



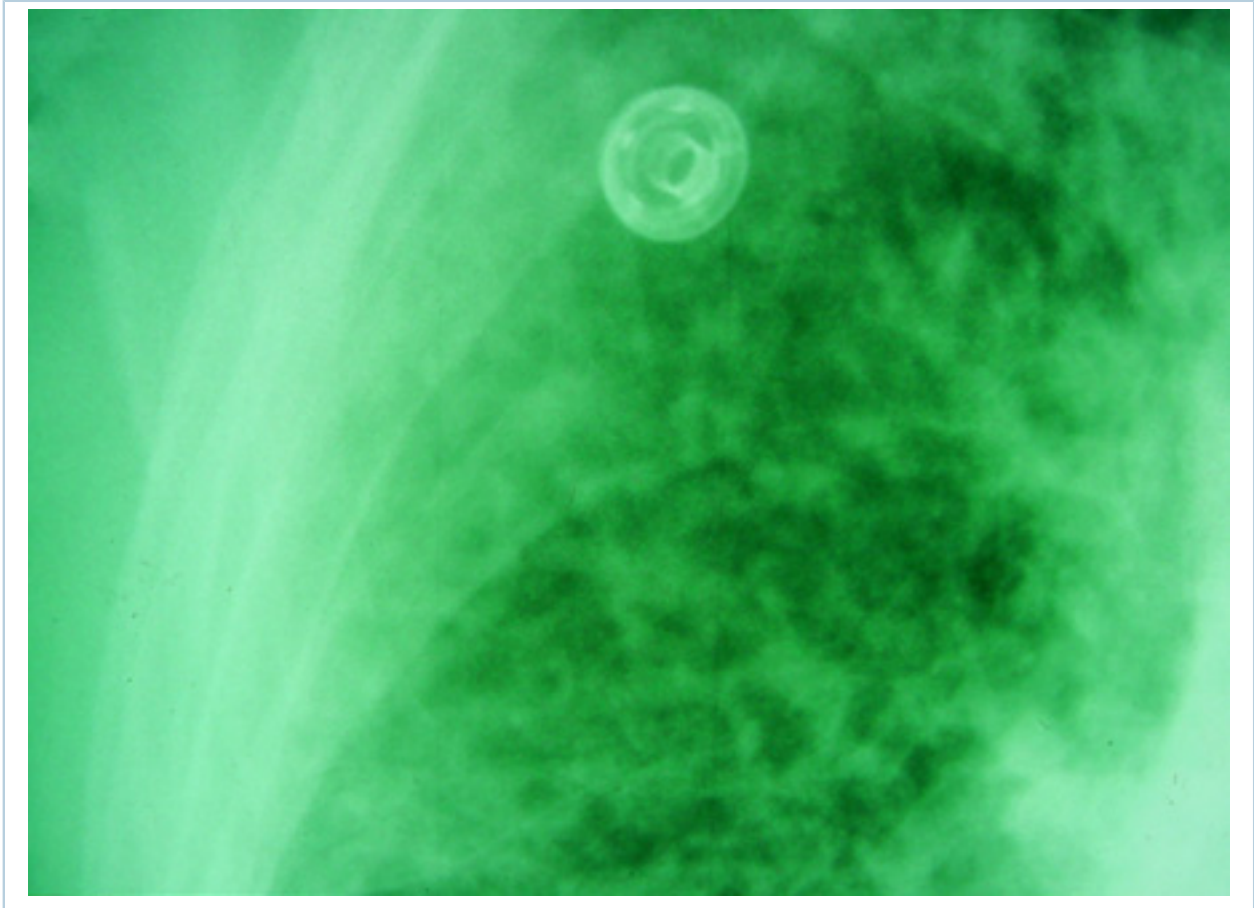
Pulmonary blastomycosis with focal infiltrates on chest radiograph

*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 radiograph

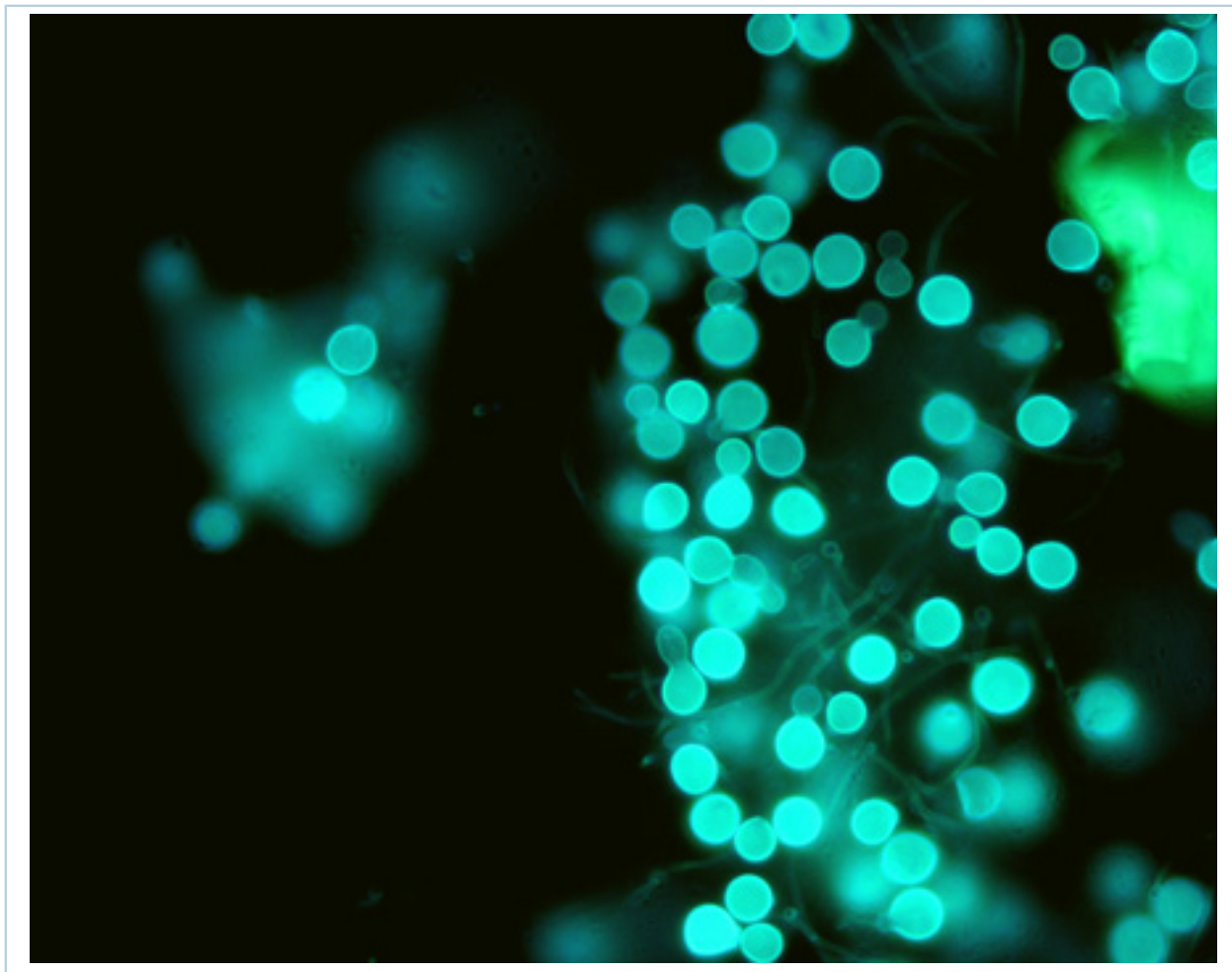
*Dr Robert Orenstein, DO, Associate Professor of Medicine,
Division of Infectious Diseases, Mayo Clinic, Scottsdale, AZ*



Close up of reticulonodular findings on chest radiography in disseminated blastomycosis

Personal files of Larry Baddour, MD

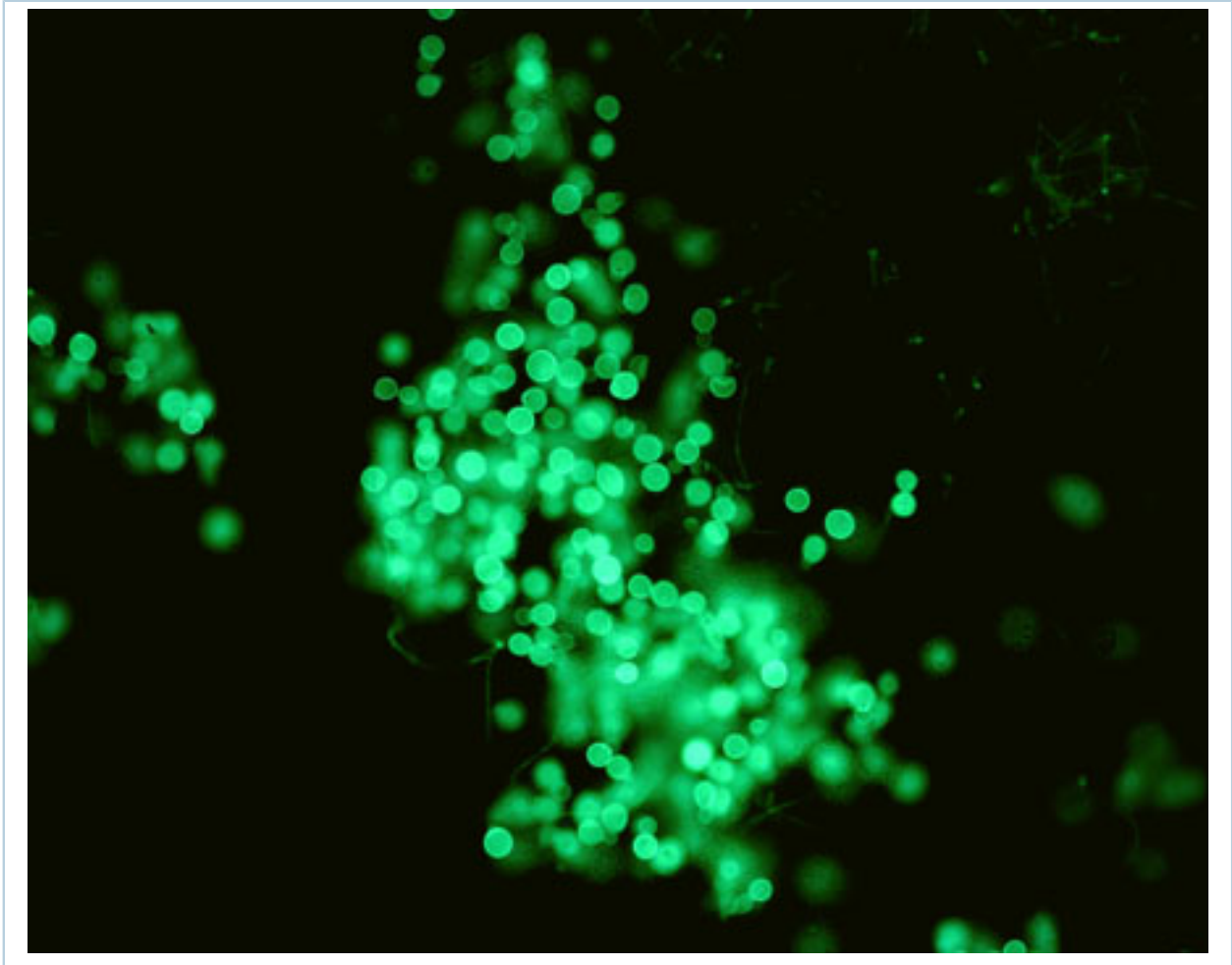
The direct pathologic examination of clinical specimens such as sputum, bronchoalveolar washings, endoscopic lymph node needle aspiration, or cutaneous lesions is sufficient to provide quick diagnosis.[2][33] The hallmark of the pathologic diagnosis is the demonstration of the characteristic yeast form,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



