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Introduction

Fungal infections or mycoses are the great neglected diseases of medical history.[1] There are numerous histories of viral, bacterial and protozoan infections, for all times and all places, but very few studies of those caused by fungi. Why? It cannot be because of prevalence. Historical sources and contemporary epidemiological investigations show that fungal infections were and are ubiquitous in human and animal populations. Everyone in Britain and the United States in the last half a century would have heard of, if not suffered from, athlete's foot or thrush. In the first half of the twentieth century, children feared the school nurse finding ringworm on their scalp and having to endure, not only the pains of X-ray depilation or having their shaven head painted with gentian violet, but also exclusion from school and the shame of being stigmatised as 'unclean'.[2]

It seems that medical historians have followed the agenda of the medical profession in showing relatively little interest in conditions, such as the majority of cases of mycoses, that do not lead to 'illness' as such, but cause inflammation, irritation and discomfort. Medical history remains dominated by studies of diseases that had, or continue to have, a high profile within medicine, or have attracted government interest and investment because they cause significant morbidity or mortality. Yet, the majority experience of ill health was, and is, of self-limiting and self-treated conditions, where sufferers did not, and do not, consult a doctor and become 'patients'. In their efforts to recover 'the patient's view', medical historians have ignored the minor illnesses, injuries and infections that were, and remain, outside of the medical gaze.[3]

But medical historians have also largely ignored the ailments brought on by medical advances, and here too the history of fungal infections

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can be instructive. The grand narrative of Western medicine in the twentieth century was one of 'progress', evidenced by greater, scientifically based knowledge of the aetiology and pathology of disease, more accurate diagnostics, improved management of symptoms and pain, more effective treatments, innovations in surgery, improved health care, falling mortality rates and greater longevity.[4] Those telling this story recognised that progress was not unalloyed, yet amongst doctors such was the step change in their effectiveness and efficiency that problems, like the development of antibiotic resistance, were discounted or seen as something that would be solved by further scientific and technological advances.[5] However, medical professionals soon realised that therapeutic and technological advances often led to intractable problems; for example, the practice of managing the adverse effects of one drug with another could lead to patients taking more medicines to manage side effects than for their primary illness. Such practices were criticised in the 1960s, but for our narrative of fungal infections Ivan Illich's book *Medical Nemesis*, first published in 1975, is most relevant.[6] Illich made *iatrogenesis* – doctor induced disease – central to his critique of modern medicine, claiming that around 10% of all clinical encounters were for such conditions. He argued that the cures of modern medicine were often worse than the disease – if indeed there was a disease in the first place, as Illich also attacked the medicalisation of everyday life, anticipating the burgeoning of risk-defined conditions that emerged in the last quarter of the twentieth century.[7]

Thrush, the most prevalent opportunistic mycosis of the twentieth century, exemplifies these trends. In the 1940s and 1950s, the emergence of resistant bacteria was only one side effect of the new drugs. More important then was the development of so-called 'superinfections', also caused by antibiotics as they removed not just disease-causing bacteria but many others, and altered the normal microbial flora of the body. These changes opened the body to opportunistic infection by other bacteria, such as *Staphylococcus aureus*, and by fungi, especially *Candida*. This fungus had previously only affected the 'external' mucus membranes in the mouth and genitalia, but emerged in the 1950s as a rare, but serious, internal and systemic infection, where fungi grew on major organs, such as the heart. It was not just patients on antibiotics who were vulnerable. There were a growing number of patients whose immune systems were weakened or immunocompromised. Initially, this situation developed as a side effect of steroids and other similar treatments, but then such states were deliberately produced by doctors to aid the acceptance of transplanted organs, or as a by-product of new

cancer therapies. In 1987, John W. Rippon, a leading American medical mycologist, reflected on the situation.

