

# The Search for the Natural Habitat of *Cryptococcus gattii*

Ferry Hagen · Teun Boekhout

Received: 1 April 2010 / Accepted: 2 April 2010 / Published online: 23 April 2010  
© Springer Science+Business Media B.V. 2010

In this issue of Mycopathologia, Loperana-Alvarez et al. [1] report that they have isolated the pathogenic yeast *Cryptococcus gattii* from trees and succulent plants in Puerto Rico, a tropical island in the Caribbean.

Until a decade ago the basidiomycetous yeast *Cryptococcus gattii* was a rare cause of cryptococcosis in humans and animals that occurred mainly in the subtropical and tropical regions in South America, Africa and Australia. However, this distribution pattern changed by an unprecedented outbreak of this yeast which emerged in 1999 in the temperate climate of British Columbia (Canada) and that subsequently expanded to the Pacific Northwest [2, 3]. In contrast to its opportunistic relative *Cryptococcus neoformans*, *C. gattii* has a preference to cause disease in apparently healthy humans and animals [2, 3]. However, it became obvious that also immunocompromised patients, like individuals receiving immunosuppressive therapy, organ transplant recipients and patients with hematological malignancies, are likely to acquire

cryptococcosis caused by *C. gattii* [2]. Furthermore, several cases of activated dormant *C. gattii* infections have been described [4]. In a recent study by Litvintseva et al. [5], *C. gattii* was identified as the cause of cryptococcal disease in more than 13% of the studied HIV-positive humans in the sub-Saharan region. These examples suggest that *C. gattii* can no longer be regarded as a primary pathogenic yeast [4].

In most cases, *C. gattii* and *C. neoformans* enter the body via the respiratory system from where it disseminates to the central nervous system to cause meningitis, which frequently has a fatal course [2, 6]. It is generally accepted that airborne basidiospores produced by *Filobasidiella bacillispora*, the teleomorph of *C. gattii* or small-sized desiccated *C. gattii* cells are the infectious propagules since encapsulated vegetative yeast cells are too large to pass through the lung alveoli [6]. Nevertheless, the sexual phases of both pathogenic *Cryptococcus* species are only known to be produced under laboratory circumstances and have not yet been found in nature or in clinical samples [6].

The natural habitat of *C. neoformans* and *C. gattii* has been intensively studied, especially in those areas where the incidence of cryptococcosis is relatively high [7]. The primary ecological niche of *C. neoformans* has been determined to be bird excreta, especially pigeon droppings, and trees [8]. Two decades ago, *C. gattii* was isolated from plant debris under a *Eucalyptus camaldulensis* tree in Australia [8]. The distribution pattern of *E. camaldulensis* has been associated with the relatively high proportion of

---

F. Hagen (✉) · T. Boekhout  
Department of Yeast and Basidiomycete Research,  
CBS-KNAW Fungal Biodiversity Centre, Uppsalalaan 8,  
3584CT Utrecht, The Netherlands  
e-mail: f.hagen@cbs.knaw.nl

F. Hagen · T. Boekhout  
Department of Internal Medicine, Division of Infectious  
Diseases and Medical Microbiology, University Medical  
Centre Utrecht, Utrecht, The Netherlands

*C. gattii* infections among rural aboriginals, compared to other areas where *C. gattii* was known from clinical sources [8]. However, shortly after this finding, Ellis and Pfeiffer, as well as other Australian investigators isolated *C. gattii* from a wide variety of *Eucalyptus* species and *Syncarpia glomulifera*, which is also a native Australian tree species [7, 9]. *Eucalyptus* trees have been exported from Australia to many countries, especially those with a subtropical or tropical climate, which is the preferred environment for *Eucalyptus* trees [7–9]. It has been speculated that the export of *Eucalyptus* seeds and trees had contributed to the dispersal of *C. gattii* [7, 8]. However, the finding of *C. gattii* in a hollow of a native *Guettarda acreana* tree in Ilha de Maracá, an unaffected area in the Northern Brazilian Amazon rainforest, indicated that probably not *Eucalyptus* but (decomposing) plant material in general is the most probable ecological niche for *C. gattii* [7, 9].

This idea became more evident after a large environmental sampling study to determine the environmental source of the ongoing Vancouver Island *C. gattii* outbreak [2, 3, 7, 9]. This study revealed that *C. gattii* was abundantly present on a broad range of native Canadian tree species, especially alder (*Alnus* spp.), cedar (*Thuja* spp.), Douglas fir (*Pseudotsuga menziesii*), grand fir (*Abies grandis*) and Garry oak (*Quercus garryana*), but that it was absent on several imported tree species such as *Eucalyptus* spp. [9].

