

# The Role of Antifungal Susceptibility Testing

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## Description

The global burden of the endemic mycoses continues to rise yearly and these infectious diseases remain a leading cause of patient morbidity and mortality worldwide. Management of the associated pathogens requires a thorough understanding of the epidemiology, risk factors, diagnostic methods and performance characteristics in different patient populations, and treatment options unique to each infection. Guidance on the management of these infections has the potential to improve prognosis. The recommendations outlined in this Review are part of the “one world, one guideline” initiative of the European confederation of medical mycology. Experts from 23 countries contributed to the development of these guidelines. The aim of this Review is to provide an up-to-date consensus and practical guidance in clinical decision making, by engaging physicians and scientists involved in various aspects of clinical management.

## Antifungal Susceptibility Testing

Many factors influence the outcome of in vitro Antifungal Susceptibility Testing (AFST), including endpoint definition, inoculum sizes, time and temperature of incubation, and growth medium used. This European Confederation of Medical Mycology (ECMM) excellence center driven study investigated Multiple Colony Testing (MCT) of five separate colonies to investigate the prevalence of Poly Resistance (PR), defined as heterogeneous MICs from a same-species *Candida* culture irrespective of the underlying resistance mechanism.

Medical mycology is one of many areas in the biomedical sciences that are served by a small, dispersed community that is below critical mass. Whilst funders may be sympathetic to the challenges in stimulating growth and research activity in such areas, they may lack appropriate funding mechanisms to create synergies and draw research communities together. This article reports on the outputs and achievements of a welcome trust strategic award in medical mycology and fungal immunology that links 13 institutions to build capacity in the field, stimulate interdisciplinary research and train a new generation of researchers in the UK and in low- and middle-income countries.

Fungi are critical to the function of the world's ecosystem, and many species provide vital chemicals, drugs and food products. As model systems, fungi have been the organisms of choice for a

dozen Nobel laureates to illustrate fundamental principles in genetics and cell biology. Some fungi are known for their ability to cause skin infections, whereas others are a feared cause of fatal human infections. Deaths per annum due to fungal infections are greater than the global mortality due to malaria, breast or prostate cancer, and are similar to that inflicted by Tuberculosis (TB) or HIV. A systematic analysis of the fungal disease burden in 2017, covering 883 million people in 14 countries, revealed that an average of 2% of people have a serious fungal infection. In many of these countries, the figures can only be estimates, due to inadequate or late diagnosis and a lack of effective reporting systems, suggesting a significantly higher actual burden. Current global estimates suggest that over a million people die of fungal infections, 10 million suffer severe fungal allergy, 100 million women are victims of recurrent vulvo vaginal infections annually, and more than a billion people suffer skin infections. There are no vaccines or immunotherapies for mycoses and only a limited arsenal of antifungal drugs to treat infections, with invasive infections often diagnosed too late to save the patient.

## Multiple Colony Testing

International student recruitment was supported by LMIC academic leaders who maintained engagement in the students' UK-based training and, upon successful completion of the training programme, facilitated their redeployment into jobs in their home countries. The students all undertook an MRes degree at the University of Aberdeen to provide basic expertise in medical mycology, molecular biology and immunology, before selecting a university within the UK to complete their PhD training.

All projects offered to the MRes/PhD students, postdoctoral researchers and clinical fellows were vetted by an International Advisory Board and local Management Board for excellence and alignment against strategic priorities. All trainees met annually at meetings of the BSMM to present their research, and attended courses in careers, scientific paper and grant writing, fellowship applications, research commercialisation, and other generic skills. This paper attempts to bring new insights to a long-standing historical debate over medical specialization by analyzing the formation of medical mycology, a somewhat marginal biomedical discipline that emerged in the mid-twentieth century around studies of fungal disease in humans.

The study of fungi predates that of bacteria and viruses, but from the 1880s it became eclipsed by bacteriology. However, in the postwar period, there were moves to establish medical mycology as an independent specialty. I trace the processes that led to the launch of professional societies in the United States, Britain and Japan, three major players in medical mycology, and more broadly in biomedicine. The analysis of the three different national contexts illustrates how geographical, medico-technological, epidemiological, political and social conditions gave the specialty a distinctive character in each country; this was further complicated by the different and changing medical fields in which fungal diseases were studied and treated. The three case studies show medical specialization as a process that is not simply cumulative but responds to specific historical events and developments.

All students also attended a workshop on fungal diagnostics and epidemiology hosted by Dr Elizabeth Johnson and colleagues at PHE in Bristol, and information sessions hosted by Wellcome on funding opportunities relevant to their future careers. The students therefore benefited from the collective expertise available throughout the MMFI consortium and from the building of a vibrant network of colleagues and expertise that extended across the whole UK sector. The MMFI consortium also worked alongside other Wellcome-funded infectious disease centres in Dundee, Glasgow and Edinburgh to present showcase events for eukaryotic medical microbiology that led to cross-disciplinary analyses, for example, drug resistance in eukaryotic pathogens.