CLOSING ADDRESS

The future of antifungal therapy

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Introduction

The vision of the future is often induced and facilitated by the study of the past. The historian not only collects material to gain information of the past but many historians try to find general rules about the course of history, a formula which describes the movement of events in the past as well as in the future. An example of this is the investigation on the increasing number of scientific journals which was carried out by Derek de Solla Price (1963). He showed a continuous movement of this development starting with less than 10 journals around the year 1700, about 100 journals around the year 1800 and nearly 1000 in 1850. From then on, every 50 years the number of journals multiplied by the factor of ten, which led to the prediction that at the end of this century there would be 1,000,000 different scientific journals in the world. This example is very impressive at first sight but it also shows that calculations of this order can be very misleading. For if we followed that line of argument we would have to predict that in about 200 years there would be one scientific journal per person in the whole world. So much for the predictability of the future from the extrapolation of the past.

A different approach would be to show future aims. For instance, a young scientist with a well equipped research unit behind him, and with a mind full of plans for future scientific work.

I will consider the future of antifungal therapy under 4 different headings: the patient; the disease; the drug; the medical mycologist.

The patient

There is no doubt that antifungal therapy is exclusively meant for the benefit of the patient. He is the central aim to which all our efforts are directed. So, at first sight, the relation between antifungal therapy and the patient seems to be very clear and straightforward but there are many unsolved problems in the field of infections with opportunistic fungi. Doctors have great doubts about when and when not to give systemic antifungal therapy. It is not easy to decide if you should give an extensive

amphotericin B infusion treatment to a patient with lung cancer complicated by pulmonary aspergillosis. One knows that one's patient will die of the cancer and that his suffering is prolonged if the aspergillosis can be cured. Many doctors in this situation would prefer to see their patient die quickly from a superimposed infection than see him painfully suffocating of his cancer. There are, however, cases where antifungal therapy of the compromised patient can improve the prognosis. Cytotoxic therapy of some forms of leukaemia is improving, transplantation surgery is progressing but fungal infections are frequent complications. The treatment of these infections is often inadequate owing to the lack of knowledge of modern antifungal drugs. So, from the patient's point of view there may be 'too much' and also 'not enough' of antifungal therapy, especially in opportunistic infections.

The disease

There are a large number of human mycoses, but only 2 groups will be discussed. Both groups are a special challenge to future efforts in antifungal therapy.

In opportunistic fungal infections, the challenge is 2-fold. Firstly, factors predisposing for such infections will probably increase in the future, especially because of new forms of immunosuppressive therapy. Secondly, the further development of immunosuppressive therapy will become more and more successful. More patients may be saved by this type of therapy but endangered by opportunistic infections.

The second group of fungal diseases are the superficial mycoses of the skin. These infections, in spite of their superficial location and of the development of several highly active and penetrating antimycotics, still have to be considered as undefeated infectious diseases. The failure of therapy is usually not a failure of the drug but a series of ecological and epidemiological factors. There is a need for more effective drugs which could be administered over

days instead of weeks, which penetrate the nail and invade the hair follicle.

The drug

It is easy to formulate verbally the qualities of the ideal antimycotic drug. Is it still possible that a zone of inhibited growth in a Petri dish will be observed, an organism isolated from the centre of this zone and a new antifungal antibiotic be discovered? Certainly, but the probability is very, very small. About 15 years ago Sir Ernst Boris Chain (1963) gave a brilliant lecture on the merits of academic research in the development of new drugs. It is fascinating to read this paper and to realize to what extent the development of new drugs has become an exclusive achievement of the chemical industries. Without the vast efforts in the research laboratories of the pharmaceutical industry there would be few modern drugs. Large amounts of money are needed for industrial research. The future for antifungal drugs depends on industrial research in co-operation with doctors and microbiologists in practice and in hospitals.

The medical mycologist

Why is it important to talk about the medical mycologist when talking about antifungal therapy? Is not the medical mycologist someone who establishes the diagnosis by identifying the causative organism, someone who perhaps has to deal with antifungals in terms of sensitivity studies or testing of blood levels? In relation to antifungal therapy the medical mycologist is much more than that. Apart from the fact that some medical mycologists are physicians and not biologists, every medical mycol-

ogist by reading, attending conferences and other activities has gained a knowledge in the field of antifungal therapy which usually exceeds greatly what is known to the general clinician. So, the clinician having patients with fungal infections will depend on advice from his medical mycologist. Unfortunately there is often a wide gap between the clinician and the medical mycologist. For many decades medical mycology remained an obscure science. To the average doctor, medical mycologists were people playing around with cultures of peculiar organisms bearing peculiar and unpronounceable names.

Any attempt to understand what mycologists were talking about would be discouraged by an ever changing terminology and, besides, the practical use of such knowledge was minimal. Mycology was a mystery. What is new in this situation is that today medical mycology is serving world-wide and important medical problems. The task before us is directly related to the future of antifungal therapy, to the future of the correct use of antifungals. The challenge is to make ourselves understood, to explain simply to our colleagues what in reality is complex and often strange.

In conclusion, the future of antifungal therapy and the antifungals depends on the need of the patient, the recalcitrance of the mycoses, free research for new drugs and, finally, the lucidity of the medical mycologist.

References

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