A New and Improved Surveillance System

"Cryptococcus gattii Pacific Northwest"



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C. neoformans vs. C. gattii



	C. neoformans	C. gattii
Distribution	• Ubiquitous, global, associated with pigeon guano-contaminated soil	• Until recently, only tropical and subtropical areas, associated with eucalyptus trees
Patients infected	 Severely immunocompromised (HIV, organ transplant) In post-AIDS era, infections in immunocompetent are rare 	 Endemic Australia and Papua New Guinea, other areas: Nearly all immunocompetent BC, US Pacific Northwest: Mostly HIV-uninfected but many immunocompromised
Diagnosis	• Typically, Cryptococcal antigen test or India Ink	 Typically, Cryptococcal antigen test, India Ink Distinction from <i>C. neoformans</i> requires plating on special media
Clinical course	 Usually presents as meningitis Cryptococcomas (fungal growths in brain, lungs, muscle) are infrequent 	 Presentation (meningitis vs pneumonia) appears to depend on strain, location, patient immune status Cryptococcomas are common
Treatment	 If non-CNS: oral fluconazole If CNS: IV amphotericin + flucytosine, 2 weeks; fluconazole, 6+ months 	 IV amphotericin + flucytosine, 2+ months; fluconazole, 6+ months May require brain or lung resections, shunts to drain CSF

Infection and pathogenesis of C. gattii

- Inhalation of spores from environment (trees, organic matter, soil around trees)
 - Colonization of nasal cavity, sinuses
 - Incubation period ~6 mos (2-13 mos)
- Symptoms and clinical findings
 - Cough, dyspnea, chest pain, fever, headache, night sweats
 - Meningitis, pneumonia
 - Cryptococcomas (brain, lungs)
- Not transmissible between mammals

Brain cryptococcoma



Lung cryptococcoma





CDC

Distribution of C. gattii infections

Before 1999	• Australia	-
	• Papua New Guinea	
	• Southeast Asia	
	• India	
	• South and Central America	
	• Southern California	
	• Mostly type VGI, VGIII	
1999-2003	• Began appearing in humans,	-
	animals in Vancouver Island and	0
	mainland BC, Canada	
	• Also among persons who traveled	
	to Vancouver Island	
	• Mostly type VGIIa, some VGIIb	
2004-2010	• Ongoing infections in BC	
	• Humans and animals, mostly in	5
	Washington and Oregon, infected	
	• Mostly type VGIIa and VGIIc.	
	someVGIIb	





C. gattii: breakdown of genotypes, human infections, US, 2004-2010



CDC



Onset year is reported for 49 patients and is estimated by initial report year for 15 patients for whom onset date was not available. 2010 data is year-to-date; data are typically lagged by several months.

Characteristics of patients included in *C. gattii* surveillance in the United States, 2004-2010. Complete information was not available for all patients.



Patient characteristic	n (%)
Demographics Age (n=59) (mean, median, range) % Male % White (1 each of Asian, Native Hawaiian, and African- American)	53, 56 (15, 95) 32 (53) 29 (91)
Symptoms (most common) Headache Cough Nausea Dyspnea Weight loss Fever	29 (58) 27 (52) 23 (51) 23 (48) 20 (43) 22 (42)
Clinical findings Pneumonia Meningitis Cryptococcoma: lung (n=45 with images) Cryptococcoma: brain (n=18 with images) Outcomes	26 (55) 23 (49) 14 (31) 5 (28)
Hospitalized Died of <i>C. gattii</i> Died of or with <i>C. gattii</i>	48 (91) 10 (20) 16 (32)

Predisposing conditions of patients included in *C. gattii* surveillance in the United States, 2004-2010.

Predisposing conditions (patients with information)	(%)
Recent history of oral steroid use	50
Lung disease (not transplant; includes asthma, bronchitis, COPD, scarring)	33
History of cancer	25
Kidney disease (not transplant)	22
Solid organ transplant	20
Cardiovascular disease (not transplant)	19
Diabetes	19
Rheumatic condition	13
Liver disease (not transplant)	9
Connective tissue disorder	7
HIV	6
Stem cell transplant (any type)	0
No identifiable condition	25

Statistically meaningful associations between exposures and outcomes among patients included in *C. gattii* surveillance in the United States, 2004-2010.



