Imported fungal infections

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Summary

Data on mycoses known to be imported into the United Kingdom are sparse. Estimates on the prevalence of fungal infections have to be based on indirect and incomplete figures, obtained from isolation figures and reports of individual cases to co-ordinating centres such as the Mycological Reference Laboratory and the Communicable Disease Surveillance Centre of the Public Health Laboratory Service.

Imported species of dermatophytes account for less than 1% of the total number of isolations made annually at mycological laboratories throughout the U.K. A suggested prevalence of dermatophytosis in this country is *c.* 250 000 cases per annum. *Trichophyton rubrum* may now be the most common species of dermatophyte.

Other estimates of the frequencies with which infections are recorded each year include mycetoma (7–10), histoplasmosis (2–5), aspergilloma (50–80), invasive aspergillosis (10–30), *Candida* vaginitis ($\geq 1\ 000\ 000$), invasive candidiasis (10–80), *Candida* endocarditis (1–2) and cryptococcosis (6–10).

Introduction

In presenting some perspectives on the prevalence of fungal infections in the United Kingdom consideration will not be confined to those mycoses known to be imported from endemic areas outside this country. Data on mycoses known to be imported are scarce and usually incomplete, and most of the mycoses being recognized and treated in Western Europe originate from indigenous species of fungi.

The data presented have been collated from several sources including the Mycological Reference Laboratory (MRL), and the Communicable Diseases Report forms produced by the Communicable Diseases Surveillance Centre of the Public Health Laboratory Service. Mycoses are not notifiable in this country, although efforts have been made in the past to obtain figures on the prevalence of mycoses in the U.K. by the Medical Mycological Committee of the Medical Research Council and more recently by the British Society for Mycopathology. On the international scene, the World Health Assembly in 1975 and 1976 recognized that mycoses are an important public health problem, and that information is required on the world-wide prevalence of mycoses.

If this leads to a better system for reporting, then more accurate assessments may eventually become available on the incidence and distribution of individual mycoses on a global scale. In many parts of the world the extent and significance of mycoses is now known. Only 15% of the members of the International Society for Human and Animal Mycology come from tropical countries. There are therefore large gaps in the understanding of the distribution of mycoses.

No attempt is being made to catalogue all the cases of mycotic infection seen in the U.K., some selection has been exercised and attention will be focused only on the major imported or endemic mycoses.

Discussion

Some of the most commonly imported mycoses in the U.K. are dermatophytoses – the ringworm infections. Their number can be assessed accurately only for those species which are not already established in this country. Over the past 3 decades there has been an increase in international travel. In Britain there is a large immigrant population, and formerly exotic species of dermatophytes are now being recognized as causes of ringworm. These include *Trichophyton violaceum*, *T. schoenleini*, *T. concentricum*, *T. gourvilii*, *T. yaoundei* and *Microsporum ferrugineum*.

These species account collectively for only about 1% of the cases of dermatophytoses where the identity of the agent has been established. *T. rubrum*, which accounts for 58% of the total number of dermatophytes identified in this country has been imported in large numbers but it is now well established in its own right, and this makes it difficult to distinguish between indigenous and imported infections.

Laboratories in the U.K. isolate and identify *c.* 5500 dermatophytes annually. Numbers of *T. rubrum* exceed the sum total of the other species. Until recently, it was generally thought that although *T. rubrum* might appear to be the most common dermatophyte in the U.K. its predominance was more apparent than real. Largely because of its chronicity and intractability, more patients infected with *T. rubrum* sought medical attention than did

those infected with any other species of dermatophyte. This resulted in a misleadingly high proportion of *T. rubrum* infections. More recent surveys suggest, however, that it may now be the most common dermatophyte affecting man in this country.

