

**19-ID-02****Committee:** Infectious Disease**Title:** Standardized Surveillance Case Definition for Blastomycosis

Check this box if this position statement is an update to an existing standardized surveillance case definition and include the most recent position statement number here: N/A.

**Synopsis:**

This position statement creates a standardized surveillance case definition for blastomycosis.

**I. Statement of the Problem**

Blastomycosis, caused by the dimorphic fungus *Blastomyces* (most commonly the species *B. dermatitidis* and *B. gilchristii*), can cause a spectrum of disease ranging from subclinical to influenza-like illness to disseminated infection. It is acquired by inhaling airborne spores from the environment, particularly in areas with moist soil and decomposing organic material near fresh water (1, 2). Most symptomatic infections likely involve self-limited pulmonary disease, although these infections are rarely diagnosed. Disseminated infections and life-threatening pulmonary disease are a major concern with blastomycosis, and a better understanding of the disease's epidemiology could lead to improved primary and secondary prevention measures. In the United States, cases of blastomycosis occur primarily in midwestern, south-central, and southeastern states, particularly areas surrounding the Ohio and Mississippi River valleys, the Great Lakes, and the Saint Lawrence River (3, 4). However, the geographic distribution of blastomycosis remains poorly understood and can be highly focal even within endemic areas. Additional pockets of disease likely occur outside of these regions. Compounding the problem, *Blastomyces* is very difficult to isolate directly from the environment and the lack of standardized or commercially available testing for environmental specimens frustrates many wanting to avoid or investigate environmental exposures (4, 5). No national standardized case definition or reporting protocol exists for blastomycosis in the United States, limiting our understanding of its epidemiology and how and why sporadic cases and outbreaks occur. This position statement proposes a standardized surveillance case definition for blastomycosis.

**II. Background and Justification**

Blastomycosis is a rare disease, though the true number of cases is unknown and difficult to estimate. Most cases occur in the United States and Canada. In states where blastomycosis is reportable, yearly incidence rates are ~1–2 cases per 100,000 (6), and up to 40 per 100,000 in some localized areas (7). About 600 patients died of blastomycosis during 1999–2017 (8). However, these figures likely underestimate the true burden of blastomycosis given substantial under-diagnosis. Many more cases may occur within and outside of the region considered endemic. The lack of standard case definition and inconsistencies in reporting make it difficult to accurately estimate its true incidence and range (9).

Infection can occur following inhalation or inoculation of *Blastomyces* spores from the environment. Symptoms usually begin 3–15 weeks after exposure (9). The clinical presentation of blastomycosis can vary considerably from mild, acute, flu-like illness to severe, chronic, disseminated disease (1, 10, 11). Many mild cases are self-limiting and go unreported (1, 12). Primary infection of the skin following traumatic inoculation occurs rarely (9). Approximately 25% of reported cases of blastomycosis involve disseminated disease, usually with skin, bone or central nervous system lesions. Unfortunately, there are no pathognomonic signs of blastomycosis. The variable course and nonspecific symptoms of blastomycosis commonly lead to delayed or missed diagnosis (1). Lack of physician awareness of

blastomycosis may also contribute to under-diagnosis and reporting (1, 2). Treatment usually involves itraconazole for patients with mild to moderate disease and amphotericin B for more severe cases (1, 11).

Many laboratory methods are available for blastomycosis diagnosis, including culture, histopathology, cytopathology, molecular assays, and antigen and antibody tests. Use of >1 test is often beneficial, as each has advantages and disadvantages (Appendix 1). These diagnostic challenges also contribute to a delay in blastomycosis diagnosis, causing unnecessary use of empiric antibiotics for presumed bacterial pneumonia, and increased morbidity and mortality (13).

In 2019, blastomycosis is reportable in Arkansas, Louisiana, Michigan, Minnesota, and Wisconsin (14). The case definitions vary by state, and although most include broadly similar criteria, the differences limit data comparability. Additionally, the jurisdictions collect different laboratory, clinical, and epidemiological data. Cases occurring in states where blastomycosis is emerging, such as New York, should be reported to public health departments. Outside of these states, cases may be reported when an unusual cluster of infections is identified (15). Standardized public health surveillance can improve our ability to detect temporal trends, geographic hotspots, and emerging risk factors with an aim toward improving patient and provider awareness, clinical diagnosis, and prevention recommendations.

