Table 1. Cure rates for the different formulations.

	After 1 week		After 4 weeks	
	Cured	Not cured	Cured	Not cured
Placebo bioadhesive tablet (n = 7)	0	7	0	7
Bioadhesive tablet with 100 mg metronidazole (n = 7)	6	1	4	3
Flagyl (n = 10)	8	2	7	3

placebo bioadhesive tablet ($0{\cdot}001 < P < 0{\cdot}01$) as compared with the two other treatment groups.

In this study where a single 100-mg metronidazole bioadhesive vaginal tablet was administered, similar cure rates were obtained as for the orally treated group, although only one-seventieth of the drug was administered locally. After four weeks a certain recurrence incidence was observed in both treated groups. Recurrence of infection is an important problem in the treatment of bacterial vaginosis. The recurrence could be due to the presence of microorganisms remaining after the period of treatment, failure of restoration of the normal lactobacilli flora after infection and reinfection via sexual contact.

Although further research is required to define the optimal tablet geometry and drug-loading limits on the residence time, the use of a bioadhesive tablet opens new perspectives in the local treatment of bacterial vaginosis, especially with a dramatic reduction in the amount of drug administered. An optimization study is continuing, to investigate the influence of drug loading, the geometry of the tablet and the polymer/drug ratio on residence time and the cure rate.

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Book Review

Crystallization Technology Handbook
Edited by A.Mersmann
Published 1994, Marcell Dekker, Inc., New York
xii + 691 pages
ISBN 0 8247 9233 5 $195.00

The stated aim of this book is to describe not only the science of crystallization, but also the design procedures of crystallizers. I believe that the book fulfils that aim.

The first chapter deals with fundamentals in a reasonable manner, however, I don't this it was targeted for the novice reader; for example Miller's indices are used but not explained.

The second chapter is entitled 'Interaction Between Balances, Processes and Product Quality'. This is a chemical engineering, and often mathematically based, section dealing in some considerable detail, with everything from mass balance, through size distribution and growth rate, classified product, agglomeration and abrasion, habit, and the influence of impurities, to caking.

The third chapter is devoted to 'Design of Crystallizers and Crystallization Processes'. Not surprisingly, this is pure chemical engineering and from my perspective seems to cover all aspects and available types of crystallizer that may be of industrial interest.

The fourth chapter is on the control of crystallizers and the fifth on reaction crystallization. The sixth is an interesting section on additives for crystal engineering, including changing morphology, aiding dissolution, polymorphism control and modelling.

Chapter seven deals with crystallization from the melt and given a comprehensive coverage of the approaches and technology which are available.

The final chapter 'Thermal Analysis and Economics of Processes' relates to aspects such as energy utilization as well as capital and other operational costs of industrial crystallization processes.

The text is presented in varying styles, some chapters being relatively easy reading (from my perspective), whilst others deal with relatively detailed mathematical concepts. In conclusion this book is suitable for people who have some scientific knowledge of the principles of crystallization which they wish to develop into a practical industrial application.

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Book Review

Antimicrobial Susceptibility Testing. Critical Issues for the 90s
(Advances in Experimental Medicine and Biology/349)
Edited by James A. Poupard, Lori R. Walsh and Bruce Kleger
Published 1994 Plenum Press, New York
xii + 191 pages
ISBN 0 306 44673 1 $69.50

To paraphrase an old joke, when two microbiologists are discussing sensitivity tests, there are three opinions. This diversity of views underpins the need for a book such as Antimicrobial Susceptibility Testing—Critical Issues for the 90s. It is correctly stated in this book that the cost of antibiotic therapy substantially exceeds the cost of the sensitivity test, so good prediction is very cost effective. This book originated from a symposium of the Eastern Pennsylvania Branch of the American Society of Microbiology and the bias is inevitably towards American susceptibility testing criteria which, surprisingly, can be different from European, thus the reader should beware.

