BOOKS RECEIVED

Models of anaerobic infection

Edited by the Steering Committee of the Anaerobe Discussion Group: M. J. HILL, S. P. BORRIELLO, J. M. HARDIE, M. J. HUDSON, R. J. LYONS and S. TOBAQCHALI. 1984. Martinus Nijhoff, Dordrecht, The Netherlands. Pp. xi and 287.

This is a series of papers originally presented at Churchill College, Cambridge in July 1983. It was the third symposium of the Anaerobe Discussion Group, an informal group of medical, veterinary and dental microbiologists and clinicians, all of whom have a common interest in anaerobic micro-organisms.

The chapters deal with animal models of anaerobic infection and with in-vitro models. The former relate to surgical wound sepsis, peritonitis and the effects of antimicrobial agents, antibiotic-associated colitis, otitis media, periodontal disease, enterocolitis, *Clostridium spiriforme* diarrhoea and sheep foot-rot. The in-vitro models include several descriptions of the effects of non-sporing gram-negative anaerobes (mainly *Bacteroides fragilis*) on polymorph function and other host defences, together with chapters on rumen fermentation, continuous culture of oral anaerobes, the application of tissue cell culture techniques to determinations of bacterial virulence, an in-vitro model of the mammalian caecum and colon, mathematical models and studies of adherence of *Clostridium difficile* and other clostridia.

Many of the contributors are internationally recognised as authorities in their fields. The standard of presentation is uniformly high. Most chapters are c. 10–12 pages in length, many with well reproduced illustrations and adequate, sometimes extensive, bibliographies. The penultimate section of the book contains a collection of abstracts of the posters that were presented at the meeting. These cover a wide range of topical areas in anaerobic microbiology. The last section contains abstracts of the papers presented at the first meeting of the Society for Intestinal Microbial Ecology and Disease held in Boston, Massachusetts in 1983.

This book is recommended to all with interests in the pathogenesis of anaerobic infections. The contributors, editorial team and publishers are to be congratulated; and the Symposium organisers (the Anaerobe Discussion Group committee) and sponsors (May and Baker) should be thanked for producing a memorable conference.

I. R. Poxton

Microbial associations and interactions in food

Edited by I. KISS, T. DEÁK and K. INCZE. 1984. Martinus Nijhoff Publishers, Dordrecht, The Netherlands. Pp. xviii and 470. £44.50.

This volume, the proceedings of the 12th International IUMS–ICFMH symposium, contains a mixture of papers of varying standards of content and presentation. The manuscripts have received only minimal editing and are largely as received from authors. A large proportion of the contributions are from Eastern European countries, a reflection of the venue of the meeting.

The 66 papers are broadly grouped as follows: plenary sessions (4), pathogenic micro-organisms (16), methods (15), spoilage micro-organisms (6), miscellaneous (4), useful micro-organisms (6) and preservation (15). The plenary sessions include an historical review of the study of microbial ecology of food (Mossel, Netherlands) and reviews of controlled atmosphere storage of fruits and vegetables (Deák, Hungary), intestinal pathogens and the environment (Hobbs, UK), and vegetables as an ecological environment for microbes (Skovgaard, Denmark). The section on pathogenic micro-organisms includes papers on most of the wide range of organisms associated with food-borne illness in man. Of interest are reports on the use of reference samples in detection methods for *Salmonella* (Beckers, Netherlands), improvement

in the microbiological quality of chicken by irradiation (Kiss *et al.*, Hungary), stability of pathogenic factors in *Yersinia enterocolitica* (Nover and Kramer, FRG) and the role (if any) of foodstuffs in the transmission of *Listeria* (Ralovich, Hungary).

There are interesting reports in the Methods section on liquid media for the enumeration of faecal coliforms in food (Søgaard, Denmark) and a comparison of different versions of Rappaport medium for the isolation of *Salmonella* (Vassiliadis, Greece). A new wonder plating medium for *Salmonella*, inhibitory to all other Enterobacteriaceae is described (Vamos *et al.*, Hungary); however, the authors are not prepared to divulge details of the medium as it is under patent application! Mehlmann (USA) gives the results of a very thorough study on a modified Anderson/Baird-Parker procedure for the enumeration of *Escherichia coli* in foods.

