

The recent *Cryptococcus gattii* outbreak

A deadly pathway...

From Trees to Lungs to Brain



by Jay Hardy, CLS, SM (NRCM)

Jay Hardy is the founder and president of Hardy Diagnostics. He began his career in microbiology as a Medical Technologist in Santa Barbara, California.

In 1980, he began manufacturing culture media for the local hospitals. Today, Hardy Diagnostics is the third largest media manufacturer in the U.S.

To ensure rapid and reliable turn around time, Hardy Diagnostics maintains six distribution centers, and produces over 3,000 products used in clinical and industrial microbiology laboratories throughout the world.

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Cryptococcus *gattii* has been in the news lately, due to a recent outbreak in the Pacific Northwest. This new, more virulent strain is expected to spread further throughout the Northwest and Northern California in the coming months.

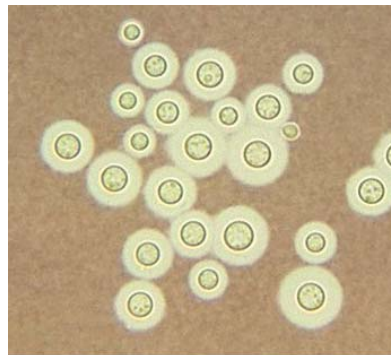


Figure 1: An India ink stain showing the capsule surrounding the *C. gattii* cells in the yeast form at 1,000X. Photo from Haley/CDC.

The organism is a fungus that is usually found in the soil and on trees. It is not spread from human to human or animal to human. However, some animals and pets have been known to contract this

disease. The route of infection is from breathing the airborne organism, which becomes lodged in the pulmonary tissues.

Symptoms

The pulmonary disease, known as cryptococcosis, develops slowly. After exposure it can take two to twelve months for symptoms to appear, with the usual onset at six or seven months.

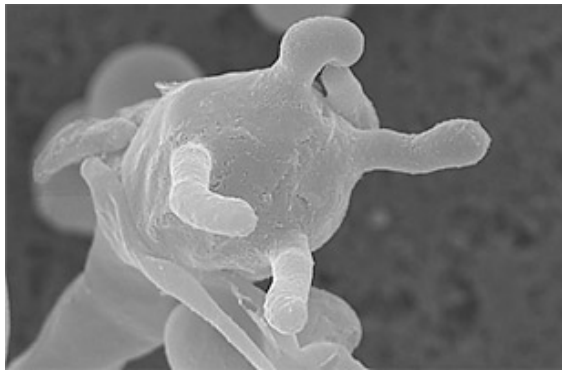
The symptoms include:

- Cough that lasts weeks or months
- Sharp chest pain
- Unexplained shortness of breath
- Severe headache
- Confusion
- Fever
- Night sweats
- Unintended weight loss

Those that are most susceptible are those with a weakened immune system,

although healthy individuals have been known to be infected as well, as seen in the recent outbreak.

More serious infections develop into meningitis and cerebral cryptococcomas.



An electron microscope view of the fungus from Duke University.

The Geography of Infection

Infections have been found in Washington, Oregon, British Columbia, and perhaps Northern California.

Most of the original cases were found on the East side of Vancouver Island in British Columbia, Canada beginning in 1999.

The New Strain

A more virulent strain has claimed six lives in Oregon and a total of 21 have become infected recently. Particularly worrisome is that the new strain can strike otherwise healthy individuals and has been known to progress into CNS tissue.

This new strain, dubbed VGIIc, has been implicated in the recent outbreak in Oregon. Another strain of the same pathogen, dubbed subtype VGIIa, was responsible for 19 deaths in Canada back in 1999. At that time, 218 people were infected on Vancouver Island, in British Columbia; nine percent of these cases were fatal. Researchers say that the new form is very similar to the old one; however, the new strain is killing one of every four victims.

It's puzzling that the North American strains of this fungus are so virulent, given that *C. gattii* has existed in South America, Africa and Australia for many years where it is commonplace, but much less dangerous.