> The mycology of human infections in the 1980s is the mycology of the soil, rotting vegetables, shower curtains, toilet bowls, leaf piles, wilted flowers and dung heaps. Organisms literally come out of the walls to infect immunosuppressed patients. Technical medical and surgical expertise is such that we can pass around hearts, lungs, and livers only to be thwarted by a *Fusarium* from a rotting plum.[8]

Rippon was pointing to a larger truth about human fungal infections, namely, that their prevalence has been linked to specific ecological conditions and interactions, not only within the body, but also within the wider social and physical environment. At the time Rippon wrote, the United States, and soon the Western world, was gripped by a popular health panic about fungal disease. Some fringe doctors promoted the view that *Candida* infection was responsible for all manner of 'modern' ailments, including chronic fatigue syndrome (CFS) and inflammatory bowel disease (IBD), in what they styled as 'the yeast connection'.[9]

In this book, we discuss the changing medical and public profile of fungal infections in the period 1850–2000. We consider four sets of diseases: ringworm and athlete's foot (dermatophytosis); thrush or candidiasis (infection with *Candida albicans*); endemic, geographically specific infections in North America (coccidioidomycosis, blastomycosis and histoplasmosis) and mycotoxins; and aspergillosis (infection with *Aspergillus fumigatus*). We discuss each disease in relation to developing medical knowledge and practices, and to social changes associated with 'modernity'. Thus, mass schooling provided ideal conditions for the spread of ringworm of the scalp in children, and the rise of college sports and improvement of personal hygiene led to the spread of athlete's foot. Antibiotics seemed to open the body to more serious *Candida* infections, as did new methods to treat cancers and the development of transplantation. Regional fungal infections in North America came to the fore due to the economic development of certain regions, where population movement brought in non-immune groups who were vulnerable to endemic mycoses. Fungal toxins or mycotoxins were discovered as by-products of modern food storage and distribution technologies. Lastly, the rapid development and deployment of new medical technologies, such as intensive care and immunosuppression in the last quarter of the twentieth century, increased the incidence of aspergillosis and other systemic mycoses.

In understanding and managing infectious diseases, scientists and doctors have long argued for thinking about them in terms of the metaphor of 'seed and soil', where the 'seed' is the infectious organism or pathogen: that is, virus, bacteria, fungi, protozoa (single cell) or metazoan (multicellular); and the 'soil' is the human body and its environs.[10] Thus, for someone with the common cold, the notion of 'seed and soil' ensures that we go beyond focusing only on infection by the virus (the seed) and consider the sufferer (the soil). This means looking at the conditions in which the person was exposed to the virus, the quantity and quality of the virus reaching the body, the nature of the body's specific immune response and the overall health of the individual. We all know that we do not 'catch a cold' every time we are exposed to the virus and that some people suffer longer and more serious illness than others do. Some variations are individual, but epidemiological studies have always shown patterns of exposure, susceptibility, sickness and recovery by age, gender, class, occupation, ethnicity and other socio-cultural variables. For example, in their history of pulmonary tuberculosis, René and Jean Dubos systematically use the notion of 'seed and soil' to discuss the disease at all levels, from biological factors influencing the susceptibility of cells and tissues, through to the socio-economic and technological variables that have shaped global trends in morbidity and mortality.[11] In this book, we frame our history of fungal infections in terms of 'seed and soil'; hence, our 'seeds' are specific fungal pathogens and we interpret 'soils' widely to include the human body, social relations and structures, and the medical, material and technological environment.

Fungi

Fungi and how they cause diseases are not well known, so it will be useful here to give a brief introduction to the nature of the 'seeds' of mycoses. Our account is part historical and part current.

Mycology is the branch of science that studies fungi and until the 1960s, it was a part of botany, at which time its subject matter was moved to the animal kingdom. Since then, fungi have been placed in their own kingdom, with the other four being plants, animals, protozoa and monera (bacteria).[12] Current estimates are that there are well over 100,000 species of fungi and many more are still to be classified, let alone discovered. Some fungi are large and multicellular, like toadstools. However, most species are microscopic, single cell organisms and are best known as industrial agents (yeast fungi in the production of bread and beer) and as medical agents (*Penicillia* spp. remain the source

of the world's mostly widely used antibiotic). The larger fungi develop as microscopic filaments called hyphae, which branch and grow into networks or colonies called mycelia, whereas smaller fungi, such as yeasts, are single cell microorganisms.

