

## Blastomycosis



This disease has also been referred to as Gilchrist's Disease, North American Blastomycosis, Chicago Disease and Namekagon River Fever.

### Case Definition

A person from whom *Blastomyces dermatitidis* is detected either by culture or direct visualization by microscopy of the characteristic broad-based budding yeast from a clinical specimen (1).

### Reporting Requirements

The true incidence of blastomycosis is not known as it is not reportable nationally in Canada or the United States (2).

**In Manitoba:** Blastomycosis has been reportable to the Communicable Disease Control Unit, Manitoba Health by laboratories as of Sept. 1, 2006 for surveillance purposes only and will generally not require Public Health follow-up.

**In Ontario:** Blastomycosis was removed from the list of reportable diseases in 1989 (3); however, a passive reporting system for laboratory confirmed cases was initiated in 2000 by the Northwestern Health Unit jurisdiction (4). As well, a database was created in 2002 to track local cases.

### Clinical Presentation and Natural History

Blastomycosis is caused by a thermally dimorphic fungus (*Blastomyces dermatitidis*), found in soil (1, 2, 5, 6). Symptomatic disease has been found to occur in less than 50 per cent of infected individuals (5, 7, 8). The high frequency of asymptomatic infection suggests that healthy people are fairly resistant to infection by *B. dermatitidis* (7). Isolated pulmonary involvement occurs in approximately 70 per cent of patients (7, 9).

#### Pulmonary Blastomycosis:

Blastomycosis is usually acquired by inhaling aerosolized spores (conidia) from a source in nature,

presumably soil (5, 10). Upon entering the lungs, the conidia transform into yeasts and may cause disease. Clinical disease with *B. dermatitidis* is variable however, and symptomatic infection usually presents as a flu-like illness with fever, chills, night sweats, productive cough, myalgia, arthralgia, weight loss and pleuritic chest pain (10-12). The pulmonary disease may be acute or chronic and mimics other fungal and bacterial infections, including tuberculosis (7, 13). Misdiagnosis with community-acquired pneumonia is not uncommon (10, 12, 14). Chronic pulmonary disease appears similar to lung cancer and tuberculosis (15). The similar presentation of blastomycosis to other illnesses may result in delayed diagnosis and treatment (12).

The radiologic appearance of pulmonary blastomycosis varies depending on the stage of infection and the clinical presentation and is not specific to blastomycosis (16). The predominant finding is air-space infiltrates, followed by mass-like and interstitial infiltrates (17). Air-space infiltrates are more often associated with acute disease, and mass-like infiltrates with chronic disease (17). Blastomycosis has been diagnosed in patients with significant underlying illnesses (6, 18), including diabetes mellitus (10) and infection with the Human Immunodeficiency Virus (HIV) (19). However, as *B. dermatitidis* has caused disease in otherwise healthy individuals, it is considered to be a primary rather than an opportunistic pathogen (15, 20, 21). Only a few reports have indicated that *B. dermatitidis* can act as an opportunistic pathogen (7). Hematogenous dissemination occurs in approximately 30 per cent of patients with pulmonary blastomycosis (9). The most common extrapulmonary sites are the skin, bone and genitourinary and central nervous systems (CNS) (9, 17, 20, 22).

**Skin:** Cutaneous blastomycosis is the most common extrapulmonary manifestation (16). Skin lesions may be the first indication of blastomycosis in patients where pulmonary infection is asymptomatic (7, 16, 23). Cutaneous lesions can be

verrucous (rough, warty) or ulcerative (7). Lesions usually appear on exposed areas such as the face, trunk and extremities (10). Lesions may also appear on the mucosa of the mouth, nose and larynx (7). Both types of lesions may be seen in the same patient (6, 7). Verrucous lesions often start as small papulopustular (small, elevated, pus-containing) lesions that may spread slowly to form crusted, heaped-up lesions. Colour varies from a gray to a violet hue (7). These lesions may appear similar to other more common diseases such as basal cell carcinoma and squamous cell carcinoma (7, 15). Ulcerative lesions present as pustules that spread as superficial ulcers or slightly raised lesions that bleed easily (6, 7). Subcutaneous nodules have also been reported in blastomycosis patients. These individuals often appear acutely ill and may deteriorate rapidly if treatment is not initiated promptly (7, 16). Spontaneous drainage has occurred (7).

**Bone and Joint:** Lesions may occur at any bony site (16) although the long bones, vertebrae and ribs are the most commonly involved sites (7). These lesions may be asymptomatic (24).

**Genitourinary:** The third most common extrapulmonary site is the urogenital system (16), mainly the prostate and epididymis (7). Prostate obstruction is a common genitourinary presentation.

**Central Nervous System (CNS):** In a normal host (immunocompetent), CNS disease is rare (7). Although blastomycosis is uncommon among HIV-infected individuals, and is not an AIDS-defining illness, when it does occur in this setting, CNS complications are common (7, 19).

