

# Mucormycosis—Emerging Fungal Threats

Subjects: Mycology

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Mucormycosis is an opportunistic fungal infection due to organisms of the Zygomycetes class and the order of *Mucorales* that can cause various types of infections. In recent years, an increasing phenomenon has been observed—invasive fungal infections especially in the healthcare setting. Among immunocompromised patients, an important clinical emergency could be represented by mucormycosis. The epidemiology of mucormycosis has shown an alarming trend and its incidence is rising globally. Four elements are fundamental for a successful treatment: rapid diagnosis, reduction of predisposing factors (if possible), surgical debridement of infected tissues, and appropriate antifungal therapy.

Keywords: emerging fungal infections ; mucormycosis ; emerging infections ; Mucorales

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The end of the 1970s was supposed to be the “end of infectious diseases”. This optimism derived from the success of the fight against infectious diseases due to the development of hygiene, environmental hygiene, the advent of anti-infective drugs, and vaccine–vaccination programs including those against smallpox. With the identification of new infectious agents (*Legionella*, rotavirus, Ebola virus, Hantaan virus, *Campylobacter*, prions, etc.), the emergence of acquired immunodeficiency syndrome (AIDS) and its global spread, as well as the progression of bacterial resistance to antibiotics, the “return of infectious diseases” was pronounced <sup>[1]</sup>.

The American Centers for Disease Control and Prevention developed a strategic plan to combat emerging infections in 1994 based on surveillance, alert and response, applied research, prevention and control, and strengthening public health facilities. The World Health Organization (WHO) therefore launched a comprehensive plan based on the same principles <sup>[2]</sup>.

As reported by Barreto et al., a communicable disease, also known as an infectious disease, could be defined as “an illness caused by a specific infectious agent or its toxic product that results from transmission of that agent or its products from an infected person, animal, or reservoir to a susceptible host, either directly or indirectly through an intermediate plant or animal host, vector or inanimate environment” <sup>[3]</sup>.

Infectious diseases can occur as both endemic (diseases constantly present in a population or in a certain geographical area) and epidemic (sudden increase in the number of cases, higher than expected). When an epidemic is geographically very extensive and affects many individuals of the population, it is called a pandemic. Epidemics and pandemics have always been conceived in the collective imagination as a dangerous threat from which it is difficult to escape in the event of contagion <sup>[3]</sup>.

Occasional and exceptional outbreaks of infectious diseases have had deep and durable effects on societies throughout history. For example, the Athenian plague is a historically documented event that occurred in 430–26 BC during the Peloponnesian War, fought between the city-states of Athens and Sparta. Thucydides provided a historic account of the Athenian plague and survived the plague, describing it in his *History of the Peloponnesian War* <sup>[4]</sup>. However, we could also note the Manzoni plague (1629); the flu pandemic known as “Spanish” flu (1918); and, recently, AIDS (1980) <sup>[5]</sup>, SARS (severe acute respiratory syndrome) (2003), and SARS-CoV 2 (2019) <sup>[6]</sup>. For centuries, humanity had to passively undergo these events until the definition of the theory of germs and the discovery of bacteria, with the identification of specific microorganisms responsible for various infectious diseases, which allowed for the subsequent discovery and development of vaccines and antibiotics. However, in recent years, despite the enormous progresses made in the biomedical field, microorganisms have continued to emerge and re-emerge and spread worldwide without any possible forecast <sup>[7]</sup>.

As Reported by Van Doorn et al., emerging infectious diseases are defined as “those whose incidence in humans has increased within the past two decades or threatens to increase in the near future. Emergence may be due to the spread of a new agent, to the recognition of an infection that has been present in the population but has gone undetected, or to the realization that an established disease has an infectious origin” <sup>[8]</sup>.

The causes of the emergence or re-emergence of microorganisms can be numerous.

Changes in the geographical footprint of pathogens or parasites could be determining factors associated with the emerging infections. This may be due to changes in the natural geographical ranges of animal hosts of zoonoses and vectors, and/or via the dispersal of pathogens in infected humans, animal reservoirs, or vectors <sup>[9]</sup>.

Instead, “adaptive emergence” is the genetic change of a microorganism that results in a phenotype that is capable of invading a new ecosystem, particularly via jumping to a new host species, including humans <sup>[10]</sup>.

In addition, all these factors can interact together and create the conditions for a microorganism to evolve, thus acquiring the ability to reach the host and to adapt and spread much more easily in humans. Depending on whether the microorganism is emerging or re-emerging, the possible causes and the prevention measures to be implemented may be different. Any infectious disease can become an emergency when it takes on an epidemic character or when it is perceived by the population as being dangerous <sup>[7][11]</sup>.

The advent of new therapies has deeply changed the treatment of cancers and autoimmune diseases, but some of these therapies (especially immunomodulators) can be complicated by the onset of invasive fungal infections. For example, the Bruton tyrosine kinase inhibitor (ibrutinib) (to treat malignant B cell tumors) could be linked to severe infections due to *Aspergillus* and *Cryptococcus*, while cryptococcosis and histoplasmosis could be a complication of treatment with Sphingosine-1-phosphate receptor modulator fingolimod (used for multiple sclerosis) <sup>[12]</sup>.

One of the most troubling changes in the epidemiology of invasive candidiasis is the emergence of *C. auris*, a potential multi-drug resistant and nosocomially transmitted organism. Since being described in Japan in 2009, *C. auris* has been reported in 32 countries on six continents <sup>[13]</sup>.

As for invasive aspergillosis (IA), it has a high mortality percentage in immunocompromised patients. *A. fumigatus*, the most common species, is often highly susceptible to new triazole antifungals such as itraconazole, voriconazole, and posaconazole. However, various countries around the world have reported *A. fumigatus* resistant to azoles <sup>[14]</sup>.

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