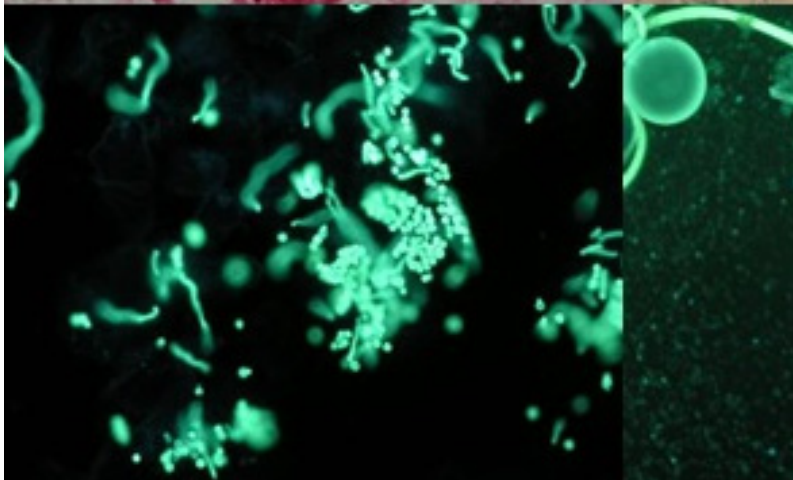
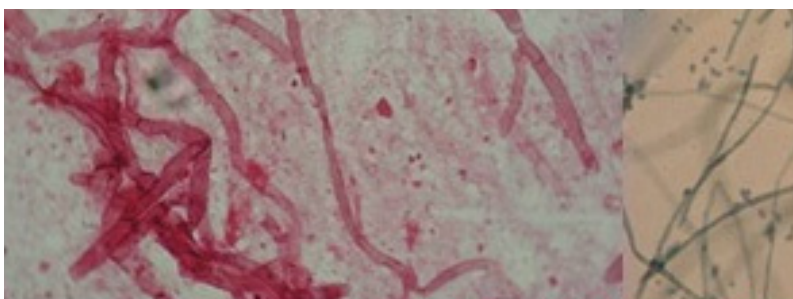
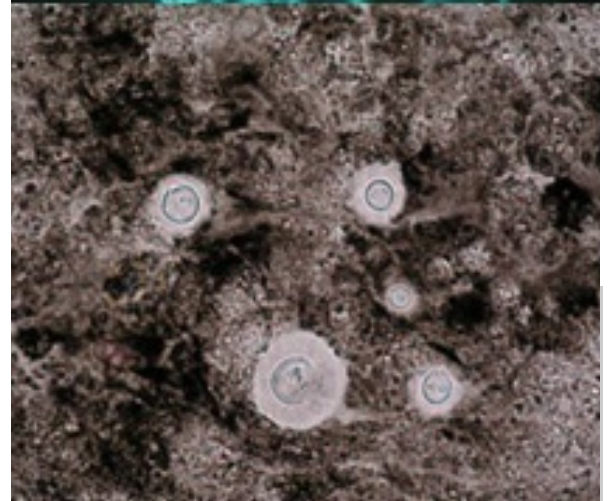
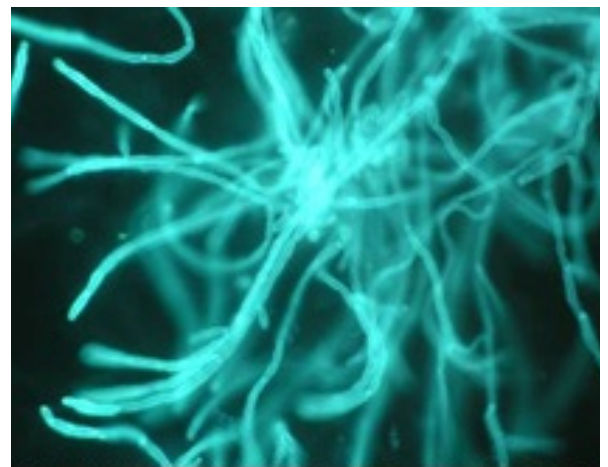
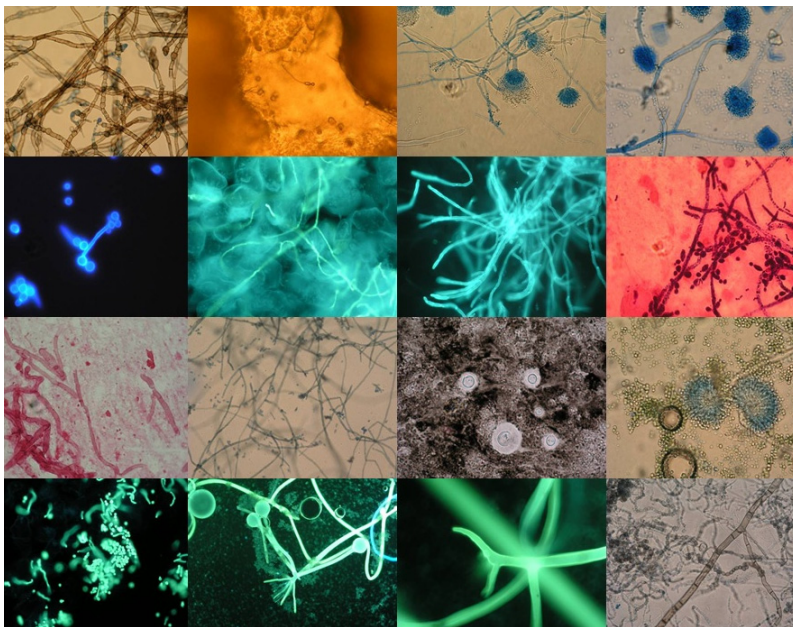