### **Primary Cutaneous Blastomycosis:**

This form of blastomycosis is rare (16, 22) and occurs by traumatic puncture of the skin with infected material. Cases have been described as the result of injuries sustained in diagnostic laboratories (22, 25, 26). The skin lesions caused by primary cutaneous blastomycosis are similar in appearance to those caused by disseminated pulmonary infection (25). The prevalence of primary cutaneous blastomycosis may be underestimated due to spontaneous resolution (25).

### **Outcomes:**

Prior to the availability of antimicrobials for the treatment of blastomycosis, the disease, as reported, had a mortality rate exceeding 60 per cent (7). With antifungal therapy, mortality rate is about five to 10 per cent (9, 11). Spontaneous recovery has been described (5, 8, 21). If adult respiratory distress syndrome (ARDS) develops, the fatality rate is higher (10); about 68 per cent (27). Immunocompromised patients with blastomycosis have a mortality rate of 30 to 40 per cent (7).

### **Etiology**

*B. dermatitidis* is the imperfect or asexual stage of the fungus *Ajellomyces dermatitidis* (7). *B. dermatitidis* grows as the mould or mycelial form at 25°C and as a yeast form at 37°C (7, 28). Upon entering the body, the mould transforms into a yeast as part of the adaptation process to new environmental conditions with a raised temperature (29).

### **Epidemiology**

**Reservoir:** *B. dermatitidis* has been found in moist soil with a low pH, especially soil that is enriched with organic debris such as decaying vegetation, rotting wood and animal excreta (high nitrogen content) (5, 8, 12, 28, 30). It remains difficult to isolate *B. dermatitidis* from the soil, even from sites that have previously yielded the organism (5, 21). Changing climatic factors such as rainfall, temperature and humidity, as well as changing soil conditions such as pH and organic content, are believed to play a role (5, 31). No studies have been done that demonstrate whether composts can act as a reservoir for *B. dermatitidis*, or whether activities associated with composting represent an increased risk to individuals for infection (32). There is no other known reservoir besides soil.

**Transmission:** Acquisition of blastomycosis usually occurs by inhalation of airborne spores and in rare cases by traumatic inoculation through the skin (11, 25, 28). Exposure to soil has been the most commonly identified risk factor for infection during outbreaks (1). Exposure to soil elements

may be increased during excavation and construction activities as well as recreational activities along waterways (5, 27). Although *B. dermatitidis* grows more abundantly in moist acidic soil, the spores aerosolize less readily under moist soil than dry soil conditions if the soil is disturbed (33). Person-to-person transmission has not been documented (7).

## Occurrence:

**General:** The vast majority of documented cases of blastomycosis are from the eastern portion of North America (15), particularly the regions bordering the Mississippi and Ohio River basins, the Midwestern states, the Canadian provinces that border the Great Lakes and Central Canada (3, 7). In 1984, blastomycosis became a reportable condition in Wisconsin following two large outbreaks (1). Cases have been reported in Africa (13), India (34) and the Middle East (28).

*B. dermatitidis* also causes disease in dogs (35) and cases have been described in cats, a horse, a captive African lion and a sea lion (28).

**Canada:** Blastomycosis is hyperendemic in the Kenora catchment area (3), which falls within the Northwestern Health Unit jurisdiction. There appears to be an increase in the incidence of blastomycosis in the northwestern region of Ontario (3). This finding may be due to improved awareness and increased testing. From 1989 to 2005, 213 cases were diagnosed in the Kenora catchment area (4), giving an estimated average annual population incidence of 1.7 per 10,000 using the population of the Northwestern Health Unit area of 77,823 in 2001 (Statistics Canada).

**Manitoba:** It is difficult to provide accurate incidence and prevalence data for blastomycosis in Manitoba as blastomycosis was not reportable to Public Health until Sept. 1, 2006 and existing published studies are based upon hospitalized patients only. Furthermore, differentiating Ontario and Manitoba cases is complicated by the fact that many residents from the Northwestern Health Unit of Ontario

region are referred to Manitoba hospitals and Manitoba residents travel to the Kenora region and may acquire their infections there (9). As of May 22, 2007, 16 cases of blastomycosis had been reported to Manitoba Health since reporting began Sept. 1, 2006 (36).

**Incubation Period:** For symptomatic infection, the average incubation period is 30 to 45 days (7, 28); however, incubation is estimated to range from 21 to 106 days (8). Shorter incubation periods have been documented (13 to 18 days) and may be related to inoculum size (25, 37).

Seasonal occurrence of blastomycosis is difficult to determine due to the variation in incubation and the often delayed diagnosis. In Manitoba, cases were diagnosed in all months of the year with a slightly higher proportion of patients becoming symptomatic from October through March (9). In the Kenora catchment area of Ontario, the initial onset of symptoms tended to occur from September to January (3).

**Susceptibility and Resistance:** Symptomatic disease occurs in about 50 per cent of people infected with *B. dermatitidis* (5, 8). The historically slightly higher incidence of disease in males compared to females was thought to reflect increased exposure of males to environmental conditions through male-dominated professions and recreational activities (4, 10).