The value of a laboratory's contribution to diagnosis varies according to the mycosis involved. Isolation of a dermatophyte, a *Histoplasma* or a *Cryptococcus* is *prima facie* evidence of infection, but recognition of *Candida* in urine or *Aspergillus* in sputum is not. In attempting to assess prevalence in the U.K. of mycoses in general, or dermatophytes in particular, another factor has to be considered in relation to laboratory isolation or identification figures. To consider dermatophyte infections as an example: the majority of individuals acquiring ringworm have the condition diagnosed and treated by their general practitioner without laboratory confirmation. There is another group comprised of those who diagnose and treat (or ignore) their own dermatophytoses. It must be recognized that for every mycosis recorded in a reporting scheme, the numbers noted represent no more than the tip of an iceberg (Ajello, 1970). If it can be accepted as possible that only 1 in 10 of patients with tinea corporis is referred by a General Practitioner for laboratory examination, and that the corresponding figure for tinea pedis is 1 in 50, then an overall projected total of diagnosed dermatophytoses in the U.K. could be of the order of 220 000 patients annually. When added to the self-diagnosed cases, an approximate annual figure of c. 250 000 is obtained. It cannot be accurately estimated what proportion of this figure represents *true* infection. From a report published by Holmes and Gentles (1956), only a small proportion of patients thought to have tinea pedis – perhaps as little as 20% – have mycological evidence of infection. A similar problem exists in estimating prevalence of *Candida* infections.

Reports of imported infections with other types of mycoses affecting skin, hair or nails are comparatively small. One condition affecting predominantly toe spaces and nails and caused by *Hendersonula toruloidea* was first described by Gentles and Evans in 1970. Since that time additional reports by Campbell *et al.* (1973) and Moore (1978) have established that it is comparatively common in dark-skinned subjects. At St John's Hospital for Diseases of the Skin, London, c. 90 cases of this dermatomycosis or the closely related *Scytalidium* have been seen (Clayton, 1978).

Subcutaneous mycoses, or mycoses of implantation, are uncommon in Britain. The most frequently diagnosed of these is mycetoma. Fifty imported cases have been investigated at the MRL in the last 17 years. In the past 3 years the numbers of cases has increased considerably, and is presently

around 7–10 confirmed cases per annum. The principal countries of origin are the Indian sub-continent, the middle East and the West Indies. Laboratory studies, in the form of microscopical examinations, culture and serology are of great value in establishing the aetiology. Because of the marked differences in response to therapy of mycetomas caused by actinomycetes and fungi respectively, distinction between the 2 forms is of considerable importance to management and prognosis. The majority of mycetoma seen in this country are caused by true fungi, including *Fusarium*, *Acremonium*, *Petriellidium* and *Madurella*. *Streptomyces somaliensis* is the most common of the actinomycetoma infections.

Systemic mycoses are uncommon in this country. Histoplasmosis caused by *Histoplasma capsulatum* is widely distributed throughout the world, having been reported from more than 70 countries. It is not endemic in the U.K. and imported cases are reported infrequently. Firm diagnoses, based on isolation and identification of the pathogen are very uncommon. Skin tests with histoplasmin and serodiagnosis, using double diffusion and complement fixation tests are sometimes used as ancillary diagnostic aids, but figures based on these tests together with clinical history and presentation can be highly misleading. The MRL receives 600–700 requests annually for *Histoplasma* serology, but these are principally for the exclusion of histoplasmosis in patients who have travelled abroad. Four proved cases have been diagnosed in the past year, 2 of whom developed the disease in the West Indies. If evidence from histological examination of pathological materials is added to estimates from other laboratories findings and reports in the literature then the national total for all cases of histoplasmosis seen in the U.K. up to this point is c. 100. Symmers (1972) described 48 cases of Asian histoplasmosis, an unusual form of the disease with characteristics which differentiate it from classical histoplasmosis.

African histoplasmosis, coccidioidomycosis, blastomycosis and paracoccidioidomycosis are seldom seen in this country, and a combined total of less than 50 cases have appeared in the records of the MRL.

The other principal mycoses endemic in the U.K. are due to *Aspergillus* spp. and *Candida* spp.

