mark. The development of the assay within the NHS setting has enabled the use of the assay within a financial envelope of £38 per patient (in-house reagent costs). The Metasin assay has evolved further and we are currently evaluating a modified formulation with a new Roche enzyme, giving a result in under 18 minutes for the PCR machine run time (cf. current 26 minutes). Metasin is a fast, sensitive and cost-effective NHS-derived solution for assessment of sentinel nodes in the intraoperative setting.

Salma Al-Ramadhani
Histopathology
University College, London

Priyadharshini Sai-Giridhar and Simon Holt
Department of Surgery and Pathology
Prince Philip Hospital, Llanelli, Wales

Ian Cree
Department of Pathology
University Hospitals Coventry And Warwickshire

Constantinos Yiangou, Neerja Agrawal and Margaret Jeffrey
Departments of Surgery and Pathology
Queen Alexandra Hospital , Portsmouth

Vasi Sundaresan
Cellular Pathology
Princess Alexandra Hospital NHS Trust, Harlow, Essex

Professor Rosemary Barnes

Dr Riina Richardson

Fungi – forgotten foes

In the UK, the public perception of fungal infection focuses on superficial and mucocutaneous infections such as athlete's foot, scalp ringworm, nail infections and thrush. Whilst overwhelmingly common, affecting approximately one in three of the population, these troublesome, painful and unsightly infections are seldom serious.

The true burden of fungal disease remains hidden and poorly perceived by the public and health providers with minimal investment from research funding bodies.[1]

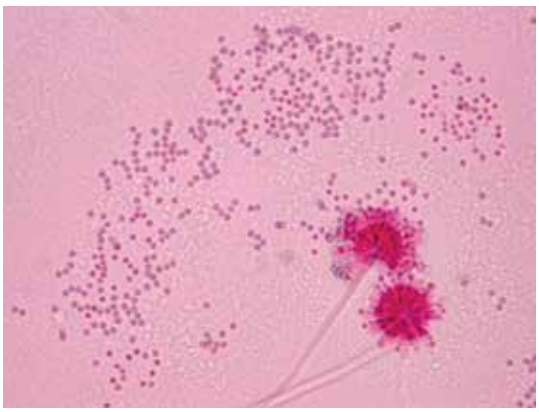
It is estimated that more 2.5 million people worldwide suffer from invasive fungal disease. The morbidity associated with these infections is considerable and with mortality greater than 50% results in more than 1.5 million deaths from invasive disease annually. Cryptococcal disease accounts for more infection-related deaths in sub-Saharan Africa than tuberculosis. Add to this chronic respiratory disease caused by fungi with approximately five million suffering from allergic bronchopulmonary aspergillosis,[2] two million from chronic pulmonary aspergillosis[3,4] and half a million sufferers with severe asthma with fungal sensitization in Europe,[5] and the burden of fungal disease becomes apparent. All these figures are estimates, as no coordinated surveillance of fungal disease is undertaken.

Expenditure on systemic antifungal drugs for the treatment of systemic opportunistic fungal infections such as candidosis and aspergillosis in the UK exceeds £112 million annually, but is outstripped by primary care prescriptions and over-the-counter sales of antifungal preparations for superficial infections. Veterinary medicine usage is also extensive and increasing, and there are major concerns regarding emerging resistance to current antifungal drugs, particularly the azoles. The azole (fluconazole) and triazole (itraconazole, voriconazole, posaconazole) agents are the most efficient and cost-effective treatment available for treating a wide range of mucocutanoeus, chronic respiratory and also life-threatening invasive fungal disease.

However, the total human and animal usage is dwarfed by agricultural use. Azole fungicides are widely used for crop protection and material preservation. They protect crops from disease, ensure yields and prevent fungal contamination of produce. Tens of millions of kilograms of triazole drugs are used in the regular spraying of crops and food commodities in UK each year[6] and the emergence of multiazole resistance in environmental isolates of aspergillosis has been clearly linked to usage. These resistant isolates are now found in clinical environments and are impacting on patient care.

