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Emerging trends in the epidemiology of invasive mycoses in England and Wales (1990–9)

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SUMMARY

Invasive fungal infections are becoming an increasing public health problem owing to the growth in numbers of susceptible individuals. Despite this, the profile of mycoses remains low and there is no surveillance system specific to fungal infections currently existing in England and Wales. We analysed laboratory reports of deep-seated mycoses made to the Communicable Disease Surveillance Centre between 1990 and 1999 from England and Wales. A substantial rise in candidosis was seen during this period (6·76–13·70 reports per million population/year), particularly in the older age groups. Rates of cryptococcosis in males fluctuated over the decade but fell overall (1·05–0·66 per million population/year), whereas rates of female cases gradually rose up until 1998 (0·04–0·41 per million population/year). Reports of *Pneumocystis carinii* in men reduced substantially between 1990 and 1999 (2·77–0·42 per million population/year) but showed little change in women. Reports of aspergillosis fluctuated up until 1996, after which reports of male and female cases rose substantially (from 0·08 for both in 1996 to 1·92 and 1·69 per million population/year in 1999 for males and females respectively), largely accounted for by changes in reporting practice from one laboratory. Rates of invasive mycoses were generally higher in males than females, with overall male-to-female rate ratios of 1·32 (95% CI 1·25–1·40) for candidosis, 1·30 (95% CI 1·05–1·60) for aspergillosis, 3·99 (95% CI 2·93–5·53) for cryptococcosis and 4·36 (95% CI 3·47–5·53) for *Pneumocystis carinii*. The higher male than female rates of reports is likely to be a partial reflection of HIV epidemiology in England and Wales, although this does not fully explain the ratio in infants and older age groups. Lack of information on underlying predisposition prevents further identification of risk groups affected. Whilst substantial under-reporting of *Pneumocystis carinii* and *Cryptococcus* species was apparent, considerable numbers of superficial mycoses were mis-reported indicating a need for clarification of reporting guidelines. Efforts to enhance comprehensive laboratory reporting should be undertaken to maximize the utility of this approach for surveillance of deep-seated fungal infections.

INTRODUCTION

Fungal infections are becoming an increasingly important cause of morbidity and mortality in many countries [1–3]. Although some fungal species commonly exist as harmless colonizers of various bodily sites [4], they are also responsible for a vast array of clinical conditions, ranging from dermatological complaints to life-threatening systemic disease.

Invasive mycoses are a particular problem in hospital settings where distinct host and environ-

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mental factors predispose patients to opportunistic infections. Fungal spores are commonly found as environmental contaminants, but their presence in hospitals is hazardous to certain patient groups. Hospital-acquired fungal infections may originate from endogenous flora in the case of yeast infections or are transmitted via healthcare workers and fomites or through the airborne spread of spores (conidia) [5]. Underlying diseases and treatments or procedures which predispose patients to invasive mycoses include those that impair the cellular immune response, the use of treatments that alter the balance of microflora, such as broad-spectrum antibiotics, invasive surgical procedures and the use of intravascular lines [6]. Invasive fungal infections are difficult to treat and can progress rapidly to death, case fatality rates of 19–65% for candidosis [7, 8] and 13–85% for aspergillosis [9, 10] have been reported. Invasive mycoses often pose the biggest threat to patients vulnerable to infection; aspergillosis is thought to be the leading cause of death following bone marrow transplantation [11].

The incidence of nosocomial fungal infection has increased over the last 20 years for a number of reasons relating to the emergence of new disease, increasing use of immunosuppressive treatments and invasive procedures, and to prolonged survival of highly susceptible patients [12–14]. The shift towards use of more intensive cytotoxic drug regimes, resulting in prolonged neutropenia, in patients with leukaemia has also led to longer risk periods in this group [15, 16]. Cancer patients are being treated with ever more aggressive chemotherapy regimens, leaving them susceptible to opportunistic infections. Organ transplantation is also becoming more common, necessitating the wider use of immunosuppressive therapy. Survival of preterm neonates is improving, creating a new group of highly susceptible patients. The onset of the HIV epidemic further added to this group of individuals with impaired immunity. These phenomena have served to increase the pool of individuals susceptible to opportunistic infections. The economic implications of nosocomial infection in England, fungal or otherwise, were estimated in a recent study to cost the NHS an additional £930 million each year [17].

Invasive mycoses pose a particular challenge to public health. Given that fungal organisms are common environmental contaminants, and colonizers of various body sites, prevention of infection is exceptionally difficult. For *Pneumocystis* and *Cryptococcus* species, and infections due to dimorphic fungi, disease can result from reactivation of infection acquired from the inhalation of airborne spores many years previously. Our ability to control these diseases is reliant on prevention of exposure and effective prophylactic treatment of vulnerable individuals, something that has been largely achieved for pneumocystis pneumonia but not for cryptococcosis.

Surveillance of mycoses in England and Wales is carried out primarily through systems monitoring hospital-acquired infections. Data are also available from routine laboratory reports of clinically significant fungal infections made to the PHLS Communicable Disease Surveillance Centre (CDSC). Laboratories throughout England and Wales are invited to report to CDSC all deep-seated fungal infections in which the organism has been isolated (or which have been diagnosed by antigen tests in the case of cryptococcosis) [18]. All reports of *Pneumocystis carinii* are accepted regardless of the method of detection. In this paper we summarize these reports in an attempt to review laboratory reporting of mycoses and, where appropriate, to describe the epidemiology of invasive fungal infection in England and Wales.

METHODS

Reports of fungal infections received by CDSC from microbiology laboratories in England and Wales between 1990 and 1999 were reviewed. Reports were made electronically through the CoSurv network or in paper format (CDR form 2 and computer-generated printouts). Ongoing checks were carried out by CDSC for possible duplication of reports.

A marker of the clinical significance of reported isolates was elicited by examination of the site of the specimen in combination with the organism reported. Specimen types were grouped according to site of infection (see Box). Isolation of a fungal species from the following site groupings was considered to indicate deep-seated infection: central nervous system; organs, tissue and tissue fluids; pulmonary (except for *Candida* spp.); blood (except for *Aspergillus* spp.); sputum (except for *Candida* spp.). Isolations of *Rhizomucor* and *Rhizopus* species from sites within the upper respiratory tract were also considered to reflect invasive disease. Isolations of *Candida* species from pulmonary sites or sputum were treated as being of indeterminate clinical significance as these were thought in many cases to be contaminants or harmless colonizers. Although possibly reflecting disseminated

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Box 1. Specimen site groupings and hierarchy

1	Central nervous system
2	Blood
3	Organs, tissue and tissue fluids
4	Pulmonary
5	Sputum
6	Genitourinary
7	Gastrointestinal and anorectal
8	Eyes
9	Upper respiratory tract
10	Ears
11	Surgical devices
12	Subcutaneous
13	Cutaneous

infection, isolations of *Aspergillus* from blood cultures were similarly placed in this indeterminate category as this organism is very difficult to isolate from blood but is a common contaminant; therefore a positive culture is not proof of infection. All other isolations were considered to reflect superficial or subcutaneous infection. This included isolations of *Aspergillus* species from the ear, which may represent significant morbidity but do not represent deep-seated or invasive disease. Reports with isolations from more than one site were assigned according to the most invasive site (see Box for hierarchical ordering of sites).

Fungal infection reports were analysed by year of report, with further analyses by age, sex and region for *Aspergillus*, *Candida*, *Cryptococcus* and *Pneumocystis* species. Both standardized clinical descriptions and free-text clinical comments accompanying reports were examined for likely clinical significance and information on predispositions to infection. Reporting rates were calculated using mid-year resident population estimates for each corresponding year, age and gender grouping in each NHS regional office (Office for National Statistics: Population Estimates Unit, unpublished data). Regional population estimates were unavailable for 1990 and therefore substituted with 1991 population denominators. Rate ratios and exact confidence intervals were calculated using statistical software (StataCorp. 1999. *Stata Statistical Software: Release 6.0*. College Station, TX: Stata Corporation).