On the more practical aspects of food preservation, there are reports on the use of CO₂-packaging as a means of prolonging the shelf life of beef (Erichsen and Molin, Sweden) and the effect of frozen storage on the aerobic flora of vacuum-packed beef (Beyer, Berlin). There is a particular emphasis on preservation by the use of irradiation, with papers on the benefits of ionising irradiation over ethylene oxide treatment (Farkas and Andrassy, Hungary), improvements in the microbiological quality of spices and the effects on the microflora of other foods such as chicken and shrimp (various workers, Netherlands). The effects of natural spices and oleoresins on *Lactobacillus plantarum* and *Staphylococcus aureus* (Nes *et al.*, Norway), yeasts (Conner and Beuchat, USA) and *Bacillus cereus*, *Staph. aureus*, *Pseudomonas* and *S. typhimurium* (Shelef, USA.) are also discussed.

Overall, an interesting assortment of papers, giving an opportunity for the reader to see some of the work being carried out in the field of food microbiology and hygiene in both Eastern Europe and the West.

DIANE ROBERTS

Role of the envelope in the survival of bacteria in infection

Edited by C. S. F. EASMON, J. JELJASZEWICZ, M. R. W. BROWN and P. A. LAMBERT. Medical Microbiology, vol. 3. 1983. Academic Press, Orlando, FA. Pp. xiii and 264. US\$ 47.00.

The editors of this series planned to include some volumes containing review articles on a common theme. In this volume, the theme linking the chapters is the role of the bacterial envelope in the survival of bacteria in infection. The book has emerged from contributions to a meeting held at Aston University and sponsored by the British Society for Antimicrobial Chemotherapy.

The first three chapters deal comprehensively with aspects of drug resistance in relation to the bacterial surface, including the role of specialised structures such as glycocalyx, and also with the influence of drugs on bacterial adhesion. This latter chapter by Vosbeck and Mett discusses critically the problems associated with different model systems for studying bacterial adhesion; it should become required reading for anyone with a serious interest in adhesion assays.

The next three linked chapters deal with the influence of the envelope on tissue invasion, humoral defences and interaction with phagocytic cells. There is throughout a strong emphasis on the ability of the bacterial cell to vary its envelope in response to the growth environment, an aspect that is highlighted in Chapter 7 by Griffiths who describes the important effects of iron availability in the ability of bacteria to survive *in vivo*, a neglected yet critical aspect of bacterial virulence.

The last two chapters illustrate how current knowledge of the bacterial surface might be exploited in the design of antibacterial agents and vaccines. The enthusiasm of these chapters makes for stimulating reading.

Although initially I had some doubts as to whether the diversity of topics covered would produce an overall patchiness, the whole, in fact, blends together well and there is remarkably little duplication of core material in the different chapters. Multi-author volumes often suffer from the variability of the standards achieved but each of these chapters is well written and, on the whole, well edited. The literature reviews throughout are extensive and reflect accurately the state of the art as at the end of 1982. It is inevitable, therefore, that subsequent progress in some of the faster-moving, popular areas will have been considerable. Nevertheless, this book will

provide valuable reading for both science and medical students. Indeed, any medical microbiologist wishing to keep abreast of current developments in areas removed from his own particular sphere of interest would do well to make use of this helpful book. Whilst the cost may put it beyond the pocket of many students, they should be able to locate this volume in the library of most departments of medical microbiology. This is another useful volume in an enjoyable and worthwhile series.

D. C. OLD

Genetics and biotechnology of bacilli

Edited by A. T. GANESAN and J. A. HOCH. 1984. Academic Press, Orlando, FA. Pp. xix and 421. £29.50.

This volume comprises the proceedings of the second International Conference on the Genetics and Biotechnology of Bacilli, held at Stanford University, July 1983.

Much has been written on the potential impact of molecular biology on health care. As Stanley Falkow points out in a thought-provoking and humorous Introduction, in the real world the majority of deaths occur through inadequate hygiene—principally the lack of clean water. Biotechnology is of little use in these circumstances.

