

III. Sex and emerging pathogens: Vancouver Island Cryptococcus gattii outbreak expands

How microbial pathogens emerge to cause outbreaks involves environmental changes, zoonotic-human transmission, and genetic evolution. We address this question with *Cryptococcus gattii* and *C. neoformans*, closely related fungal species that are common causes of meningitis. In contrast to worldwide distribution of *C. neoformans*, *C. gattii* has been geographically restricted to tropical/subtropical regions, associated with trees rather than pigeon guano, and causes infection in hosts with normal immunity. An outbreak of *C. gattii* infections (humans and animals) began in 1999 on Vancouver Island, British Columbia, Canada and is ongoing. Environmental sampling (Karen Bartlett, UBC) reveals the organism is endemic in soil and common indigenous tree species (Douglas Firs) and particles small enough to be infectious spores are in the air.

Genetic and high-resolution MLST genomic approaches reveal the outbreak is caused by two clonal isolates, a hypervirulent major genotype (VGIIa) (95%) and a less virulent minor genotype (VGIIb) (5%). Both are mating-type α and sexually fertile. Their genomes are closely related and share 50% overall identity. The major outbreak genotype is unique and geographically restricted to the Pacific Northwest although isolates with a similar but not identical MLST genotype are present in South America. The minor genotype is identical with isolates from a sexually recombining population in Australia, and further studies are ongoing in collaboration with Dee Carter from the University of Sydney. Unisexual mating, global warming, and imported trees or migrating animals are all hypothesized to have contributed to the origins and ongoing outbreak. Recent studies reveal the outbreak is expanding beyond Vancouver Island, causing human infections on the mainland in British Columbia, on Orcas Island in the San Juan Islands, USA, and in Oregon and Washington State. Continued analysis of veterinary, human, and environmental isolates is ongoing in collaboration with Kieren Marr and Dee Carter and colleagues. A variety of genotypically distinct *C. gattii* VGI and VGII isolates are present in the Pacific Northwest; their relationship to the outbreak, if any, is unknown. This unusual fungal outbreak raises concerns about further expansion and illustrates how microbial pathogens emerge in novel geographic locales.