

BRIEFING

Human Fungal Diseases

- Over 1 billion people are affected by fungal diseases globally.
- Life-threatening fungal diseases affect millions of immunocompromised people, causing an estimated 1.5 million deaths each year.
- New and affordable diagnostics and antifungal therapies, and strengthened public health and research capabilities are needed.

SUMMARY

Human fungal diseases pose a significant, but often overlooked, burden on public health, affecting over 1 billion people worldwide. Superficial fungal infections (e.g. nail, skin and urogenital) affect most people at some point in their lifetimes, but are usually curable when treated with antifungal drugs. Nevertheless, they affect quality of life and burden health services.

Life-threatening fungal infections that invade the blood, lungs and other organs pose a serious risk to millions of immunocompromised people, such as those living with HIV/AIDS, or receiving chemotherapy. Despite available antifungal drugs, invasive fungal infections are associated with high mortality rates worldwide, causing an estimated 1.5 million deaths each year, a number comparable to tuberculosis.

Fungal infection burden could be greatly reduced by improving development of, and global access to, new antifungal treatments and rapid diagnostics, and by strengthening public health capabilities and research on understanding and preventing fungal infection.

INVASIVE FUNGAL INFECTIONS

Invasive fungal infections are potentially life-threatening opportunistic infections of the blood and organs, which usually affect people with compromised immune systems. Fungi commonly causing these infections live on humans (e.g. *Candida* species) or in the environment (e.g. *Aspergillus*, *Cryptococcus*, *Pneumocystis* species), normally without harm to healthy people.

In recent decades, invasive fungal infection incidence has increased substantially, driven by growing



numbers of susceptible people, such as those with HIV/AIDS and patients undergoing organ transplantation, immunosuppressive therapies and surgery. Consequently, fungal infections impact advances made in the treatment of other diseases. European studies of economic impact, although limited, suggest additional drug and hospitalisation costs of around €10,000–€51,000 for a patient with invasive fungal infection.

In lower-income countries, lack of access to diagnosis and antifungal drugs is a major problem. For example, cryptococcal meningitis is a leading cause of death for HIV/AIDS patients in sub-Saharan Africa. The best antifungal drugs to treat this infection have existed since the 1970s yet remain unavailable in many countries.

FUNGAL RESPIRATORY DISEASES

Aspergillus moulds occur worldwide in different environments, but inhalation of airborne particles can cause life-threatening infections in susceptible patients, including invasive pulmonary aspergillosis in hospitalised immunocompromised patients (e.g. leukaemia and transplant patients), which can spread from the lungs to other organs. Chronic pulmonary aspergillosis is a long-term destructive fungal lung infection, which affects people with pre-existing lung diseases; it may affect over 3 million people and kill over 450,000 worldwide each year.

Aspergillus and other airborne fungal particles are also a major cause of allergic diseases of the lungs and sinuses, which can seriously worsen asthma and cystic fibrosis. Severe asthma with fungal sensitisation may affect over 6 million people worldwide.

Despite advances in antifungal therapies, inadequate access to treatment, suboptimal diagnostics and drug-associated limitations contribute to poor outcomes for invasive fungal infection patients worldwide, with high mortality rates that often exceed 50%.

ANTIFUNGAL DRUGS

Many current antifungal drugs face limitations, such as drug resistance, harmful side effects, negative interactions with other drugs, and an inability to be administered orally. Extensive, and often inappropriate, use of antimicrobial drugs is leading to the emergence of difficult-to-treat drug-resistant infections. Intensive fungicide use in agriculture and horticulture has been linked to the emergence of multidrug-resistant strains of *Aspergillus*.

While new antifungal drugs are needed, few are currently in development. Antifungal development is scientifically challenging, taking many years and high levels of investment. Much development only focuses on improving the efficacy of existing drug classes.

Preventative vaccination in some high-risk groups could be part of the solution. Currently, no antifungal vaccines are approved for human use, although vaccines for *Candida* infection are beginning clinical trials.

DIAGNOSTICS

Developing more accurate, rapid and affordable diagnostic tests for fungal infections is essential for improving patient outcomes, reducing delayed and inappropriate treatment. Fungal diagnostics have been revolutionised by advances in molecular and immunological biotechnologies, CT scanning and mass spectrometry. For example, a rapid point-of-care immunological test for detecting *Cryptococcus* infection has been developed, while genetic tests for other fungal infections are quicker and more sensitive than older methods. However, diagnosis of many infections still depends on suboptimal diagnostics that are too slow (e.g. culturing fungi from clinical samples) or imprecise, and some diagnostics are unaffordable in low-income healthcare settings.

RESEARCH

Medical mycology (the study of human fungal diseases) is essential for improving diagnosis and treatment. Our increasing understanding of fungal disease genomics and immunology may, for example, enable both the development of novel immunotherapy treatments, and genetic tools to identify high risk people for preventative care.

MICROBIOLOGY SOCIETY BRIEFINGS

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CANDIDIASIS INFECTIONS

Many healthy people carry species of yeast-like *Candida* fungi in and on their bodies without harm. However, these species commonly cause superficial candidiasis infections such as oral and vaginal thrush, which although treatable, affect quality of life and burden health services. For example, 50–75% of premenopausal women worldwide suffer at least once episode of vaginal thrush, with around 100 million women suffering four or more episodes annually.

More seriously, these *Candida* species can disseminate to cause life-threatening invasive candidiasis infections of the blood and organs following severe trauma or immunosuppression. Conservative estimates suggest over 250,000 cases of invasive candidiasis and over 50,000 deaths worldwide each year. Even with antifungal therapy, mortality is often around 40%.

However, the medical mycology research base is comparatively small. For example, it accounted for an estimated 2% of infectious disease research funded in UK institutions between 1997 and 2010, with strengths identified in preclinical research, but limited translational research. Recent Wellcome Trust and Medical Research Council investments aim to strengthen UK medical mycology.

PUBLIC HEALTH AND SURVEILLANCE

Improving public health awareness and surveillance of fungal diseases is important to implement strategies to reduce their burden. Currently, there is no World Health Organization fungal diseases programme and only a few countries – including the USA, UK and France – conduct surveillance, which is limited in scope to very few diseases. A lack of high-quality surveillance data means that estimates of incidence are often inexact and some burdens may be underestimated. Strengthening skills and infrastructure for clinical mycology, diagnostic services and surveillance is a key challenge, especially in lower-income countries.

FURTHER READING

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Elizabeth Johnson (Public Health England), Neil Gow (University of Aberdeen), Robin May (University of Birmingham), and David Denning, Nick Read and Paul Bowyer (University of Manchester). Image credit: X-ray of aspergillosis lung infection (upper left); Sovereign, ISM/Science Photo Library.

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