

OREGON PUBLIC HEALTH DIVISION • OREGON HEALTH AUTHORITY

**CRYPTOCOCCUS GATTII: THE FUNGUS AMONG US**

A new strain of a tropical fungal interloper has been discovered in the United States...but no matter how it arose, this party crasher looks like “it’s going to stick around...”

**INTRODUCTION**

*Cryptococcus gattii* is an encapsulated, pathogenic yeast, closely related to *Cryptococcus neoformans*.<sup>\*</sup> Until 1999, it had been thought limited to tropical and subtropical climates; but in that year it emerged on Vancouver Island, resulting in one of the highest incidences of *C. gattii* infection reported anywhere in the world.<sup>1-3</sup> Human illnesses caused by *C. gattii* were subsequently confirmed on the British Columbia mainland, in Washington State, and, since 2004, in Oregon.

**THE PATHOGEN**

*Cryptococcus gattii* is most easily distinguished from *C. neoformans* by the blue color it produces when plated on differential CGB<sup>†</sup> agar.<sup>4</sup> The natural reservoir of *C. gattii* seems to be soil and plant debris; the fungus has been associated with numerous tree species including eucalyptus, fir, Garry oak, etc.<sup>5-6</sup> When inhaled, it may infect humans and a variety of mammals such as dogs, cats, goats, elk, ferrets, etc.<sup>7</sup>

Multilocus sequence typing subcategorizes the organism into four genotypes: VGI, VGII, VGIII, and VGIV. Further genetic analysis divides the VGII genotype into three subtypes: VGIIa, VGIIb, and VGIIc.<sup>8-9</sup> Although VGII is the genotype most commonly found recently in the Pacific Northwest and in British Columbia, it is uncommon in other *C. gattii*-endemic parts of the world, where VGI is isolated most frequently.<sup>10</sup> Interestingly, VGIIc has been isolated only from humans, animals in Washington and Oregon and so far only from Oregon soil.

**EPIDEMIOLOGY**

In the wake of the Vancouver Island outbreak, in November 2004 the Oregon Public Health Division began

to solicit cryptococcal isolates from Oregon clinical laboratories for testing at the Oregon State Public Health Laboratory (OSPHL). *C. gattii* infections were soon confirmed among Oregonians, including some who had never traveled to British Columbia.<sup>11</sup> Of 91 *Cryptococcus* isolates processed by the OSPHL sixty cases (66%) of *C. gattii* infection were reported in Oregon between November 2004 and October 2011; most cases were identified after September 2008 when we began to solicit cases more actively (Figure 1). Thirty-three (55%) of the cases were female. The median age was 57 years (range, 10 months – 96 years; Figure 2).

**HUMAN ILLNESS**

*Cryptococcus gattii* appears to differ from its sibling species *C. neoformans*, both in its clinical manifestations and in its ecologic niche. *C. gattii* may be more likely to cause cryptococcomas and less susceptible to antifungal drugs.<sup>12,13</sup> In addition, whereas the primary risk factor for *C. neoformans* cryptococcosis is severe immunosuppression (e.g., from HIV infection), both immunocompromised and previously healthy individuals seem to be at risk for *C. gattii* infection.<sup>12-14</sup> *Cryptococcus gattii* causes life-threatening infection of the pulmonary and central nervous systems in all hosts.

Through November 2010, 46 of the Oregon cases have been reviewed thoroughly. Of these, 21 (46%) were primarily pulmonary, 12 (26%) primarily CNS, 9 (20%) CNS and pulmonary, 1 (2%) bloodstream alone and 3 (6%) were other (nail bed infection, thrush, urinary tract infection).

Of those, 34 (74%) had an underlying chronic medical condition. Twenty-four (52%) patients had an immunosuppressing condition, including nine with solid organ transplants and 11 with a variety of autoimmune diseases. This is a bit at odds with the pictures of *C. gattii* infection as reported from British Columbia, where only 41 (39%) of 124 confirmed cases during 1999–2007 were immunocom-

promised; and Victoria, Australia, where 0 of 20 cases identified during 1980–1990 were immunocompromised.<sup>2,14</sup> Perhaps cases in immunocompetent patients in Oregon were missed, given that reporting was voluntary. N.B.: as of August 19, 2011, cryptococcal infection is now reportable in Oregon; and laboratories will be required to forward the isolates to OSPHL for speciation.<sup>‡</sup>

