Editorial: Direct fungal infection of the eye and its prevention

The paper from Nigeria (page 607) makes a welcome and important contribution that expands our knowledge of the world-wide distribution and clinical importance of fungal infection of the eye (Gugnani, Talwar, Njoku-Obi, and Kodilinye, 1976). For some time it has seemed likely that loss of eyes from fungal infection in the humid tropical world is much more common than the literature would suggest (Jones, 1975a). Diagnostic facilities have seldom been available there, and in the absence of effective treatment there has been little point in pursuing the precise causation of such infections. A mycologically proved diagnosis was made in 21 out of 36 of the corneal ulcers presenting in the University of Nigeria Teaching Hospital at Enugu during a two-year period. Because of the selection of cases for study it is likely that many more fungal infections went unrecognized because they were not investigated. Most of these patients were agricultural workers and in many cases the infection followed trauma with palm tree or other vegetable material.

This report appears to be the result of the expansion of academic ophthalmology in the African continent rather than the result of a recent invasion of that region by Fusarium solani. It is likely therefore that it represents a first sampling of an important and widespread cause of loss of eyes in rural populations over a vast area in Central Africa. It is known that this is the case in the south eastern United States of America, India, and South East Asia and it will probably be shown to be so throughout Indonesia, New Guinea, the Pacific Islands, Northern Australia, tropical Central and South America, and the Caribbean area.

The predominant organism in the West African series was F. solani (12 out of 21 identified). The second most frequent was Aspergillus fumigatus and other Aspergillus species (five out of 21). In Europe, Britain, and the northern United States of America A. fumigatus and other Aspergillus species of environmental origin and Candida albicans, of which the reservoir is in humans, have been the commonest fungi responsible (Jones, Richards, and Morgan, 1969c).

Although F. solani has come to be recognized as an ocular pathogen only during the last 10 years, this finding has been reported extensively from the southern United States of America (Jones, Sexton, and Rebell, 1969d) and from a number of other countries including England (Jones, 1975a; Gugnani and others, 1976). Fusarium ulcers may present as superficial and rather unimpressive lesions, more often they progress rapidly to deep corneal disease or extensive corneal abscess formation, sometimes with scleral invasion (Jones, 1975a and b). As with other fungi there is a strong tendency for fungal invasion of the posterior chamber to lead to seclusion of the posterior chamber followed by forward displacement of the lens and iris from pressure of aqueous behind, with progressive shallowing of the anterior chamber giving rise to a malignant glaucoma that requires lens extraction with anterior vitrectomy and sometimes corneal transplantation (Jones, Jones, Lim, Bron, Morgan, and Clayton, 1969a; Jones, Jones, and Richards, 1969b; Jones 1975a and b). The most striking feature of ocular infections with F. solani is the speed and destructiveness with which they can develop. This commonly misleads the clinician to think that he is dealing with a bacterial infection.

The virulent pathogenic nature of ocular isolates of F. solani is clearly established: the ocular disease that occurs in man with infection by this organism has been reproduced in animals (Jones and others, 1969a). Furthermore, in all cases in which the biology of the ocular isolates has been reported, the organisms have grown especially well at 37°C and have had other biological differences from the more common isolates made from plant disease (Jones and others, 1969a; Jones, 1969d; Gugnani and others, 1976). This suggests that among the vast population of F. solani in the environment, much greater in the humid tropical areas than in the arid or cooler regions, there is an undetermined proportion of strains of F. solani that are especially well suited to invade the eye. Although many cases of infection by F. solani have followed trauma, some have had no history of injury (three out of 12 in the African report), nor have immunodeficiencies figured in the background of reported cases.