Fungal Diseases in the UK

The current provision of support for diagnosis and treatment:
assessment and proposed network solution





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Report of a working group of the Health Protection Agency Advisory Committee for Fungal Infection and Superficial Parasites

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Front cover picture: assorted fungi kindly supplied by Dr RP Hobson,
Mycology Reference Centre, Leeds

Executive summary

The health burden of diseases caused by fungi is considerable. In 2002, almost 10,000 patients in England were estimated to have suffered a deep-organ fungal infection as a negative corollary to otherwise successful treatment for a serious illness; almost half of them died from their fungal disease. Fungal infections such as athlete's foot and vaginal thrush are ubiquitous throughout the population. The financial impact of all fungal diseases is reflected in a national expenditure on antifungal drugs exceeding £90M in 2002. This cost has been rising annually and could rise even further with the recent introduction of important new antifungal drugs. Specialised support services for fungal diseases are few and patchily distributed throughout the UK. A coherently administered network of medical microbiologists with a specialised interest in clinical fungi could dramatically improve diagnosis and optimise antifungal therapy, thus reducing morbidity, mortality and drug costs associated with fungal disease.

In England in 2004, there are only 3 specialised laboratories for fungal diseases, employing 6 Grade B and 1 Grade C Clinical Scientists; none is located in the capital. In Scotland there is one further specialised laboratory. The numbers of UK personnel specialised in fungal laboratory tests has been decreasing steadily since the early 1980s. Certain specialised tests (such as antifungal drug monitoring and antifungal susceptibility testing) impact directly on care, and it is recognised that increased hospital infection, deaths and additional expense accrue from poor therapy. In addition, much unnecessary therapy contributes to the £40M annual community drug expenditure on antifungal agents.

Developing programmes for susceptibility testing of fungi involved in invasive infections is specifically mentioned as part of the Health Protection Agency's (HPA) strategic goal to prevent and reduce the impact and consequences of infectious diseases.

A Working Group of the Advisory Committee for Fungal Infection and Superficial Parasites was convened to identify how the provision of support services for fungal diseases in the UK can be improved, with the effect of optimising antifungal therapy. The key recommendations are as follows:

Key recommendations

- **Each region should have access to a comprehensive fungal testing service. This service should involve a clinician with a major interest in fungal infection to assist in all aspects of diagnosis, treatment and surveillance.**
- **A UK-wide HPA network should be set up to co-ordinate development of the service via training, SOPs and national surveillance. Development of the service will be supported by the British Society for Medical Mycology, which is already established in the provision of mycology training and standards of care. Funding for England will be pursued through the HPA and Workforce Development Confederations. Funding for the rest of network would need to be pursued from other sources.**
- **The fungal surveillance system needs to be strengthened, and should include antifungal resistance. This process should be jointly led by the HPA Mycology Reference Laboratory (Bristol) and Communicable Disease Surveillance Centre (now part of the Centre for Infections) (London), capturing data from all laboratories undertaking sensitivity testing.**

Introduction

Invasive fungal infections are increasing in frequency in all western countries as a result of modern medicine and increased survival from otherwise lethal diseases (Cohen, 2000). While there is some world class expertise in fungal diseases in the UK in some locations, service provision at all levels (routine, specialist, reference laboratory services and clinical care) is tenuous and poorly distributed nationally. Major advances have been made in diagnosis and treatment over the last 10 years (fluorescent microscopy, antigen detection, PCR, CT scanning, validated susceptibility testing, therapeutic drug monitoring, 2 new antifungal agents), but very few are in routine practice in the UK, except for usage of the new (expensive) drugs.