Many writers divide fungi into 'good' and 'bad', judged by their impact on human existence; fungi themselves, of course, are just filling niches that allow them to multiply and survive. In popular writing, the 'good' fungi are those used in industrial processes or medicine, such as yeasts and penicillins mentioned above, plus those that can be eaten, break down waste or work in plant roots to fix nitrogen. The 'bad' fungi are those that produce diseases in plants, animals and humans. In terms of impact on humanity, fungi do most harm as causes of crop diseases and amongst farm animals, but they are also a threat to homes, where their ability to breakdown organic matter is seen most strikingly in the dry rot fungus which can destroy wooden structures very rapidly. Most fungi are saprophytic, that is, they obtain their nutrients from breaking down organic matter, normally dead tissues, and absorbing the products to 'feed' their metabolism. They mostly live on or within the material on which they are feeding. A small number of fungi, and of course the ones that concern medical mycologists, derive their nutrients from infecting living tissue, either by destroying it, or through establishing a symbiotic relationship that affects human tissues and their functioning.

Following long-established Linnaean principles, the classification of fungi was mainly by their reproductive and sexual characteristics. Thus, the 1911 *Encyclopaedia Britannica* divided fungi into three groups: the *Basidiomycota,* which produce club-like fruit bodies that spread spores (e.g. mushrooms); the *Ascomycota*, which produce fruit bodies on special pods or sac structures (e.g. baker's yeast, penicillin and most human fungal pathogens); and the *Phycomycetes* that reproduce sexually by spores joining (e.g. black bread mould). These classifications held for most of the twentieth century, though with many refinements and revisions with individual groups, genera and species. Certain fungi proved very difficult to classify as they had different forms in different stages of their life cycle. In the final decades of the century, the whole basis of ordering fungi changed as the new types of analysis of their DNA (their genome or genotype) revealed different relationships from those of their form and function (phenotype). The fluidity of understanding of the nature and classifications of fungi was evident with the microorganism known currently as *Pneumocystis jiroveci*. Through the 1980s, this organism was regarded as a protozoan and named *Pneumocystis carinii*, when it was the subject of extensive research as it was a major cause of pneumonia

and death in HIV/AIDS sufferers.[13] Indeed, *Pneumocystis carinii* pneumonia (PCP) was an early marker of the epidemic and allegedly responsible for the deaths of celebrities such as Freddie Mercury. The redesignation of the organism as a fungus was first made in 1988, based on work using the new techniques of DNA sequencing, though this remained controversial until the late 1990s when the reclassification was finally accepted.[14]

Fungal diseases

Geoffrey Ainsworth, who has written most extensively on the history of fungal diseases, argues that fungi are amongst the oldest recognised causes of infection in humans.[15] Hippocrates seemingly wrote on 'aphthae' (sores in the mouth) in 500 BC, which modern mycologists have identified as thrush. Two millennia later, ringworm infection was present on the skin and in the hair of the subjects of Old Masters' paintings. In the modern medical era, the first systematic writings on fungi as a source of human disease were by the Hungarian born, Paris-based physician and microscopist David Gruby in 1842–1844. At the time, fungi were understood to be the sources of a number of diseases and attracted considerable scientific interest. In the 1830s, the Italian entomologist Agostino Bassi published claims that the devastating muscardine disease of silkworms was due to a microscopic fungus *Tritirachium shiotae*, which was eventually renamed in his honour as *Beauveria bassiana*.[16] Bassi was a major influence on Louis Pasteur, both in his work on the silkworm diseases of *pébrine* and *flacherie* in the 1860s and on the idea that living microorganisms might cause infectious diseases. The work of Bassi and Pasteur showed that fungal infections were, and in fact still are, the cause of economic problems in agriculture and related industries.[17] Ainsworth goes on to make the point that most 'mycologists' in Britain and the United States work as plant pathologists, with a disciplinary allegiance to botany, and that medical mycologists were and remain quite a small minority, with a quite different orientation.