The blastomycosis consensus case definition was developed in response to a common desire of states with reporting, states investigating clusters, and CDC for more robust and impactful surveillance for this disease. This case definition is intended for the standardized reporting of cases and is not intended for clinical decision making. It will allow for collection and comparison of standardized data, incidence rates, and disease trends in states conducting blastomycosis surveillance or investigations.

### **III. Statement of the desired action(s) to be taken**

CSTE recommends the following actions:

1. Implement a standardized surveillance case definition for blastomycosis.
  - A. Utilize standard sources (e.g. reporting\*) for case ascertainment for blastomycosis. Surveillance for blastomycosis should use the recommended sources of data to the extent of coverage presented in Section V/Table V.
  - B. Utilize standardized criteria for case identification for blastomycosis presented in Section VI and Table VI in Technical Supplement.
  - C. Utilize standardized criteria for case classification for blastomycosis presented in Sections VII and Table VII in Technical Supplement.

\*Reporting: process of a healthcare provider or other entity submitting a report (case information) of a condition under public health surveillance to local, state, or territorial public health. Note: notification is addressed in a Nationally Notifiable Conditions Recommendation Statement and is the process of a local, state, or territorial public health authority submitting a report (case information) of a condition on the *Nationally Notifiable Conditions List* TO CDC.

### **IV. Goals of Surveillance**

To provide information on the temporal, geographic, and demographic features of outbreak-associated and sporadic blastomycosis cases in the United States. These data will inform understanding of risk factors, including geographic risk, and changing trends, allowing for improved public and medical outreach and clinical decision making, which are essential for reducing delays in diagnosis and treatment.

**V. Methods for Surveillance: Surveillance for blastomycosis should use the recommended sources of data and the extent of coverage listed in Table V.**

Laboratory reporting will be the most common source of data. Electronically-generated reports for positive tests should be reported, as well as microbiology and pathology reports identifying suspected *Blastomyces*, which may require manual records review. In states where blastomycosis is reportable, laboratories should report all tests meeting the criteria listed in Section VI subsection A to public health authorities. Additionally, healthcare providers and facilities who diagnose or become aware of blastomycosis cases should report them to public health authorities. Other data sources (e.g. hospital discharge data, diagnosis codes or death certificates) may be used as supplementary case finding methods.

**Table V. Recommended sources of data and extent of coverage for ascertainment of cases of blastomycosis.**

Source of data for case ascertainment	Coverage	
	Population-wide	Sentinel sites
Clinician reporting	X	
Laboratory reporting	X	
Reporting by other entities (e.g., hospitals, veterinarians, pharmacies, poison centers), specify:	X	
Death certificates	X	
Hospital discharge or outpatient records	X	
Data from electronic medical records	X	
Telephone survey		
School-based survey		
Other, specify:		

2019 Template

**VI. Criteria for case ascertainment**

**A. Narrative: A description of suggested criteria for case ascertainment of a specific condition.**

In public health jurisdictions where blastomycosis is classified as a reportable disease, clinicians, laboratories, and healthcare facilities should report to public health authorities based on the below criteria.

Reporting should be all-inclusive, ongoing, and routine. Reporting should occur in a timeframe consistent with local jurisdiction rules.

**A1. Clinical Criteria for Reporting**

**A2. Laboratory Criteria for Reporting**

Any of the following laboratory criteria listed are sufficient to prompt reporting to public health authorities:

- Culture of *Blastomyces* spp. from a clinical specimen
- Identification of characteristic *Blastomyces* spp. yeast in tissue or body fluid by histopathology.
- Identification of characteristic *Blastomyces* spp. yeast in tissue or body fluid by cytopathology (i.e., fungal smear).
- Demonstration of *Blastomyces*-specific nucleic acid or proteins in a clinical specimen or isolate using a validated molecular assay (e.g., PCR, DNA Probe, MALDI-TOF).

- Detection of *Blastomyces* spp. antigen in serum, urine, or other body fluid by enzyme immunoassay (EIA).  
Detection in serum of antibodies to *Blastomyces* spp. by immunodiffusion (ID), enzyme immunoassay (EIA), or complement fixation (CF).