This paper sets out the current situation in England, analyses the deficits and identifies areas in which major improvements could be made, at minimal cost. Provision for fungal disease services in the rest of the UK is not notably different from that in England.

The burden of fungal diseases in England

Fungal diseases can be divided into three broad groups:

- Invasive life-threatening infections, especially those due to *Candida* and *Aspergillus* spp.
- Superficial infections such as thrush, athletes foot, scalp ringworm, nail infections etc.
- Allergic fungal disease of the sinuses or chest

Our understanding of the overall burden of fungal infections in the UK is very limited as there are no infectious disease surveillance programmes specific to fungal infections currently in existence. However, some data are available from surveillance activities designed to capture a range of infectious disease diagnoses. As these programmes were not designed to specifically capture data on the incidence of fungal infections, they each have their limitations.

Invasive fungal infections

The only source of national surveillance data for invasive fungal infections are derived from routine microbiology laboratory reports made to CDSC (now Centre for Infections) via regional Health Protection Agency units. As these data are derived from microbiological diagnoses, their robustness is dependent on the diagnostic laboratory's capacity to make the diagnosis, as well as their consistency and quality of reporting. These data are likely to be of most value for invasive candidosis, owing to its relative ease of microbiological diagnosis. A review of reports made between 1990 and 1999 identified substantial increases in invasive candidosis over this period, from 6.8 to 13.7 per million population in England and Wales (Lamagni *et al.*, 2003). Invasive candidosis was the most commonly reported invasive

mycosis during this review period. Since 2002, reports of candidaemia are published each year in the CDR Weekly, and show further year-on-year rises in numbers of diagnoses, a total of 1148 being reported for England, Wales and Northern Ireland in 2002 (HPA, 2003).

Another approach to quantifying the burden of fungal infections is to estimate likely numbers of cases from studies measuring incidence in a specified time, place and patient group and applying this to defined populations of patient groups. What follows are estimates of the burden of disease in the UK (Denning, pers comm. 2003). If the patient groups below in table 1 were to be summed, this would give 5466 cases of invasive candidosis/candidaemia and 4120 cases of invasive aspergillosis, although there may be overlaps between these groups.

Table 1: Invasive fungal infection - estimated number of cases, 2002

Patient group	Number of patients	Invasive candidosis/ candidaemia risk estimates**	Expected number invasive candidosis/ candidaemia	Invasive aspergillosis risk estimates®	Expected number invasive aspergillosis
AlloBMTx	793	4%	32	10%	79
Solid organ Tx	2953	5%	148	1.9%	56
Leukaemia	16269	3%	488	6%	976
Solid tumour (neutropenic)	28955	3%	869	2%	579
Advanced cancer	131678	1%	1316	1.5%#	1975
ICU	210130	1%	2101	0.2%	420
Burns	378	5.6%	21	1.9%	7
Renal dialysis	24536	0.2%	490	0.02%	5
HIV/AIDS	661	0.2%	1	4%	26

** no estimate for surgical patients, but some are in ICU, or have advanced cancer

@ no inclusion of most chronic chest, steroid-treated patients, an increasing group

the literature figure is 6%, but felt to be autopsy selection bias, so reduced by 75%.

Mortality statistics, based on information provided on deaths certificates, are a further potential source of national data on fungal infections. However, at present the only routinely available mortality statistics are based on underlying cause of death, and are therefore of limited use in enumerating the role opportunistic pathogens, such as fungi, in patients' deaths.

Invasive mycoses have been shown in many studies to be associated with relatively high levels of mortality. Invasive candidosis has an overall mortality of approximately 30% (Kibbler, 2003), a reduction from 55% in the early 1990's (Wey, 1988). Of this approximately half is attributable mortality, the remainder a function of co-morbidity. Survivors are usually completely cured, although ~5-10% suffer complications such as unilateral or bilateral blindness, bone infections or surgical complications related to treatment.

Invasive aspergillosis has a high mortality (~60%), higher if the diagnosis is delayed (von Eiff *et al.*, 1995), and in highly immunocompromised patients. Survivors have limited sequelae, unless they get brain infection. Because the treatments are suboptimal, and tissue damage often extensive, delay in treatment of the underlying disease (notably anti-leukaemia therapy) is