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

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Assistant Professor of Microbiology and 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 mold to yeast form at 98.6°F (37°C). However, most laboratories use a commercially available DNA probe assay to confirm the mold form as *B dermatitidis*. [4][36][37]

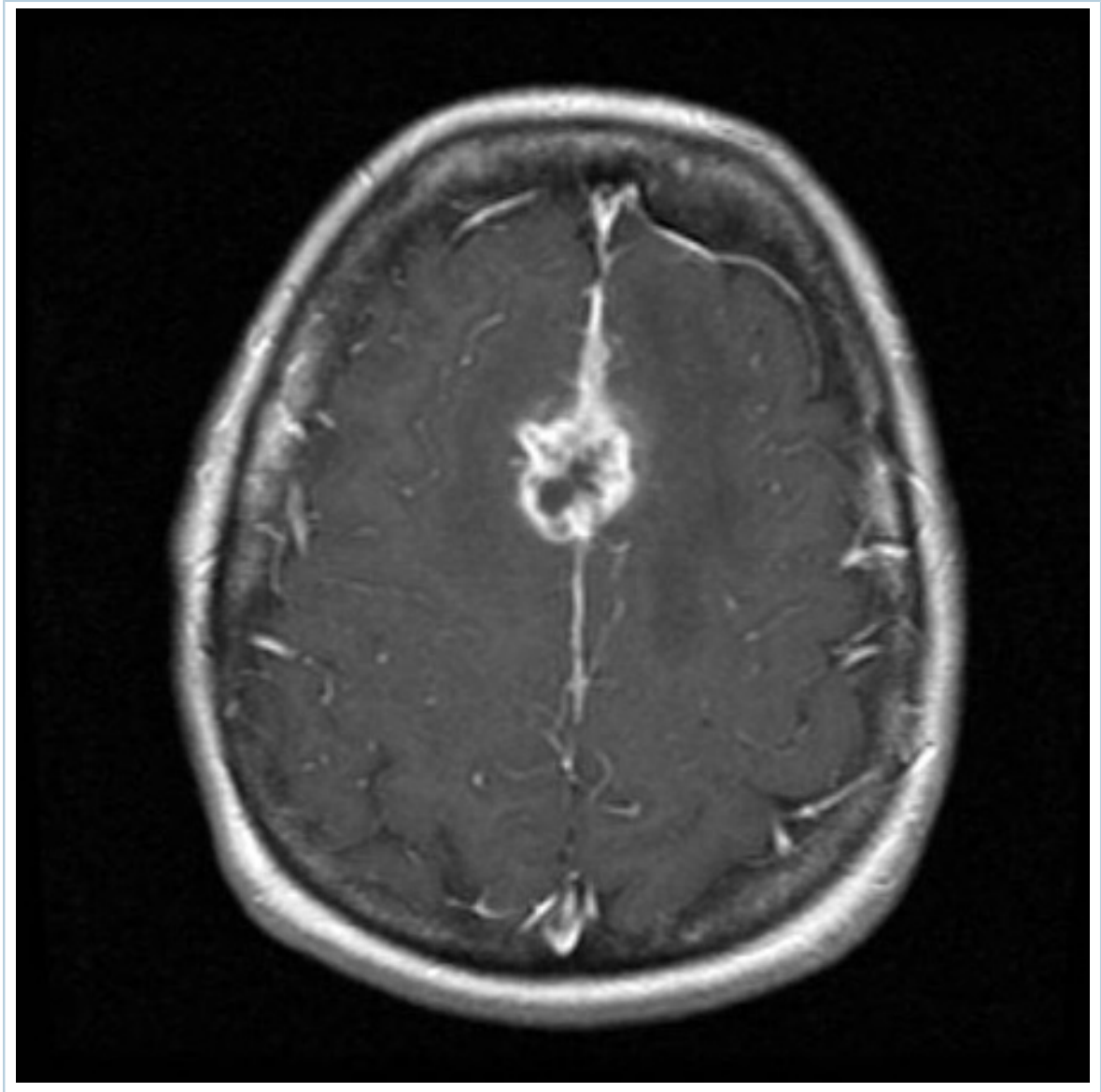


Direct potassium hydroxide preparation at 20x magnification of a sputum specimen

*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 serology 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.
- Pathologic examination of lesions associated with blastomycosis generally reveals findings of acute inflammation with or without necrosis, granuloma formation, and multinucleated 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 radiograph, and disseminated disease spread hematogenously 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.



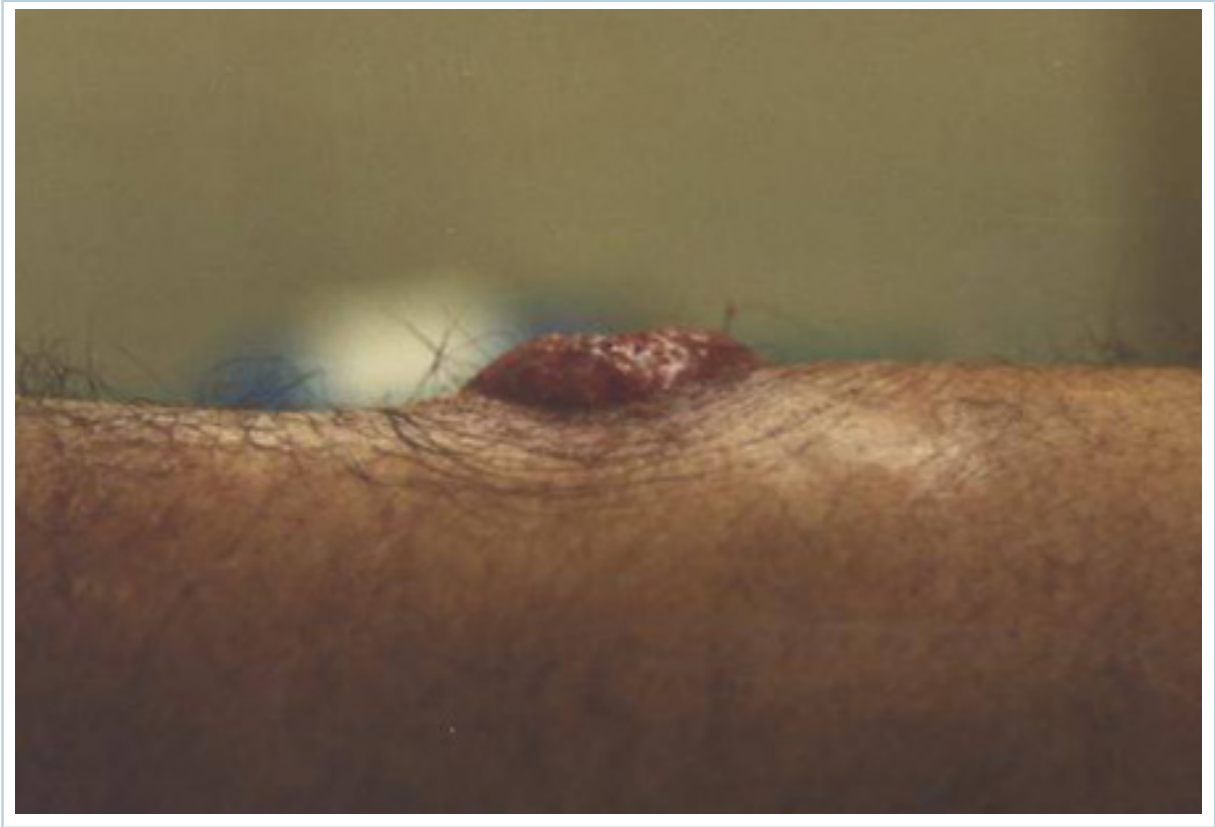
Cutaneous blastomycosis on the lower extremity

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



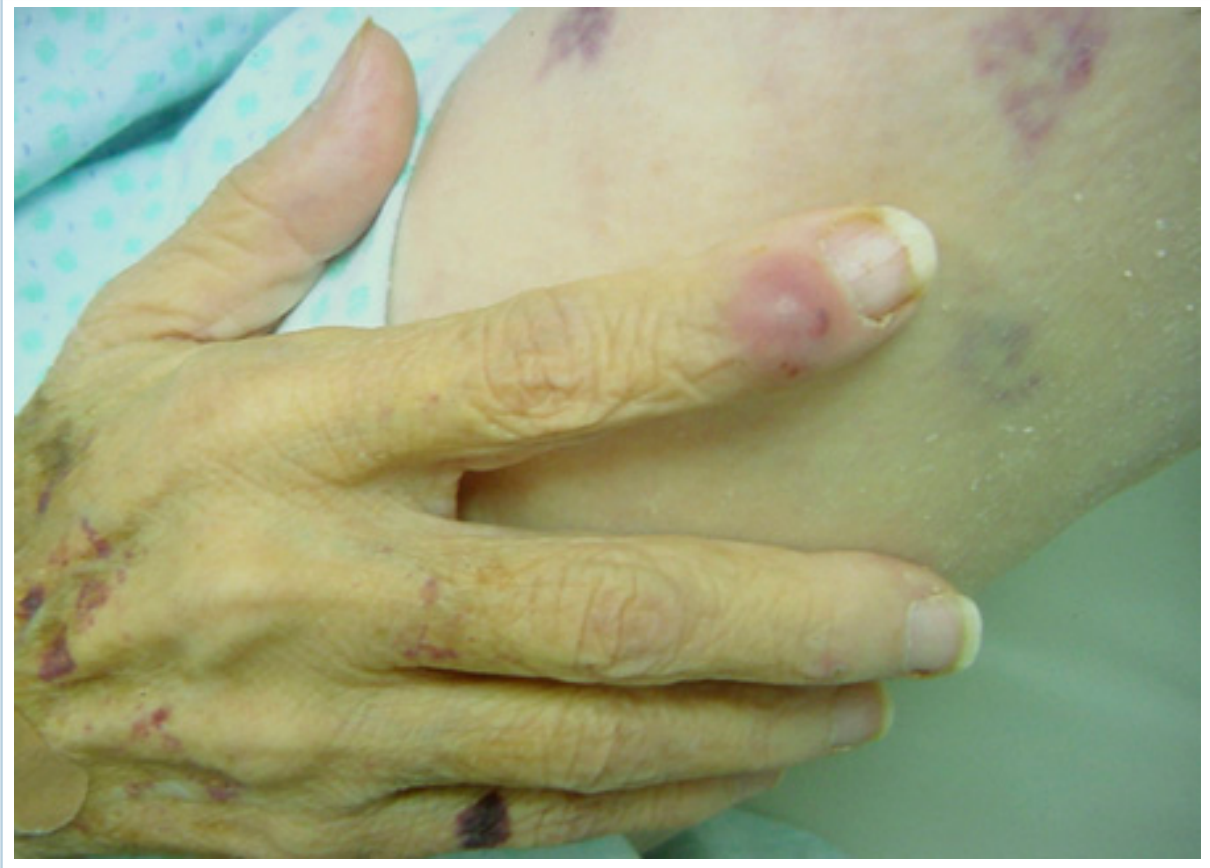
Cutaneous blastomycosis on the lower extremity

