

Podcast #4: Broad Based Budding Yeast - Diagnosis of Blastomycosis

JM: Hello and welcome to Think Blasto! I am Dr. Joe McBride, an infectious diseases specialist at the University of Wisconsin.

GG: Yes, welcome to Think Blasto! I am Dr. Greg Gauthier, I am also an infectious diseases specialist at the University of Wisconsin. This podcast series is designed to describe and outline a disease that is more common in Wisconsin than in most parts of the world: an infection called blastomycosis.

JM: The title of today's podcast is "Broad-Based Budding Yeast – Diagnosis of blastomycosis?"

GG: Thus, we will be talking about how blastomycosis is diagnosed in human patients. In a separate podcast we will discuss diagnosis of blastomycosis in animals.

JM: Greg, let's start with an example. You are evaluating a patient that has had fevers, worsening cough, increasing shortness of breath for 6 weeks. The patient has received 2 courses of antibiotics without improvement in symptoms. A chest x-ray shows pneumonia. Take me through how you would figure out if this illness could be blastomycosis?

GG: To help figure out if this could be fungal infection including blastomycosis, I would first assess the patient's risk for fungal exposure by asking several questions about activities involving disruption of dirt. This would include where they live and whether or not there are lakes, streams, or rivers on their property, do they visit a cabin, have they traveled to a blastomycosis "hot spot", has there been recent landscaping or construction near their home including road and building construction, recent well digging, remodeling of their home, cabin, or barn, and use of a community compost pile. I also ask about recreational activities such as hunting, canoeing, kayaking, tubing on a river, and fishing. In addition, I ask if they have a family member or a pet that has had or is currently being treated for blastomycosis. Finally, I ask if they have had exposure to beaver dams.

JM: Why ask about exposure risks?

GG: Determining if there has been an exposure is important because it helps us as physicians assess the risk for fungal infection and gives us a clue to where the person may have acquired blastomycosis. Studies from Wisconsin and Minnesota indicate that about 60% of patients with blastomycosis have a risk factor for environmental exposure to *Blastomyces*.

JM: Why do you ask about family members and pets having blastomycosis?

GG: When a family member or a pet such as a dog has blastomycosis, it suggests a common source of environmental exposure. Approximately 4 to 9% of patients with blastomycosis will have a family member with current or prior blastomycosis. Studies from Wisconsin and Minnesota indicate that about 8 to 10% of patients with blastomycosis have a pet with current or prior blastomycosis.

JM: Is *Blastomyces* transmitted from person-to-person or animal-to-human?

GG: No it is not. Blastomycosis is acquired from the environment, not from other people or animals.

JM: And why do you ask about beaver dams?

GG: One of largest outbreaks of blastomycosis occurred following exposure to soil around beaver dams. This occurred in the mid-1980's in Northern Wisconsin. During the investigation of this outbreak, *Blastomyces* was cultured from the soil, which was an amazing accomplishment because it is extraordinarily difficult to isolate *Blastomyces* from the soil. Thus, soil around beaver dams is favorable for the growth of *Blastomyces*. In addition, we have seen several patients with blastomycosis at the University of Wisconsin that have had exposure to beaver dams.

JM: It is worth noting that in general *Blastomyces* prefers to grow in soil around fresh water whether or not beaver dams are present. Also, beavers do not transmit blastomycosis to humans.

You mentioned that about 60% of patients have risk factors, which means that 40% don't have environmental risk factors for blastomycosis. Thus, in the absence of risk factors you cannot rule out blastomycosis as the diagnosis.

GG: Joe, that is right, diagnostic testing is needed to figure out if a person has blastomycosis or not.

As it turns out, our patient regularly visits his cabin in northern Wisconsin, which recently underwent renovation and landscaping.

JM: What diagnostic testing would you use to diagnose blastomycosis?

GG: There are several tests that can help doctors diagnose blastomycosis. However, in my opinion, the most critical diagnostic test is to think about blastomycosis as a diagnosis. If you cannot think of the diagnosis, you cannot make the diagnosis. In addition to thinking blastomycosis, one of the most important tests is obtaining a specimen for fungal culture and fungal staining. If a patient has pneumonia, the specimen would be a sputum sample. If the patient has a skin lesion that would include a biopsy of the skin lesion. A dermatologist typically does the biopsy.

JM: What if patient is coughing but is not bringing up enough sputum or phlegm for testing. Is there still a way to get a sputum sample for testing?

GG: Yes, there is. We can help induce sputum production by having the patient inhale a saline mist. This is typically done with the assistance from our colleagues in respiratory therapy. Alternatively, our colleagues in pulmonary medicine can do something known as bronchoscopy in which they put a special scope known as a bronchoscope into the lungs, instill some saline fluid, then suck it back up into the bronchoscope and submit it to the microbiology lab. During bronchoscopy the patient is given sedation to keep them comfortable. Most patients with blastomycosis do not require bronchoscopy, it is typically reserved for patients who are very sick with a pulmonary infection and a diagnosis is needed sooner rather than later.

