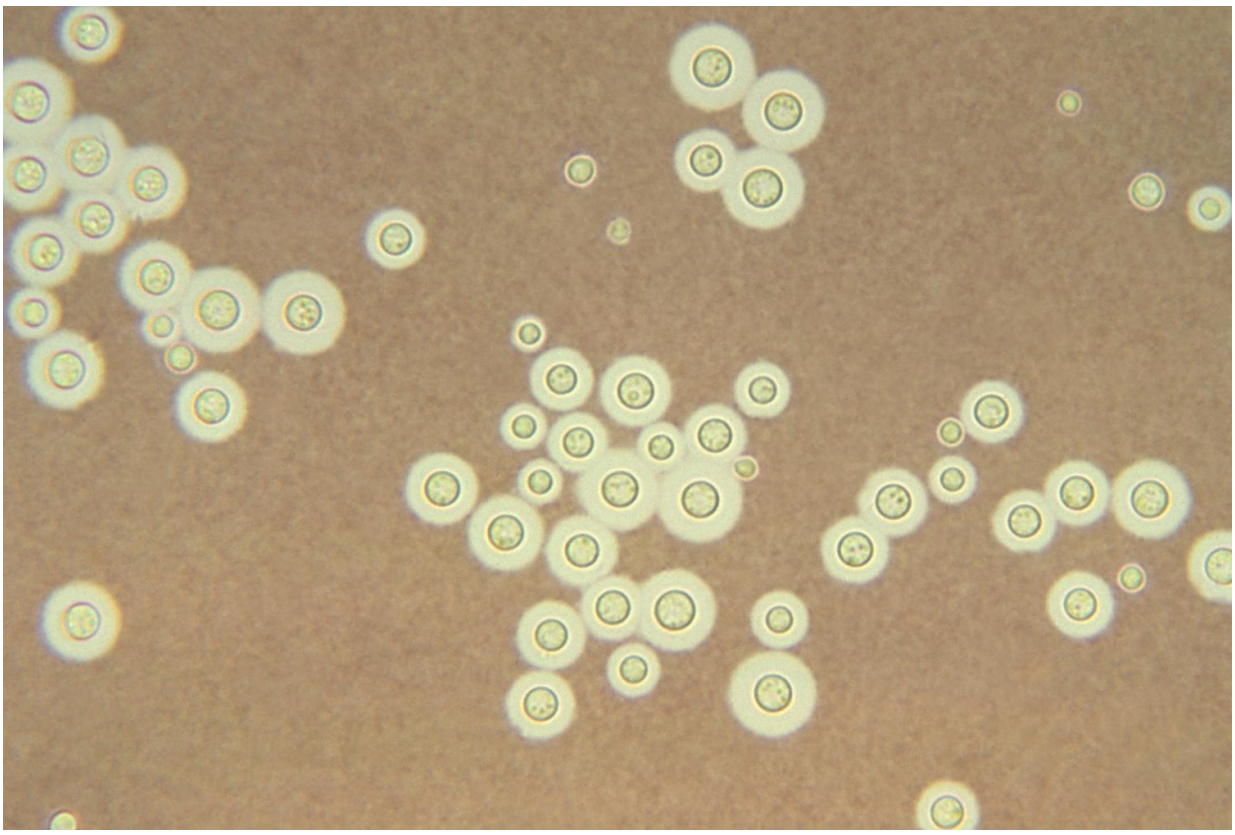
Did long ago tsunamis lead to mysterious, tropical fungal outbreak in Pacific northwest?

October 1 2019



This photomicrograph depicts Cryptococcus neoformans using a light India ink staining preparation. Credit: CDC

The Great Alaskan Earthquake of 1964 and the tsunamis it spawned may

have washed a tropical fungus ashore, leading to a subsequent outbreak of often-fatal infections among people in coastal regions of the Pacific Northwest, according to a paper co-authored by researchers at the Johns Hopkins Bloomberg School of Public Health and the nonprofit Translational Genomics Research Institute (TGen), an affiliate of City of Hope.

In the paper, to publish Oct. 1 in the journal *mBio*, the co-authors confront the mystery of the *Cryptococcus gattii* outbreak in the Pacific Northwest. The outbreak, involving at least several hundred known cases, has been ongoing since 1999, with cases still occurring in humans and wildlife. It has long puzzled epidemiologists because the fungal subtypes isolated from the vast majority of infected patients resemble subtypes normally seen in Brazil and nearby areas of South America.