In medicine in the 1830s, and in keeping with the then fashionable focus on pathological anatomy and lesions, distinctive and specific fungal infections of the skin, such as favus and ringworm, were well recognised. Classifications or nosologies of skin diseases were produced in the early nineteenth century, most influentially in Thomas Bateman's *A Practical Synopsis of Cutaneous Diseases According to the Arrangement of Dr Willan* (1813) and an atlas *The Delineations of Cutaneous Disease*

in 1817.[18] Many authors followed the French physician Jean Louis Alibert in using extensive colour illustrations and some copied the wax models (*les moulages*) that he collected at the Hôpital Saint-Louis in Paris.[19] The use of colour illustrations continued with photography, as in Charles-Philippe Lallier's *Leçons cliniques sur les teignes*, published in 1878.[20]

The contagious and infectious aspects of fungal disease meant that, from the 1860s, doctors and scientists regarded them as 'germ diseases'.[21] Early historians of germ theories of disease certainly traced the familiar lineage from van Leeuwenhoek through Bassi to Pasteur, and the natural philosophers and medical men who used microscopy and culturing to study fungi. David Gruby first linked specific fungi to favus, sycosis and ringworm infections of the human scalp in the 1840s. For the latter, he first described the clinical condition of tinea tonsurans (scalp ringworm), though the terms 'herpes tonsurans' and 'teigne tondante' also enjoyed currency.[22] In the 1850s, botanists and dermatologists agreed on *Trichophyton* – literally hair-fungus due to its shape seen through microscopes – as the main ringworm germ and, in line with the wider switch to naming diseases by their causes rather than their signs and symptoms, in France tinea tonsurans became 'trichophytie'. As we discuss in Chapter 1, these developments were followed by leading dermatologists, such as William Tilbury Fox and Thomas M'Call Anderson, but most doctors and dermatologists remained focused on morbid anatomy and nosologies based on signs and lesions.

Fungus theories of infectious disease were popular in the 1840s and the best known was the 'cholera fungus'.[23] In a paper read to the Microscopical Committee of the Bristol Literary and Philosophical Institution in 1849, 'fungoid' bodies were reported in the faeces of cholera sufferers.[24] The authors emphasised analogies between the growth and decay of fungi, and the rise and fall of zymotic diseases in individuals and in populations over epidemic periods. However, given that contemporaries thought that fungi were the 'appointed executioners and nimble scavengers of nature', any such organisms were understood by contemporary doctors to be the consequences rather than the causes of cholera. Medical views on the causal role of living organisms in disease waxed and waned from the 1840s to the 1880s, until bacterial germs were accepted as major pathogens.[25] At this time, bacteria were termed as the 'Schizomycetes', literally the splitting fungi, so named because they reproduced by the division of cells, and were believed to be a type of fungi because of their microscopic form and physiological function as saprophytes.

One of the first British textbooks on the new science of germs was German Sims Woodhead and Arthur Hare's *Pathological Mycology* published in 1885.[26] However, this was the only time 'mycology' was used in this context; the German term *Bacteriologie* soon took over. In the new manuals and textbooks on 'bacteriology' and 'microbiology', fungi as causes of infection were, at best, described briefly and typically in a final chapter or appendix. For example, Muir's and Ritchie's influential *Manual of Bacteriology*, published in 1899, had a chapter entitled 'Non-Pathogenic Micro-organisms – Fungi', and presented them as likely laboratory contaminants rather than pathogens. The authors discussed *Mucor* spp., *Oidium* spp., *Aspergillus niger*, *Penicillium glaucum*, plus yeasts, and ended with the comment, 'Certain fungi closely related to the above are pathogenic agents.' Readers were referred to Anton De Bary's *Comparative Morphology and Biology of the Fungi, Mycetozoa and Bacteria*, first published in 1886, for further details.[27]

In the twentieth century, fungi were recognised as causing three types of disease in humans and animals. First, there were infections where fungi develop parasitically in the tissues of the host, at (literally) three levels: superficial mycoses, like athlete's foot, where infection is limited to the outermost layers of the skin, nails and hair; subcutaneous mycoses, like the tropical disease of Madura foot (mycetoma), where the growth extends to the underlying layers of the skin and perhaps into bone; and systemic mycoses, like aspergillosis, where infection spreads through internal organs and tissues.