RESULTS

Overview of reports

A total of 11 702 fungal isolates were reported to CDSC between 1990 and 1999 from laboratories across England and Wales (Table 1). Reports were received from 267 PHLS and NHS laboratories, with 55% (6418/11 702) of all isolates being reported from PHLs. Seventy-three different fungal species were reported, 69 of which were fully identified. Isolations were made from 100 different specimen sites, with fungi isolated from more than one site in 6% (685/11 702) of reports.

Over half (59%; 6902) of all fungal isolates reported between 1990 and 1999 were of *Candida* species. A fifth (21%; 2510) of reports were of *Trichophyton* species, the next most commonly isolated species were *Aspergillus* (7%; 873), *Pneumocystis carinii* (6%; 668) and *Cryptococcus* (3%; 301).

Examination of specimen sites of fungal reports indicated a third (4012) to be superficial or subcutaneous infections and 6% (691) of indeterminate significance. Four percent (458) had missing information on site of isolation. The remaining 6541 reports appeared to indicate invasive infection. Reports of invasive mycoses from 46 different species were received, 43 of which were fully identified. Numbers of yearly reports of invasive mycoses by species are given in Table 2, excluding the following species for which less than 10 reports were received between 1990 and 1999 (number of reports): *Absidia corymbifera* (6); *Acremonium* sp. (3); *Blastoschizomyces capitatus* (1); *Cunninghamella bertholletiae* (1); *Exophiala dermatitidis* (2); *Fusarium* sp. (4); *Geotrichum* sp, (2); *Histoplasma* sp. (8); *Penicillium* sp. (5); *Phialophora richardsiae* (1); *Rhizomucor pusillus* (2); *Rhizopus sp*. (2); *Sporothrix schenckii* (1). Although not associated with invasive disease, five isolations from invasive sites of *Microsporum* sp. and two of *Trichophyton rubrum* were also reported.

Aspergillosis

A total 873 *Aspergillus* isolates were reported between 1990 and 1999 to CDSC (Table 1). The clinical significance of 172 *Aspergillus* reports isolated from serum alone was questionable, so these were excluded from further analysis. A further 312 isolates were excluded on the basis of missing specimen information (53 reports) or because the sites from which they were isolated were not thought to represent invasive disease as follows: inner/outer ear (201), cutaneous/subcutaneous sites (38), upper respiratory tract (12), eyes (4), gastrointestinal/anorectal sites (2), genitourinary sites (1) and surgical device (1).

In total, 389 reports *Aspergillus* were thought to

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Table 1. *Laboratory reports of all fungal isolates, by year of report (England and Wales: 1990–9)*

Species	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	1990–9
Absidia corymbifera		1	2		3	4		1	1		12
Acremonium spp.	1			1		5	3	1	3	2	16
Aspergillus spp.	44	48	63	39	42	31	17	166	207	216	873
Blastoschizomyces capitatus	1										1
Botrytis spp.				1							1
Candida spp.	356	328	361	399	485	644	636	1103	1279	1311	6902
Chrysosporium keratinophilum									1		1
Coccidioides immitis									1		1
Cryptococcus spp.	27	30	25	37	29	41	29	17	34	32	301
Cunningamella bertholletiae										1	1
Epidermophyton floccosum			5		2	11	2	2	8	1	31
Exophiala spp.	1			1	1	1				1	5
Fusarium spp.			1	4		5	3	3	6	9	31
Geotrichum spp.								2		2	4
Histoplasma spp.	3	2			1				2	1	9
Hyphozyma spp.									1		1
Malassezia spp.	2	3			8	48	5	7	3	2	78
Microsporum spp.			6	3	8	29	15	9	16	4	90
Mucor spp.			1	2				1			4
Penicillium spp.		1					1	2	3		7
Phialophora richardsiae	1										1
Pneumocystis carinii	78	152	87	26	50	58	61	53	54	49	668
Pseudallescheria boydii			1			1					2
Rhizomucor pusillus	1				1						2
Rhizopus spp.	1						4			2	7
Rhodotorula spp.	2		1	1	3	4	3	3	5	10	32
Saccharomyces spp.	2		1	2	1	1	2	4	3	24	40
Scopulariopsis spp.				2		14	8	3	11	7	45
Scytalidium dimidiatum									1		1
Sporothrix spp.							1		2	1	4
Trichophyton spp.			1		352	667	299	275	578	338	2510
Trichosporon spp.	4	2	1	2	2	5	1		3	1	21

Table 2. *Laboratory reports of invasive mycoses, by year of report (England and Wales: 1990–9)*

Species	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	1990–9
Aspergillus spp.	27	18	20	17	15	8	4	83	95	102	389
Candida spp.	344	317	349	387	463	536	552	683	804	722	5157
Cryptococcus spp.	27	30	25	36	25	41	25	15	27	28	279
Malassezia spp.	2	3			4		1	1	1	2	14
Pneumocystis carinii	78	152	85	26	48	56	57	35	39	19	595
Rhodotorula spp.	1		1	1	3	4	2	3	5	10	30
Saccharomyces spp.	2		1	2		1	2	4	3	5	20
Trichosporon spp.	3	2	1	2	2	1				1	12
Other species*	9	4	0	0	3	4	3	6	8	8	45

* Species with less than 10 reports received between 1990 and 1999.

represent invasive infection (Table 2). The majority specified *A. fumigatus* (338) as the causative organism, with a further 12 isolates identified as *A. flavus* and 6 each of *A. niger* and *A. terreus* (27 reports did not fully identify the organism).

The majority of *Aspergillus* isolates were from sputum (342) or pulmonary sites (32), indicative of lung disease. Other sites reported were CNS (5 cases) and organs, tissue and tissue fluids (10).

Two-thirds (265) of reports of aspergillosis contained standardized or free-text clinical information. Underlying diseases reported included: bronchiectasis (13 cases), neoplasms (12), chronic obstructive airway disease (9), leukaemia (8), Waldenström's macro-

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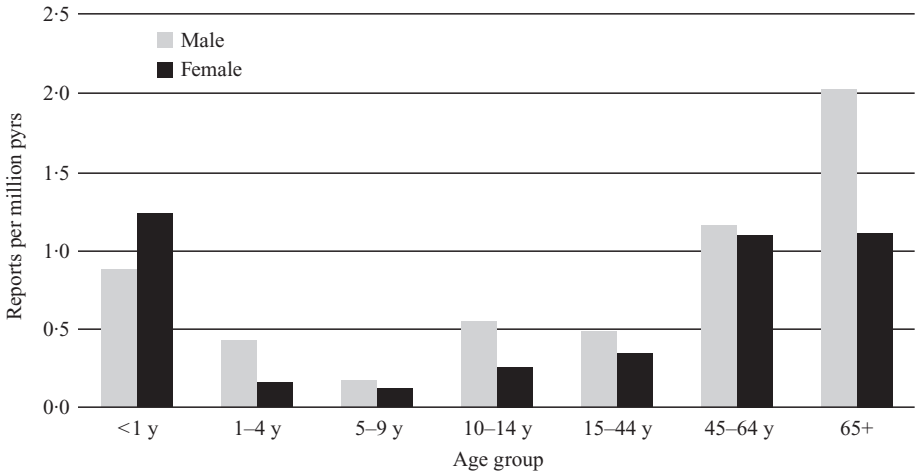

Fig. 1. Rates of aspergillosis laboratory reports, by age and sex (England and Wales: 1990–9).