### **A3. Epidemiologic Linkage Criteria for Reporting**

An epidemiologic linkage (e.g., common environmental exposure, which may be suspected among family members, coworkers, friends, etc.) is only necessary for reporting in patients with a clinical suspicion of blastomycosis in the absence of a positive laboratory test. Such a linkage is not necessary when any of the other criteria are met. Report any suspected blastomycosis outbreaks to public health authorities.

### **A4. Vital Records Criteria for Reporting**

A death certificate listing of blastomycosis is sufficient for reporting.

### **A5. Other Criteria for Reporting**

A health record diagnosis of blastomycosis is sufficient for reporting.

## **B. Disease-specific data elements to be included in the initial report**

The following disease specific data elements are expected to be included in all reports to public health agencies:

#### Laboratory Information:

- Collection date of first specimen that indicated blastomycosis
- For each specimen indicating blastomycosis
  - Specimen type
  - Collection date
  - Laboratory test performed
  - Results, including *Blastomyces* species, if known

Further clinical or epidemiological information may be available to those reporting. If possible, the following data elements are also requested\*.

#### Clinical Information:

- Description of clinical symptoms and signs of illness
- Date of illness onset
- Hospitalization
- Any underlying diseases or co-infections

#### Epidemiological Information:

- Occupation
- Epidemiological link to another blastomycosis case, if known
- Environmental exposure that likely contributed to risk, if known
- Travel history in past 12 months

\*Minnesota and Wisconsin have standardized case investigation forms available to share with states that are considering expansion of their disease surveillance to include blastomycosis (16, 17).

## **VII. Case Definition for Case Classification**

### **A. Narrative: Description of criteria to determine how a case should be classified.**

#### **A1. Clinical Criteria**

Clinical presentation should include:

- At least two of the following findings:
  - Cough
  - Fever or chills or night sweats
  - Shortness of breath
  - Poor appetite or weight loss
  - Myalgia (muscle pain)
  - Arthralgia (joint pain) or bone pain
  - Fatigue

OR

- At least one of the following findings determined to be likely attributed to *Blastomyces* infection:
  - Abnormal lung findings on chest imaging (e.g., pulmonary infiltrates, nodule, or mass-like lesions)
  - Single or multiple skin lesions (often verrucous or ulcerated)
  - Bone or joint abnormality (e.g., osteomyelitis, pathologic fracture)
  - Meningitis, encephalitis, or focal brain lesion
  - Abscess, granuloma, or lesion in other body system (e.g., genitourinary, ocular)

#### **A2. Laboratory Criteria**

*Confirmatory laboratory evidence\**:

- Culture of *Blastomyces* spp. from a clinical specimen
- Identification of characteristic *Blastomyces* spp. yeast in tissue or body fluid by histopathology
- Identification of characteristic *Blastomyces* spp. yeast in tissue or body fluid by cytopathology (i.e., fungal smear)
- Demonstration of *Blastomyces*-specific nucleic acid or proteins in a clinical specimen or isolate using a validated molecular assay (e.g., PCR, DNA Probe, MALDI-TOF)

*Presumptive laboratory evidence\**:

- Detection of *Blastomyces* antigen at or above the minimum level of quantification in serum, urine, or other body fluid by enzyme immunoassay (EIA) test\*\*
- Detection in serum of antibodies against *Blastomyces* by immunodiffusion

\*Additional details regarding diagnostic characteristics of laboratory methods used for diagnosis of blastomycosis are described in Appendix 1.

\*\*The EIA threshold is not set based on clinical or epidemiological data but rather to err on the side of specificity rather than sensitivity. Cross-reactivity is a known problem with the EIA antigen test, and cases known to be infected with another fungal infection should not be counted as blastomycosis cases. This cutoff is to be used in surveillance case definitions and not for making clinical decisions.

#### **A3. Epidemiologic Linkage**

Epidemiologically linked (e.g., common environmental exposure, which may be suspected among family members, coworkers, friends, etc.) with a confirmed case.

#### **A4. Case Classifications**

*Confirmed:*

A clinically compatible case that meets confirmatory laboratory criteria.