Falkow, also in the Introduction, gives his opinion of *Escherichia coli* K12—"a nice enough micro-organism but it had little personality". *Bacillus subtilis*, the principle subject of this volume, could not be included in this category. The recent advances in the molecular genetics of this intriguing and, in the opinion of the reviewer, often confusing and annoying micro-organism, are fairly comprehensively covered in five sections, on chromosomal organisation, secretion, transcription, cloning and sporulation; further sections are devoted to phage, spores and general genetics. Biotechnologists will be particularly interested in the section on secretion. One of the advantages of *B. subtilis* is the potential for isolating the desired gene product from the culture medium after gene cloning in a secretion vector. The expression of foreign genes may be temporally controlled, with respect to the cell cycle, by putting them under the control of sporulation promoters—a feature that may be attractive to the biotechnologist working with a lethal gene product.

Much of the information contained has been published previously and therefore this volume might be regarded as a luxury by some workers in the field. At £29.50, I feel that a little more care should have been taken in proof-reading, as there are numerous errors; the most glaringly obvious is "post-experimental growth" instead of presumably, "post-exponential growth", on page 409. Despite these distracting oversights, I consider it a useful collection of papers which gives a fairly up-to-date account of the principle areas of research.

E. KENNY

Malaria and the red cell

Edited by J. W. EATON and G. J. BREWER. 1984. Alan R. Liss Inc., New York. Pp. xi and 174. £28.00.

The papers presented and the subsequent discussions at a Malaria Workshop held in conjunction with the Sixth International Conference on Red Cell Metabolism and Function at Ann Arbor, Michigan, on October 2 1983, form the basis of this book. The contents are divided into three sections.

In the first chapter of section one, metabolism, Eckman deals with the competition between the malaria parasite, *Plasmodium falciparum*, and the host erythrocyte for glutathione which plays a key role in protecting the red cells from the oxidant stress imposed on them by the parasites. Superoxide dismutase also serves to protect both parasite and host. Evidence is presented in the next paper by Fairfield, Meshnick and Eaton to show that the rodent parasite, *P. berghei*, does not synthesise this enzyme for itself but makes use of that produced by its host cells, one of the rare examples of this phenomenon in the genus *Plasmodium*. A number of drugs that inhibit the enzyme are also inhibitory to growth of the intraerythrocytic parasites. Calcium ions play a key regulatory role in all eukaryotes. The presence of another rodent parasite, *P. chabaudi*,

in rat erythrocytes increases the permeability of the host cell membranes to Ca^{2+} and the calcium content of the parasitised cells increases greatly. Mikkelsen and his colleagues, on the basis of experiments with lysed red cells, indicate that this is brought about by an uncoupling of ATP hydrolysis and ion translocation. In the final chapter of this section by Roth *et al.* the role of glucose 6-phosphate dehydrogenase (G6PD) deficiency in protecting the host against falciparum malaria is reviewed in relation especially to the increase in tocopherol levels of infected erythrocytes. The author conclude that oxidant stress is insufficient as an explanation of the limiting effect of G6PD deficiency on parasite growth.

Section two deals with membranes and membrane proteins. Howard, Varki and Reese describe a novel technique for the identification of metabolically labelled merozoite proteins and show that *P. falciparum* synthesises little or no sialic acid from the monosaccharide precursors, glucosamine and N-acetylmannosamine. The parasites were found not to incorporate fucose. Details are given of the merozoite proteins detected in these experiments which suggest that *P. falciparum* does synthesise N-linked oligosaccharides. Leech and his associates review studies of the nature of proteins associated with the "knobs" of *P. falciparum*-infected red cells that cause the erythrocytes to adhere to capillary endothelium. This is inhibited by immune serum and adhering cells may be released. The knobs themselves are associated with an unusual histidine-rich protein (HRP) of parasite origin lying beneath the surface membrane of the red cell. It is proposed that the adhering ligand may be a further parasite protein, but not the HRP itself. The nature of HRP is further pursued by Lorand *et al.* They provide evidence on the basis of experiments following the fate of ^{35}S -methionine-labelled *P. falciparum* *in vitro*, that the erythrocyte "knobs" contain parasite peptides linked to host cell protein, and discuss possible biochemical routes by which this linkage could be achieved. Ockenhouse, Schulman and Shear confirmed that H_2O_2 released from monocyte derived macrophages is capable of killing *P. falciparum* in red cells *in vitro* and that catalase blocks this action. "Knobless" infected erythrocytes do not attach to macrophages nor cause the oxidative burst that results in the production of "crisis forms" of the parasites and their death. There is evidence that antimalarial antibody promotes this attachment to monocytes and macrophages. Wallach and Sarkar show that the genes and RNA responsible for the synthesis of HRP are highly conserved evolutionary characters found in both simian and avian species of *Plasmodium*.