In Manitoba, the highest incidence of disease was found in the 50 to 69 year-old age group (9) whereas in Northwestern Ontario the highest incidence was in the 40 to 59 year-old age group (4). A higher annual incidence rate was found among Aboriginal people than among non-Aboriginal people (3, 9) in both Manitoba and the Kenora region of Ontario. Blastomycosis may also occur in children (21).

*B. dermatitidis* is not a common opportunistic pathogen in immunocompromised hosts (7, 19).

**Period of Communicability:** There is no direct person-to-person transmission (28). It is not known how long spores can retain their infectivity.

## Diagnosis<sup>1</sup>

*B. dermatitidis* is a biosafety level three organism, and, if suspected in a clinical specimen, should be referred immediately to the appropriate reference laboratory for further investigation (38). Diagnosis is based on detection of *B. dermatitidis*. This may include isolation of *B. dermatitidis* in culture or visualization of *B. dermatitidis* yeast forms by microscopy in pathologic or microbiologic specimens. The characteristic broad-based budding yeast form must be present.

Clinical specimens used for diagnosis may be obtained from respiratory sites, skin, urine or other body fluids such as pleural fluid or CSF (cerebrospinal fluid) (39).

Staining with potassium hydroxide (KOH) wet mount is a simple, rapid test for identification of *B. dermatitidis* (39); however, it is not widely available.

Specimens are plated on BHI (brain heart infusion) agar, inhibitory mould agar and Sabouraud agar (39). Cultures are confirmed using a DNA probe which yields same-day results (39).

### Serology:

Although serological testing is available, the sensitivity and specificity are poor, and therefore it is not generally recommended.

## Key Investigations

Most reported cases of blastomycosis are sporadically occurring (1) and will not require Public Health investigation. However, a cluster of two or more cases may be investigated at the judgment of the regional Medical Officers of Health in consultation with Manitoba Health. Such investigations should include the following:

- Identify the source of the infection. This investigation will involve looking at the patient's exposure to soil from work or recreational activities, as well as documenting travel to endemic areas.

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<sup>1</sup> Always check with the laboratory prior to submitting a specimen.

## Control

### Management of Cases:

Consultation with an infectious disease specialist is recommended. Blastomycosis is not vaccine-preventable. Most patients require treatment. Treatment is indicated for all patients with progressive pulmonary or extrapulmonary disease as well as those patients who are immunocompromised (40). Surgical procedures have been performed in the past, including incision and drainage of subcutaneous abscesses in conjunction with antifungal therapy (6, 7). With appropriate therapy, blastomycosis has a mortality rate of less than 10 per cent (40). Recurrence of blastomycosis after adequate antifungal therapy is uncommon (17). Therapeutic options for blastomycosis have been described in a guideline by the Infectious Diseases Society of America (40) and are summarized as follows:

- Patients who are immunocompromised or who have life-threatening disease such as ARDS or who have CNS involvement should be treated with amphotericin B (0.7–1 mg/kg/d; total dose 1.5–2.5 g).
- Patients having mild to moderate disease should be treated with itraconazole at a dosage of 200–400 mg/d for a minimum of six months. Ketoconazole or fluconazole at a dosage of 400–800 mg/d for six months are alternatives to itraconazole.

### Special Circumstances:

- Amphotericin B is recommended for treating blastomycosis in pregnant women. Azoles should not be used owing to their teratogenic potential.
- Children with life-threatening or CNS disease should receive amphotericin B. For pediatric patients with non-life-threatening, non-CNS disease, itraconazole at a dosage of 5–7 mg/kg/d has been used successfully.

## Prevention

Definitive preventive measures are unknown (28), in part because the nature of *B. dermatitidis* and its ecological role are poorly understood (15). Activities that bring individuals closer to rotting

wood or moist soil near water may confer a higher risk of infection (12). However, as the habitat of *B. dermatitidis* is not well-characterized, avoidance of all potentially infected sites is difficult (8). Decontamination is not possible and soil-testing is not reliable (12).

There is no direct evidence that wearing masks during outdoor activities will reduce the risk of acquiring blastomycosis. It is reasonable to believe that masks may offer some protection by reducing exposure to blastomycosis spores when they are present in the environment. However, there is insufficient evidence to support a recommendation of wearing masks in all of the many settings where exposure to blastomycosis spores may occur.

## Additional Resources

### Information for Health Professionals

- National Institutes of Health Mycoses Study Group <http://www.niaid.nih.gov/dmid/fungal/>
- Microbiology and Immunology On-Line, University of South Carolina School of Medicine <http://pathmicro.med.sc.edu/mycology/mycology-6.htm>

### Information for the Public

- In Manitoba, contact your doctor, your local Public Health Unit or Health Links-Info Santé at 1-888-315-9257 or 204-788-8200
- See the Manitoba Health fact sheet on blastomycosis available at: <http://www.gov.mb.ca/health/publichealth/cdc/factsheets.html>
- In Ontario, contact the Ontario Northwestern Health Unit at 1-800-830-5978 or 807-468-3147.

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