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



Cutaneous blastomycosis on the forearm

Personal files of Larry Baddour, MD



Cutaneous manifestation of disseminated blastomycosis

Personal files of Larry Baddour, MD

animal exposure (uncommon)

- A previous or coincident 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 neurologic 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

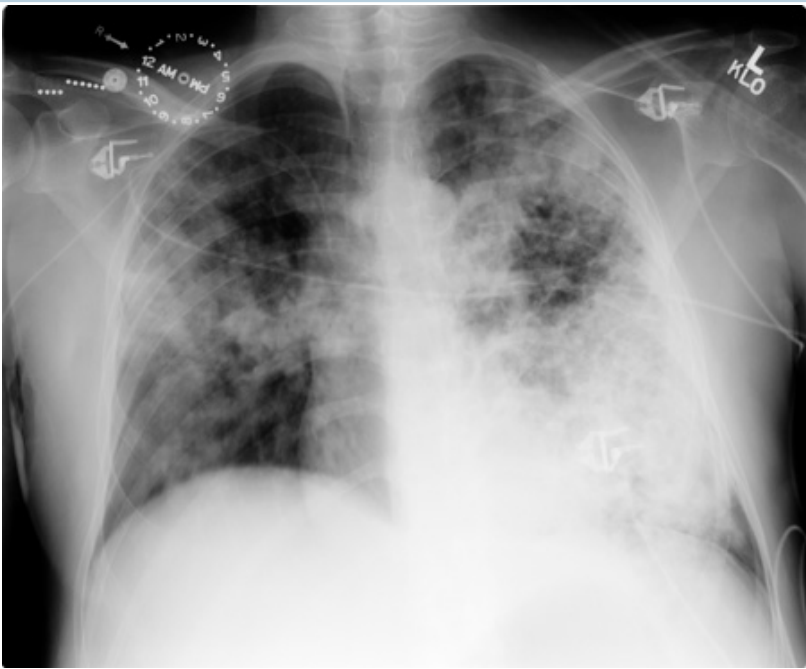
- Cases in men typically outnumber those in women, with a ratio between 4:1 and 15:1 depending on the series. However, this is generally thought to be secondary to increased environmental exposure in men as opposed to an actual sex predilection.[15]

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 defense of blastomycosis, and patients with HIV/AIDS generally have T-cell defects but intact neutrophil function.

Investigations

1st test to order

Test	Result
<p>Blastomyces dermatitidis enzyme immunoassay (EIA) urine antigen testing</p> <ul style="list-style-type: none"> 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]} 	<p>positive for <i>B dermatitidis</i> galactomannan antigen</p>
<p>chest x-ray</p> <ul style="list-style-type: none"> Posteroanterior and lateral chest radiograph 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.  <p><i>Pulmonary blastomycosis with focal infiltrates on chest radiograph</i> <i>Dr Robert Orenstein, DO, Associate Professor of Medicine,</i> <i>Division of Infectious Diseases, Mayo Clinic, Scottsdale, AZ</i></p>	<p>lobar pneumonia, mass-like or cavitory lesions, diffuse interstitial infiltrates, or signs of adult respiratory distress syndrome</p>

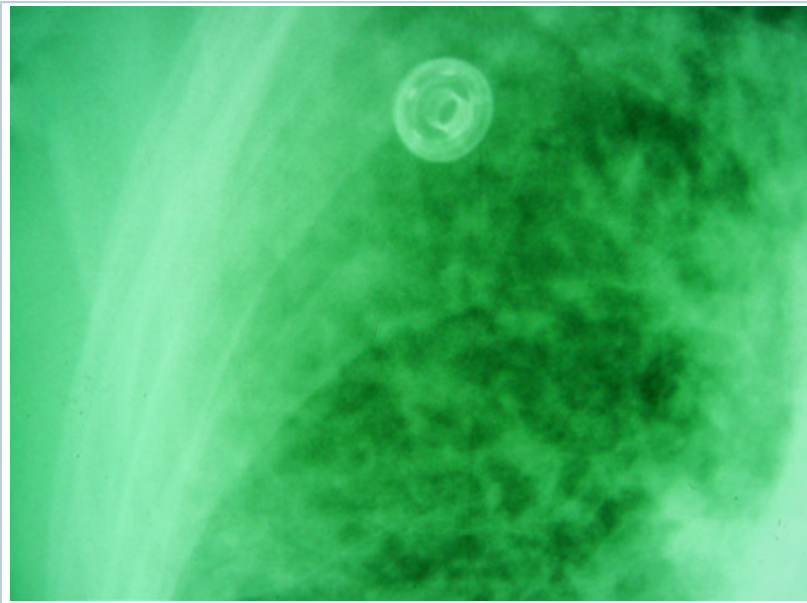
DIAGNOSIS

Test

Result



Pulmonary blastomycosis presenting as a miliary pattern on chest radiograph
 Dr Robert Orenstein, DO, Associate Professor of Medicine,
 Division of Infectious Diseases, Mayo Clinic, Scottsdale, AZ



Close up of reticulonodular findings on chest radiography in disseminated blastomycosis
 Personal files of Larry Baddour, MD

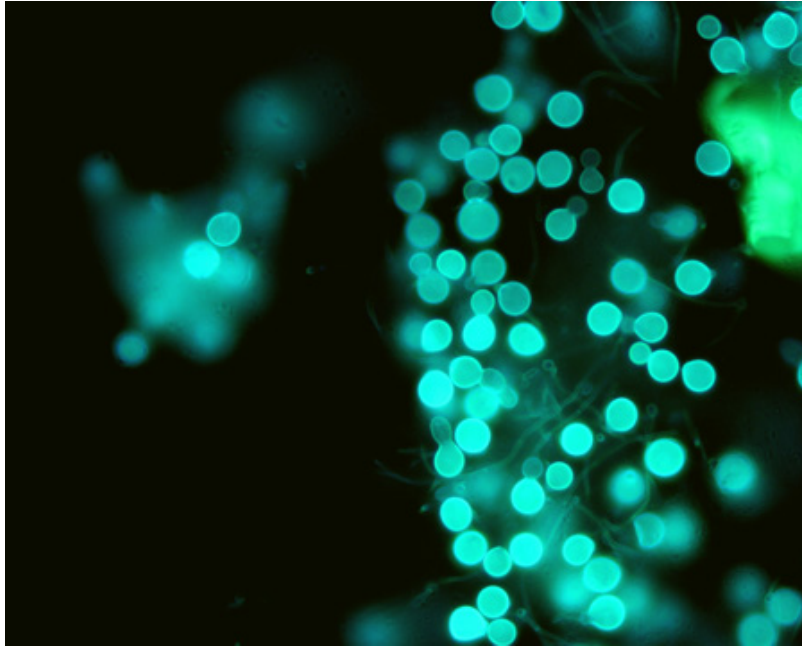
respiratory tract specimen smear and culture

- 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

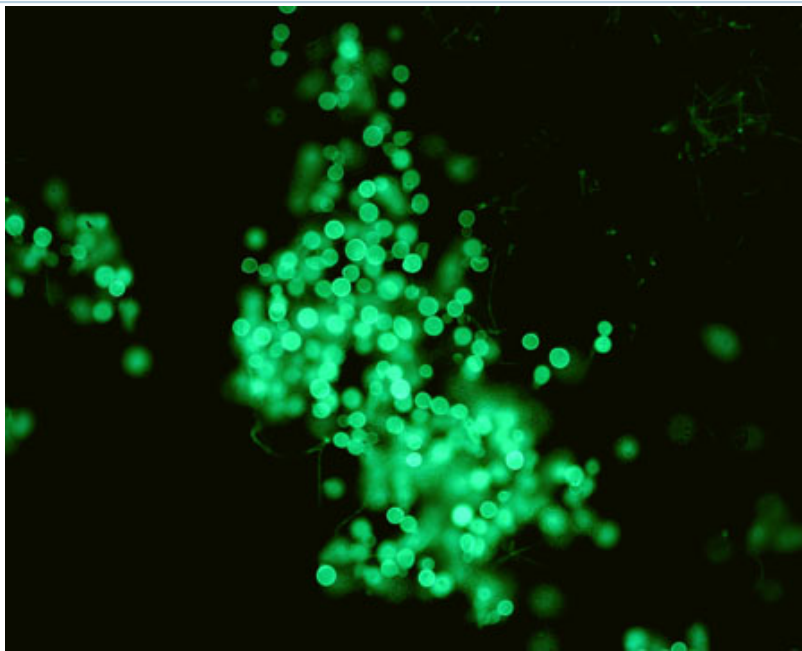
Test

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 and Lab Medicine, Mayo Clinic, Rochester, MN*



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

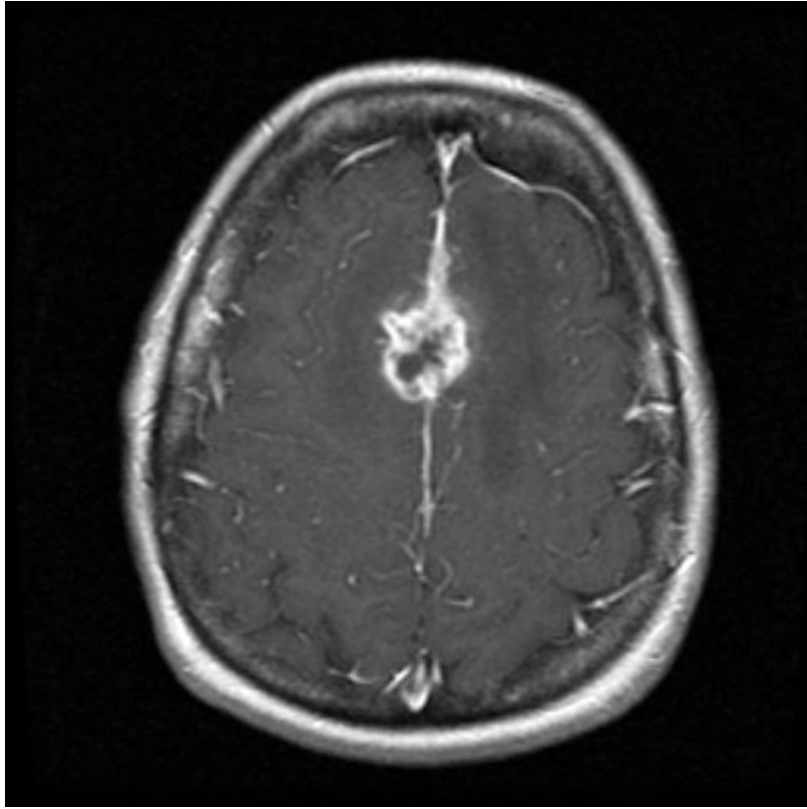
*Nancy L. Wengenack, PhD, D(ABMM), Director of Mycology
and Mycobacteriology Laboratories, Assistant Professor of
Microbiology and Lab Medicine, Mayo Clinic, Rochester, MN*

- 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
<p>diagnosis usually requires culture confirmation, which can take 2 to 4 weeks.</p> <ul style="list-style-type: none">• 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 mold form should be tested for <i>Blastomyces dermatitidis</i> with a commercially available DNA probe assay.	