*Probable:*

A clinically compatible case that meets presumptive laboratory criteria\*, OR

A clinically compatible case that does not meet laboratory criteria\* but is epidemiologically linked to a confirmed case, OR

A case with confirmatory laboratory criteria but no clinical information available

*Suspect:* N/A

\*Illness in a person with compelling evidence (e.g., culture, histopathology, seroconversion) of a different fungal infection, such as histoplasmosis or coccidioidomycosis, and meeting only non-confirmatory laboratory criteria for blastomycosis should not be counted as a case of blastomycosis since other fungal infections can cause false positive *Blastomyces* antigen and antibody test results.

#### **B. Criteria to distinguish a new case of this disease or condition from reports or notifications which should not be enumerated as a new case for surveillance**

To minimize duplicate counting of infections that are due to relapse or reactivation, a given person should be counted only once as a probable or confirmed case of blastomycosis despite repeated positive testing over time.

#### **VIII. Period of Surveillance**

Surveillance should be ongoing.

#### **IX. Data sharing/release and print criteria**

1. CSTE recommends the following case statuses\* be included in the 'case' count released outside of the public health agency:

- Confirmed
- Probable
- Suspect
- Unknown

\* Which case statuses are included in the case counts constitute the "print criteria."

2. Jurisdictions (e.g., States and Territories) conducting surveillance under this case definition can voluntarily submit de-identified case information to CDC, if requested and in a mutually agreed upon format.

Production of national data summaries and national data re-release for non-NNCs:

- Prior to release of national data summaries CDC should follow the CDC/ATSDR Policy on Releasing & Sharing Data, issued on April 16, 2003 and referenced in 11-SI-01 and custodians of such data should consult the CDC-CSTE Intergovernmental Data Release Guidelines Working Group report ([www.cste2.org/webpdfs/drgwgreport.pdf](http://www.cste2.org/webpdfs/drgwgreport.pdf)) which contains data release guidelines and procedures for CDC programs re-releasing state, local, or territorial-provided data.

- CDC programs have a responsibility, in collaboration with states, localities, and territories, to ensure that CDC program-specific data re-release procedures meet the needs of those responsible for protecting data in the states and territories.

#### **X. Revision History**

Not applicable. This is the initial surveillance case definition for blastomycosis.

#### **XI. References**

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## Appendix 1: Laboratory Methods for Diagnosis of Blastomycosis

Several clinical laboratory methods are available for blastomycosis diagnosis. Fungal culture is the gold standard, with a sensitivity ranging from 67-86%, but can take over a month to yield a result, complicating treatment decision making (13). *Blastomyces* can also be identified in clinical specimens using histopathology or cytopathology (i.e., fungal smear) by its characteristic broad-based budding yeast form. Molecular assays such as PCR, DNA probe, and MALDI-TOF, are often used for confirmation of culture or pathologic identification. PCR can also be used on clinical specimens directly, but is not widely performed (1). Fungal antigen enzyme immunoassays (EIA) may be performed on a variety of body fluids and faster time to results, but are not universally available. The diagnostic sensitivity of the antigen EIA is affected by specimen type and the anatomical location and severity of clinical disease. The assay has been found to be most sensitive ( $\leq 93\%$ ) testing urine from patients with moderate to severe pulmonary blastomycosis (18, 19). The high rate of cross-reactivity with other fungi, such as *Histoplasma* and *Paracoccidioides*, and consequently lower diagnostic specificity limit its use to a non-confirmatory diagnostic test, but is reported to be clinically useful in monitoring fungal disease burden during antifungal treatment (20). Serum antibody tests are available; with immunodiffusion assays of host antibody to *Blastomyces* having high specificity but relatively low sensitivity, whereas ELISA has higher sensitivity but lower specificity. Antibodies can take two months to reach detectable levels and can persist long after infection (5, 19).