JM: So now that you have a sputum specimen, what happens next?

GG: The sputum specimen is sent to the microbiology laboratory for staining and culture. This includes doing special stains that allow us to see *Blastomyces* yeast. Stains that are specific for

fungi must be used. That is because stains used for bacteria, such as the Gram stain, don't stain fungi very well.

Most microbiology laboratories use a fungal stain called calcofluor white, which stains the cell wall of fungi making them appear pretty, bright blue under the fluorescent microscope. On the website, we have a picture of calcofluor-stained *Blastomyces* yeast. If calcofluor white is not available, then 10% potassium hydroxide solution is often used.

For culture, the sputum specimen is inoculated on special media that support the growth of fungi. Culture media used to grow bacteria don't work to grow fungi.

JM: What about a tissue specimen such as a skin biopsy? What happens next?

GG: A tissue specimen should be submitted to the microbiology lab for culture and the pathology lab for staining. For the pathologist to be able to see fungi in the tissue specimen using a microscope, special fungal stains must be used. The most common stain used in the pathology laboratory to help identify fungi is the silver stain, which makes the fungal cell wall look black, which makes it easier to identify *Blastomyces* yeast. On the website, we have a picture of silver-stained *Blastomyces* yeast. In addition to silver staining, there are several other stains that can be used by pathologists to identify fungi.

Similar to the sputum sample discussed previously, special culture media are needed to support growth of fungi. Culture media used to grow bacteria don't work for fungi.

JM: How long does it take for *Blastomyces* to grow in culture?

GG: *Blastomyces* grows quite slow. It takes about 5- 28 days for it to grow on culture media.

Joe, In addition to staining and cultures of sputum or tissue, are there other ways to diagnosis blastomycosis?

JM: Yes, there is a *Blastomyces* antigen test that can be very helpful in diagnosing blastomycosis.

This test detects a specific type of sugar known as galactomannan, which is found in the cell wall of *Blastomyces* yeast. When *Blastomyces* yeast cells grow, they shed this galactomannan from their cell walls and this test can be used to detect it in the body. Most commonly, this galactomannan can be detected in blood or urine samples. Thus, it is considered a non-invasive test.

GG: In addition to blood and urine, can the *Blastomyces* antigen test be used on other specimens?

JM: Yes, if a patient has meningitis due to blastomycosis, spinal fluid can be obtained by spinal tap and submitted for *Blastomyces* antigen testing. In addition, fluid obtained from lung bronchoscopy can also be submitted for the *Blastomyces* antigen test.

GG: So the antigen test can be used for diagnosis using urine, blood, lung fluid from a bronchoscopy, and spinal fluid obtained from a spinal tap. Can the antigen test be used in place of staining or culture?

JM: No. The antigen test does not replace the importance of staining and culture. The antigen test should be used in conjunction with staining and culture.

Lets go back to our patient who has a chest X-ray that shows pneumonia. Greg, are there specific findings on chest X-ray that could suggest this is blastomycosis and not bacterial pneumonia?

GG: No, there are no chest X-ray findings that would definitively suggest blastomycosis. On chest x-ray blastomycosis can look like bacterial pneumonia, viral pneumonia, tuberculosis, and even lung cancer.

JM: The patient has received 2 different antibiotics without improvement. Is that an important clue for blastomycosis?

GG: Yes, it is an important clue that the patient could have blastomycosis or another type of fungal pneumonia. Antibiotics work against bacteria not fungi. Thus, any person that has pneumonia that does not respond to antibiotics fungi such as *Blastomyces* should be considered and looked for by diagnostic testing

JM: Greg, that is helpful. So let's summarize what we have learned today about diagnosing blastomycosis.

GG: It is important to Think Blasto, otherwise blastomycosis cannot be diagnosed.

JM: Most but not all persons with blastomycosis have risk factors for exposure to *Blastomyces* in the environment.

GG: For some patients, family members or a pet will have blastomycosis, which suggests a common site of environmental exposure.

JM: For patient with pneumonia, sputum specimens should be obtained for fungal staining and fungal culture.

GG: For patients with skin lesions, a skin biopsy should be obtained for analysis in the pathology lab along with fungal staining and culture in the microbiology lab.

JM: For any patient with suspected blastomycosis, antigen testing of urine or blood can be helpful.

GG: Antigen testing can also be done on lung fluid obtained by bronchoscopy and spinal fluid obtained from a spinal tap.

JM: To our audience thank you very much for your time and interest. Greg, I look forward to discussing more aspects of blastomycosis with you in the future.

GG: And until next time, Think Blasto!