Table 3. *Laboratory reports of aspergillosis per million population*, by region* (*England and Wales: 1990–9*)

	Year of report										
Region	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	1990–9
Eastern											
Number	15	8	4	8	0	3	0	1	0	2	41
Rate	2·91	1·55	0·77	1·54	0·00	0·57	0·00	0·19	0·00	0·37	0·78
London											
Number	2	6	2	1	1	1	1	0	0	26	40
Rate	0·29	0·87	0·29	0·14	0·14	0·14	0·14	0·00	0·00	3·57	0·57
North West											
Number	0	1	1	1	0	0	1	77	93	68	242
Rate	0·00	0·15	0·15	0·15	0·00	0·00	0·15	11·89	14·36	10·51	3·74
Northern and Yorkshire											
Number	0	0	1	1	1	1	0	2	1	1	8
Rate	0·00	0·00	0·16	0·15	0·15	0·15	0·00	0·31	0·15	0·15	0·12
South East											
Number	0	0	0	1	9	2	1	2	1	2	18
Rate	0·00	0·00	0·00	0·12	1·07	0·24	0·12	0·23	0·12	0·23	0·21
South West											
Number	8	1	5	2	1	0	1	1	0	0	19
Rate	1·70	0·21	1·05	0·42	0·21	0·00	0·21	0·21	0·00	0·00	0·40
Trent											
Number	0	0	0	0	1	0	0	0	0	1	2
Rate	0·00	0·00	0·00	0·00	0·20	0·00	0·00	0·00	0·00	0·19	0·04
Wales											
Number	0	0	0	0	0	1	0	0	0	0	1
Rate	0·00	0·00	0·00	0·00	0·00	0·34	0·00	0·00	0·00	0·00	0·03
West Midlands											
Number	2	2	7	3	2	0	0	0	0	2	18
Rate	0·38	0·38	1·33	0·57	0·38	0·00	0·00	0·00	0·00	0·37	0·34
England and Wales											
Number	27	18	20	17	15	8	4	83	95	102	389
Rate	0·53	0·35	0·39	0·33	0·29	0·15	0·08	1·59	1·81	1·94	0·75

* Yearly regional population estimates used except for 1990 (1991 population denominator used).

globulinaemia (2), leucopenia (5), cystic fibrosis (5), sarcoidosis (2), HIV infection (2) and emphysema (1). In 40 cases the infection followed bone marrow or solid organ transplant and other invasive surgical procedures in 11 cases. Cytotoxic or steroid treatment was recorded for 7 cases.

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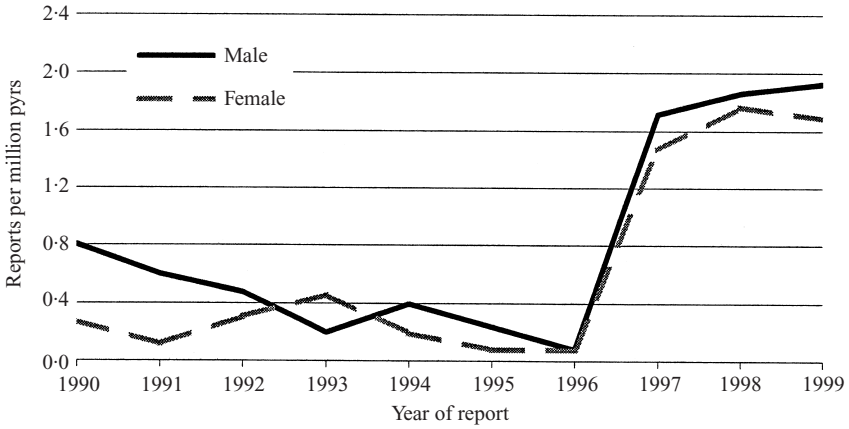

Fig. 2. Annual rates of aspergillosis laboratory reports, by sex (England and Wales: 1990–9).

Annual rates of aspergillosis by age group and sex are given in Figure 1. Age-specific rates of aspergillosis were highest for males in those 65 and over and for females in infants under 1 year. Rates were higher in males than females overall (rate ratio = 1·30, 95% CI 1·05–1·60), and in all age groups except in infants under 1 year. Only in the over 65 age group did this reach statistical significance (2·01 and 1·11 per million per year for males and females respectively; rate ratio = 1·82, 95% CI 1·25–2·65).

Regional yearly rates of all aspergillosis reported between 1990 and 1999 showed considerable variation, ranging from 0·03 (Wales) to 3·74 (North West) per million population per year (Table 3). Reports from the North West rose substantially in 1997, from 1 or 2 annual reports between 1990 and 1996 to 77 received in 1997, 93 in 1998 and 68 in 1999. Of the 280 aspergillosis reports received between 1997 and 1999, 169 originated from one laboratory.

Yearly changes in numbers of reports per million population are shown in Figure 2. Rates of reported aspergillosis in males and females remained between 0·08 and 0·80 per million between 1990 and 1996, after which reports rose to reach 1·92 and 1·69 per million respectively, mainly accounted for by the change in numbers of reports from one laboratory.

Candidosis

A total of 6902 laboratory reports of *Candida* species were received by CDSC between 1990 and 1999 (Table 1). Of these, 1745 did not meet our criteria for invasive disease and were excluded from further analysis. The majority (1108) of these exclusions were isolations from sites commonly colonized by *Candida* species or thought to reflect superficial or subcutaneous infection: gastrointestinal/anorectal sites (356), subcutaneous/cutaneous (307), ear (241), genitourinary sites (112), upper respiratory tract (50), surgical devices (16), eyes (15), pulmonary sites (11). Specimen information was missing from 118 reports. A further 519 reports were isolated from sputum specimens and therefore excluded as yeasts are a rare cause of pulmonary infection and the diagnosis is histological.

Reports of systemic candidosis formed over three-quarters (5157/6541) of all invasive mycoses reported to CDSC between 1990 and 1999 (Table 2). *C. albicans* was isolated in most (60%; 3104) of the candidosis reports, with substantial reports of *C. parapsilosis* (545) and *C.* (*Torulopsis*) *glabrata* (484) also being received. Other causative agents reported were *C. tropicalis* (195), *C. krusei* (78), *C. guillermondi* (33), *C. lusitaniae* (17), *C. famata* (22), *C. kefyr* (9), *C. inconspicua* (6), *C. lipolitica* (2) and one case each of *C. ciferrii*, *C. pelliculosa*, *C. norvegensis*, *C. humicola* and *C. rugosa*. Thirteen percent (657) were recorded as unnamed *Candida* species. The proportion of candidosis reports with *C. albicans* as the underlying agent showed little change between 1990 and 1999. Little variation was seen in the species distribution between males and females. Although *C. albicans* was the most commonly reported species across all age groups, distribution of other species varied across age groups. Nearly a quarter (23%; 172/757) of all paediatric (less than 15 years) candidosis cases were caused by *C. parapsilosis*, compared to only 9% (353/4144) of adult cases. Conversely, adult cases of candidosis showed higher proportions *C. glabrata*

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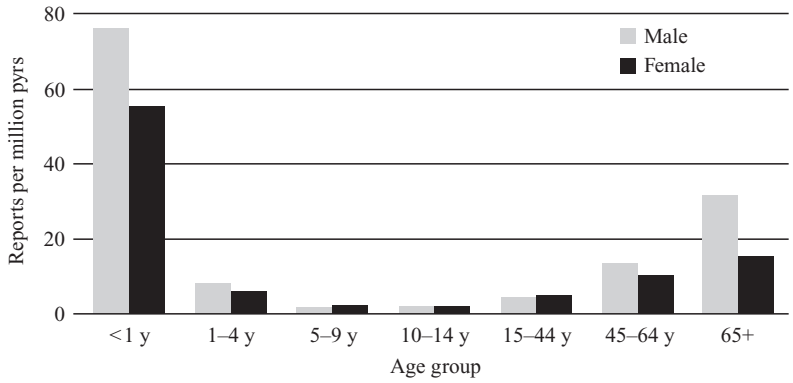

Fig. 3. Rates of candidosis laboratory reports, by age and sex (England and Wales: 1990–9).