In 1962 John McLean said ‘Our defences against fungi are indeed weak and clumsy’. The recent advances in chemotherapy of oculomycosis now mean that although few fungal infections of the eye are so trivial that they can be managed lightly, few are so severe that they should be despaired of, provided they can be treated at a centre with the required combination of skills. This has been brought about by the rational use of amphotericin B within its limited range of usefulness, the introduction of the wide spectrum polyene antifungal, natamycin, and the development of the imidazole antifungals: clotrimazole, miconazole, econazole, and thiabendazole, together with appropriate use
of flucytosine for yeast-like fungi. These newer antifungals penetrate the eye well but are more selective in their action than the poorly penetrating but widely active natamycin (Jones, 1975a and b). Optimal antifungal treatment must therefore be guided by isolation and species identification of the infecting organism, with direct measurement of the antifungal sensitivities of the patient's own fungus.

The development of effective chemotherapy of fungal infection of the eye has a number of important implications. There is a strong case for the rapid referral of patients with oculomycosis for emergency management in a few centres especially equipped for and experienced in this work.

The second implication results from the frustrating delays that hold up the making available of a preparation or drug that is likely to be of use only for saving eyes infected with fungi: the forseeable therapeutic market may be unlikely to cover the costs of securing approval to market it in a variety of countries. If the compound is, like thiabendazole, already in widespread veterinary and agricultural use there may be further obstacles to its availability for treating oculomycosis. It is therefore desirable that national or international agencies should undertake or support the work to provide the data needed for approval to use and to market selected preparations.

The third implication is greatly accentuated by the report from West Africa. Topical antifungal chemotherapy of individuals at times of high risk should substantially reduce these potentially disastrous infections. These times are following oculomycosis, especially with plant or vegetable material. Fungal infection is only part of the overall problem of loss of eyes from suppurative keratitis, which should be amenable to a considerable measure of prevention. It should now be possible to produce a combined antifungal and antibacterial preparation for widespread and immediate prophylactic first aid use after trauma, especially in rural areas. Further surveys are needed however, to define the causes of suppurative keratitis leading to loss of eyes in various regions. These include Gram-positive and Gram-negative bacteria, a wide variety of ocular fungi especially Fusarium species and Aspergillus species and probably also anaerobic bacteria. It will be of great interest to determine the world wide prevalence of ocular infection by Acanthamoeba polyphaga, A. Castellani, and other pathogenic freshwater amoebae, for these protozoa can cause suppurative corneal and intraocular infections resembling those due to fungi (Nagington, Watson, Playfair, McGill, Jones, and Steele, 1974; Watson, 1975; Nagington, 1975; Jones, McGill, and Steele, 1975; Ashton and Stamm, 1975; Jones, Visvesvara, and Robinson, 1975). These surveys require the provision and distribution of kits for diagnostic cultures and the provision of facilities for identification and the measurement of antimicrobial sensitivities. Local, national, regional, and international collaborations can contribute in thisendeavour. Fortunately, the techniques required for bacteria, fungi, and the pathogenic freshwateramoebae are all simple and straightforward.

Further animal experimental work is needed to define optimal formulation of various antifungals and the effect of combinations of antifungals and antibacterials. But a likely combination to be used in an ointment might well be natamycin, polyoxyn B, and an aminoglycoside such as gentamicin. Clotrimazole because of its wide spectrum of antifungal action, especially against Aspergillus species, and its good ocular penetration, would have a case for inclusion, as would econazole (Jones, 1975a and b).

In this Prevention of Blindness Year it would be appropriate for the World Health Organization to take the lead in catalysising the designation of a small number of institutions as reference centres for research in oculomycosis and related suppurative infections of the eye. This should boost and assist the collaborative endeavours that are essential in order to avoid the loss of eyes from suppurative infections.

References

--------- (1975b) Amer. J. Ophthal., 79, 719
---------, and RICHARDS, A. B. (1966b) Ibid., 89, 887
---------, MCGILL, J. I., and STEELE, A. D. MCG. (1975) Ibid., 95, 210
---------, RICHARDS, A. B., and MORGAN, G. (1966c) Ibid., 89, 727
JONES, D. B., SEXTON, R., and REBELl, G. (1966d) Ibid., 89, 781
---------, VISVESVARA, G. S., and ROBINSON, N. M. (1975) Ibid., 95, 221
NAGINGTON, J. (1975) Ibid., 95, 207