Just how virulent is this new strain? A recent study by Edmund Byrne at Duke University found that the Oregon strain of *Cryptococcus gattii* killed 25 percent of the people it infected, but the overall numbers of people infected were small. In lab animals, the disease was found to be 100% fatal, which is not the case with previous strains.

The public has been cautioned against becoming panicked, while being reminded of the extreme rarity of this disease. Even so, there is currently no

way to protect against the spread of this organism.

History

C. gattii is a close relative of *Cryptococcus neoformans*, which is often implicated in HIV/AIDS patients due to their impaired immunity. *C. gattii* is more likely to strike healthy individuals than is *C. neoformans*. It is also more likely to progress from the lungs to the brain (meningitis) than *C. neoformans*.



Figure 2: Colonies of Cryptococcus will turn brown on [Caffeic Acid Agar](#) also known as [Bird Seed Agar](#).

The infection was once considered endemic, occurring sporadically in the tropics and subtropics where the fungus was known to grow on the eucalyptus trees. In 1999, the range of this pathogen expanded to Vancouver Island, British Columbia, Canada. Since 2004, over 50 cases of *C. gattii* infection have been documented in the Pacific Northwest of the United States. The source is usually traced back to trees. Over 50

species of trees have been found as a source of *C. gattii* spores.

During a recent study on Vancouver Island in Canada, the organism was isolated in high traffic areas in automobile wheels and footwear. Another common location was in woodchips used for landscaping.

Recently, there have been several reports of a more deadly strain that is a hybrid of *C. neoformans* and *C. gattii* found in Europe and Canada.

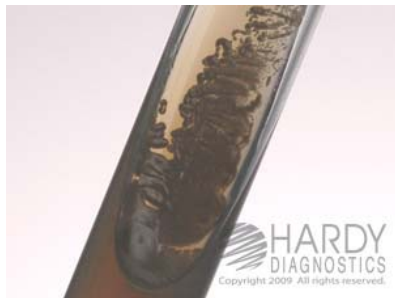


Figure 3: A three day old culture of *Cryptococcus* on a Caffeic Acid Agar Slant.

Identification

Cryptococcus spp. are easily cultured on typical fungal media. [Caffeic Acid Agar](#) will cause the colonies to turn brown. Another more rapid method involves the use of a [paper disk](#) containing caffeic acid.



Figure 4: A [rapid caffeic acid disk](#) can be used to identify *Cryptococcus* within four hours.

An [India ink](#) prep is useful in detecting the polysaccharide capsule surrounding the irregularly sized yeast cells.



Figure 5: Colonies showing reddish brown pigment production on [Caffeic Acid Agar](#) (Bird Seed Agar).

One way to distinguish *C. neoformans* from *C. gattii* is with the use of [CGB Agar](#). This highly selective medium utilizes the ability of *C. gattii* to create an alkaline shift in pH when creatine is degraded to ammonia. This causes the media to turn from yellow-green to cobalt blue.

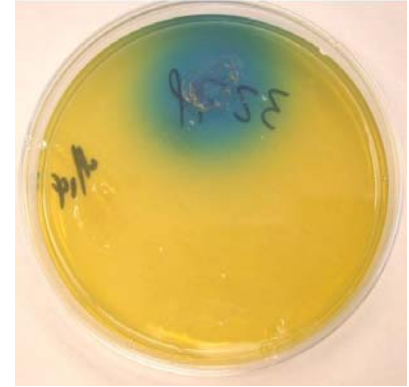


Figure 6: *C. gattii* turning the media blue on a [CGB Agar plate](#) within five days. This media will distinguish *C. gattii* from *C. neoformans*.

All strains of *C. neoformans* are not capable of producing this color change.

Treatment

Once correctly diagnosed, *C. gattii* is treated with the anti-fungals, amphotericin B and fluconazole. Treatment is prolonged (3 to 12 months) and is oftentimes less effective than with *C. neoformans* infections.

Now that we are over the H1N1 Influenza pandemic, we are once again challenged with a new outbreak to keep our eyes on in the coming months. As a somewhat “new” organism, further study of *C. gattii* is definitely warranted.

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