In the third section of this book Fitch and his co-workers review their studies on ferriprotoporphyrin IX (FP) which is formed when the malaria parasite digests host-cell haemoglobin. FP is highly haemolytic through a detergent-like action on biological membranes and is normally sequestered within the malaria parasite by complexing with a parasite-derived protein. They believe that chloroquine competes with this protein to bind with FP, rendering the latter even more haemolytic than it is on its own, and that FP acts as a high-affinity binding site also for other antimalarial drugs. Scheibel *et al.* investigated the antimalarial action of proteinase inhibitors and showed that a number of them were inhibitory to the growth of *P. falciparum* *in vitro*. Neither the antimalarial action of cyclosporin A nor of artemisinin could be attributed to proteinase inhibition. Whan, Brown and Chiang report that SIBA and deaza-SIBA, two methyl-thioadenosine analogues, inhibit the growth of this parasite and result in an elevation of intraparasitic spermidine levels. Their mechanism of action is debated and the authors warn against directly interpolating such in-vitro experiments to the action of drugs *in vivo*. In the final paper, Wood, Rock and Eaton return to the question of haemoglobin digestion and confirm that chloroquine-resistant *P. berghei* degrades relatively more of it and at a higher rate than do parasites of a chloroquine-sensitive strain. However, the residue of the digested haemoglobin (i.e., haemozoin formed from FP plus its sequestering protein) is greater in chloroquine-sensitive parasites. The reasons for the different rates of haemoglobin catabolism and haemozoin formation remain to be clarified.

This collection of papers provides an excellent update of research on malaria and the red cell as well as several stimulating ideas for further research in this field. It should be read by anybody interested in the challenging problem of developing new chemotherapeutic and immunologic approaches to the combatting of malaria, which remains, today, one of the world's most frustrating public health problems.

W. PETERS

Human antiparasitic drugs: pharmacology and usage

Edited by D. M. JAMES and H. M. GILLES. 1985. John Wiley & Sons Ltd, Chichester. Pp. xiii and 288. £15.50.

In the course of teaching pharmacology to medical and science students in the tropics, the principal author perceived the need for a text that exclusively addresses the pharmacology of antiparasitic drugs. It is considered that this requirement is now even more relevant with institutions worldwide becoming increasingly involved in parasitic infections, since drugs play an integral role in parasitic disease studies both in their curative and related pharmacological effects and as tools to explore the aetiology of such diseases. It is believed that a knowledge of drug properties in the context of parasitic disease is therefore axiomatic for such studies.

The first section, which covers fundamental principles, provides a basis for the two other sections in which the appropriate drugs for the two sub-kingdoms (Protozoa and Helminths) are considered. In these latter sections, drugs in current use, as well as some in an advanced stage of development, are discussed in detail, while some obsolete drugs which are still of academic interest are included where relevant. Section A, that provides a background to parasitic diseases and drug treatment, contains three chapters which cover general considerations. In Chapter 1, methods of control, the role of drugs, and the introduction of specific antiparasitic drugs are considered. This provides a useful introduction to the use of now available, selective, highly effective and safe compounds in control strategies for population-based chemotherapy and targeted treatments.

