

and stated clearly that, like thermodynamics, special relativity was a framework theory to which all specific physical theories had to conform—until of course his own general relativity came along and superseded it. The following paper 4 on mass energy equivalence is very brief. It is only necessary to point out that neither the phrase 'rest mass energy' nor the formula ' $E=mc^2$ ' occur in it explicitly. The statement however is made that 'The mass of a body is a measure of its energy content'.

The 'revolutionary' paper 5 is historically the second most important paper in the development of quantum theory, after Planck in 1900 had announced his law of black body radiation. Here Einstein's mastery of statistical thermodynamics, the roles of probability and entropy and the Boltzmann principle, are just stunning. His examination of the high frequency Wien limit of Planck's radiation law, and extracting the volume dependence of the entropy of such radiation, are strokes of sheer genius: he knew that it was here that departures from classical ideas would show up. It was the similarity of this volume dependence to the case of a gas of free molecules that led him to the idea of quanta of light. This link to the Wien limit of Planck's law, an approximation, is mentioned by him repeatedly. And after having arrived at the light quantum hypothesis in this way—expressed in the historic statement 'monochromatic radiation of low density (within the range of validity of Wien's radiation formula) behaves thermodynamically as if it consisted of mutually independent energy quanta of magnitude  $R\beta\nu/N$ '—he looks at three different situations where his ideas can be checked: Stokes rule for photoluminescence, the photoelectric effect, and the ionization of gases by ultraviolet light. As everyone knows, it was not relativity but the explanation of the photoelectric effect that was cited in his Nobel award in 1921.

This is a precious volume, meant for both the mature and the gifted young. There is an indescribable thrill in reading these classics of science, and in reminding oneself that physics was different before them. We see the sources from which Einstein learnt his physics, the connections he made in his mind among its various areas, the new conceptions that sprang from his imagination, all in the historical context. Remembering what he

said about Mahatma Gandhi, one can scarce believe that such a one as this walked this earth and achieved so much in the span of a single year, while earning his living as a patent office clerk. But then volume 17 of the *Annalen* exists to convince the incredulous!

N. MUKUNDA

*Centre for Theoretical Studies and  
Department of Physics,  
Indian Institute of Science,  
Bangalore 560012, India*

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**Therapeutic Strategies for Modulating Inflammatory Diseases.** B. M. Weichman (ed.). Birkhauser Verlag, Postfach 133, CH 4010, Basel, Switzerland. 1998. Price: SFR 78. 107 pp.

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One of the many problems with this book (and others of its genre) is of dates: The date of publication of the book is 1998 (although the catalog entry is from 1997), the editor's preface is dated August 1997—a year ago—, and the book is based on a conference in October 1996—almost two years ago! So the question is: What is new?

It is a generic problem, rooted in the cumulative nature of scientific endeavour, that books in science become outdated. This is especially true of books whose major, if not sole, *raison-d'etre* is their novelty or 'currency',—they suffer as terribly as bell-bottom trousers. Since the major reason (or at least, the major academic one) for conferences is topicality, a publication of the proceedings two years after the event is a sorry spectacle. If one is bent on publishing the proceedings of ephemeral conferences, should one not do it within months, at least, of the event itself?

The second difficulty with the book is in deciding what to expect, even after one has finished reading it. The blurb on the back cover says that it presents the latest results from molecular, preclinical and clinical investigations on the mechanisms of inflammatory diseases, by international experts in the field of inflammation research, and should be a valuable resource for pharmacologists,

immunologists, molecular biologists, and medicinal chemists involved in inflammation research and drug discovery. That is indeed a tall order to live up to! Then one starts at the beginning and discovers that the book simply presents 'many highlights of the eighth international conference of the inflammation research association'. That is not a letdown; it is a crash.

Associated quibbles also arise: There is no uniformity in the pieces presented in the book. While some are reviews, others are actual data reports. Some of the data reports are those of clinical phase I trials, meaning preliminary studies of new drug toxicity and pharmacokinetics in volunteers, saying nothing about efficacy. Why on earth are these 'valuable resources'? A large part of the book is poster presentation summaries, which in the nature of things are even more ephemeral. Another quibble, admittedly a minor one, is about hype. 'International experts', the blurb proclaims, yet with one exception from the UK, all authors are from the USA. One hopes at least that the poster sessions had a more international flavour. All the five editors are from industry, as are a majority of the authors. This sets the tone for the writings which, despite claims to the contrary in the blurb, say nothing whatsoever about mechanisms of inflammatory diseases. What are 'inflammatory diseases', anyway? As far as the book is concerned, this is not an etiological or mechanistic definition but only a clinical therapeutic one, meaning all those diseases where anti-inflammatory therapy helps. Thus from so-called 'autoimmune' inflammation to degenerative diseases, like osteoarthritis, a wide range of pathophysiological states is grist to this mill. Every piece exhorts the troops about the 'immense therapeutic possibilities' in this that or the other,—the industry-based authors with pushy vim, the academics with chilly caution.

So why do academics write in such books at all, given its exceedingly limited readership? This is a 'non-peer-reviewed publication', and therefore of no great use to the bio-data of a working scientist. One reason could be to pad the bio-data of a junior colleague such as a doctoral student or a post-doctoral associate, but the junior collaborator authors in the book do not appear to need that. Another reason could be to write a review of currently controversial preoccupations in the field,

with a personal interpretation to offer. In separate articles, Jenkins and Sharpe, along with their coauthors, do valiantly attempt this.

