Book Reviews

EFFECTS OF MICROBES ON THE IMMUNE SYSTEM

Edited by MW Cunningham and RS Fuginami. Lippincott Williams and Wilkins, Hagerstown (MD), 1999. 662 pages.

Price: approximately A$214

This book focuses on the immunopathology of infectious disease, but also tells much about the protective immune response. It covers a wide range of pathogens and is aimed at clinicians, microbiologists, immunologists and pathologists; that is, health professionals rather than undergraduate students. Whether clinicians as such would find it useful I wonder, but I found it fascinating to dip into. It is a reminder of the compromises made by the immune system, the immunopathology that arises during the defence of the body against infection. It also opens our eyes to the complexity of the immune response to infection, compared with the response induced by the pure protein antigens beloved of immunologists until recently.

The range of this book is broad. The pathogens covered include staphylococci, streptococci, chlamydia, mycobacteria, listeria, shigella, salmonella, Escherichia coli, treponema, neisseria, haemophilus, measles virus, lymphocytic choriomeningitis virus (LCMV), picornaviruses, coronaviruses, human T-lymphotropic virus (HTLV)-1, lentivirus, herpes simplex virus, cytomegalovirus, Epstein–Barr virus, hepatitis C virus, toga/flaviviruses, poxviruses, bunyavirus, leishmania, nematodes, trypanosomes, fungi, Helicobacter and rabies virus, more or less in that order. Topics covered include autoimmunity in its various manifestations associated with infection, mucosal immunity, immunosuppression and immunomodulation as a result of infection. Superantigens of different sources are covered in separate chapters.

Most chapters relate to a particular infection. They lead us from the basic background of the subject to the latest research. The book is strong on experimental work that throws light on the clinical, rather than being clinical per se.

Each of the 38 chapters is written by an expert or experts prominent in their field, yet the editorial control is strong enough to produce a uniform format and style. The figures are clear and useful. Some even display a sense of humour, as in Fig. 6 of Chapter 16, where B cells are depicted as toy soldiers with swords drawn or missing in the case of anergic cells. When they suffer apoptosis, they lie flat on their backs with toes in the air! Each chapter is accompanied by copious references to research papers. There is an extensive index.

To get a flavour of the book, it is necessary to give some examples at random of the material covered. Each author has followed his/her own interests and approach.

Chapter 1 on ‘Autoimmunity and microbial infection’ deals largely with the role of the hsp60 family of heat shock proteins in arthritis. It begins with a thoughtful discussion of mechanisms of bacterial signalling to the innate immune response and ends with discussion on the maintenance of self tolerance.

Chapter 11 gives a coherent account of the extensive knowledge of Listeria monocytogenes, which has formed the paradigm of cell-mediated immunity to intracellular bacterial pathogens. Without the concepts derived from this largely experimental murine model, our understanding of leprosy, for example (chapter 10), would have been much slower coming. Chapter 10 deals with the immune complications that occur at both ends of the leprosy spectrum: tuberculoid leprosy, where the Th1 response is associated with nerve damage, to lepromatous leprosy, where the Th2 response is unable to control infection and antibody complexes cause damage.

Chapter 37 on Helicobacter pylori covers virulence factors, innate and acquired immune responses, potential vaccines and serological diagnosis.

Chapter 26 on EBV presents an excellent analysis of the range of diseases associated with this fascinating virus. It contains an historical background, the molecular basis of interaction of the virus with B cells and other cells, a section on the manifestations of the disease including lymphoid disorders, modulation of immune function and immune evasion.

Measles virus (Chapter 18) is presented as a relatively recent human pathogen that arose from a variant of rinderpest 2500 years ago. The time scale is based on the fact that the virus needs several hundred thousand susceptible individuals to maintain itself, and it was not until this time that populations of this size were available. The ability of the virus to modulate immune function and induction of postinfection encephalomyelitis are discussed.

Leishmania (Chapter 33) is an infection that fascinates those interested in the Th1/Th2 model of immune responses. Epidemiology and clinical features are explained, followed by host/parasite relations, first in the experimental mouse, then in humans. Vaccination and immunotherapy are discussed.

Chapter 36 on ‘Cell mediated immunity and medically related fungi’ is a general one in which trichophyton, Candida albicans, Pneumocytis carinii, Aspergillus, Blastomyces, Coccidioides, Histoplasma and Cryptococcus neoformans all get a mention in just 22 pages! The effort to condense relevant information is reflected in the 400-odd references. It is evident that this pithy book could not have been split into a number of chapters, but this is already a substantial book.