Chapter 2 is devoted to the principles of drug treatment in parasitic diseases, and the many aspects of pharmacodynamics and pharmacokinetics. Chapter 3 deals with drug development and the problems that face the pharmaceutical industry in producing drugs for parasitic infections, including Third World economic factors, and the now more exacting legislation in developing all drugs for use in man. Drug formulation is of increasing pharmaceutical interest and many sophisticated methods are considered which are in the process of development to facilitate the delivery of biologically active molecules, including a number of macromolecules, liposomes and erythrocytes.

Section B contains eight chapters that cover the antiprotozoal drugs. It is considered paradoxical that so little progress has been made in the chemotherapy of the trypanosomiasis, despite its long-established screening methodology and the significant advances that have been made in the biology of the parasites. In relation to leishmaniasis, it is anticipated that the finding that liposomes can greatly enhance the delivery of the standard drugs in the in-vivo experimental models may lead to improved methods of drug delivery in man. In the case of amoebiasis, it is believed that metronidazole and its derivatives come closest to the ideal drug, exerting some activity in the lumen in addition to having high activity at tissue sites. Further work is, however, desirable to confirm that the drug is devoid of mutagenic and carcinogenic potential in man. Attention is drawn to the value of the drugs with effective luminal activity only, such as diloxanide furoate, which can perform an important role in controlling the disease.

In reviewing the drugs for malaria it is concluded that the greatest need is for blood schizontocides that are as effective and rapid in action as chloroquine and as well tolerated. It is thought that mefloquine may be a likely candidate to replace chloroquine or chloroquine plus sulphonamides with pyrimethamine, in cases where drug resistance is a problem.

The rarer protozoal infections such as toxoplasmosis, *Pneumocystis* infection, *Isospora* and *Sarcocystis* infections, etc., have had to rely on the results of limited empirical trials of antimicrobial and antiparasitic drugs in man, but it is noted that two medications that have had wide application within this group of infections are the sulphonamide-pyrimethamine combination and metronidazole or its derivatives. It is considered that there is a need for alternative drugs to supplement or displace the few in present use which are deficient in efficacy or are of uncertain safety, and that much more basic research is required on their common biochemical characteristics.

Section C contains four chapters covering the anthelmintics. The wide range of effective anthelmintics for the intestinal nematodes that have become available during the past 25 years is noted, as is their high tolerability. The mechanisms of anthelmintic activity for this group of drugs, however, are either unknown or incompletely understood. The value of drugs that have

effects other than against adult parasites, such as ovicidal action or which interfere with larval development, is emphasised. The dearth of drugs for treating infections in man due to tissue nematodes is highlighted, and the need for a macrofilaricidal compound for onchocerciasis is noted. Certainly the benzimidazole carbamates offer new hope as a development of clinical value for trichinosis.

It is considered that the treatment of cestode infection has been very much improved during the past decade with the emergence of the two important drugs, praziquantel and mebendazole. The most significant advance is considered to be the discovery of drug activity against metacestodes—i.e., mebendazole that has some effect in hydatid disease and praziquantel that can cure some cases of cysticercosis. The advent of the broad spectrum anthelmintic praziquantel is again highlighted as the most exciting development in the treatment of schistosomiasis and other human trematode infections.

The standard treatment schedules of antiprotozoal agents, antimalarial drugs and anthelmintic agents are given in Appendices I, II and II, respectively. These excellent appendices list the diseases, the drugs by generic name, ranks of choice, forms of preparation available, the dosage regimens, and main adverse reactions. Although oxamniquine is listed as the drug of first choice in the treatment of *S. mansoni* infection, it should be noted that the recommended dosage of 15–20 mg/kg body weight is applicable only to strains of *S. mansoni* from the Caribbean and South America, and effective treatment of *S. mansoni* in Africa and the Middle East requires at least double these doses. The recommended dosage of metrifonate in the treatment of *S. haematobium* should also read: “3 times at 2-weekly intervals”.

Each chapter has selected references for further reading and there is a very useful Index. This well written publication, which spans several disciplines, provides an excellent introduction to antiparasitic drugs for pharmacologists, parasitologists and microbiologists, while clinicians can find up-to-date information on current chemotherapy. It is a valuable and most useful addition to medical literature.

G. WEBBE