Figure 1. *C. gattii* human cases reported, Oregon 2004–2011

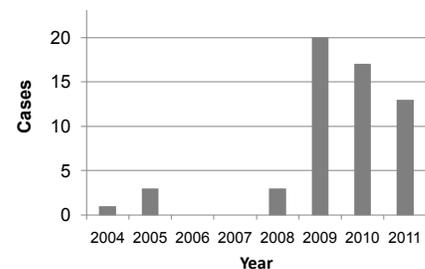
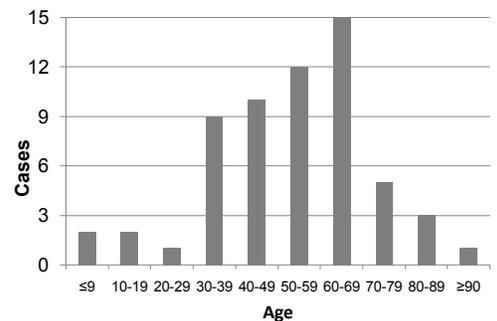


Figure 2. *C. gattii* by age group, Oregon, 2004–2011



**EPIZOOTIOLOGY**

Oregon veterinarians and veterinary laboratories have reported *C. gattii* cases since 2008. Through October 2011, the Oregon State University’s Veterinary Diagnostics Laboratory (VDL) has identified 40 cases: 15 cats, 9 dogs, 5 alpaca, 5 goats, two elk, a ferret, a horse, a dolphin and a sheep (Figure 3, verso). Of the *C. gattii* isolated at VDL, 10 were isolated from lungs, 10 from nasal cavities, 9 from skin abscesses, 7 from the brain or CSF, 2 from kidneys, and one each from an oral lesion and a rectal sample. Of the 40 isolates, 39 were serotyped: 23 were VGIIa, 6 VGIIb, 9 VGIIc and 2 VGIII.

‡ Oregon Administrative Rules 333-018-0015 and 333-018-0017

\* In fact, its former moniker was “*Cryptococcus neoformans* var. *gattii*.”  
† L-canavanine glycine bromothymol blue



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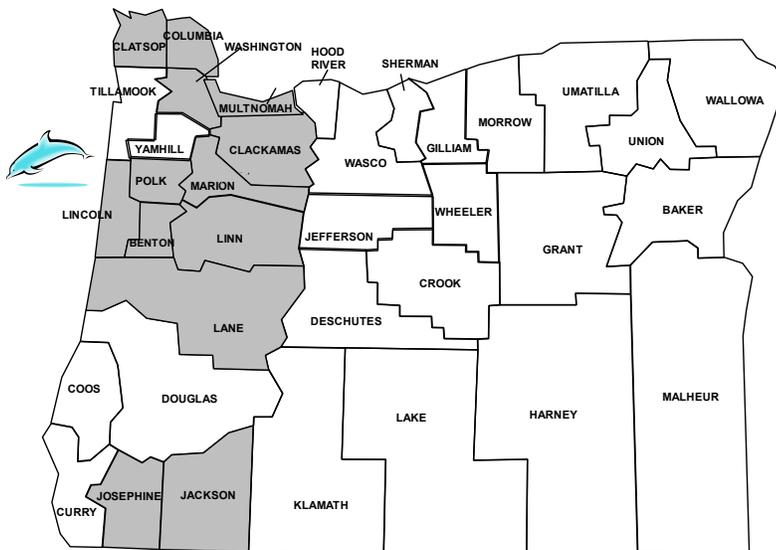
Because human beings are wont to travel, and the incubation period for *C. gattii* infection is long (median, 6–7 months; range of 2–13 months),<sup>11</sup> it's difficult to know where a given human case acquired his or her infection. Figure 3 shows where the non-human cases resided — probably indicating more reliably where the fungus abides.

the better to define the ecology of this fungal pathogen in Oregon.

### CONCLUSION

*Cryptococcus gattii* appears to be established in Oregon, and case counts may be rising. Both immunosuppressed and previously healthy persons appear to be at risk. More information is needed about the effective-

Figure 3. Geographic location of animal *C. gattii* cases, Oregon, 2008–2011



### ECOLOGY

To zero in on environmental niches, we collected samples from around the residence of a 9-month-old dog (with no travel history!) from which *C. gattii* VGIIa was cultured. The soil and tree bark samples of a *Pseudotsuga menziesii* var. *menziesii*<sup>§</sup> collected a year apart yielded *C. gattii* VGI, VGIIa, VGIIb and VGIIc. We hope to collect more environmental samples around the homes of animal cases without travel history, § a Douglas fir to most of us.

ness of azole antifungal agents in treating it. All cryptococcal infections are now reportable in Oregon; we hope that the data bolster our understanding of *C. gattii* risk factors, treatment and prognosis.

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