Table 4. *Laboratory reports of candidosis per million population*, by region* (*England and Wales: 1990–9*)

	Year of report										
Region	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	1990–9
Eastern											
Number	14	18	20	25	32	44	36	32	39	58	318
Rate	2·72	3·50	3·86	4·81	6·13	8·37	6·80	6·00	7·25	10·70	6·05
London											
Number	92	79	78	80	76	84	87	107	127	77	887
Rate	13·35	11·47	11·30	11·54	10·91	11·99	12·30	15·02	17·67	10·57	12·64
North West											
Number	57	54	49	54	76	95	78	117	135	154	869
Rate	8·82	8·36	7·57	8·33	11·72	14·65	12·04	18·07	20·84	23·80	13·42
Northern and Yorkshire											
Number	35	47	34	63	56	75	53	74	92	65	594
Rate	5·45	7·32	5·28	9·76	8·66	11·60	8·20	11·46	14·23	10·06	9·20
South East											
Number	37	27	38	46	69	86	73	97	96	70	639
Rate	4·48	3·27	4·58	5·52	8·23	10·18	8·59	11·32	11·14	8·05	7·58
South West											
Number	33	30	35	24	38	52	74	58	57	56	457
Rate	6·99	6·36	7·37	5·03	7·92	10·77	15·28	11·90	11·63	11·35	9·50
Trent											
Number	38	25	39	29	51	28	34	49	63	79	435
Rate	7·55	4·97	7·71	5·71	10·01	5·48	6·64	9·55	12·27	15·35	8·54
Wales											
Number	12	11	21	31	24	30	55	47	84	65	380
Rate	4·15	3·80	7·25	10·67	8·24	10·29	18·83	16·06	28·64	22·13	13·04
West Midlands											
Number	26	26	35	35	41	42	62	102	111	98	578
Rate	4·94	4·94	6·63	6·62	7·74	7·91	11·66	19·17	20·82	18·37	10·91
England and Wales											
Number	344	317	349	387	463	536	552	683	804	722	5157
Rate	6·76	6·20	6·81	7·52	8·97	10·34	10·61	13·08	15·34	13·70	9·97

* Yearly regional population estimates used except for 1990 (1991 population denominator used).

(11%; 453/4144) than in paediatric candidosis (2%; 17/757).

The majority (98%; 5075) of patients with systemic candidosis had positive blood culture (candidaemia). Other sites from which *Candida* species were isolated include the CNS (42) and organs or tissue fluid (40).

Standardized clinical comments were available for 29% (1521) of candidosis cases (117 of cases less than

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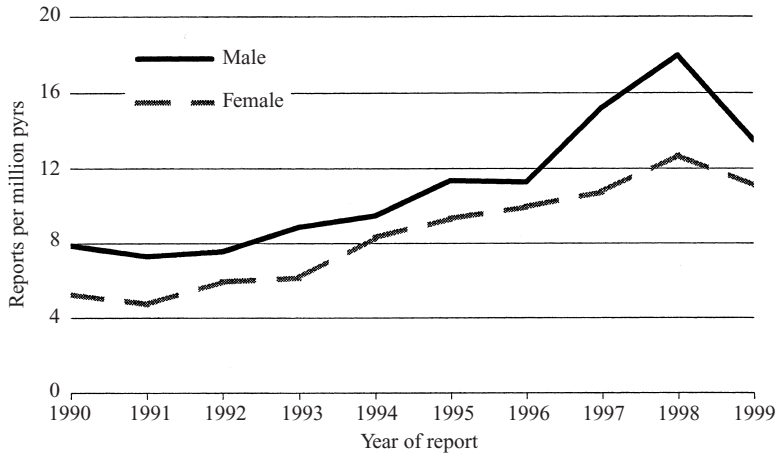

Fig. 4. Annual rates of candidosis laboratory reports, by sex (England and Wales: 1990–9).

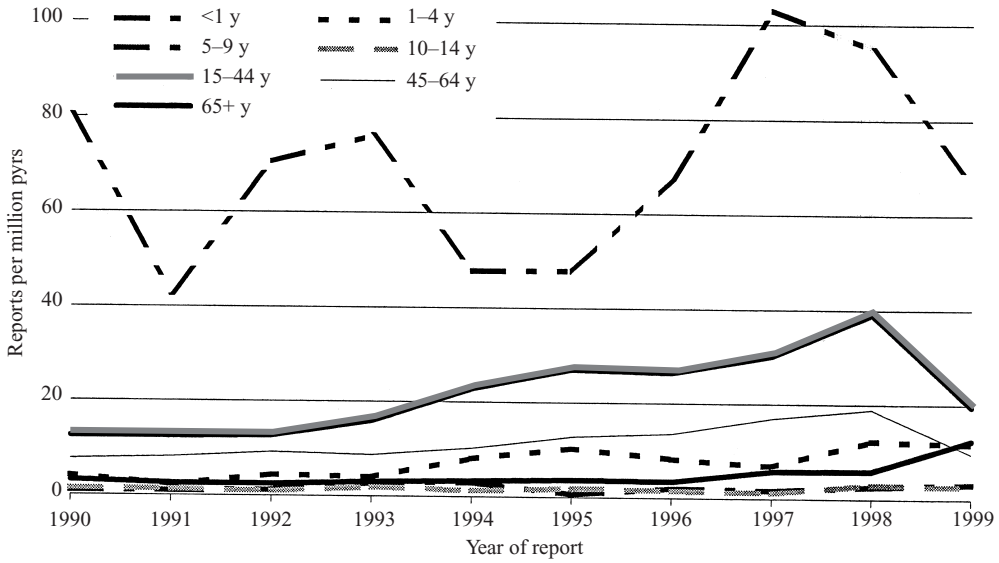

Fig. 5. Age-specific annual rates of candidosis laboratory reports (England and Wales: 1990–9).

1 year of age). Of these, a third (478) indicated that patients were immunocompromised (21% in under ones; 24/117), with use of intravenous catheters mentioned in 186 of these (12 of under ones). Use of intravenous catheters was mentioned in a further 918 cases (78 of the under ones). Additional free-text comments were recorded in 2401 reports (252 of under ones). Of these, 130 patients were noted as receiving total parenteral nutrition. Other predisposing factors noted included preterm birth (135 cases), pancreatitis (83), leukaemia (59), leucopenia (29), pancytopenia (2), neoplasms (49), cystic fibrosis (36), diabetes (31) and Whipple's disease (13). Four-hundred and eighty patients developed candidosis following invasive surgical procedures and a further 27 subsequent to solid organ or tissue transplant. Fifteen post burns cases were also reported.

Annual rates of candidosis reports by age and sex are shown in Figure 3. Highest rates were observed in infants under 1 year of age, 76·0 and 55·5 cases per million population per year for males and females respectively (rate ratio = 1·37, 95% CI 1·13–1·67). The majority of candidosis cases in infants occurred in those under 1 month old (58%; 260/446). Annual rates in age groups between 1 and 4 and 15 and 44 were less than 10 per million per year for males and females. Rates of reports were higher in males than females in most age bands, especially in those aged 65 plus, where rates in men were twice those in women (31·5 and 15·1 per million; rate ratio = 2·08, 95% CI 1·89–2·29).