The search for the presence of *C. gattii* in the environment is usually initiated after the emergence of clinical and veterinary cases [2, 3, 7, 9]. Since *C. gattii* has been isolated from a wide variety of natural habitats in North and South America, the presence of *C. gattii* in the Caribbean could be expected [7]. Earlier attempts to isolate *C. gattii* from the environment in Puerto Rico and Cuba were unsuccessful [10, 11]. Loperana-Alvarez and colleagues investigated the same regions in Puerto Rico that were sampled two decades ago, but this time both pathogenic *Cryptococcus* species were found [1, 11]. Trees that were known to be positive for *C. gattii*, like the almond (*Terminalia cattapa*) and mango tree (*Mangifera indica*), were found to yield *C. gattii* [1, 7, 9]. Strikingly, the majority of *C. gattii* strains were isolated from lesions on *Cephalocereus royenii* cacti. This cactus species belong to a group of succulent plants that are known to harbor non-pathogenic *Cryptococcus* yeasts [1]. With the knowledge that

*C. gattii* can survive in lesions of succulent plants, it may be a matter of time before cacti in other geographic regions of the world will be found to harbor *C. gattii*.

The question remains how *C. gattii* has colonized the cacti lesions. Loperana-Alvarez et al. [1] suggested that invasive insects, causing lesions on plants, could be the mode of transfer for *C. gattii*. This hypothesis deserves to be investigated since *C. gattii* has been isolated from several insect-related sources in the past [1, 12]. The current investigations clearly demonstrate that our understanding of the ecology of *C. gattii* is only partly known. What will be the next surprise?

## References

1. Loperana-Alvarez Y, Ren P, Li X, Bopp DJ, Ruiz A, Chaturvedi V, Rios-Velazquez C. Genotypic characterization of environmental isolates of *Cryptococcus gattii* from Puerto Rico. *Mycopathologia*. 2010. doi:10.1007/s11046-010-9296-3.
2. Datta K, Bartlett KH, Baer R, Byrnes E, Galanis E, Heitman J, Hoang L, Leslie MJ, MacDougall L, Magill SS, Morshed MG, Marr KA. *Cryptococcus gattii* working group of the Pacific Northwest. Spread of *Cryptococcus gattii* into Pacific Northwest region of the United States. *Emerg Infect Dis*. 2009;15:1185–91.
3. Kidd SE, Hagen F, Tschärke RL, Huynh M, Bartlett KH, Fyfe M, Macdougall L, Boekhout T, Kwon-Chung KJ, Meyer W. A rare genotype of *Cryptococcus gattii* caused the cryptococcosis outbreak on Vancouver Island (British Columbia, Canada). *Proc Natl Acad Sci U S A*. 2004;101:17258–63.
4. Hagen F, Van Assen S, Luijckx GJ, Boekhout T, Kampinga GA. Activated dormant *Cryptococcus gattii* infection in a Dutch tourist who visited Vancouver Island (Canada): a molecular epidemiological approach. *Med Mycol*. 2010; 48:528–531.
5. Litvintseva AP, Thakur R, Reller LB, Mitchell TG. Prevalence of clinical isolates of *Cryptococcus gattii* serotype C among patients with AIDS in Sub-Saharan Africa. *J Infect Dis*. 2005;192:888–92.
6. Velagapudi R, Hsueh YP, Geunes-Boyer S, Wright JR, Heitman J. Spores as infectious propagules of *Cryptococcus neoformans*. *Infect Immun*. 2009;77:4345–55.
7. Springer DJ, Chaturvedi V. Projecting global occurrence of *Cryptococcus gattii*. *Emerg Infect Dis*. 2010;16:14–20.
8. Ellis DH, Pfeiffer TJ. Natural habitat of *Cryptococcus neoformans* variety *gattii*. *J Clin Microbiol*. 1990;28:1642–4.
9. Kidd SE, Chow Y, Mak S, Back PJ, Chen H, Hingston OA, Kronstad JW, Bartlett KH. Characterization of environmental sources of the human and animal pathogen *Cryptococcus gattii* in British Columbia, Canada, and the Pacific Northwest of the United States. *Appl Environ Microbiol*. 2007;73:1433–43.

10. Illnait-Zaragozi MT, Martínez-Machín GF, Fernández-Andreu CM, Boekhout T, Meis JF, Klaassen CHW. Microsatellite typing of clinical and environmental *Cryptococcus neoformans* var. *grubii* isolates from Cuba shows multiple genetic lineages. PLoS ONE. 2010;5:e9124.
11. Ruiz A, Vélez D, Fromtling RA. Isolation of saprophytic *Cryptococcus neoformans* from Puerto Rico: distribution and variety. Mycopathologia. 1989;106:167–70.
12. Kidd SE, Sorrell TC, Meyer W. Isolation of two molecular types of *Cryptococcus neoformans* var. *gattii* from insect frass. Med Mycol. 2003;41:171–6.