Second, there were fungal poisons, either toxins in the fungi themselves, as with poisonous toadstools, or toxins produced by the growth of fungi on foodstuffs, as with aflatoxins (produced by *Aspergillus flavus*). Third, there were allergic reactions to fungal spores and moulds, which range from mild to acute, depending on the dose and susceptibility of the host; thus, fungi are a common cause of asthma. There was a fourth type of disease that was 'discovered' in the 1980s and remains highly contested – 'fungal overgrowth'. As we show in Chapter 3, this condition has been widely dismissed by the medical profession as a fiction, yet it had wide currency with the public and was linked to CFS and other 'diseases of modernity'. In the cultural climate in North America and Europe, where lifestyle was increasingly regarded as a cause, as well as a solution, to ill health, books such as William G. Crook's *The Yeast Connection* (1983), which attributed various chronic conditions to the overgrowth of *C. albicans*, became a best seller and spawned many imitators. Crook also had the cure: dietary and lifestyle changes, plus a

course of antifungal antibiotics, which was surprising given his pedigree in 'alternative medicine'.

The history of medical mycology

The multi-faceted career of medical mycology's leading historian Geoffrey Ainsworth exemplifies the diverse and changing character of the field in the twentieth century. He studied pharmacy at University College, Nottingham, and then pursued a dual career in plant pathology and medical mycology.[28] He first worked on the virus diseases of plants at Britain's two leading botanical institutions, the Rothamsted Experimental Station and the Experimental and Research Station in Cheshunt. He spent the Second World War at the Imperial Mycological Institute at Kew, developing abstracting services on all aspects of mycology. After the war, he moved to the pharmaceutical industry, as head of the mycological department of the Wellcome Research Laboratories at Beckenham, Kent. There he led work on the antibiotics produced by fungi, such as streptomycin and penicillin. He then moved, first, to the London School of Hygiene and Tropical Medicine and later to the University of the South West (later the University of Exeter), before returning to the now Commonwealth Mycological Institute, where he stayed until his retirement in 1968. Ainsworth published widely on all aspects of fungi. His major works were *Dictionary of the Fungi* (1943), *British Smut Fungi* (1950) with Kathleen Sampson, *Medical Mycology* (1952), and the multi-volume *The Fungi: An Advanced Treatise* (1965–1973) with A. S. Sussman and F. K. Sparrow.

Towards the end of his career, Ainsworth developed an interest in the history of mycology and published three books that have been immensely valuable in the research and writing of this book: *Introduction to the History of Mycology* (1976), *Introduction to the History of Plant Pathology* (1981) and *Introduction to the History of Medical and Veterinary Mycology* (1987).[29] In his preface to the latter volume, he sets out his approach and the scope of the topic.

> Although possessing deep, if slender roots that can be traced back to ancient times, medical and veterinary mycology is essentially a development of the twentieth century, especially the last fifty years during which time several mycoses at first considered to be rarities have been shown to affect millions of men, women, and children and their domesticated animals .... Here the attempt made to sketch in

> the historical background, by illustrating the approaches to a series of basic problems, is limited to what might be described as the 'natural history' of human and animal mycoses.[30]

While we agree with Ainsworth on the point that the development of medical mycology was a phenomenon of the twentieth century, our work differs in two ways. First, we do not take the specialism of medical mycology as given, or historically constant, rather as a social institution that had to be created and sustained. Second, we do not set out a lineage of ideas, but rather discuss changing knowledges in specific institutional and social settings, and also explore practices and meanings.[31]

The history of medical mycology in the United States in the twentieth century has been described in great detail in a monograph by Ana Victoria Espinel-Ingroff published in 2006.[32] Her narrative is comprehensive and wonderfully rich in characters and institutional detail. It focuses on training and mapping the professional networks that have shaped medical mycology across the country. At the same time, the author tells the story of discoveries in the understanding and management of the main fungal infections that affect Americans. It is history informed by disciplinary politics, as Espinel-Ingroff's reference point is what she sees as a crisis in medical mycology in the United States. On the one hand, the importance of mycoses has grown with their increased prevalence and the arrival of effective antifungal drugs. Yet, on the other hand, the field seems to be fragmenting, being drawn at one end to molecular approaches and basic biology, and at the other to applied clinical research, leading to the neglect of the old, middle ground of taxonomy, aetiology, physiology and pathogenesis.