Other tests to consider

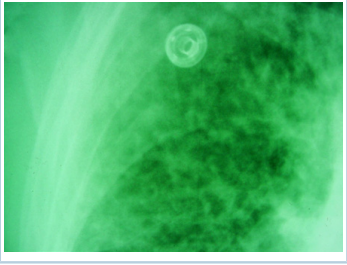
Test	Result
bronchoscopy <ul style="list-style-type: none"> Performed when sputum samples are unobtainable or nonrevealing in patients with pulmonary involvement. 	washings with large, oval, broad-based budding yeast; or tissue specimen with granuloma
tissue biopsy or cytology (lung, skin, or bone) <ul style="list-style-type: none"> Transbronchial biopsy of lung lesions, or biopsy of suspicious skin or bone lesions. 	acute inflammation with or without necrosis, granuloma formation, and multinucleated giant cells
arthrocentesis <ul style="list-style-type: none"> 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 <ul style="list-style-type: none"> Including complement fixation, immunodiffusion, and enzyme immunoassay, this measures antibodies to <i>Blastomyces dermatitidis</i>. 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 <ul style="list-style-type: none"> Positive fungal blood cultures can be seen in disseminated disease and offer a noninvasive diagnostic strategy. A negative fungal blood culture does not rule out disseminated disease. Can take up to 2 weeks for results. 	positive
MRI brain <ul style="list-style-type: none"> 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
 <p data-bbox="277 1016 1007 1104"><i>Axial T1 gadolinium-enhanced MRI image of cerebral blastomycosis</i> Dr William Marshall, MD, Assistant Professor of Medicine, Division of Infectious Diseases, Mayo Clinic, Rochester, MN</p>	
<p data-bbox="165 1122 727 1153">B dermatitidis#polymerase chain reaction</p> <ul data-bbox="201 1167 1011 1292" style="list-style-type: none"> • 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] 	<p data-bbox="1066 1122 1410 1184">presence of <i>Blastomyces dermatitidis</i></p>

Differentials

Condition	Differentiating signs / Differentiating tests symptoms	
<p>Community-acquired pneumonia</p>	<ul style="list-style-type: none"> Acute pulmonary blastomycosis is commonly mistaken for community-acquired pneumonia. Failure to respond to antibacterial therapy and extrapulmonary manifestations are clues to the etiology.[30] 	<ul style="list-style-type: none"> Findings of blastomycosis on chest radiograph can be atypical for community-acquired pneumonia, and include mass-like or cavitary lesions or diffuse interstitial infiltrates. <div data-bbox="1082 562 1426 846" data-label="Image"> </div> <p data-bbox="1118 871 1394 1099"><i>Pulmonary blastomycosis with focal infiltrates on chest radiograph</i> Dr Robert Orenstein, DO, Associate Professor of Medicine, Division of Infectious Diseases, Mayo Clinic, Scottsdale, AZ</p> <div data-bbox="1082 1144 1426 1429" data-label="Image"> </div> <p data-bbox="1107 1453 1406 1682"><i>Pulmonary blastomycosis presenting as a miliary pattern on chest radiograph</i> Dr Robert Orenstein, DO, Associate Professor of Medicine, Division of Infectious Diseases, Mayo Clinic, Scottsdale, AZ</p>

DIAGNOSIS

Condition	Differentiating signs / Differentiating tests symptoms	
		 <p data-bbox="1110 510 1401 712"><i>Close up of reticulonodular findings on chest radiography in disseminated blastomycosis</i> Personal files of Larry Baddour, MD</p> <ul data-bbox="1007 714 1430 965" style="list-style-type: none"> • A positive <i>Blastomyces dermatitidis</i> enzyme immunoassay (EIA) urine antigen test indicates probable acute pulmonary blastomycosis, though this may not be available in some centers.[30][31]
<p>Histoplasmosis</p>	<ul data-bbox="603 1037 954 1350" style="list-style-type: none"> • 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. 	<ul data-bbox="1007 1037 1430 1384" style="list-style-type: none"> • Differentiation between these 2 diseases often relies on culture data. <i>Histoplasma</i> yeast are typically smaller, have narrow-based budding, and are found intracellularly within macrophages in clinical specimens. There is some cross reactivity with serologic and antigen assays for these 2 organisms.
<p>Coccidioidomycosis</p>	<ul data-bbox="603 1417 946 1664" style="list-style-type: none"> • Coccidioidomycosis and blastomycosis share many of the same clinical manifestations. However, the endemic area of <i>Coccidioides</i> is the desert region of the southwestern US. 	<ul data-bbox="1007 1417 1430 1637" style="list-style-type: none"> • Serologic testing for coccidioidomycosis is of higher sensitivity than for blastomycosis, and the yeast in pathologic specimens appears as the characteristic spherule.
<p>Paracoccidioidomycosis</p>	<ul data-bbox="603 1697 938 1955" style="list-style-type: none"> • Acute/subacute paracoccidioidomycosis more often presents with lymphadenopathy, hepatosplenomegaly, and bone marrow dysfunction, while chronic paracoccidioidomycosis 	<ul data-bbox="1007 1697 1430 1984" style="list-style-type: none"> • <i>Paracoccidioides</i> yeast are typically smaller than <i>Blastomyces dermatitidis</i> 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
	<p>generally presents with dry cough and dyspnea.</p> <ul style="list-style-type: none"> Paracoccidioidomycosis is also endemic to Central and South America. 	
Sporotrichosis	<ul style="list-style-type: none"> The cutaneous lesions of sporotrichosis are similar in appearance to blastomycosis. However, lymphadenitis (generally nodular, and subacute to chronic) is pathognomonic in sporotrichosis. 	<ul style="list-style-type: none"> Microbiologic and pathologic examination of skin biopsies will yield the diagnosis.
Tuberculosis	<ul style="list-style-type: none"> Cutaneous disease is less common in tuberculosis than in blastomycosis. 	<ul style="list-style-type: none"> 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 sensitized lymphocytes are also helpful in diagnosis of tuberculosis.
Nocardiosis	<ul style="list-style-type: none"> Nocardiosis and blastomycosis share many of the same clinical features. <i>Nocardia</i> is more common in people who are immunocompromised and has a worldwide distribution. 	<ul style="list-style-type: none"> Microbiological examination of clinical specimens in nocardiosis reveals thin, branching gram-positive bacilli that stain positively by the modified acid fast stain. Culture of <i>Nocardia</i> species is confirmatory of that diagnosis.
Malignancy	<ul style="list-style-type: none"> The pulmonary, cutaneous, osteoarticular, and central nervous system manifestations of blastomycosis can all be mistaken for primary or metastatic neoplasms. 	<ul style="list-style-type: none"> Pathologic 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 hospitalization: more severe pulmonary disease, central nervous system or bone disease, or disease in pregnant or immunosuppressed patients. However, clinical judgment 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 microbiologic 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 medications with activity against *Blastomyces dermatitidis*. These include amphotericin-B preparations and azole antifungals.[2] Of the available azoles that have been studied in small randomized 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 judgment is involved in treatment decisions, and infectious diseases consultation should be considered in the management of hospitalized 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 workup of an acutely ill patient, the decision on whether to hospitalize a patient with an outpatient diagnosis of blastomycosis must be individualized. There are no formal guidelines that outline criteria for hospitalization 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 nonpregnant 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 hospitalized 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.

Hospitalized immunocompetent nonpregnant 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 centers. However, there is no evidence or expert consensus supporting this.[2]

Immunosuppressed nonpregnant 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 postdelivery 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 specialist 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, hypokalemia, and hypomagnesemia. 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 medication 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,

rechallenge with the same medication 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, hypokalemia, 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 dermatologic 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 nonpregnant adults			
	1st	itraconazole maintenance	
hospitalized immunocompetent nonpregnant adults			
<ul style="list-style-type: none"> ■ with CNS disease 	1st	amphotericin-B	
	plus	azole antifungal maintenance therapy	
<ul style="list-style-type: none"> ■ with pulmonary, osteoarticular, or genitourinary disease 	1st	amphotericin-B	
	plus	itraconazole maintenance therapy	
immunosuppressed nonpregnant adults with or without CNS disease			
	1st	amphotericin-B	
	plus	prolonged itraconazole maintenance therapy	
pregnant			
	1st	amphotericin-B	
	plus	postdelivery itraconazole maintenance therapy	
neonates <30 days old			
<ul style="list-style-type: none"> ■ without CNS disease 	1st	amphotericin-B deoxycholate	
<ul style="list-style-type: none"> ■ with CNS disease 	1st	amphotericin-B lipid formulation	
infants/children ≥30 days old			
<ul style="list-style-type: none"> ■ immunocompetent ambulatory 	1st	itraconazole	
<ul style="list-style-type: none"> ■ immunosuppressed or hospitalized: without CNS involvement 	1st	amphotericin-B deoxycholate	
	plus	itraconazole maintenance therapy	

Ongoing

(summary)

■ immunosuppressed or hospitalized: 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 nonpregnant 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, hypokalemia, and peripheral neuropathy. Azole antifungals undergo many significant drug-drug interactions.

hospitalized immunocompetent nonpregnant 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, hypokalemia, and hypomagnesemia.

plus azole antifungal maintenance therapy

Ongoing

■ with pulmonary, osteoarticular, or genitourinary disease

1st

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, hypokalemia, and peripheral neuropathy.