Numbers of reports received from each region showed considerable variation (Table 4). The lowest incidence was observed in the Eastern region (6·05 per

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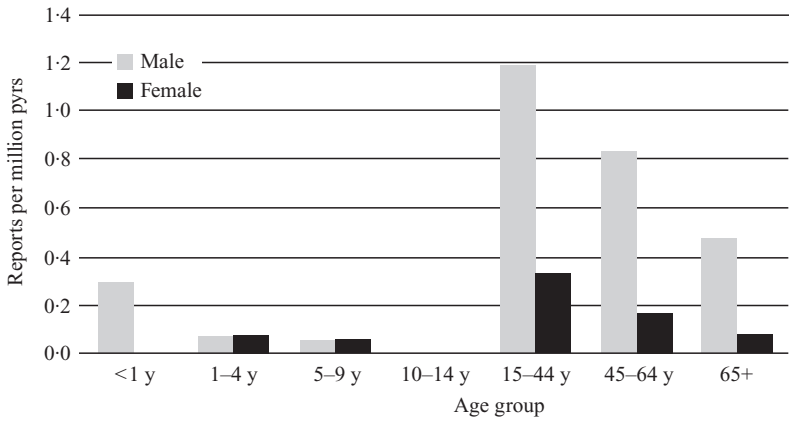

Fig. 6. Rates of cryptococcosis laboratory reports, by age and sex (England and Wales: 1990–9).

million population per year) and the highest in the North West (13·42 per million/year). All regions showed a general rise in candidosis reports between 1990 and 1999.

Annual reporting rates for candidosis showed a rising trend between 1990 and 1998, from 6·76 to 15·34 per million population, with a drop in 1999 to 13·70 per million. Rates of both male and female candidosis reports rose during this period (Fig. 4). Rates of male cases outnumbered female across the entire period (rate ratio = 1·32, 95% CI 1·25–1·40), incidence in males ranging from 13% higher (1996) to 54% higher (1991) than females. The rise in candidosis reports was seen in most age groups (Fig. 5) aside from infants less than 1 year of age, with rates in all age other groups at least doubling between 1990 and 1998.

Cryptococcosis

Between 1990 and 1999, 279 reports of invasive cryptococcal infection were received (Table 2), 263 of which were fully identified as *C. neoformans* and one as *C. albidus* infection.

Half of reports (83/173) came with accompanying clinical comments indicating patients to be immunocompromised. Underlying HIV infection was known in 57 cases. Other reported underlying predisposing factors included hepatitis C infection (2 cases) and diabetes (1 case).

Age and sex-specific incidence of cryptococcosis reports are shown in Figure 6. Rates were low in children and highest in 15–44 year olds. Substantially higher rates were reported for men than women (rate ratio = 3·99, 95% CI 2·93–5·53 overall), from 4 times greater in 15–44 year olds (rate ratio = 3·57, 95% CI 2·45–5·31), to 5 (rate ratio = 4·86, 95% CI 2·43–10·78) and 6 times (rate ratio = 5·85, 95% CI 1·89–24·05) greater in those aged 45–64 and 65 plus, respectively.

Regional reporting rates of cryptococcosis are given in Table 5. Highest rates were observed in London (1·97 per million population per year). Outside London, annual rates ranged from 0·20 in Trent to 0·46 per million in the South West.

Annual laboratory reports of cryptococcal infection were substantially higher in males than females between 1990 and 1995 (Fig. 7). Rates of male cryptococcosis fell substantially between 1995 and 1997, from 1·38 to 0·31 per million although showing a slight rise subsequently to 0·66 per million in 1999. Rates in women increased between 1990 and 1998, from 0·04 to 0·41 per million, although falling in 1999 to 0·11 per million.

Pneumocystis carinii

P. carinii infection was the second most commonly reported deep mycosis, 595 reports were received between 1990 and 1999 (Table 2). Over half (55%; 327) of the infections were detected through sputum specimens, most of the others (44%; 261) were diagnosed from other pulmonary specimens, 6 were detected from blood samples and 1 from bone marrow.

Of the 595 *P. carinii* reports, 409 had accompanying clinical information. One hundred and eighty-seven (46%) were described as immunocompromised. Underlying HIV infection was present in 181 patients. Other conditions associated with immunosuppression mentioned include organ/tissue transplant (11 cases), lymphoma (3), leukaemia (2), Wegener's granulomatosis (2), cystic fibrosis (1), severe combined immune deficiency (1) and systemic lupus erythematosus (1).

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Table 5. *Laboratory reports of cryptococcosis per million population*, by region* (*England and Wales: 1990–9*)

Region	Year of report										
	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	1990–9
Eastern											
Number	2	1	2	0	2	1	4	1	1	1	15
Rate	0·39	0·19	0·39	0·00	0·38	0·19	0·76	0·19	0·19	0·18	0·29
London											
Number	16	19	14	14	14	21	10	8	14	8	138
Rate	2·32	2·76	2·03	2·02	2·01	3·00	1·41	1·12	1·95	1·10	1·97
North West											
Number	2	3	0	4	1	3	2	0	2	3	20
Rate	0·31	0·46	0·00	0·62	0·15	0·46	0·31	0·00	0·31	0·46	0·31
Northern and Yorkshire											
Number	0	4	0	1	0	2	2	0	2	3	14
Rate	0·00	0·62	0·00	0·15	0·00	0·31	0·31	0·00	.031	0·46	0·22
South East											
Number	4	3	3	7	3	7	0	2	3	2	34
Rate	0·48	0·36	0·36	0·84	0·36	0·83	0·00	0·23	0·35	0·23	0·40
South West											
Number	1	0	2	7	3	4	1	0	2	2	22
Rate	0·21	0·00	0·42	1·47	0·63	0·83	0·21	0·00	0·41	0·41	0·46
Trent											
Number	0	0	2	2	0	1	2	1	0	2	10
Rate	0·00	0·00	0·40	0·39	0·00	0·20	0·39	0·19	0·00	0·39	0·20
Wales											
Number	1	0	0	1	0	0	1	1	0	2	6
Rate	0·35	0·00	0·00	0·34	0·00	0·00	0·34	0·34	0·00	0·68	0·21
West Midlands											
Number	1	0	2	0	2	2	3	2	3	5	20
Rate	0·19	0·00	0·38	0·00	0·38	0·38	0·56	0·38	0·56	0·94	0·38
England and Wales											
Number	27	30	25	36	25	41	25	15	27	28	279
Rate	0·53	0·59	0·49	0·70	0·48	0·79	0·48	0·29	0·51	0·53	0·54

* Yearly regional population estimates used except for 1990 (1991 population denominator used).

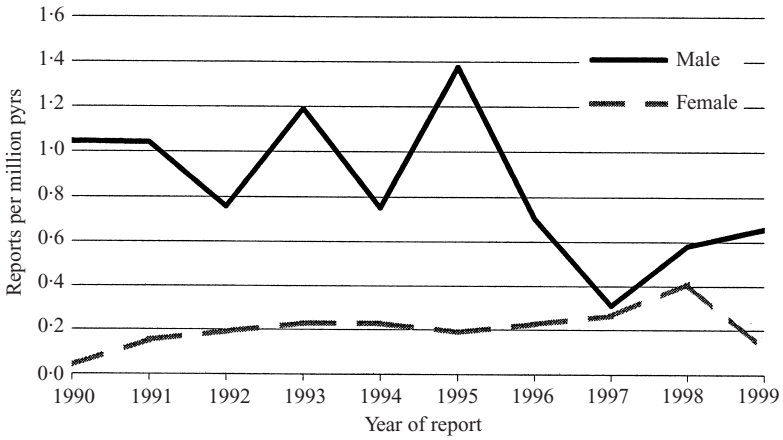

Fig. 7. Annual rates of cryptococcosis laboratory reports, by sex (England and Wales: 1990–9).