Woven into Espinel-Ingroff's history narrative is a narrative of developments in the field in the twentieth century, with five periods defining her chapters. The discussion of the 'Era of Discovery (1894–1919)' explores how work on fungi followed that in bacteriology in seeking the causal organisms of specific infections and the understanding of basic fungal biology. The 'Formative Years (1920–1949)' are characterised by the establishment of training programmes, laboratory services and epidemiological studies of common diseases, such as athlete's foot and thrush, or the then very rare systemic mycoses. The period 1950–1969, the 'Advent of Antifungal and Immunosuppressive Therapies', was dominated by drug discoveries (nystatin, amphotericin B, griseofulvin) and the increased incidence of severe opportunistic systemic fungal infections that were linked to antibiotics and immunosuppressive therapies. The 'Years of Expansion (1970–1979)' are portrayed as the apogee of

medical mycology, seen in the establishment of services to deal with the increased incidence of infections, basic research to underpin clinical innovations and the recognition of the specialty by the American Society for Microbiology (ASM). Finally, the 'Era of Transition (1980–1996)' saw continued increase in the incidence of opportunistic infections in cancer and transplant patients, and amongst AIDS patients, but also the fragmentation and relative neglect of the specialism.

What few histories there are of fungal infections are largely embedded in accounts of the development of the specialty of medical mycology, but there are a number of books and journal articles on specific infections. There is only one monograph on a disease discussed in this book, Thomas Daniel and Gerald L. Baum's *Drama and Discovery: The Story of Histoplasmosis*.[33] Their narrative follows the emergence of the disease from social changes in its endemic areas and the research networks in which new understandings of its epidemiology, aetiology, pathology and treatment developed. It is typical of much work on the history of mycoses, as with Ainsworth and Espinel-Ingroff, in being written by medical mycologists, but is quite different and richer as it explores the social as well as medical history of histoplasmosis.[34] There are no book length histories of coccidioidomycosis and blastomycosis comparable to *Drama and Discovery*, but there are very useful practitioner histories, for example, Jan Hirschmann's account of the early history of coccidioidomycosis in America.[35]

Yet, as we have indicated, 'biographies' of mycoses written by medical historians are rare. Aspergillosis has no thoroughgoing histories.[36] Ringworm has few historians in Britain and the United States, and even reflections by practitioners are rare.[37] It has only excited attention in Israel, in relation to the controversy of the long-term effects on children of X-ray treatment of the scalp and popular representations of the practice as the 'Ringworm Holocaust'.[38] It is also surprising that historians of medicine in the United States, who have thoroughly investigated popular medications and health activism, have missed athlete's foot, a condition that plagued not only the athletes but the country's youth, soldiers and miners.

Mycoses and medical history

In this book, we aim to do more than provide a narrative of a group of neglected infections. Our study also gives new perspectives on the history of twentieth-century medicine on a number of fronts: specialisation; minor illnesses and self-treatment; and 'orphan diseases'. Firstly,

we present an account of an area of medicine – medical mycology – that for most of the twentieth century was small and marginal, and where practitioners struggled to establish an area of specialist work. The development of specialisms and specialisation has long interested historians of medicine.[39] George Rosen's study of ophthalmology was path breaking and work since then has linked the division of labour to many factors within medicine and outside. George Weisz, in the most recent and comprehensive study on the topic, finds that 'divide and conquer' best explains the overall process in medicine, as these terms '[express] a fundamental intellectual strategy', whereby medical professionals were, in a matter of a century, divided into 'smaller and more manageable groups based on common attributes' and conquered by 'organization based on a novel kind of expertise'.[40]