Surprisingly, Jenkins and Pape, despite pioneering recent studies on the fate of responding T cells *in vivo*, simply restate what is by now said frequently enough: that inflammatory cytokines induced from accessory cells by pathogens or their mimics ('adjuvants') are important in regulating fate of the responding T cells. Sharpe and Schweitzer do better trying to address the current controversy over whether the two costimulatory molecules, CD80 and CD86, do or do not separately control Th1 and Th2 responses. They argue that the differential kinetics of CD80 and CD86 induction, coupled with the differences in the kinetics of the disease processes, may explain conflicting results in differing experimental systems. However, they do not even acknowledge a similar controversy on the possible inhibitory and activatory roles of the T cell costimulation receptor CTLA-4 that can also be explained as a matter of differential kinetics.

The rest of the book deals more directly with therapeutic possibilities. Overstatement remains the order of the day. So Wong says, in discussing the ICE family proteases in inflammation and apoptosis, 'inhibition of ICE represents an approach in which the levels of several cytokines can be modulated simultaneously, and offers greater therapeutic impact in the treatment of a variety of inflammatory diseases'. This flies in the face of conventional drug development, where careful selection of a single target pathway is crucial, since if multiple events are affected, unrealized and unwanted side effects multiply. Similarly, Noelle, Pape and Jenkins, Schweitzer and Sharpe, all say that interrupting T cell priming *via* costimulation is a good therapeutic bet, since it can be done regardless of knowledge of the precise molecular target being recognized by the responding T cells. That any concomitant infection during the course of this suppression of costimulation may have potentially catastrophic consequences is not a possibility that they even acknowledge.

In fact, if one looks at the 'real' drugs being tested in this book, especially in the poster summaries, it is obvious that the pharmaceutical industry is quite hard-headedly aware that traditional methods

of drug discovery are currently far more profitable with the incorporation of structure-activity relationship analyses and rational design strategies than any leads from molecular physiology. Of course, this is not to say that industry does not keep its options open on the biotech bandwagon—the piece by Narula and colleagues about the possible therapeutic uses of interleukin-10 reads every bit as gung-ho as those by the academic authors, despite similar potential limitations.

A curious feature of the current state of biotechnology emerges. Not only does the promise of biotechnology far outstrip its performance so far, even the rate of increase in the feverishness with which promises are made outstrips the rate of increase in tangible results. By and large, the promises being made are about interventions in antigen-specific, adaptive B and T cell immune responses, while the new drugs actually being tested affect various inflammatory pathways in innate immunity. Clearly, analyses of T and B cells have a long way to go before they translate at high frequency into usable products in everyday medicine. Until then, aspirin and its cohorts rule.

SATYAJIT RATH

*National Institute of Immunology,  
Aruna Asaf Ali Marg,  
New Delhi 110 067, India*

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**Drug Supply and Use: Towards a Rational Policy in India.** Anant Phadke. Sage Publication India Pvt Ltd, M-32, Market, Greater Kailash I, New Delhi 110 048. 1998. Price: Rs 295 (cloth), Rs 165 (paper). 183 pp.

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There has been a 700-fold increase in drug production during the last 50 years. Yet, chronic shortage of drugs continues to plague the public health facilities like Primary Health Centres. As a result, the poor patients, who are the main beneficiaries of these public health facilities, are deprived of the drugs they need. On the contrary, in the private sector, the poor have been spending their meager income on irrational drug formulations, prescribed by private doctors, in the hope of better medical treatment.

The author of this book, Anant Phadke, a full-time social worker and the Coordinator of the Rational Drug Policy cell of the Medico-Friend Circle, Pune, has not only highlighted the production of irrational drug formulations, but also described the maladies which result with the irrational use of drugs in India. Currently, availability of irrational drug formulations and irrational use of essential drugs are both contributing to the wasting of people's money as well as of Government. The role of drug industry as well as doctors in perpetuating the use of irrational drugs has been well documented and substantiated with detailed evidence.

The author rightly complements the drug companies for introducing new drugs, which are useful, through their intensive research. But he criticizes them for continuing to market toxic drugs by suppressing information about the side effects of these drugs. Because of this practice, he cites that a large number of drugs, which are irrational or of doubtful efficacy, are marketed aggressively by the drug companies in collusion with the doctors through commercial gimmicks and, in certain cases, indulgence in corrupt practices.

The genesis for the increased production of irrational combination of drugs and shortfall of essential drugs, with practical examples based on Drug Price Control Order of Government of India, is well presented. In addition, lack of appropriate regulation of ayurvedic drugs sale has been cited as the main reason for this abnormal increase in the introduction of irrational drugs of all kinds in the markets in recent years. The author questions the present policy of allowing commercial production of ayurvedic drugs without testing their safety and efficacy through modern scientific research, although he has recognized the need for propagation of ayurvedic therapies, which have been found to be effective and safe.

Drug companies are known to add unnecessary ingredients and make irrational drugs to gain extra profits. But, the question is, why do doctors prescribe such drugs. The answer lies in that there are 4,00,000 allopathic doctors and twice as many non-allopathic (homeopathic and ayurvedic) doctors in India. The large-scale use of allopathic drugs by these non-allopathic doctors is one of the main factors responsible for large-scale sale of