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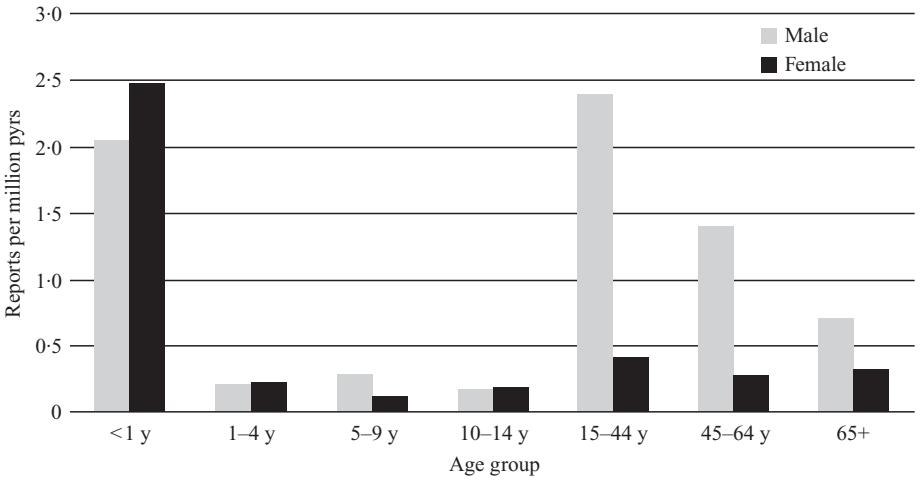

Fig. 8. Rates of *Pneumocystis carinii* laboratory reports, by age and sex (England and Wales: 1990–9).

Table 6. *Laboratory reports of* Pneumocystis carinii *per million population**, *by region* (*England and Wales: 1990–9*)

	Year of report										
Region	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	1990–9
Eastern											
Number	4	6	7	3	3	7	3	3	7	4	47
Rate	0·78	1·17	1·35	0·58	0·57	1·33	0·57	0·56	1·30	0·74	0·89
London											
Number	54	91	41	3	3	0	5	3	1	0	201
Rate	7·84	13·21	5·94	0·43	0·43	0·00	0·71	0·42	0·14	0·00	2·86
North West											
Number	1	0	2	0	1	1	0	0	4	0	9
Rate	0·15	0·00	0·31	0·00	0·15	0·15	0·00	0·00	0·62	0·00	0·14
Northern and Yorkshire											
Number	0	27	10	4	0	3	5	0	2	2	53
Rate	0·00	4·20	1·55	0·62	0·00	0·46	0·77	0·00	0·31	0·31	0·82
South East											
Number	6	2	1	3	12	10	11	1	2	0	48
Rate	0·73	0·24	0·12	0·36	1·43	1·18	1·29	0·12	0·23	0·00	0·57
South West											
Number	2	7	10	3	19	18	15	4	10	3	91
Rate	0·42	1·48	2·11	0·63	3·96	3·73	3·10	0·82	2·04	0·61	1·89
Trent											
Number	10	17	12	9	9	14	13	20	9	6	119
Rate	1·99	3·38	2·37	1·77	1·77	2·74	2·54	3·90	1·75	1·17	2·34
Wales											
Number	0	2	0	0	0	3	5	3	1	2	16
Rate	0·00	0·69	0·00	0·00	0·00	1·03	1·71	1·02	0·34	0·68	0·55
West Midlands											
Number	1	0	2	1	1	0	0	1	3	2	11
Rate	0·19	0·00	0·38	0·19	0·19	0·00	0·00	0·19	0·56	0·38	0·21
England and Wales											
Number	78	152	85	26	48	56	57	35	39	19	595
Rate	1·53	2·97	1·66	0·51	0·93	1·08	1·10	0·67	0·74	0·36	1·15

* Yearly regional population estimates used except for 1990 (1991 population denominator used).

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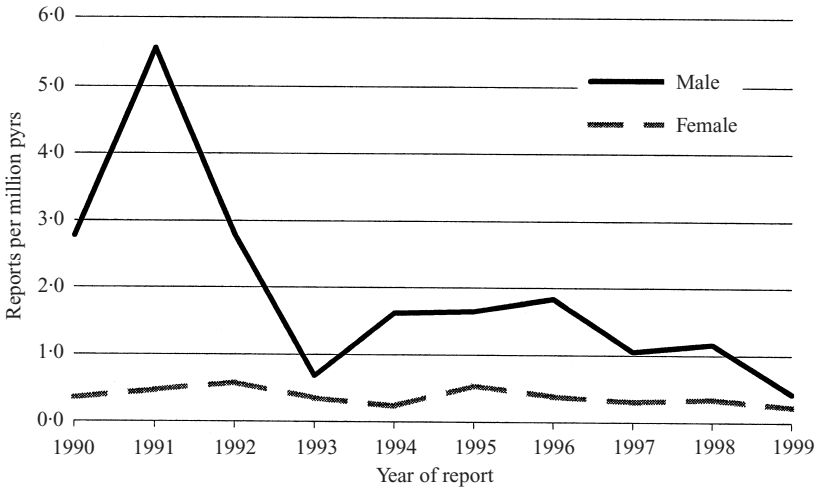

Fig. 9. Annual rates of *Pneumocystis carinii* laboratory reports, by sex (England and Wales: 1990–9).

The age distribution of *P. carinii* reported infections in men and women is shown in Figure 8. Significantly higher rates of *P. carinii* were reported for men than women overall (rate ratio = 4·36, 95% CI 3·47–5·53). Rates of paediatric *P. carinii* were similar in males and females, with the majority of reports being in infants less than 1 year old (2·06 and 2·48 per million population per year, respectively). Reporting rates remained below 0·30 per million per year up to age 14. Adult male and female cases differed markedly, with significantly higher rates in men than women observed in all adult age groups. In 15–44 year olds, rates of 2·39 in men and 0·42 in women per million per year were reported (rate ratio = 5·75, 95% CI 4·18–8·07). The gender discrepancy in *P. carinii* reports was also seen in older age groups, rates in men were 5 times higher than in women in the 45–64 year age range (rate ratio = 5·13, 95% CI 2·98–9·40), and 2 times higher in those aged 65 plus (rate ratio = 2·19, 95% CI 1·12–4·42).

Regional reporting rates of *P. carinii* are shown in Table 6. Annual rates of *P. carinii* showed considerable fluctuation between 1990 and 1999, although reports generally declined in most regions. Cumulative reports received during this period were highest in London (2·86 per million population), with Trent and the South West reporting the highest numbers of infections outside London (2·34 and 1·89 per million population, respectively).

Yearly reporting rates for *P. carinii* for males and females are given in Figure 9. Reporting rates were considerably higher for men than women throughout the period, although reports in males decreased substantially between 1991 and 1993, from 5·56 to 0·67 per million population per year. Reports of *P. carinii* infection in females remained fairly constant over this period.

Other invasive mycoses

A further 121 reports of deep-seated fungal infections, involving 24 different species, were received between 1990 and 1999. The majority of these were fungaemias (77%; 93/121). Other sites from which fungi were isolated were sputum (15), organs, tissue/fluids (5), pulmonary (3), CNS (3) and upper respiratory tract (2). Underlying conditions included leukaemia (10 cases), premature birth (5), HIV infection (5), neutropenia (5), pancytopenia (1), post-surgery/tissue transplant (3) and neoplasms (2). Seven reports of invasive mycoses were in patients receiving total parenteral nutrition.

DISCUSSION

This analysis of laboratory reports of fungal infections has illustrated some important trends in England and Wales, especially with regard to candidosis.

The laboratory reports analysed in this paper are restricted to actual isolations of fungal organisms, which will considerably underestimate the true numbers of invasive mycoses, given the difficulty in isolating the causative organism in many cases of invasive disease. Variations in completeness of reporting between regions will further underestimate the true numbers of isolations made. These limitations primarily affect our ability to estimate the true burden of invasive mycoses but do not entirely prevent any meaningful interpretation of either trends over time or between different subgroups within the population.