The book is divided into chapters written by different authors. The first chapter is historical and, except for the student of such history, unlikely to thrill. The second chapter on testing methods and interpretative problems is much more stimulating. It questions why sensitivity tests are performed and makes the timely reminder that the sensitivity test measures the interaction between bacterium and antibiotic, and does not tell you whether the antibiotic will control the organism at the site of infection. The author discusses the merit of disc diffusion tests and microdilution assays and warns against the current trend towards the latter. R. C. Bartlett has a chapter on when we should use sensitivity tests and emphasizes how specimens should be taken and maintained, how care must be taken to avoid mixed cultures, and how the tests employed should be appropriate for the organism and the antibiotic; much of this should be basic knowledge for the diagnostic microbiologist. He does, however, discuss how much information should be provided; an important point as some specimens are now being sent to private laboratories that do not provide consultant recommendation. There is a particularly provocative piece by Janet Hindler on the actual execution of sensitivity tests and the pitfalls that can be encountered. This chapter is essential reading for all involved in any sensitivity test with antibiotics and she emphasizes the importance of quality control and adequate training. I found the latter part of her chapter on the potential inaccuracies very revealing. There are further chapters that examine new techniques for minimum inhibitory concentration (MIC) and sensitivity testing. These include automated systems such as VITEK and ALADIN; these techniques may be more common on the other side of the Atlantic, but our diagnostic laboratories have yet to adopt them. A section that should have been important was the one that discusses MIC testing by gradient techniques. The most important version of this in the UK at the moment is the E-test. It is actually mentioned on page 9 in the Introduction, but the author promises it will be discussed in more detail later on. This promise was not kept, for although the E-test was mentioned twice later in the book (pages 137 and 156), it was only in passing. This was a serious omission as the E-test is the centre of much current debate.

The book continues with a number of philosophical questions such as "Is One Laboratory In Town Enough?"; to which virtually every UK microbiologist will simply answer "NO". The last section of the book discusses a few of the posters presented at the meeting from which the book was taken. These are quite esoteric, though I personally found the one on β-lactamase combinations by Barry particularly illuminating.

I am lucky enough to have been given this book because I am reviewing it. Sensitivity testing interests me so I would have bought it. If the reader is looking for a book to tell all they want to know about sensitivity tests, including how to do them, then this is not the book for them. It dips into the subject, with some superb discussions on specific points, but it is, by no means, a comprehensive guide.

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Book Review

Analysis of Addictive and Misused Drugs
Edited by John A. Adamovics
Published 1994, Marcel Dekker Inc., New York
800 pages
ISBN 0 8247 9238 6 $195.00

Analysis of Addictive and Misused Drugs is an "examination of contemporary techniques used to evaluate the non-medical use of drugs". It is an informative, in-depth review and discussion of the mechanisms underlying drug separations by enzyme immunoassay, high-performance liquid chromatography using both reversed-phase systems and the less commonly used systems involving bare, unmodified silica with polar methanolic and methanolic/aqueous solvents, thin-layer chromatography and capillary electrophoresis. The use of gas chromatography and gas chromatography/mass spectrometry is given a more cursory examination. Some chapters include a step-by-step approach featuring recipes applicable to drug testing in athletes whereas another illustrates the guidelines recommended for toxicologists working with banned and abused substances in South America. There is a critical appraisal of the Toxi-Lab, commerical-kit, thin-layer chromatography system and an update on the still limited by growing application of robotics and automation in the laboratory. The chapter on the availability of biosensors for near-patient testing is short and demanding; an opportunity may have been missed to illustrate more clearly this growth field.

There is an extensive appendix designed to supplement and complement the preceding ten chapters by offering referenced methodologies for the detection and characterization of over 400 substances listed by the International Olympic Committee as banned drugs and the US Drug Enforcement Administration as controlled substances, whether in bulk form, as pharmaceutical preparations or present in biological fluids. This is certain to be of interest to senior analysts and their less experienced juniors who may be unaware of the best approach to the detection and measurement of compounds they may be encountering for the first time.

All toxicologists will find this a valuable and interesting addition to their library.