The weakness of the book lies in the apparently random choice of topics and the seeming lack of a logical structure. Chapter 1 concerns the role of mycobacterial heat shock proteins in arthritis. Arthritis also appears in chapter 5 on Lyme disease and chapter 8 on spondyloarthropathies. It is reasonable that arthritis appears in a number of chapters, because it is believed to be one of the major immunological sequelae of infection, but why not group the chapters? Of the intervening chapters, chapters 2 and 3 deal with superantigens from, respectively, staphylococci and streptococci. We next encounter superantigens in chapter 7 on Mycoplasma arthritidis. Streptococci are again the major subjects of chapters 9 and 17. There is also no consistency between very general chapters, for example Chapter 15 ‘Mucosal immunity’, and very specific, such as Chapter 31 ‘Regulation of apoptosis by poxviruses’. Maybe this criticism is unreasonable, but it seems to me that for someone coming from outside the field, a useful approach would be a general chapter on a particular problem followed by some specific examples. Alternatively, grouping according to pathogen would be a simple logic.
More worrying, there are some glaring gaps in the coverage. For example, whereas *Mycobacterium leprae* rates a chapter, *Mycobacterium tuberculosis* does not, and what greater example of immunopathology! Of the various hepati-
tis viruses, only hepatitis C rates a chapter. As explained
earlier, there is only one chapter on the pathogenic fungi and just three on parasites. AIDS as such is not covered, except under the broader heading of lentiviruses. Given the amount written on this infection, this may be regarded as refreshing!

In summary, despite its shortcomings, I would strongly recommend this book as a rich source of information for anyone with an interest in this field. It is broad in its scope, readable and abundantly referenced. It has gaps, so just make sure your particular interest is covered.

CHRISTINA CHEERS
Department of Microbiology
University of Melbourne
Parkville, Vic.
Australia

CYTOTOXIC CELLS

Edited by MV Sitkovsky and PA Henkart. Lippincott Williams and Wilkins, Philadelphia, 1999. 472 pages. Price: US$295

This book is a follow up to a very successful edition of *Cyto-
toxic T Cells* published in 1993 by the same editors. A great deal of work has been done on understanding the process of cytotoxic T cell (Tc) killing of target cells since that time and this book amounts to a collection of comprehensive reviews by experts in the field bringing together recent advances in the area. A number of chapters also include much-needed historical perspectives of the field, acknowledging the contributions of early workers so often overlooked now.

As well as being a useful historical perspective, the intro-
ductive chapter sets the scene for the format of the book by succinctly reviewing the three stages of killing by Tc cells, namely target recognition, delivery of the lethal hit and target cell disintegration. The following chapters are covered in this order followed by a number of contributions dealing with clinical exploitation of Tc cells. The book is divided unequally into six major sections dealing with target recognition, effector cell signalling, effector cell molecules, *in vivo* effects, memory and medical applications.

Recognition of target cells by Tc cells is covered in five chapters, providing in-depth coverage of the nature of MHC interactions with both T cell and NK cell receptors and drawing out the differences in the two types of interactions. The upregulation of accessory adhesion molecules is covered in detail, including signals for de-adhesion of the Tc cell after the lethal hit. A useful chapter explores the role in patho-
genesis of innocent bystander killing by antigen-specific Tc cells during long-term chronic infections accompanied by persistent presence of antigen-expressing targets.

Effector cell signalling pathways are covered in only two chapters. This includes a chapter on the detail of early sig-
alling events involving tyrosine kinase activity and inhibitory signalling in NK cells. A second chapter in this section explores the evidence to date for the role of non-immune extracellular signalling molecules, such as ATP and adenosine, in effector function. These molecules may play a role in control of effector cell function, including suppression, by the local tissue environment such as in a tumour mass.

Effector molecules are covered in nine chapters, including a useful overview of effector cell mechanisms. Two chapters are reserved exclusively for perforin, one of the first cytolytic molecules isolated from Tc cells. These chapters cover the early observations of the role of perforin as a disease marker to regulation of perforin and its role in effector cell activity. That perforin is not simply an agent for punching holes in cells, but occupies a more central role than originally thought, is explored in chapter 12 on internal delivery of the all-important granzyme molecules to the cell. In this chapter, evidence for the proposal that granzyme B is delivered to the cytosol of the cell with the help of sublytic concentrations of perforin following endocytosis is presented. The granzyme then induces apoptotic cell death by activating downstream caspases, such as caspase 3. The following chapter then includes an extensive review of granzymes, their structure and all-important regulation by endogenous inhibitors, followed by a chapter focusing on the role of granzymes in controlling virus infection. Natural killer cells are not neglected, with a section on granulysin and NK-lysin.