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Candida species were responsible for the majority of invasive mycoses reported between 1990 and 1999. Rates of candidosis for both males and females were highest in infants. Lack of clinical information accompanying reports prevents full ascertainment of underlying vulnerability in these infants. However, of the candidosis reports with clinical information available, the majority noted use of central venous catheters and prematurity *was* reported in over half of those under 1 year old. Other studies have also documented these risk factors for neonatal candidaemia, along with use of antibiotics, steroids and total parenteral nutrition [19–22]. Central venous catheters have similarly been found to be the source of over 85% of paediatric hospital-acquired bacteraemia [23]. Development of normal flora can be disrupted in neonates admitted to intensive care units, through exposure to different (hospital) flora, the use of antibiotics and methods of feeding, regardless of underlying disease [24]. Colonization by *Candida* species has been shown to be common in low birth weight infants, especially in those delivered vaginally [24], leaving preterm infants susceptible to development of systemic fungal infection [4, 20]. Several outbreaks of invasive *Candida* infection have been reported in neonatal intensive care units, with evidence of transmission facilitated through the hands of health care workers [22, 25].

Markedly higher rates of candidosis were reported in males than females in every year and across most age groups, from 40% higher in infants to 200% higher in those aged 65 plus. Similar male biases in candidosis have been reported in other countries [26]. The bulk of the published literature on the epidemiology of candidosis fails to present sex-specific rates, making our finding difficult to interpret. As the cases presented in this paper were observed through population-based laboratory surveillance, resident population estimates were used as denominators. The majority of these cases are likely to have been acquired in hospital, and as such the higher incidence may reflect either a male bias in the general or a speciality-specific inpatient hospital population at particular risk of opportunistic fungal infection. Hospital Episode Statistics for 1998/99 showed a male bias for many of the common major operations, such as heart bypass (79% male), which could contribute to the higher rates in men in the older age groups [27].

Male sex was associated with a higher likelihood of neonatal candidaemia in a case-control study, matched on birth weight and date of birth, with 80% of cases and 40% of controls being male, although the sample was small and the differences consequently not statistically significant [28]. A small cross-sectional study of candidosis in neonates in intensive care units with normal birth weight ($>$ 2500 g) found 15 of 17 cases to be male, although baseline gender characteristics of neonates in the unit were not given [29]. In this study, nearly all had congenital abnormalities. A further cross-sectional study in India reported 71% of neonatal candidosis cases being male [30], while a cohort study carried out in Finland reported a 30% higher male incidence of paediatric cases of bacteraemia [31]. A cohort study based in neonatal intensive care units failed to find a gender-associated increased risk of candidosis [20], suggesting that the higher rates in male infants observed in this paper could be explained by a higher proportion of male births requiring intensive care. Infant mortality is known to be higher in male than female infants, 6352 deaths per million population for males under 1 compared to 5016 for females in 1998 [32]. Although rare, a number of genetic immunodeficiency disorders affecting cell-mediated immunity are sex linked to the Y chromosome, as shown by mortality rates in infants. Mortality rates due to underlying 'endocrine, nutritional and metabolic diseases and immunity disorders' in infants under one year in England and Wales are 71 *vs*. 48 per million population in males and females respectively [32]. Diabetes, a recognized risk factor for candidosis [6], is also more common in males than females in the United Kingdom [27]. Hyperglycaemia has also been found to be a risk factor for fungal dermatitis in low-birth weight neonates [33]. Investigations using animal models suggest a possible protective effect of oestrogen on fungaemia caused by the dimorphic fungus, *Paracoccidioides brasiliensis* species [34], but there is no evidence that such an explanation could account for the gender bias observed for *Candida* species.

Rates of candidosis reporting varied greatly between regions, being lowest in the Eastern region and highest in the North West. Although this could reflect a genuine difference in burden of disease, it is equally likely to reflect different levels of reporting by different laboratories.

C. albicans was the most common cause of candidosis in all age-groups, although the distribution of non-*albicans* species did vary according to age-group, with *C. parapsilosis* predominating in paediatric cases and *C. glabrata* in adult cases. Similar species-age patterns have been reported in other

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countries [7], with some studies reporting a secular shift from *C. albicans* to *C. parapsilosis* as the predominant cause of neonatal candida infection [35, 36].

Marked increases in candidosis reports were seen in the last 10 years, a trend found in other countries in Europe and outside [12, 35]. Rates of candidosis in England and Wales doubled between 1990 and 1999, from 6·76 to 13·70 per million population per year. Rates increased in both males and females, across most age groups and in all regions. The uniformity of the rise would suggest a genuine increase in disease, rather than a reporting artefact. This probably reflects an increase in the pool of susceptible individuals, following the secular trends in more widespread use of treatments inducing immunosuppression, invasive devices facilitating infection and increased survival of vulnerable individuals.

Interpreting laboratory reports of *Aspergillus* species isolated over the past decade presents many problems. Unlike candidosis, aspergillosis is often difficult to diagnose from culture alone, requiring histological examination for proof of infection, which is often not carried out until post-mortem if at all [37]. Laboratory specimens are also particularly prone to contamination with airborne *Aspergillus* conidia. The low sensitivity and specificity of culture for diagnosis of infection by *Aspergillus* species is also likely to result in increasing use of antigen testing as a diagnostic tool rather than attempts at isolating the causative organism [38]. These issues mean that differences in numbers of reports between laboratories or over time are as likely to represent changes in diagnostic techniques utilized and fluctuations in the levels of airborne contaminants as true differences in incidence.

Ascertaining the clinical significance of reports of the laboratory isolation of *Aspergillus* species made over the last decade has also been problematic. Although laboratories were asked to report deep-seated fungal infections only [18], it was clear that superficial infections were reported in great numbers. An attempt was made to differentiate between likely cases of invasive aspergillosis and superficial infections or culture contaminants by applying criteria to *Aspergillus* reports based on specimen site. Isolations from blood culture alone were rejected on the basis that *Aspergillus* fungaemia is rare [10, 39–41], whilst *Aspergillus* species are frequent blood culture contaminants [41, 42]. Insufficient clinical information was provided in most cases to differentiate genuine aspergillus fungaemia from contaminations [42]. Isolations made from sputum specimens were analysed, although not all of these were likely to be indicative of pulmonary aspergillosis [10].

Laboratory reports of aspergillosis observed between 1990 and 1999 rose substantially after 1996 in both men and women, from less than 10 reports per annum to around 50 each for men and women. The rise was restricted to one region, the North West, with over half originating from one laboratory. Further investigations revealed a local change in reporting practice following the introduction of a region-wide automated reporting system around this time.

In both men and women, aspergillosis rates were highest in infants and adults aged 45 plus. A general gender bias in aspergillosis cases was evident, with rates in males outnumbering those in females for most age groups. Due to the small number of cases, rates were only significantly higher in those aged 65 plus. This could be due to a larger male than female population of hospitalised patients vulnerable to opportunistic pathogens, as described for candidosis and also including HIV positive patients, although HIV is very uncommon in those over 65 [43].