Aspergillosis, caused principally by *A. fumigatus* is most commonly encountered as an allergic manifestation to substances produced by non-invasive growth of the fungus in the respiratory tract. Patients with asthma, transient pulmonary infiltrates, a positive Type I skin test to *A. fumigatus*, eosinophilia, and who have *A. fumigatus* in the sputum show the essential features of allergic bronchopulmonary aspergillosis. Serological tests based in

part on studies at the Brompton Hospital, London (Longbottom and Pepys, 1964), are often used as diagnostic aids, because patients with allergic aspergillosis usually have low levels of specific IgG antibody to *A. fumigatus*. By 1972, serodiagnostic tests accounted for 70% of the requests for assistance received each year by the MRL. Seventy per cent. of these serological requests were for precipitin tests to *A. fumigatus*. Up to 10 000 requests for *Aspergillus* serology were handled annually and although approximately 1300 sera contained antibodies to *A. fumigatus*, no direct quantitative relationship to clinical disease could be recognized, since details of the patient's condition were seldom provided.

Aspergilloma caused by *A. fumigatus* and other *Aspergillus* spp. is less common than allergic aspergillosis. The diagnosis depends primarily on clinical and radiological evidence although the laboratory can assist materially by cultivation of the agent and serodiagnostic testing. It is estimated that 50–80 cases of aspergilloma may be seen each year in the U.K.

Invasive aspergillosis, where the agent becomes established in living tissues, is essentially a disease of severely compromised patients. Laboratory findings are of limited value as diagnostic aids, since cultural and serological findings are frequently negative, even when *Aspergillus* is later shown to have been present. In the U.K., there is no evidence to suggest that the number of cases exceeds 10–30 per annum. Renal units which previously encountered *Aspergillus* infections as a post-transplantation complication have more recently reported that they have diminished in importance as a cause of sepsis.

In non-atopic subjects, *Aspergillus* may colonize diseased airways and cause symptoms associated with chronic inflammatory responses. *Aspergillus* can be demonstrated in their sputum, and precipitin levels are generally very high. No data are available on the frequency of this 'saprophytic' form of aspergillosis, but its distinction from other forms of aspergillosis is a matter of some relevance in evaluating the choice and response to therapy.

If problems exist in trying to assess numbers of cases of aspergillosis in the U.K., they are much simpler to resolve than those relating to candidiasis. Apart from the more obvious manifestations of the disease as thrush of mucosal surfaces, the spectrum of candidiasis is wide and establishment of a diagnosis is often difficult.

Candidiasis is not commonly reported in this country. For this disease, as for ringworm, the ratio between case numbers (based on available reporting systems and data) and the number of occasions for which anti-*Candida* therapy is prescribed is extremely low. Estimates of the numbers of infections are therefore very inaccurate.

Invasive candidiasis may be confirmed in 10 to 80 cases per annum, with numbers of clinically significant cases of candidaemia being in the same range. *Candida* endocarditis may be even less common, with only one to 2 cases per annum. Only by careful evaluation of the patient's condition and the selective and meticulous application of laboratory procedures can a reliable diagnosis be established.

One final mycosis should be mentioned, since its prognosis depends to a large extent on prompt diagnosis and management. This is cryptococcosis, a rare and severe fungal infection affecting the lungs, skin, bones or CNS. In this country, it is best known as cryptococcal meningitis. Between 1962 and 1977, 60 cases of cryptococcosis were reported to the MRL, but proved infections are being recorded at present at the rate of almost one per month. These originate in many parts of the country, and it is clear that the disease is widespread here. In view of the availability of specific laboratory tests it is disappointing to find that cryptococcosis is not more frequently considered and investigated earlier in patients with predisposing factors.

In conclusion, although excellent laboratory facilities exist in this country for the assistance with diagnosis, the true prevalence of fungal infections still remains highly conjectural. Mycoses can be life-threatening, and in these cases can be eradicated only by rapid and accurate diagnosis, combined with carefully selected and effective courses of management. This is perhaps a good point to restate the absolute need for co-ordination between the physician in charge of the patient and the laboratory undertaking back-up investigations. This, of course, is as true for attempts to gauge incidence of mycoses as it is for their diagnosis and management.

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