Most histories of specialisation and specialisms are of successful enterprises and can be teleological, charting the seemingly inevitable journey to the present division of labour in medicine. Our narrative of medical mycology runs against this grain, though it does not present medical mycology as a failed specialism, rather one, as Espinel-Ingroff's work makes clear, the position and status of which was always problematic. For most of the twentieth century, it was small, institutionally fragmented and dispersed geographically. Its practitioners tried to 'divide' themselves off from other specialisms but were relatively unsuccessful because their services were never in sufficient demand to form a critical mass either numerically or politically. Thus, we challenge the accepted, though often implicit, view that specialisation was an inevitable path in twentieth-century medicine, where it becomes ever more populated with full-time 'mono-specialists'; that is, clinicians and scientists who worked on a single disease or group of diseases, a particular organ or organ system, specific technologies or a restricted patient group, say, by age or sex. Our research on the doctors and researchers who treated and studied fungal infections shows a different, and perhaps equally common, pattern of work: clinicians and scientists making a living as working in and combining a number of specialisms.[41]

We suggest that it is useful to think about twentieth-century medicine generally in terms of the doctors, and other health workers for that matter, developing careers in a number of 'specialist practices'. Historians of medicine often overlook the fact that doctors and medical scientists had to 'make a living', and that in less wealthy times, when health was a lower priority in private and state budgets, this was done by earning where they could and what they could.[42] In this context, 'medical mycology' was an area of 'specialist practice' for certain

botanists, dermatologists, bacteriologists, hospital physicians and surgeons, infectious disease doctors, microbiologists, general practitioners or, of course, combinations of these. Typically, 'specialist practice' was in cognate areas; hence, the first 'medical mycologists' were mostly botanists, or those who created the specialism of dermatology. Nevertheless, in the late nineteenth century few doctors were able to work full-time on skin diseases, so dermatologists were often general practitioners, who functioned as part-time specialists, part-time in hospital outpatient clinics.

Secondly, and as noted already, fungal infections represent the overwhelming experience of illness, then and now, like the common colds, sickness and diarrhoea, and sore throats that are self-limiting, self-treated or treated after one short consultation with a general practitioner.[43] Research in the 1980s revealed that on average only one in 20 'symptom episodes' led to a medical consultation, a pattern that was termed the 'iceberg of illness'.[44] If that was the position in a country with a National Health Service, offering care that was 'free at the point of delivery', the proportion would almost certainly be lower in pay-for-service medical and healthcare systems, then and now. There are few studies, except for the era of 'bedside medicine', of the everyday experience of illness, and of decisions on when and how to self-treat, and when and how to seek medical consultation and become a patient.[45] That said, our focus is on the *medical* history of mycoses – a sufferer's history would be quite different and, in fact, very difficult to research. However, we do try to capture sufferers' agency, for example, in our discussion of the proliferation of proprietary remedies for athlete's foot and thrush.

Thirdly, and at the other end of the scale of prevalence, systemic fungal infections have been classified as 'orphan diseases'; that is, those too rare to attract the attention of research agencies or the interest of many clinicians and researchers.[46] The term originated in the United States and the Orphan Drug Act, 1983, promoted by the National Organization for Rare Disorders and the Federal Drugs Agency (FDA). In the United States 'orphan diseases' are those with a prevalence of less than 2,000 cases per year. By the end of the twentieth century, the rise in the incidence of mycoses meant that this designation only applied to the geographically localised infections and the rarer types of hospital acquired or nosocomial infections. Yet, for most of the twentieth century, opportunistic, invasive mycoses were rare and medical mycologists and other interested parties bemoaned their neglect. In part, this was because such infections were seen as 'diseases of the diseased' and affected patients who were seriously ill and close to death. In fact, doctors spoke of these

patients receiving 'salvage therapies', where ethical standards were different and there was scope of experiment and the non-standard use of standard drugs. Interestingly, when invasive mycoses ceased to be 'rare', they attracted the attention of many surgical and medical specialists, and researchers in pharmaceutical companies, who sought to transfer their successes with mass market, external antifungals to invasive, systemic disease. Indeed, the story of medical mycology in the second half of the twentieth century is dominated by the development of new antifungal antibiotics, principally polyenes (e.g. nystatin and amphotericin B), azoles (e.g. clotrimazole and ketoconazole), triazoles (e.g. fluconazole and itraconazole) and echinocandins (e.g. caspofungin), targeted at the 'seeds' of infection.