P. carinii infections were the second most common invasive mycosis reported by laboratories in England and Wales between 1990 and 1999. Although rates of *P. carinii* infections were relatively high in infants (2 and 2·5 per million per year for males and females respectively), actual numbers of cases were very few (15 altogether). Reported cases of *P. carinii* infection in females were uncommon, totalling 98 throughout the period. Reports of *P. carinii* were four times as common in men than women, probably largely a reflection of pneumocystis pneumonia in HIV-associated immunodeficiency. As for laboratory reports of cryptococcosis, aspergillosis and candidosis, reports of *P. carinii* were more common in men than women in older age groups, five times higher in 45–64 year olds and twice as high in those 65 plus. Other studies of pneumocystis pneumonia in patients with a variety of predisposing factors unrelated to HIV infection, have shown a moderate to large male bias in cases [44–46]. This could indicate that the gender difference seen in our laboratory reports is not entirely due to underlying HIV infection, but could relate to other predisposing conditions in which cellular immunity is impaired [47]. Diagnostic statistics from 1998/9 suggest that more men than women undergo renal, heart, lung and liver transplantation in England [27], operations which necessitate the use of immunosuppressive therapy to prevent organ rejection. Diagnoses of lymphoma, leukaemia

and combined immune deficiency were also more common in men than women, although this was not the case for other known predisposing diseases such as cystic fibrosis and systemic lupus erythematosus. Interestingly, a published case series of pneumocystis pneumonia in patients diagnosed with Wegener's granulomatosis found 9 of 11 cases to be male, despite the similar incidence of Wegener's granulomatosis in males and females (10 of the cases were known to be HIV-negative, 1 remained untested) [48].

Despite the considerable number of *P. carinii* pneumonia cases seen since the advent of the HIV epidemic, there remains a considerable lack of understanding of its natural history. Although pneumocystis pneumonia was long considered to result from reactivation of latent infection in vulnerable individuals, this has been challenged by documented clusters and possible outbreaks of disease [49]. As well as suggesting that recent infections of *P. carinii* can result in pneumocystis pneumonia, this further suggests a common source of infection or person-to-person transmission, something which has never been demonstrated. Given the availability of effective prophylactic treatment against pneumocystis pneumonia, understanding the risk factors for this opportunistic infection will help effective targeting of those at risk.

There is evidence of substantial under-reporting of *P. carinii* by laboratories over the last decade. Data are available on pneumocystis pneumonia from a separate HIV/AIDS surveillance scheme, which records opportunistic infections present at the time of AIDS diagnosis [50]. By June 2000, 3031 diagnoses had been reported to CDSC, for the period 1990–9, in which a definitive diagnosis of *P. carinii* pneumonia had been made for the initial AIDS defining event. Laboratories reported only a fifth of these clinical diagnoses (595) to CDSC. As an unknown number of AIDS patients will have developed pneumocystis pneumonia further into disease progression (i.e. after the initial AIDS defining event), additional clinical diagnoses are likely to have been made in AIDS patients. Although this appears to indicate substantial under-reporting by laboratories, two things should be borne in mind. The definitive pneumocystis pneumonia diagnoses made in these AIDS patients are done through microscopy (histology or cytology) using staining techniques, and not isolations from culture, and as such it would be unclear under current reporting guidelines as to whether they should be included. This is further compounded by *P. carinii* having only been definitively identified as a fungus in recent years and as such it would have been unclear as to which reporting criteria would apply to this organism.

Between 1990 and 1999, 279 laboratory reports of cryptococcosis were made to CDSC. In both males and females, reporting rates were highest in young adults (15–44 years). Rates were significantly higher for males than females across all adult age groups (few paediatric cases were reported), from 4 times higher in 15–44 year-olds rising to 6 times higher in those over 64. The male bias in young adult cryptococcosis cases is likely to reflect the epidemiology of HIV infection in the United Kingdom [43]. Although AIDS cases in the United Kingdom have been concentrated in adults less than 45 [43], sufficient cases are reported in older age groups to explain the male excess of cryptococcosis reports in those aged 45 plus, especially given the small numbers of cryptococcal reports in these age groups.

Other predisposing factors could also contribute to the male excess in older age groups, a case series of cryptococcal disease reported prior to the AIDS epidemic typically described a 2–3 fold male excess of cases [51], as have subsequent studies in HIV-negative individuals [52]. The higher incidence of cryptococcal disease in men than women could relate to higher levels of exposure to environmental reservoirs of cryptococcal yeasts or basidiospores [53], a history of outdoor occupations such as landscaping and building having been associated with increased risk of cryptococcosis [54]. Given that these occupations have traditionally been more common in men than women, reactivation of latent occupationally acquired infection [53] could go some way to explaining the increased incidence in men. Smoking has also been found to increase the risk of cryptococcal infection, independently of occupational risk or male gender [54], a behaviour which has historically been more common in men than women and could exacerbate any existing differences [55]. Another relevant factor could be underlying diabetes mellitus, more common in men than women in the United Kingdom [27], a condition thought to predispose individuals to cryptococcal disease [51], and mycoses in general [6], possibly through associated impairment of cell-mediated immune function and/or the glucose-rich environment. Another possible reason for the higher male incidence of cryptococcal disease is the reported hormonal influence on pathogenesis [52].

An indication of the magnitude of laboratory under-reporting of cryptococcosis comes from the Mycology Reference Laboratories in Leeds and

Bristol on specimens sent for serological detection and cultures sent for identification and/or susceptibility testing. Between 1997 and 1999, cultures and specimens from 135 patients with cryptococcosis were referred to the reference laboratories, only half (70) of these were reported by the source laboratories to CDSC.

There are severe limitations to using this laboratory-based system for surveillance of deep-seated mycoses, arising from sporadic or consistent under-reporting from some laboratories, which hamper any estimates of the burden of infection. For conditions such as aspergillosis, laboratory reports of *Aspergillus* isolation will always greatly underestimate the burden of disease given the difficulty in culturing this species and the reliance on clinical presentation (or post-mortem detection) for diagnosis. This is also possibly the case for *P. carinii* pneumonia, as illustrated by the substantial discrepancy in numbers of clinical diagnoses and laboratory reports received. In the absence of any other national population-based surveillance schemes for invasive mycoses, it is difficult to judge the level of under-reporting or under-estimation from the reporting of infection on CDSC's LabBase.

Although detailed clinical information was often absent from laboratory reports, by analysis of the site from which fungal isolations were made, in conjunction with the known pathogenicity of the particular species, it seems that as many as a third of all reports received between 1990 and 1999 were indicative of superficial or subcutaneous infection. This further illustrates the problems with laboratory reporting of mycoses, given that only deep-seated mycoses should have been reported to CDSC. Coupled with the general under-reporting, it seems unlikely that it is solely resource or motivational constraints which are responsible for the mis/under-reporting, but that there is a lack of clarity as to which fungal infections laboratories should be reporting [56].

Although problems of under-reporting hinder our interpretation of laboratory surveillance data, they do not entirely prevent a cautious analysis of these data. Laboratory reporting of mycoses could provide a reasonably robust means of surveillance for some mycoses in England and Wales, especially for candidosis and cryptococcosis. The value of any laboratory-based surveillance for monitoring *P. carinii* pneumonia and aspergillosis, whose causative organism cannot be readily cultured and are occasionally diagnosed on clinical presentation, or in the case of pneumocystis pneumonia, microscopy only, is likely to remain limited. Clearly hospital acquired infection surveillance schemes will have an important role in monitoring invasive mycoses, but the use of a population-based system could play a useful complementary role in monitoring mycoses occurring in both outpatient and inpatient populations. Laboratory reports to CDSC are generally made shortly after isolation of the organism, making the system particularly valuable in detection of infectious disease outbreaks, as has been the case for mycoses in the United Kingdom [5]. However, without detailed clinical information it will continue to be difficult to interpret the clinical significance of reports to enable colonisation or contamination to be distinguished from infection and disease.

Improvements need to be made to obtain more complete reports from laboratories, and to clarify reporting guidelines such that only invasive mycoses are reported to CDSC. Access to information on underlying disease or immunosuppressive treatments is essential to the interpretation of trends in laboratory reports as it will allow risk groups to be identified. Better completion and expansion of the standardised descriptions available to reporting laboratories to include terms such preterm birth, underlying disease, use of immunosuppressive treatment and whether the report is from an inpatient would greatly help our understanding of laboratory mycoses reports and the epidemiology of mycoses in England and Wales.

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