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Book Review

The Metabolism of Drugs and Other Xenobiotics: Biochemistry of Redox Reactions
Bernard Testa
Published 1995 Academic Press Limited, London
xviii + 471 pages
ISBN 0 12 685391 6 £75.00

This volume, Biochemistry of Redox Reactions is the first in an ambitious and welcome series of books by Professors Testa and Caldwell, under the title of The Metabolism of Drugs and Other Xenobiotics. Although recent advances in the study of cytochromes P450 and related enzyme systems have been little short of astounding, perhaps an excessively reductionist approach to this work has accumulated a mountain of detailed knowledge and techniques with less emphasis on the integration of these advances in the context of a living system. In Biochemistry of Redox Reactions, Professor Testa has redressed this imbalance in that he has attempted to acquaint the reader with the philosophy of these systems as well as much of their detail. However, rather than supply an exhaustive 'vocabulary' of redox reactions, the reader is encouraged to learn the 'language' of these systems. Knowledge of this language is intended to facilitate the study of new therapeutic entities as well as potential toxins. The book is thus both demanding and extremely rewarding to study.

Many of the pitfalls of distilling the contents of hundreds of papers into one volume have been anticipated and impressively circumvented. The accusation that textbooks are often immediately out of date may be partly refuted by the strenuous efforts to include current material as close to the publication deadline as possible and papers published up to the end of 1993 have been included. The benefits of this approach have enabled the latest comprehensive nomenclature of cytochromes P450 to be outline in Chapter 3. The authors are keenly aware that sections on different topics will age according to the pace of advances in knowledge of those topics. However, for example, the nomenclature controversies of cytochromes appear to have been mostly resolved for now and our understanding of the mechanisms of P450-mediated catalysis is much improved. These subjects have been dealt with so that they are accessible and understandable to readers with a variety of biochemical backgrounds. As the quantum leap of crystallization of smooth endoplasmic reticulum based P450 has apparently not yet been made, this textbook should not age too rapidly in these areas. Another strength of this volume, is that it does not confine itself to oxidation reactions of P450 alone. A range of other enzyme systems is covered to a comprehensive degree, including oxidases, peroxidases and oxidoreductases. There is a valuable chapter (11) concerning the oxidation of a number of inorganic ions, which is especially relevant in view of increasing concern over environmental pollution by these substances. From a practical point of view, the layout of the text and typeface is both pleasing and conducive to extended periods of study. In addition, the liberal use of chemical structures is of great help in the understanding of the text. Diagrams are also plentiful, clear and informative, often taken (with permission) from the original references. The referencing system is easy to use and is well structured.

Recent studies have revealed redox enzyme systems such as cytochromes P450 to be increasingly involved in subjects as diverse as ion-channel regulation of cytokine-mediated nitric oxide synthesis. Although no text can possibly keep up with the breakneck pace of research, this volume can provide a bedrock of understanding of both detailed mechanisms and general context. In view of the author's achievements in this first volume, subsequent books in this series should be eagerly awaited.

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Book Review

Animal Test Alternatives.
Refinement•Reduction•Replacement
Edited by Harry Salem
Published 1994, Marcel Dekker, Inc,. New York
360 pages
ISBN 0 8247 9284 X $135.00

The steady rise of in-vitro toxicology has spawned a number of 'review' books of which this is the latest example. Indeed, many of the authors of particular chapters in this book have been in print in previous publications of this type. Against this background, then, it is pertinent to ask what new ideas are presented in this book, and I consider that at least two can be identified.

The first is the addition of a fourth R—responsibility—to those first set out by Russell and Burch (refinement, reduction, replacement). By this is meant the responsibility of scientists to engage in alternatives research and to ensure that the results so obtained are used sensibly. This aspect is laid out clearly in the Preface and threads its way through the book before resurfacing again in the Epilogue. The second new idea stems directly from the interests of the editor, namely, the use of animal alternatives in research of relevance to the armed forces, with chapters on isopropylamine, antidotes to cyanide poisoning, munitions, antivesicants, and toxic gases.

The book attempts a very broad sweep of material in terms of methodology and types of toxicity. Thus, the book contains chapters, inter alia, on physiological modelling, structure–activity relationships, target-organ toxicity, skin and ocular toxicity, and developmental toxicity, these interspersed with chapters largely historical in nature or concerned with regulatory requirements and validation of alternatives. Much of this will be familiar to those who have read other review books in this subject area.