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

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, hypokalemia, and hypomagnesemia. 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

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, hypokalemia, and peripheral neuropathy. Azole antifungals undergo many significant drug-drug interactions.

immunosuppressed nonpregnant 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, hypokalemia, and hypomagnesemia. 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, hypokalemia, 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, hypokalemia, and hypomagnesemia.

» 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 postdelivery 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

» Providing 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 specialist 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, hypokalemia, 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**: consult specialist for guidance on dose

» The duration of treatment is not well defined.

» Amphotericin-B is associated with nephrotoxicity, hypokalemia, and hypomagnesemia.

■ with CNS disease

1st

amphotericin-B lipid formulation**Primary options**

» **amphotericin B lipid complex**: consult specialist for guidance on dose

OR

» **amphotericin B liposomal**: consult specialist for guidance on dose

» 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, hypokalemia, and hypomagnesemia.

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, hypokalemia, and

Ongoing

■ immunosuppressed or hospitalized: without CNS involvement

1st

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

amphotericin-B deoxycholate**Primary options**

» [amphotericin B deoxycholate](#): consult specialist for guidance on dose

» Amphotericin-B is associated with nephrotoxicity, hypokalemia, and hypomagnesemia.

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, hypokalemia, and peripheral neuropathy. Azole antifungals undergo many significant drug-drug interactions.

■ immunosuppressed or hospitalized: with CNS involvement

1st

amphotericin-B lipid formulation**Primary options**

» [amphotericin B lipid complex](#): consult specialist for guidance on dose

OR

» [amphotericin B liposomal](#): consult specialist for guidance on dose

» 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, hypokalemia, and hypomagnesemia.

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, hypokalemia, 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. Isavuconazonium, a prodrug of isavuconazole, has demonstrated in vitro activity against *Blastomyces dermatitidis*, but reported clinical use in this setting is limited.[47] [48] [49] Isavuconazonium is approved in the US and Europe (as isavuconazole) for the treatment of adults with invasive aspergillosis and mucormycosis.

Primary prevention

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

Secondary prevention

- The only secondary preventive 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 medication-related side effects, particularly the development of signs or symptoms of hepatotoxicity such as jaundice or stool color 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.

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

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 optimal to balance therapeutic efficacy and risk of toxicity.[53]
- 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.
- Radiographic abnormalities should be followed up with repeat exams every 1 to 3 months until resolution.
- It is important to monitor for drug interactions between the azole antifungals and other medications metabolized by the cytochrome P450 system, particularly warfarin (using INR) or statins (symptoms of rhabdomyolysis). However, routine laboratory monitoring for rhabdomyolysis is not warranted.

Complications

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

Prognosis

Prognosis

Although unrecognized and untreated blastomycosis can be a fatal disease, the prognosis for treated blastomycosis is quite good, with most symptoms and radiologic 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.[52]

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 serologic and skin antigen testing. However, this specific immunity is not necessarily protective, and reinfection can occur in the face of repeated exposure.

Diagnostic guidelines

International

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>) [30]

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>) [33]

Published by: American Thoracic Society Clinical Practice Guideline

Last published: 2019

Global guideline for the diagnosis and management of the endemic mycoses (<https://pubmed.ncbi.nlm.nih.gov/34364529/>) [2]

Published by: European Confederation of Medical Mycology; International Society for Human and Animal Mycology

Last published: 2021

Treatment guidelines

International

Endemic fungal infections in solid organ transplant recipients (<https://pubmed.ncbi.nlm.nih.gov/30924967>) [50]

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>) [51]

Published by: American Thoracic Society

Last published: 2011

Global guideline for the diagnosis and management of the endemic mycoses (<https://pubmed.ncbi.nlm.nih.gov/34364529/>) [2]

Published by: European Confederation of Medical Mycology; International Society for Human and Animal Mycology

Last published: 2021

Online resources

1. Centers for Disease Control and Prevention: fungal diseases - blastomycosis (<http://www.cdc.gov/fungal/diseases/blastomycosis/index.html>) (*external link*)
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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 \(http://www.ncbi.nlm.nih.gov/pubmed/34364529?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34364529?tool=bestpractice.bmj.com)
- Limper AH, Knox KS, Sarosi GA, et al. American Thoracic Society Fungal Working Group. An official American Thoracic Society statement: treatment of fungal infections in adult pulmonary and critical care patients. *Am J Respir Crit Care Med*. 2011 Jan 1;183(1):96-128. [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/21193785?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/21193785?tool=bestpractice.bmj.com)

References

1. Castillo CG, Kauffman CA, Miceli MH. Blastomycosis. *Infect Dis Clin North Am*. 2016 Mar;30(1):247-64. [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/26739607?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/26739607?tool=bestpractice.bmj.com)
2. 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 \(http://www.ncbi.nlm.nih.gov/pubmed/34364529?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34364529?tool=bestpractice.bmj.com)
3. Wheat LJ. Antigen detection, serology, and molecular diagnosis of invasive mycoses in the immunocompromised host. *Transpl Infect Dis*. 2006 Sep;8(3):128-39. [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/16913971?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/16913971?tool=bestpractice.bmj.com)
4. Linder KA, Kauffman CA, Miceli MH. Blastomycosis: a review of mycological and clinical aspects. *J Fungi (Basel)*. 2023 Jan 14;9(1):117. [Full text \(https://www.mdpi.com/2309-608X/9/1/117\)](https://www.mdpi.com/2309-608X/9/1/117) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/36675937?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/36675937?tool=bestpractice.bmj.com)
5. McBride JA, Gauthier GM, Klein BS. Clinical manifestations and treatment of blastomycosis. *Clin Chest Med*. 2017 Sep;38(3):435-49. [Full text \(https://www.doi.org/10.1016/j.ccm.2017.04.006\)](https://www.doi.org/10.1016/j.ccm.2017.04.006) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/28797487?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/28797487?tool=bestpractice.bmj.com)
6. Schwartz IS, Muñoz JF, Kenyon CR, et al. Blastomycosis in Africa and the Middle East: a comprehensive review of reported cases and reanalysis of historical isolates based on molecular data. *Clin Infect Dis*. 2021 Oct 5;73(7):e1560-9. [Full text \(https://www.doi.org/10.1093/cid/ciaa1100\)](https://www.doi.org/10.1093/cid/ciaa1100) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/32766820?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/32766820?tool=bestpractice.bmj.com)
7. Yamely RV, Andrés SV, María CVA, et al. Cutaneous and pulmonary blastomycosis infection: a case report. *Oral Surgery Oral Medicine Oral Pathology Oral Radiology*. 2021 Jul;132(1):E38-9.

Full text ([https://www.oooojournal.net/article/S2212-4403\(21\)00324-2/abstract](https://www.oooojournal.net/article/S2212-4403(21)00324-2/abstract)) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/insert?id?tool=bestpractice.bmj.com>)

8. Klein BS, Davis JP. A laboratory based surveillance of human blastomycosis in Wisconsin between 1973 and 1982. *Am J Epidemiol*. 1985 Nov;122(5):897-903. Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/4050777?tool=bestpractice.bmj.com>)
9. Centers for Disease Control and Prevention. Surveillance for Coccidioidomycosis, Histoplasmosis, and Blastomycosis - United States, 2019. Aug 2022 [internet publication]. Full text (<https://www.cdc.gov/mmwr/volumes/71/ss/ss7107a1.htm>)
10. Mazi PB, Sahrman JM, Olsen MA, et al. The geographic distribution of dimorphic mycoses in the United States for the modern era. *Clin Infect Dis*. 2023 Apr 3;76(7):1295-301. Full text (<https://www.doi.org/10.1093/cid/ciac882>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/36366776?tool=bestpractice.bmj.com>)
11. McDonald R, Dufort E, Jackson BR, et al. Notes from the field: Blastomycosis cases occurring outside of regions with known endemicity - New York, 2007-2017. *MMWR Morb Mortal Wkly Rep*. 2018 Sep 28;67(38):1077-1078. Full text (<https://www.cdc.gov/mmwr/volumes/67/wr/mm6738a8.htm>) Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/30260940?tool=bestpractice.bmj.com>)
12. Centers for Disease Control and Prevention. Using insurance claims data to estimate blastomycosis incidence, Vermont, USA, 2011-2020. Feb 2024 [internet publication]. Full text (https://wwwnc.cdc.gov/eid/article/30/2/23-0825_article#r6)
13. Crampton TL, Light RB, Berg GM, et al. Epidemiology and clinical spectrum of blastomycosis diagnosed at Manitoba hospitals. *Clin Infect Dis*. 2002 May 15;34(10):1310-6. Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/11981725?tool=bestpractice.bmj.com>)
14. Morris SK, Brophy J, Richardson SE, et al. Blastomycosis in Ontario, 1994-2003. *Emerg Infect Dis*. 2006 Feb;12(2):274-9. Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/16494754?tool=bestpractice.bmj.com>)
15. Klein BS, Vergeront JM, Davis JP. Epidemiologic aspects of blastomycosis, the enigmatic systemic mycosis. *Semin Respir Infect*. 1986 Mar;1(1):29-39. Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/3317597?tool=bestpractice.bmj.com>)
16. Klein BS, Vergeront JM, DiSalvo AF, et al. Two outbreaks of blastomycosis along rivers in Wisconsin. *Am Rev Respir Dis*. 1987 Dec;136(6):1333-8. Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/3688635?tool=bestpractice.bmj.com>)
17. Frean JA, Carman WF, Crew-Browne HH, et al. Blastomyces dermatitidis infections in the RSA. *S Afr Med J*. 1989 Jul 1;76(1):13-6. Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/2662433?tool=bestpractice.bmj.com>)
18. Carman WF, Frean JA, Crew-Browne HH, et al. Blastomycosis in Africa. *Mycopathologia*. 1989 Jul;107(1):25-32. Abstract (<http://www.ncbi.nlm.nih.gov/pubmed/2682252?tool=bestpractice.bmj.com>)
19. Larone D. Medically important fungi, a guide to identification. Herndon, VA: ASM Press; 2018.