Despite massive azole usage, fungi continue to decimate food production, accounting for bil-

Micrograph of aspergillus



lions of pounds of food wastage and contributing to global poverty. Scenarios analogous to the Irish potato famine are being repeated throughout the world as wheat, rice, corn and barley crops are totally destroyed by fungal pathogens. The situation is set to worsen as global warming and climate change contribute to the problem. Recent episodes of flooding are likely to exacerbate the situation further. Home dampness and indoor mould growth are associated with asthma, rhinitis and other respiratory conditions. Controlling indoor dampness and subsequent mould growth will reduce the burden of these diseases.[7]

Emerging fungal diseases maintain the vicious cycle of environmental destruction. Dutch elm disease, ash dieback, sweet chestnut blight, sudden oak death, red band needle plight of pines and massaria disease of plane trees are all caused by fungal pathogens. The deforestation results in increased carbon dioxide emissions and contributes to global warming,[7] paradoxically promoting further growth of thermotolerant fungal species. Other diseases attack insect populations crucial for plant pollination. For example, a microsporidial fungal infection contributes to colony collapse disorder that has brought about a massive decline in domestic honeybee populations and is thought to have eradicated wild honeybees from parts of Europe. Crop yields are decreased by as much as one third when bee pollination is affected. Other emerging diseases have led to the extinction of entire species of frogs, bats and other animals – sometimes before the species has even been discovered. Coral reefs and sea flora and fauna are not immune.[8] Such devastating extinction events have a major impact on biodiversity and ecosystems and are potentially threatening larger and more complex mammals further up the food chain. Indeed, dinosaur extinction 75 million years ago has been attributed to massive fungal proliferation following global warming, with a meteorite merely a triggering event.[9]

Fungi are immensely versatile and readily adapt to circumstances such as increasing globalisation and climate change. Unless we also adapt to meet these challenges, they pose a significant threat to human life in earth.

Professor Rosemary Barnes
Cardiff University, School of Medicine
Institute of Infection and Immunity
Department of Medical Microbiology and Infectious Diseases

Dr Riina Richardson
The University of Manchester
Faculty of Human and Medical Sciences
Institute of Inflammation and Repair
University Hospital of South Manchester

References

1. Brown GD, Denning DW, Gow NAR, Levitz SM, Netea MG, White TC. Hidden Killers: Human Fungal Infections. *Sci Transl Med* 2012;4:165rv13.
2. Denning DW, Pleuvry A, Cole DC. Global burden of allergic bronchopulmonary aspergillosis with asthma and its complication chronic pulmonary aspergillosis in adults. *Medical Mycology* 2013;51:361–370.
3. Denning DW, Pleuvry A, Cole DC. Global burden of chronic pulmonary aspergillosis as a sequel to pulmonary tuberculosis. *Bulletin of the World Health Organization* 2011;89:864–872.
4. Denning DW, Pleuvry A, Cole DC. Global burden of chronic pulmonary aspergillosis complicating sarcoidosis. *European Respiratory Journal* 2013;41:621–626.
5. European Lung Foundation. *Lung Health in Europe: Facts and Figures*, 2013.
6. ECDC. Risk assessment on the impact of environmental usage of triazoles on the development and spread of resistance to medical triazoles in Aspergillus species. ECDC Stockholm; 2013.
7. Peden DB, Bush RK. Advances in environmental and occupational disorders in 2012. *J Allergy Clin Immunol* 2013;131:668–674.
8. Fisher MC, Henk DA, Briggs CJ, Brownstein JS, Madoff LC, McCraw SL *et al.* Emerging fungal threats to animal, plant and ecosystem health. *Nature* 2012;484:186–194.
9. Casadevall A. Fungal virulence, vertebrate endothermy, and dinosaur extinction: is there a connection? *Fungal Genet Biol* 2005;42:98–106.