The co-authors, microbiologist Arturo Casadevall, MD, Ph.D., Alfred and Jill Sommer Professor and Chair of Molecular Microbiology and Immunology at the Bloomberg School, and epidemiologist David Engelthaler, Ph.D., associate professor at the Translational Genomics Research Institute, posit that increased shipping after the 1914 opening of the Panama Canal brought *C. gattii* from south to north, possibly in ships' ballast tanks. Decades later, the tsunamis following the Great Alaskan Earthquake of 1964 brought the fungus widely ashore and into coastal forest area. After several decades, as it evolved to cope with its new habitat, *C. gattii* began to infect people. The 9.2 quake of 1964 remains the largest ever recorded in the northern hemisphere, and the effects of the tsunami were felt as far away as Hawaii and beyond.

"The big new idea here is that tsunamis may be a significant mechanism by which pathogens spread from oceans and estuarial rivers onto land and then eventually to wildlife and humans," says Casadevall. "If this hypothesis is correct, then we may eventually see similar outbreaks of *C. gattii*, or similar fungi, in areas inundated by the 2004 Indonesian

tsunami and 2011 Japanese tsunami."

According to the Centers for Disease Control and Prevention (CDC), more than 300 *C. gattii* infections have been reported in the Canadian and U.S. Pacific Northwest region since the first case on Vancouver Island in 1999. Prior to that time, infections with this fungus had been confined almost entirely to Papua New Guinea, Australia, and South America. The fungus typically infects people through inhalation. It can cause a pneumonia-like illness, and may also spread to the brain, causing a potentially fatal meningoencephalitis. Published case reports suggest a mortality rate of more than 10 percent.

Epidemiologists have found evidence of *C. gattii* in the soil and trees of coastal areas of British Columbia, Washington, and Oregon, as well as in the shore waters—infections by the fungus have been recorded even in marine mammals. Yet, how this tropical pathogen established itself in such a cool northern area were unclear. Theories have included global warming and the import of tropical eucalyptus trees.

About ten years ago, the CDC asked Engelthaler to investigate. He and his colleagues applied a "molecular clock" analysis to the DNA sequences of isolated *C. gattii* subtypes, and concluded that these subtypes had arrived from Brazil or near Brazil 60-100 years earlier. This time frame would have corresponded to a period shortly after the Panama Canal's opening, when shipping increased significantly between Atlantic and Pacific ports. Engelthaler hypothesized that the fungus, washing into South American shore waters from local rivers, likely had been brought to North America via a common mode of transport for invasive species: ballast water. Ships in those days routinely took on such water in one port and simply discharged it, without treatment, in another.

That left the question of how *C. gattii* had managed to colonize so much of the Pacific Northwest coastline. What could have brought not just one

but several subtypes from coastal waters onto the shore en masse?

After further study, Engelthaler deduced that the Great Alaska Earthquake of March 1964 might have been the key factor. The quake had its epicenter in southeastern Alaska but spawned tsunamis throughout the North Pacific. These tsunamis inundated coastal areas of British Columbia, Washington, Oregon, and California. And, the affected regions correspond broadly to the locations where *C. gattii* has been found and human infections have occurred.

There were multiple pieces to this puzzle. It appeared that a singular event, like a natural disaster, could have been the missing piece that brought the whole picture together, notes Engelthaler. The tsunami idea seemed to fit the "when, where, and why" of this disease emergence.

Then, more than 30 years passed before the fungus began infecting humans in the region which was another unresolved issue. Relevant to this aspect of the puzzle is Casadevall's previous research which suggested, for example, that another human-infecting *Cryptococcus* species closely related to *C. gattii* can evolve potent defenses as a result of being preyed on in the wild by amoebas—defenses that can make it more virulent when it infects people.

"We propose that *C. gattii* may have lost much of its human-infecting capacity when it was living in seawater, but then when it got to land, amoebas and other soil organisms worked on it for three decades or so until new *C. gattii* variants arose that were more pathogenic to animals and people," Casadevall says.

The researchers now hope to continue testing their hypothesis with detailed analyses of *C. gattii* prevalence—in soils within and outside tsunami-inundated areas of the Pacific Northwest, and with searches of DNA datasets collected from other parts of the world—to see if the

same *C. gattii* subtypes found in Brazil and the Pacific Northwest are more widely present in seawaters around ports.

"On the emergence of Cryptococcus gattii in the Pacific Northwest: ballast tanks, tsunamis and black swans" was written by David Engelthaler and Arturo Casadevall.

Provided by Johns Hopkins University Bloomberg School of Public Health