## Council of State and Territorial Epidemiologists Technical Supplement

**Table VI. Table of criteria to determine whether a case should be reported to public health authorities.**

Criterion	Reporting Blastomycosis	
<b><i>Clinical Criteria for Reporting</i></b>		
Clinical suspicion of blastomycosis		N
<b><i>Laboratory Criteria for Reporting</i></b>		
Culture of <i>Blastomyces</i> spp. from a clinical specimen	S	
Identification of characteristic <i>Blastomyces</i> spp. yeast in tissue or body fluid by histopathology	S	
Identification of characteristic <i>Blastomyces</i> spp. yeast in tissue or body fluid by cytopathology (i.e., fungal smear)	S	
Demonstration of <i>Blastomyces</i> -specific nucleic acid or proteins in a clinical specimen using a validated molecular assay (e.g., PCR, DNA Probe, MALDI-TOF)	S	
Detection of <i>Blastomyces</i> antigen in serum, urine or other body fluid by enzyme immunoassay test	S	
Detection in serum of antibodies against <i>Blastomyces</i> by immunodiffusion (ID), enzyme immunoassay (EIA), or complement fixation (CF) assay	S	
<b><i>Epidemiological Linkage Criteria for Reporting</i></b>		
Epidemiologically linked to a confirmed case of blastomycosis		N
<b><i>Vital Records Criteria for Reporting</i></b>		
Death certificate lists blastomycosis as cause of death or significant contribution to death	S	
<b><i>Other Criteria for Reporting</i></b>		
Health record diagnosis of blastomycosis	S	

Notes:

S = This criterion alone is SUFFICIENT to report a case

N = All "N" criteria in the same column are NECESSARY to report a case.

O = At least one of these "O" (ONE OR MORE) criteria in **each category** (categories=clinical evidence, laboratory evidence, and epidemiological evidence) **in the same column**—in conjunction with all "N" criteria in the same column—is required to report a case.

**Table VII. Classification Table: Criteria for defining a case of blastomycosis.**

Criterion	Probable			Confirmed
<b>Clinical Evidence</b>				
Abnormal lung findings on chest imaging (e.g., pulmonary infiltrates, nodule- or mass-like lesions)*	O	O		O
Single or multiple skin lesions (often verrucous or ulcerated)*	O	O		O
Bone or joint abnormality (e.g., osteomyelitis, pathologic fracture)*	O	O		O
Meningitis, encephalitis, or focal brain lesion*	O	O		O
Abscess, granuloma, or lesion in other body system (e.g., genitourinary, ocular)*	O	O		O
At least 2 of the following findings: <ul style="list-style-type: none"> <li>o Cough</li> <li>o Fever or chills or night sweats</li> <li>o Shortness of breath</li> <li>o Poor appetite or weight loss</li> <li>o Myalgia</li> <li>o Arthralgia or bone pain</li> <li>o Fatigue</li> </ul>	O	O		O
Clinical information is unavailable			N	
<b>Laboratory Evidence</b>				
Culture of <i>Blastomyces</i> spp. from a clinical specimen			O	O
Identification of characteristic <i>Blastomyces</i> spp. yeast in tissue or body fluid by histopathology			O	O
Identification of characteristic <i>Blastomyces</i> spp. yeast in tissue or body fluid by cytopathology (i.e., fungal smear)			O	O
Demonstration of <i>Blastomyces</i> -specific nucleic acid or proteins in a clinical specimen using a validated molecular assay (e.g., PCR, DNA Probe, MALDI-TOF)			O	O
Detection of <i>Blastomyces</i> antigen at or above the minimum level of quantification in serum, urine, or other body fluid by enzyme immunoassay (EIA) test	O			
Detection in serum of antibodies against <i>Blastomyces</i> by immunodiffusion (ID)	O			
Lack of compelling laboratory evidence of a different fungal infection causing illness	N	N		
<b>Epidemiologic Linkage Evidence</b>				
Epidemiologically linked with a confirmed case of blastomycosis		N		
<b>Criteria to distinguish a new case:</b>				
Not previously counted as a probable or confirmed case		N		N

**Notes:**

N = All “N” criteria in the same column are NECESSARY to classify a case. A number following an “N” indicates that this criterion is only required for a specific disease/condition subtype (see below). If the absence of a criterion (i.e., criterion NOT present) is required for the case to meet the classification criteria, list the absence of criterion as a necessary component

O = At least one of these “O” (ONE OR MORE) criteria in **each category** (categories=clinical evidence, laboratory evidence, and epidemiologic evidence) **in the same column**—in conjunction with all “N” criteria in the same column—is required to classify a case. A number following an “O” indicates that this criterion is only required for a specific disease/condition subtype.

\*Clinical finding determined to be clinically compatible with blastomycosis.