20. Baumgardner DJ, Paretsky DP. The in vitro isolation of *Blastomyces dermatitidis* from a woodpile in north central Wisconsin, USA. *Med Mycol*. 1999 Jun;37(3):163-8. [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/10421847?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/10421847?tool=bestpractice.bmj.com)
21. Brown EM, McTaggart LR, Zhang SX, et al. Phylogenetic analysis reveals a cryptic species *Blastomyces gilchristii*, sp. nov. within the human pathogenic fungus *Blastomyces dermatitidis*. *PLoS One*. 2013;8(3):e59237. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3606480\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3606480) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/23533607?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/23533607?tool=bestpractice.bmj.com)
22. Dukik K, Muñoz JF, Jiang Y, et al. Novel taxa of thermally dimorphic systemic pathogens in the Ajellomycetaceae (Onygenales). *Mycoses*. 2017 May;60(5):296-309. [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/28176377?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/28176377?tool=bestpractice.bmj.com)
23. Bradsher RW, Chapman SW, Pappas PG. Blastomycosis. *Infect Dis Clin N Am*. 2003 Mar;17(1):21-40, vii. [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/12751259?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/12751259?tool=bestpractice.bmj.com)
24. Gray N, Baddour L. Cutaneous inoculation blastomycosis. *Clin Infect Dis*. 2002 May 15;34(10):E44-9. [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/11981746?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/11981746?tool=bestpractice.bmj.com)
25. Vaaler AK, Bradsher RW, Davies SF. Evidence of subclinical blastomycosis in forestry workers in northern Minnesota and northern Wisconsin. *Am J Med*. 1990 Oct;89(4):470-6. [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/2220880?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/2220880?tool=bestpractice.bmj.com)
26. Habte-Gabr E, Smith IM. North American blastomycosis in Iowa: review of 34 cases. *J Chronic Dis*. 1973 Sep;26(9):585-94. [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/4759582?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/4759582?tool=bestpractice.bmj.com)
27. Lowry PW, Kelso KY, McFarland LM. Blastomycosis in Washington, Parish, Louisiana, 1976-1985. *Am J Epidemiol*. 1989 Jul;130(1):151-9. [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/2787106?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/2787106?tool=bestpractice.bmj.com)
28. Frye MD, Seifer FD. An outbreak of blastomycosis in eastern Tennessee. *Mycopathologia*. 1991 Oct;116(1):15-21. [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/1766458?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/1766458?tool=bestpractice.bmj.com)
29. Gauthier GM, Safdar N, Klein BS, et al. Blastomycosis in solid organ transplant recipients. *Transpl Infect Dis*. 2007 Dec;9(4):310-7. [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/17428278?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/17428278?tool=bestpractice.bmj.com)
30. Smith DJ, Free RJ, Thompson GR 3rd, et al. Clinical testing guidance for coccidioidomycosis, histoplasmosis, and blastomycosis in patients with community-acquired pneumonia for primary and urgent care providers. *Clin Infect Dis*. 2024 Jun 14;78(6):1559-63. [Full text \(https://www.doi.org/10.1093/cid/ciad619\)](https://www.doi.org/10.1093/cid/ciad619) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/37802909?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/37802909?tool=bestpractice.bmj.com)
31. Centers for Disease Control and Prevention. Blastomycosis: testing algorithm for blastomycosis. Apr 2024 [internet publication]. [Full text \(https://www.cdc.gov/blastomycosis/hcp/testing-algorithm\)](https://www.cdc.gov/blastomycosis/hcp/testing-algorithm)

32. Linder KA, Kauffman CA. Current and new perspectives in the diagnosis of blastomycosis and histoplasmosis. *J Fungi (Basel)*. 2020 Dec 29;7(1). [Full text \(https://www.doi.org/10.3390/jof7010012\)](https://www.doi.org/10.3390/jof7010012) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/33383637?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/33383637?tool=bestpractice.bmj.com)
33. Hage CA, Carmona EM, Epelbaum O, et al. Microbiological Laboratory Testing in the Diagnosis of Fungal Infections in Pulmonary and Critical Care Practice. An Official American Thoracic Society Clinical Practice Guideline. *Am J Respir Crit Care Med*. 2019 Sep 1;200(5):535-50. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6727169\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6727169) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/31469325?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/31469325?tool=bestpractice.bmj.com)
34. Berger J, Zamora F, Podgaetz E, et al. Usefulness of lymphoid granulomatous inflammation culture obtained by endobronchial ultrasound-guided transbronchial needle aspiration in a fungal endemic area. *Endosc Ultrasound*. 2016 Jul-Aug;5(4):243-7. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4989405\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4989405) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/27503156?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/27503156?tool=bestpractice.bmj.com)
35. Taxy JB. Blastomycosis: contributions of morphology to diagnosis. *Am J Surg Pathol*. 2007 Apr;31(4):615-23. [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/17414110?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/17414110?tool=bestpractice.bmj.com)
36. Mazi PB, Rauseo AM, Spec A. Blastomycosis. *Infect Dis Clin North Am*. 2021 Jun;35(2):515-30. [Full text \(https://www.doi.org/10.1016/j.idc.2021.03.013\)](https://www.doi.org/10.1016/j.idc.2021.03.013) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/34016289?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/34016289?tool=bestpractice.bmj.com)
37. Centers for Disease Control and Prevention. Blastomycosis: clinical overview of blastomycosis. Apr 2024 [internet publication]. [Full text \(https://www.cdc.gov/blastomycosis/hcp/clinical-overview/index.html\)](https://www.cdc.gov/blastomycosis/hcp/clinical-overview/index.html)
38. Babady NE, Buckwalter SP, Hall L, et al. Detection of Blastomyces dermatitidis and Histoplasma capsulatum from culture isolates and clinical specimens by use of real-time PCR. *J Clin Microbiol*. 2011 Sep;49(9):3204-8. [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/21752970?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/21752970?tool=bestpractice.bmj.com)
39. Sidamonidze K, Peck MK, Perez M, et al. Real-time PCR assay for identification of Blastomyces dermatitidis in culture and in tissue. *J Clin Microbiol*. 2012 May;50(5):1783-6. [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/22403418?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/22403418?tool=bestpractice.bmj.com)
40. Frost HM, Novicki TJ. Blastomyces antigen detection for diagnosis and management of blastomycosis. *J Clin Microbiol*. 2015 Nov;53(11):3660-2. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4609701\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4609701) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/26338856?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/26338856?tool=bestpractice.bmj.com)
41. National Institute of Allergy and Infectious Diseases Mycoses Study Group. Treatment of blastomycosis and histoplasmosis with ketoconazole. *Ann Intern Med*. 1985 Dec;103(6 (Pt 1)):861-72. [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/2865921?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/2865921?tool=bestpractice.bmj.com)
42. Dismukes WE, Bradsher RW Jr, Cloud GC, et al. Itraconazole therapy for blastomycosis and histoplasmosis. NIAID Mycoses Study Group. *Am J Med*. 1992 Nov;93(5):489-97. [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/1332471?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/1332471?tool=bestpractice.bmj.com)

43. Pappas PG, Bradsher RW, Chapman SW, et al. Treatment of blastomycosis with fluconazole: a pilot study. *Clin Infect Dis*. 1995 Feb;20(2):267-71. [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/7742428?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/7742428?tool=bestpractice.bmj.com)
44. Ta M, Flowers SA, Rogers PD. The role of voriconazole in the treatment of central nervous system blastomycosis. *Ann Pharmacother*. 2009 Oct;43(10):1696-700. [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/19724015?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/19724015?tool=bestpractice.bmj.com)
45. Freifeld A, Proia L, Andes D, et al. Voriconazole use for endemic fungal infections. *Antimicrob Agents Chemother*. 2009 Apr;53(4):1648-51. [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/19139290?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/19139290?tool=bestpractice.bmj.com)
46. Bariola JR, Perry P, Pappas PG, et al. Blastomycosis of the central nervous system: a multicenter review of diagnosis and treatment in the modern era. *Clin Infect Dis*. 2010 Mar 15;50(6):797-804. [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/20166817?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/20166817?tool=bestpractice.bmj.com)
47. Yamazaki T, Inagaki Y, Fujii T, et al. In vitro activity of isavuconazole against 140 reference fungal strains and 165 clinically isolated yeasts from Japan. *Int J Antimicrob Agents*. 2010 Oct;36(4):324-31. [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/20674282?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/20674282?tool=bestpractice.bmj.com)
48. Thompson GR 3rd, Rendon A, Ribeiro Dos Santos R, et al. Isavuconazole treatment of cryptococcosis and dimorphic mycoses. *Clin Infect Dis*. 2016 Aug 1;63(3):356-62. [Full text \(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4946023\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4946023) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/27169478?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/27169478?tool=bestpractice.bmj.com)
49. Sclarici MJ, King C, Sterkel A, et al. The role of Isavuconazonium Sulphate for the treatment of blastomycosis: a case series and antifungal susceptibility. *Open Forum Infect Dis*. 2022 Jul;9(7):ofac220. [Full text \(https://www.doi.org/10.1093/ofid/ofac220\)](https://www.doi.org/10.1093/ofid/ofac220) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/35821730?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/35821730?tool=bestpractice.bmj.com)
50. Miller R, Assi M, AST Infectious Diseases Community of Practice. Endemic fungal infections in solid organ transplant recipients-Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. *Clin Transplant*. 2019 Sep;33(9):e13553. [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/30924967?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/30924967?tool=bestpractice.bmj.com)
51. Limper AH, Knox KS, Sarosi GA, et al. American Thoracic Society Fungal Working Group. An official American Thoracic Society statement: treatment of fungal infections in adult pulmonary and critical care patients. *Am J Respir Crit Care Med*. 2011 Jan 1;183(1):96-128. [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/21193785?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/21193785?tool=bestpractice.bmj.com)
52. Carignan A, Denis M, Abou Chakra CN. Mortality associated with Blastomyces dermatitidis infection: a systematic review of the literature and meta-analysis. *Med Mycol*. 2020 Jan 1;58(1):1-10. [Full text \(https://www.doi.org/10.1093/mmy/myz048\)](https://www.doi.org/10.1093/mmy/myz048) [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/31111911?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/31111911?tool=bestpractice.bmj.com)
53. Hope WW, Billaud EM, Lestner J, et al. Therapeutic drug monitoring for triazoles. *Curr Opin Infect Dis*. 2008 Dec;21(6):580-6. [Abstract \(http://www.ncbi.nlm.nih.gov/pubmed/18978525?tool=bestpractice.bmj.com\)](http://www.ncbi.nlm.nih.gov/pubmed/18978525?tool=bestpractice.bmj.com)

