Miconazole: a new antymycotic drug

Whereas bacterial infections are often transmitted from man to man this rarely happens with the mycoses. Fungal infections are usually due to inhaling or the inoculation of spores, widespread in the environment, most of which are common animal pathogens. Candida albicans is an exception, for it is part of the normal flora of the gastrointestinal tract. How these organisms establish themselves in the body is obscure. Some fungi require a local alteration in the host, such as a cavity for Aspergillus to grow within, or a generalised disturbance, such as immunosuppression. Another feature of the disease process is the development of hypersensitivity, sometimes localised— as in the allergic pneumonitis associated with aspergillosis— and sometimes more generalised, provoking a reaction such as erythema nodosum.

Many of the fungal infections such as blastomycosis, coccioidiomycosis, histoplasmosis, and sporotrichosis described in the textbooks are rare in Britain. Nevertheless, cryptococcosis should always be included in the differential diagnosis of meningitis, particularly if it starts insidiously. Candida infections, on the other hand, are common: as well as the typical oral or vaginal thrush this yeast-like organism may cause chronic paronychia, membranous oesophagitis, and more serious systemic infections.

The treatment of systemic candidiasis and other deep fungal infections remains difficult. Nystatin is not absorbed from the intestinal tract. Amphotericin B may be given intravenously and, though effective, it is toxic and may affect the kidneys and the heart as well as causing fever, nausea, or vomiting. A less toxic alternative is 5-fluorocytosine, which can be given by mouth, but resistant organisms may emerge when it is used in the long-term treatment of chronic conditions such as cryptococcosis and systemic candidiasis. Clotrimazole is highly active, well absorbed, and gives sustained blood levels, but up to 18%, of patients tolerate it poorly.

For these reasons an agent combining safety with high efficacy would be a welcome addition to the antimicrobial armament. Miconazole is a contender for this role. Like clotrimazole, it is an imidazole derivative, and it is active against a wide range of fungi including dermatophytes and yeasts; some strains of aspergillus are not very sensitive. The drug is absorbed moderately well from the intestinal tract, or it may be given intravenously. There is some evidence that miconazole acts by inhibiting peroxidative enzymes, at least in C albicans. The first clinical reports described experience with miconazole as a topical agent in vaginal candidiasis and skin infections. Nevertheless, we now have some information on its systemic use, which has included the treatment of mycotic infections such as coccioidiomycosis, South American blastomycosis, and aspergillosis, as well as systemic candida infections. Commonly these conditions are associated with some underlying disorder that weakens the host's resistance, and here miconazole performed fairly well, even though treatment had to be prolonged in many cases. Side effects were infrequent, diarrhoea being the most often reported, and one case of drug-induced thrombocytopenic purpura was seen.

Assessment of any new antymycotic drug is always difficult, since any one investigator can treat only a limited number of the rare systemic infections. At this stage, however, miconazole looks like a promising newcomer and further reports will be of wide interest.


Poor-risk prostatectomy

Is prostatectomy a safe and reliable operation with a trivial mortality? A recent paper from Australia has raised doubts and has questioned this currently held belief. In a series of cases in an Adelaide teaching hospital Sach and Marshall reported an overall mortality of 2.3% at the end of one month, while the mortality rate for the patients aged over 80 was 9% at three months.

Perhaps one man in every ten will require a prostate operation sooner or later, so that initially these figures seem alarming—and would be worse were not some special factors in the Australian series. What must first be questioned is the statement by Sach and Marshall that, while the mortality rate has improved in general, the rate in high-risk patients has reached a plateau. This is surely incorrect when the benefits of skilled anaesthesis, careful selection, accurate haemostasis, and the transurethral operation are considered. Secondly, Sach and Marshall did not indicate how many patients were refused operation because they were unfit; and they did not find any increased mortality in patients with acute retention. Yet comparable figures elsewhere record only a 0.75% to 1% mortality for transurethral resection, even though many of the patients were far from ideally fit. In Jameson's series of 1600 consecutive prostatectomies one-third had respiratory troubles or had had a coronary thrombosis within two years previously, and a further third were admitted with acute retention. All 1600 patients were followed up for at least nine months to assess results. Jameson also recorded a series of 24 prostatectomies in patients with cardiac pacemakers without any deaths, all being dealt with by transurethral resection, with no patient refused operation. It can be accepted that generally the mortality for transurethral resection is less