CDC

Exposure	Outcome or presentation variable	RR	р
Age group (years)	Death from or with <i>C. gattii</i>		
<18	C	4.25	0.30
18-29		0.88	1.00
30-49		REF	n/a
50-69		1.54	0.07
70+		2.05	0.03
Pre-existing condition vs	Pneumonia	1.89	0.05
none	Meningitis	0.48	0.02
	Headache	0.48	0.003
	Nausea	0.47	0.02
	Weight loss	0.38	0.005
	Loss of appetite	0.29	0.009
	Muscle pain	0.35	0.03
	Neck stiffness	0.30	0.02
	Night sweats	0.32	0.03
	Blurry vision	0.16	0.02
	Photophobia	0.01	0.04
Death from or with C. gattii	Dyspnea	2.00	0.03
	Nausea	0.17	0.05

- Patients >70 years old were more likely than younger patients to die of or with infection
- Having a pre-existing condition was positively associated with pneumonia at presentation, but negatively associated with many other signs and symptoms, including CNS signs
- Death was positively associated with dyspnea at presentation, but negatively associated with nausea

Statistically meaningful associations between genotype or subtype of infection and presenting signs and symptoms of infection among patients included in *C. gattii* surveillance in the United States, 2004-2010.

Genotypes / subtypes	Presenting sign or symptom	RR	р
VGI infections vs [VGII, VGIII]	Seizure	40.0	0.05
VGII infections vs [VGI, VGIII]	Cough Dyspnea Neck stiffness Blurry vision	57.0 53.0 0.26 0.10	0.02 0.05 0.04 0.007
VGIIb infection vs all others	Nausea	0.02	0.02
VGIII infection vs [VGI, VGII]	Neck stiffness	4.78	0.05

- Genotype-specific differences found by presenting signs / symptoms
 - VGI and VGIII-type infections more likely to present with central nervous system signs; VGII-type infections
 were more likely to present as respiratory disease
- No associations found between genotype / subtype and:
 - Presence of cryptococcoma (lung or head)
 - Pneumonia or meningitis
 - Pre-existing condition
 - Death
- Small sample size may obscure or enhance associations



Comparisons between characteristics of US patients included in *C. gattii* surveillance in the United States, 2004-2010, and *C. gattii* patients in British Columbia, 1999-2007 (from Galanis *et al*, 2010).



*When limited to pre-existing conditions considered in BC (Galanis *et al*, 2010), only 61% have a predisposing condition. Among seven patients excluded by the BC definition, 1 was diabetic; 1 had cardiovascular disease and asthma; 1 had a rheumatic condition; 2 had both cardiovascular and kidney disease; 1 had unspecified lung disease; 1 had Nocardia infection of the lungs.



Veterinary Reporting

- Public health for veterinarians
 - Reporting forms and reports



of fuman services Oregon	Veterinary 🕻	oonose	s kepo	orting		
Date: / /	Veterinarian:			Phone: ()	-
Disease (circle one):	Onset of	illness:		Status	(circle	e one):
Bartonella	MRSA	Rabies		Clini	ical	Confirmed
Campylobacteriosis Giardiasis Leptospirosis	Plague Psittacosis Ringworm	Salmonello Toxoplasm	osis Iosis	lf Confi	rmed:	
Other disease of public health importance: (9		ich as Crypto	ococcus)	Lab N	ame:	
				Туре	of Test	
Species (circle one):	Breed	:	A	ge:	Sex	(circle one):
🔈 🏂 🋀					Mal N /	e Female
City:				Zip:		

Comments:

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Veterinary cases

Animal type	Ν
Cats	25
Dogs	11
Llama/alpaca/camelids	6
Horse	2
Elk	2
Goat	2
Bird	1
Sheep	1
Dolphin / porpoise	5

	State	Ν	
	OR	27	
	WA	23	
	CA	4	
	HI	1	
		0/	
G	enotype	% 0	
G V(GI	% 4	
V V V	GI GIIa	4 57	
G V(V(V(GI GI GIIa GIIb	4 57 17	
G V(V(V(V(GI GIIa GIIb GIIc	%	
	GI GIIa GIIb GIIC GIII	% 4 57 17 13 6	

Locations of known veterinary cases



- More VGIIb, less VGIIc among animals than humans
- Recent dropoff in reporting of animal cases



Environmental: Soil sample collection

- Samples were collected from 10 different sites
- 2 isolates were cultured
- VGI and VGIIa
- VGIIa matched that of the dog!





Conclusions



- Cryptococcus gattii is a serious, emerging infection in the US Pacific Northwest
- Patient profile differs from reports of infections in historically endemic areas (Australia, Papua New Guinea) and British Columbia for reasons that are not yet clear
- Risk factors for infection in US Pacific Northwest include being age 50-69 years, HIVinfected, otherwise immunocompromised
- *C. gattii* subtypes appear to correlate with presenting syndrome but not necessarily pre-existing patient condition
 - VGI, VGIII appear to cause more CNS disease, while VGII types cause more respiratory infections
 - However, sample size is small, particularly for VGI and VGIII types; true differences in patient tropism by strain genotype might be obscured
 - Genotype-specific treatment guidelines might be warranted; this should be sufficient incentive to continue surveilling
- Concerted continued epidemiologic surveillance is needed to determine best practices for patient care

Cryptococcus in the news

<u>http://www.youtube.com/watch?v=j0WqZ5F2</u>
 <u>eK8&NR=1&feature=fvwp</u>