Images

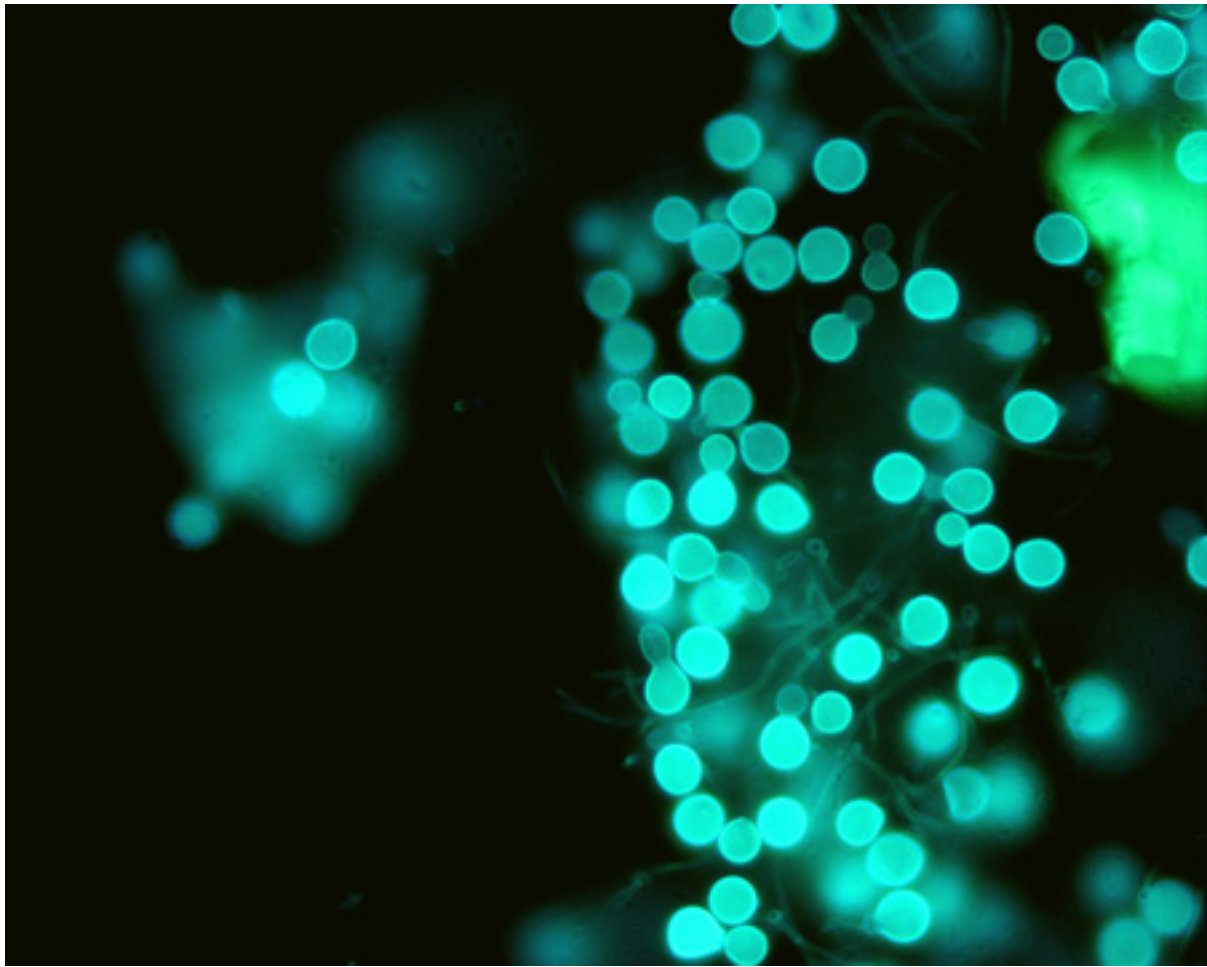


Figure 1: Direct potassium hydroxide preparation at 40x magnification of a sputum specimen

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

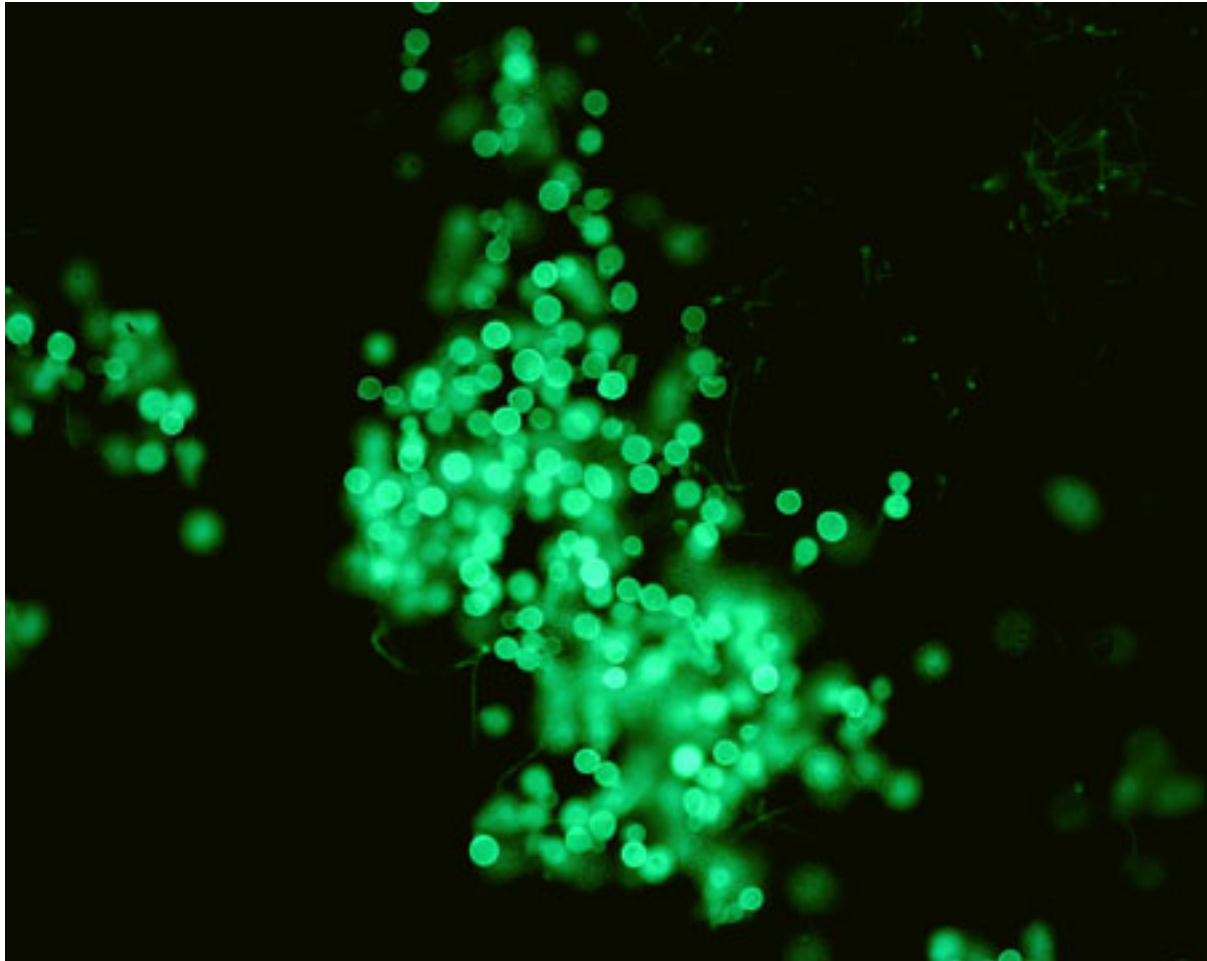


Figure 2: Direct potassium hydroxide preparation at 20x magnification of a sputum specimen

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

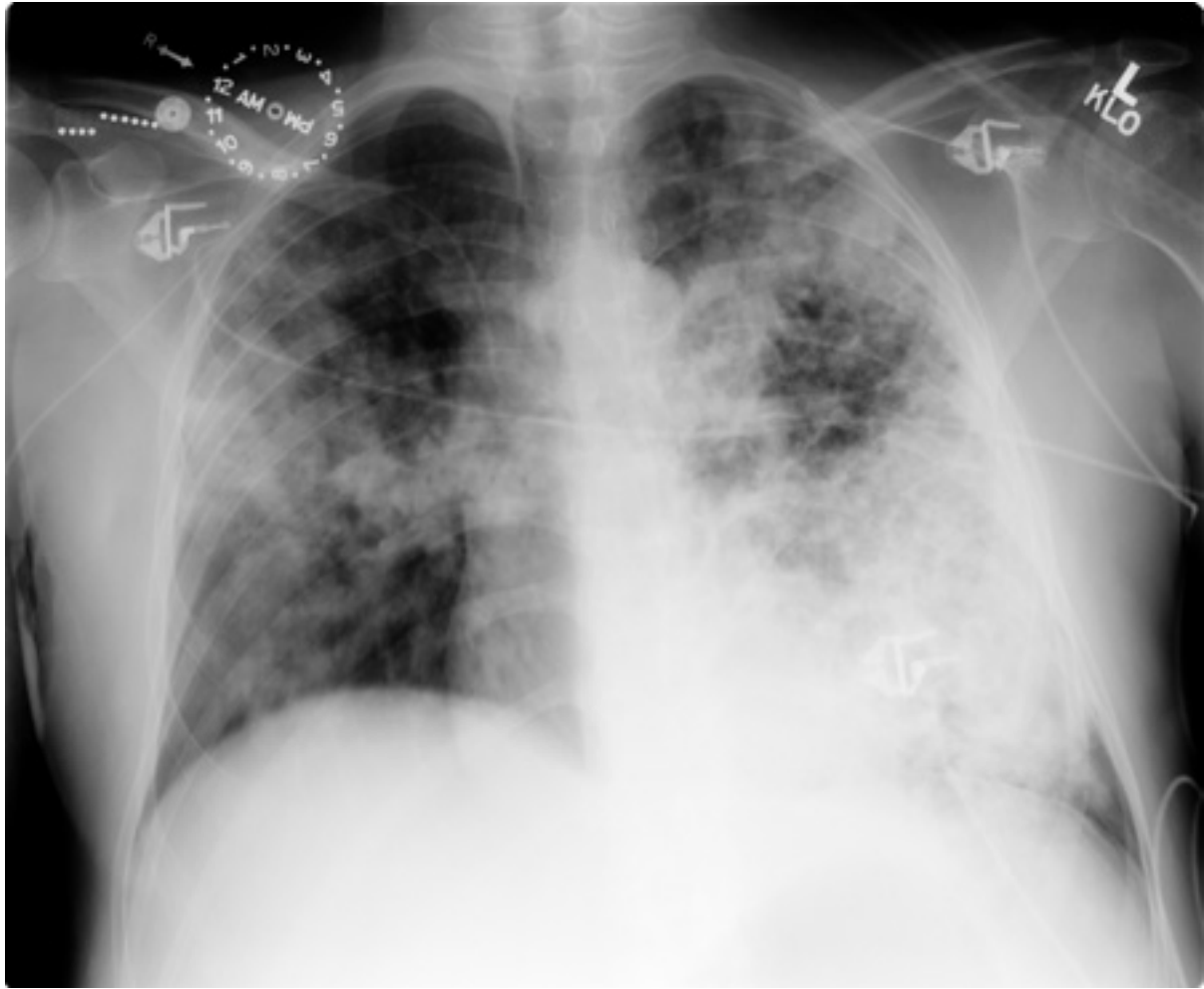


Figure 3: Pulmonary blastomycosis with focal infiltrates on chest radiograph

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



Figure 4: Pulmonary blastomycosis presenting as a miliary pattern on chest radiograph

