Chemical warfare against viruses

B.W.J. Mahy

Approaches to Antiviral Agents. Edited by Michael R. Harnden. *Macmillan, London/ VCH, Deerfield Beach, Florida: 1985. Pp.326. £45, $72.50.*

BECAUSE viruses are intracellular parasites, drugs which block virus replication usually damage the host cell, with consequent harmful side-effects. For this reason (and in contrast to the many antibiotics available to control bacterial infections), only a handful of chemotherapeutic agents have been identified for use against human virus diseases; currently, five such drugs are licensed for use in Britain, four against herpes and one against influenza. Prophylactic immunization has thus been the main weapon in the war against virus infection, but some infections are difficult to control in this way and interest in antiviral agents has continued.

This multi-author volume considers the mechanisms of action, biological properties and clinical application of known antiviral agents, and the available approaches to the discovery of new compounds. After a brief assessment of the world-wide clinical need for antiviral drugs, five contributions are devoted to specific inhibitors of viral replication. The recent discovery of a range of nucleoside analogues active against herpes infections has given a considerable boost to this area of research. These compounds do not harm uninfected cells but become activated in herpes-infected cells owing to specific phosphorylation by virus-encoded enzymes, with the result that virus-infected cells alone are destroyed. Such compounds might not have been discovered without a detailed knowledge of molecular events in the virus replication cycle, so other potential targets for selective inhibition are considered here. Two further chapters review published work on synthetic nucleosides, and must include descriptions of every analogue which has ever been tested against a virus, while the traditional random screening of synthetic or natural compounds with potential antiviral activity is described in detail in another two chapters.

There follow four accounts of the modulation of host defence mechanisms, which mostly discuss interferon and related substances. Interferon is one of the body's natural defences against viruses but, despite recent advances made through the application of recombinant DNA technology, the practical uses of interferons, either as antivirals directly or as immunostimulating agents, are at present very limited. The final chapter deals with the clinical evaluation of antiviral drugs.

On the whole, the eleven contributions are thorough, well-referenced and contain much stimulating discussion. There is a mood of optimism throughout, implying that new antiviral agents are just around the corner and that, given sufficient research effort, new drugs can be developed and put into clinical use. Like bacteria, however, viruses readily mutate to produce resistant strains in the face of inhibitory compounds, and perhaps too little attention is paid to such problems. Nevertheless, research workers involved in chemical warfare against viruses should have access to a copy of this book, and there is much of interest here for the general virologist as well. □

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Parasite parts

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The Biology of Trypanosomes. Edited by Leslie Hudson. *Springer-Verlag: 1985. Pp. 183. DM 124.*

SYMPOSIUM volumes on trypanosomes are now appearing at the rate of three or four a year. Most of them give prominence to how the parasite artfully eludes the host's immune attack or how the host overreacts to the parasite's presence. This collection of nine short essays is no exception. It is not, as the publisher claims, "the only recent review of trypanosome biology as a generic entity". It deals with only limited aspects of experimental work on the two species that infect man, *Trypanosoma brucei* and *T. cruzi*, and is thus far more restricted than (for example) the recent number of the *British Medical Bulletin* devoted to trypanosomiasis.

What the various contributors do bring out nicely is how the host — parasite relationship is reflected in the nature of the surface of these two very different parasites. The sleeping sickness trypanosome, *T. brucei*, multiplies in body fluids and escapes host antibody assault by repeatedly changing the exposed antigen in its monomolecular glycoprotein coat; in the book, the chemical basis of this process of antigenic variation is discussed in detail. The parasite of Chagas' disease, *T. cruzi*, multiplies inside macrophage or muscle cells and has no need for antigenic variation. The stage in the life cycle that ventures out into the host's blood to infect new cells carries on its surface a variety of glycoproteins, and evidence is presented here that many of these participate in entry into the host cell by binding to receptors or enzymatically exposing receptors for the parasite.

Two of the articles are strikingly novel. One introduces the intriguing possibility that DNA sequence rearrangements, known to play a part in antigenic variation in *T. brucei*, may be more widely involved in trypanosome differentiation. The other is a spirited attack on the problem of how non-immune mechanisms limit parasite numbers in the blood in *T. brucei* infections.

Some of the most exciting areas of current trypanosome research are conspicuously absent from the book; indeed the most flourishing enterprise of all — the molecular genetics of antigenic variation — was purposely excluded by the editor on the grounds that it is amply covered elsewhere. Yet half the topics in the book have also appeared in other reviews of late, especially macrophage-mediated immunosuppresion in *T. brucei* infections and autoimmunity in Chagas' disease. The editor also regrets omission of an article on the sex life of trypanosomes. So do we all. For too long this has been the subject of rumour and innuendo, and it is high time that somebody put a stop to it by setting down the incontrovertible evidence in black and white. □

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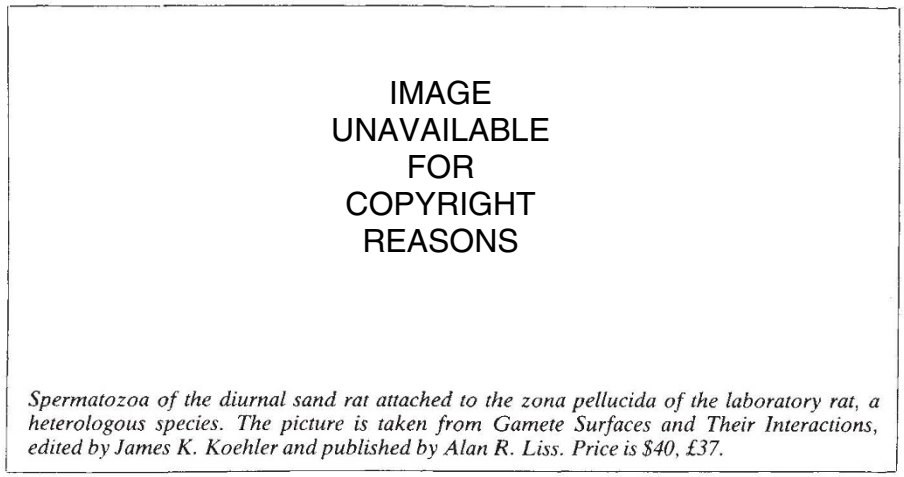

Spermatozoa of the diurnal sand rat attached to the zona pellucida of the laboratory rat, a heterologous species. The picture is taken from Gamete Surfaces and Their Interactions, edited by James K. Koehler and published by Alan R. Liss. Price is $40, £37.