Cytolysis by Tc cells is generally considered to be via a two-edged sword, the second component being lysis by the CD95 ligand/CD95 pathway, otherwise known as the FasL/Fas or APO-1 route. Although thought to be mainly involved in immune regulation, this pathway does appear to be important for Tc cell killing of target cells, particularly as target cell Fas levels can be modulated by a variety of circumstances. Regulation of the Fas ligand by TCR signalling and transcriptional regulation of Fas ligand is well established and is covered in chapter 16. These sections could have included more on mechanistic and signalling aspects of killing by engagement of the Fas receptor.

Five chapters on Tc cells *in vivo* follow, covering perforin-
dependent autoimmunity, specific discussion of hepatitis B and Tc cells and responses to intracellular pathogens. The importance of perforin in tumour surveillance is covered in these sections. This is followed by coverage of the important area of Tc cell generation and memory.

The final five chapters cover medical aspects of Tc cells, beginning with tumour antigens recognized by Tc cells with several contributions on the contentious area of tumour vaccines and immunotherapy for treatment of HIV.

This is a comprehensive survey of this expanding area of research by leaders in the field, although some areas, such as Fas killing and cytokines, were covered lightly. There was little mention of TNF, for example. Some of the data appeared to be original and unpublished, which is out of place in such a format as this. This would be extremely useful to students and non-experts initiating a study in the area, providing that they can cope with the massive price of the book.

PAUL WARING
Division of Immunology and Cell Biology
John Curtin School of Medical Research
Australian National University
Canberra, ACT
Australia
NUTRITION AND IMMUNOLOGY
Edited by ME Gershwin, JB German and CL Keen. Humana Press, Totowa (NJ), 1999. 504 pages. Price: US$149.50

This is a well-assembled book that has successfully bridged the two seemingly disparate disciplines of immunology and nutrition. A panel of leading researchers and clinicians have written 38 chapters of information on basic nutrition and clinical consequences of nutritional imbalance and deficiencies, culminating in a series of review papers on the effects of nutrition, diet and disease on immune responses. This book will serve not only as a reference source to specialist nutritionists and immunologists, but will also provide illuminating information for public health specialists and pharmacologists. Graduate and postgraduate students will find this book extremely useful to access information derived from many diverse fields, including plant products and herbal medicine, food allergies, toxicology, cancer, oral disease, probiotics and anti-oxidants.

The first section, on ‘Nutritional assessment’, provides a comprehensive description of methodologies for dietary, anthropometric, clinical, biochemical and functional assessments used by the physician to evaluate global and individual malnutrition. The third chapter provides a brief appraisal of the immune system and lists the consequences of general diet deficiencies on immune function. The need for vitamins, trace elements and anti-oxidants for optimal immune responses is also included in this section.

The second section consists of eight separate chapters on specific nutrient requirements and covers caloric intake, protein/amino acids, vitamins and nucleotides. The roles of alpha-lipoic acid as an anti-oxidant, $n$-$3$ polyunsaturated fatty acids on T-cell activation and dietary phytochemicals in modulating human immune function are included in this section. All of these chapters are more than adequately illustrated with biochemical pathways and chemical formulas that serve to summarize a mass of easily digestible information for the less than avid reader.

The third section of the book consists of only two chapters, describing in a more holistic manner the impact of nutritional status on immune integrity. A chapter on the nutritional modulation of inflammation by polyunsaturated fatty acids provides some of the latest concepts on how health can be influenced by appropriate consumption of ‘friendly’ precursor molecules in our diet.

‘Clinical issues’ represents by far the largest section in the book and consists of 24 chapters that describe one or more aspects of the interaction between nutritional components and diet and the immune responses associated with a wide range of clinical disorders. In assembling these chapters, there has been a tendency for individual articles to reiterate commonalities of immune function, such as the inflammatory process and the role of cytokines in inflammation. Nevertheless, this information can only serve to reinforce fundamental immunological concepts for readers who are non-immunologists. Several topical subjects, such as cigarette smoking and substance abuse, breast-feeding, obesity, diabetes, food allergies and food toxicology and their effects on immunity, have been portrayed in depth. Another useful feature in this section is the information on the anti-inflammatory effects of Chinese herbs and the impact of complementing normal diets with probiotic bacteria on the immune system.

Most of the chapters in the book are well illustrated with tables summarizing key concepts and pathways. Up to date references have been included to justify the extensive coverage given to the impact of diet on a range of clinical issues and immune status. As well as being informative, this book provides enjoyable reading and has succeeded admirably in preserving a central theme throughout the book on the use of diet to treat the onset and progression of chronic disease in relation to immune responses.

JAMES CHIN
Immunology
Elizabeth Macarthur Agricultural Institute
Camden, NSW
Australia