The book

We discuss our four sets of infection in five chapters: two on ringworm (dermatophytosis), and one each on thrush, the geographically specific mycoses and mycotoxins, and aspergillosis. We present histories of each disease group and while our approach is essentially thematic, there is an overall movement through time. Thus, the first chapter on ringworm begins in the mid-nineteenth century and ends around 1910, while the final chapter on aspergillosis is mainly about changes in the last quarter of the twentieth century. Our narrative moves between Britain and the United States following the changing locations where medical and social interest and activity was greatest. We are neither comprehensive nor comparative in our discussion of medical mycology in these two national contexts. However, we use the fact that work on fungal infections in the twentieth century, as demonstrated by the work of the International Society for Human and Animal Mycology (ISHAM), was dominated by an Anglo-American axis, though this is not to diminish in any way activities in other countries, which we discuss as appropriate.

Our first chapter frames ringworm as a disease of schools and schoolchildren. The disease had been reported previously in orphanages and similar institutions, but its incidence and profile increased with the arrival of mass schooling, which provided ideal conditions for its spread, both through increased opportunities for contagion (seeding) and the exposure of poor children (weakened soil). We look at responses to the problem, one of which was special schools for the isolation and treatment of sufferers, and which became sites for the use of the new X-ray technologies, not to kill the seeds of infection, but to alter the

soil by removing hair, the locus of infection. In the second chapter, we move from head to toe, from Britain to the United States, and focus on athlete's foot. Concern over ringworm infection of the feet, along with infection of the crotch, armpit and similar areas of the body, began in the 1920s, principally amongst sportsmen and women. Athlete's foot was described as a perverse consequence of the nation's attempt to improve the health and fitness of its youth, especially with the burgeoning of college sports and improved hygiene facilities. The infection was met with the tools of modern public health propaganda, being presented in some instances as equivalent to a sexually transmitted disease, and by new methods of treatment produced by the pharmaceutical industry, first in a rash of proprietary medicines and then antifungal antibiotics.

Thrush, the subject of our third chapter, was regarded at the start of the twentieth century as a disease of weak children, but moved in the medical and public view to a genital infection, principally of women and was linked mainly to alterations in the body due to pregnancy and lifestyle changes.[47] We then discuss how, in the second half of the twentieth century, thrush was linked in different ways to the development of antibiotics. It was soon recognised as a side effect of penicillin therapy, while the search for new and better bacterial antibiotics led to the discovery of nystatin – the first modern antifungal antibiotic, which soon became a specific treatment for thrush. Systemic *C. albicans* infection, known as invasive candidiasis, became, paradoxically, more prevalent in patients taking bacterial antibiotics, but also in those with cancers, transplants and inflammatory conditions. This problem was met by a search for new antifungal drugs, with successes improving the institutional position of medical mycology. We end the chapter with a discussion of 'The Yeast Connection' phenomenon.

In Chapter 4, we discuss the regionally specific fungal infections in the United States that came to the fore as a consequence of the economic development of certain regions in the South and Midwest, where population movement brought in non-immune groups who were vulnerable to endemic mycoses. The forms of economic development were also important, as new methods of production and types of industrial and domestic construction created new environmental conditions, and in some cases literally transformed and transported fungi-laden soil dust. In the same vein, we show how new technologies of food production, transportation and storage produced a new class of hazardous compounds – mycotoxins. In our final chapter, we discuss aspergillosis, the most serious of the invasive mycoses that have emerged from

new medical technologies, such as intensive care and immunosuppression. An important theme here is iatrogenesis, as attempts to control aspergillosis exemplified the now routine issue in modern medicine of balancing the benefits and adverse effects of primary treatment, with secondary and tertiary interventions.