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



Figure 5: Cutaneous blastomycosis on the lower extremity

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



Figure 6: Cutaneous blastomycosis on the lower extremity

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

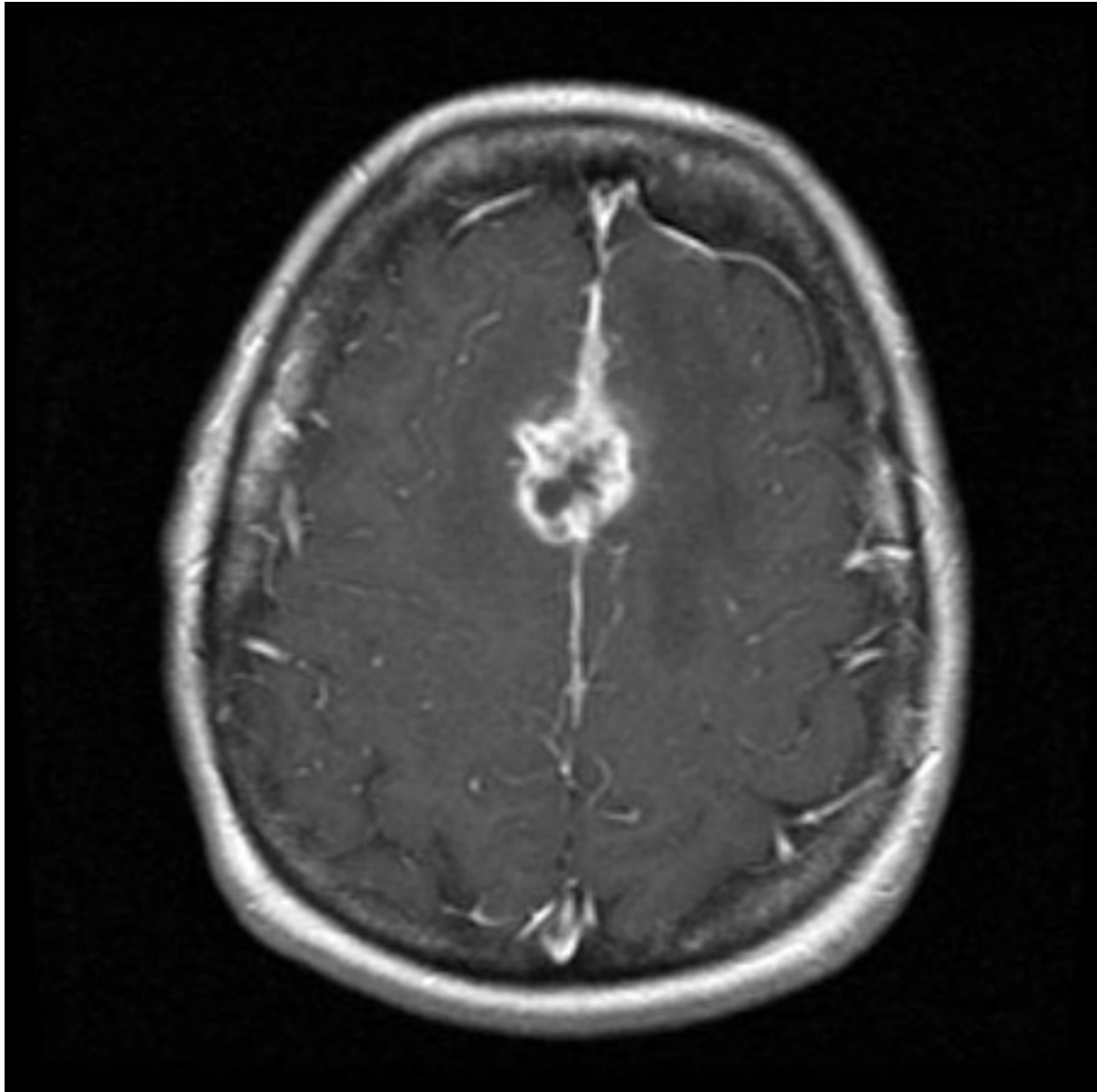


Figure 7: Axial T1 gadolinium-enhanced MRI image of cerebral blastomycosis

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

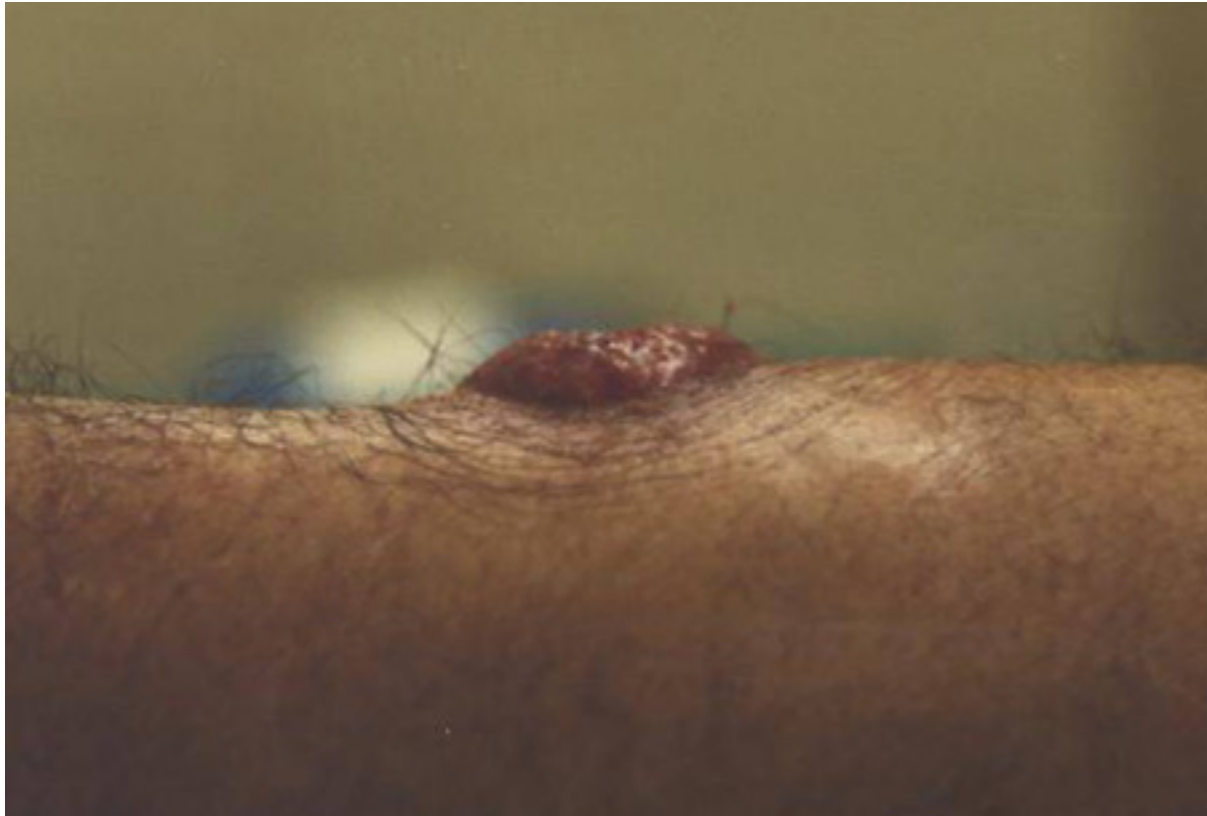


Figure 8: Cutaneous blastomycosis on the forearm

Personal files of Larry Baddour, MD



Figure 9: Cutaneous manifestation of disseminated blastomycosis

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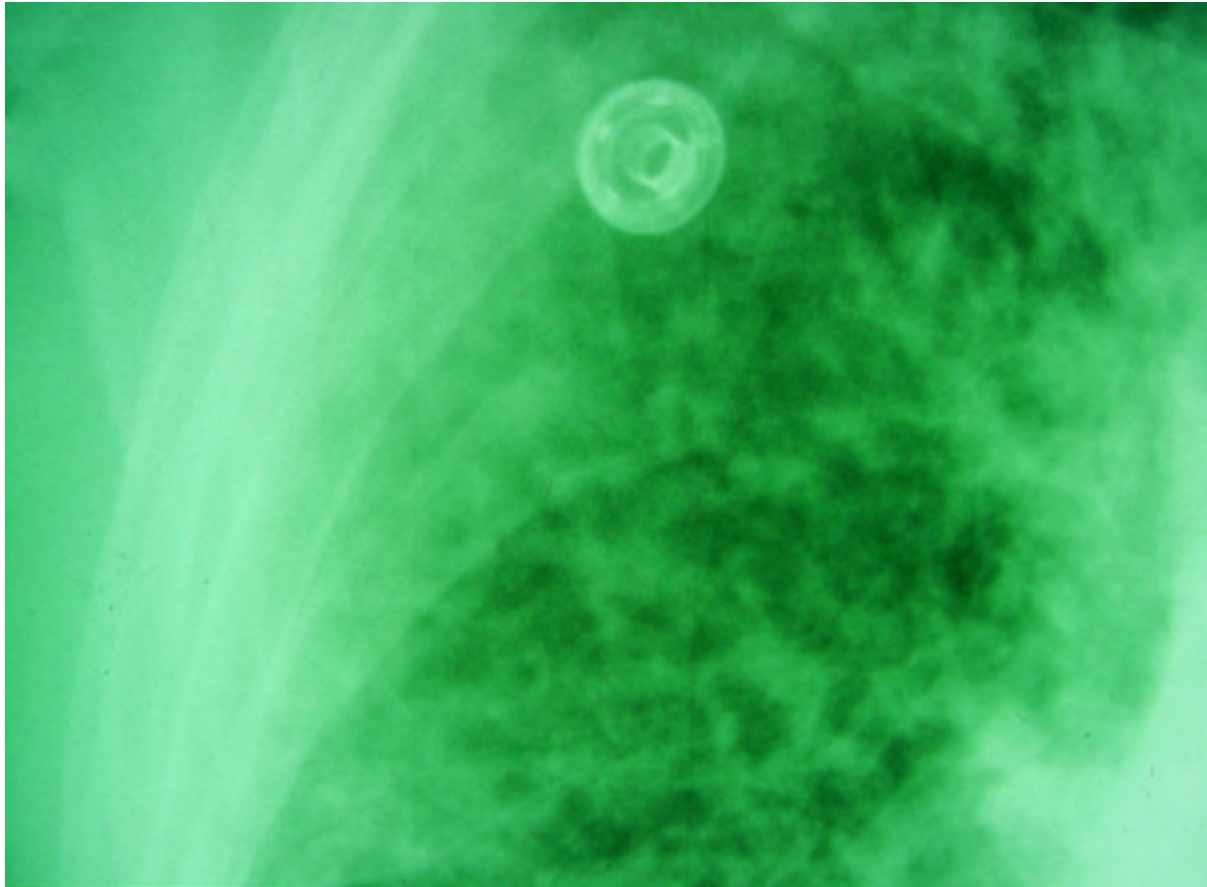


Figure 10: Close up of reticulonodular findings on chest radiography in disseminated blastomycosis

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Figure 1 – BMJ Best Practice Numeral Style

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