These various topics are each covered in a group of chapters, although there are no signposts for these topics in the contents list; these would be useful for those new to this subject area. Furthermore, in some instances there is considerable overlap in the material covered in related chapters, a common problem of multi-author works. At times the impression is one of the authors 'going through the motions', an example of this being one chapter of three pages in length, of which the main body comprises less than 1 page of text! There are also some instances of poor editing, e.g. a mismatch between a figure and its caption (page 123) and references not cited in text (chapter 15, references 9–11).

These grumbles aside, there are some useful and interesting chapters. Highlights of these for this reviewer were those by Andersen and Krishnan on physiological modelling, by Hobson on alternatives to skin toxicity evaluation (with the point that in-vitro does not necessarily equate with easier), and by Stephens and Spence on the role of in-vitro tests in safety testing of cosmetics and consumer products (with its discussion of 'managing in-vitro toxicity').

I consider that this book has a lot to offer to those who are new to in-vitro toxicology, but not to those already familiar with this area, although one or two of the thirty eight chapters will inevitably provide new insights for this latter group.

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Book Review

The Blood–Brain Barrier. Cellular and Molecular Biology
Edited by William M. Pardridge
Published 1993 Raven Press Ltd, New York
494 pages
ISBN 0 7817 0015 9 $107.50

This book is a collection of up-to-date and pertinent reviews by internationally recognized contributors to research into the cellular biology of the blood-brain barrier. The book provides a very wide ranging, but carefully focused and integrated series of monographis which will provide the reader with a rapid appraisal of current thinking, together with an indication of potential future areas of interest in research, concerning the functioning of the blood-brain barrier. The book's content necessitates some familiarity with molecular biological techniques and therefore a novice would have a little difficulty in understanding a number of the concepts. However, I am sure that this book will rapidy, and deservedly so, assume the position of a major standard reference text to which active research workers will repeatedly refer. The book also provides a well rounded overview of research in the blood-brain barrier and would, I suggest, be of great value to honours degree undergraduates or postgraduate students and will serve to illustrate to them the emergence, and application, of the new technologies in cellular and molecular biology. I have used this book in recently conducted classes for an honours degree in neuroscience, and, with a little careful selection of suitable reading material, it has proved a major stimulus to discussion in tutorial groups.

There is a logical progression of ideas throughout this book. The book is divided into four parts. The first two parts discuss cell-cell interactions and subcellular organelle function in the induction, formation and structure of the blood-brain barrier derived from both in-vitro and in-vivo analyses, the interaction between endothelial cells, endothelium and astrocytes, or between antigen presenting cells and endothelium and smooth muscle/pericytes. There are, as of necessity, several restatements in a number of chapters of the basic concepts of the distinction between brain endothelium and endothelia elsewhere in the body, transport activity and markers, and the polarity of the endothelium. Since the chapters in this book are written by internationally acknowledged experts there is on occasion a failure to fully explain abbreviations, which makes understanding by a novice difficult. However, the first two sections of the book provide the opportunity to gain an authoritative understanding of the complexity of the structure, development and functioning of the blood-brain barrier.

The latter two sections of the book, signal transduction mechanisms and gene expression, provide a modern overview of the molecular control of blood-brain barrier function, the transport of larger molecules across the barrier and suggest possible mechanisms of drug delivery to the brain. The latter is becoming of increasing importance for clinical practice or therapy after brain injury or with regard to ageing changes. But these sections also serve to illustrate that our knowledge of blood-brain barrier function is expanding rapidly. This book provides a good overview for new or young research workers, but also serves to alert an investigator to the necessity for regular and frequent perusal of the literature from a variety of subject areas. Deficiencies in modern techniques are indicated and these should serve to allow the development of new technologies for furtherance of our understanding of the blood-brain barrier – for example the contribution to blood-brain barrier function/integrity mediated through dietary manipulation, the detection of microvascular injury by free radicals, or the inadequacy of long-term tissue culture to provide a model for the analysis of therapeutic strategies.

This is a book which rewards rereading and consultation. I would suggest that active research workers will find it illuminating to consult and that this book should have a well-deserved place in any institutional library. It is also a very suitable avenue for the student to gain an appreciation of current concepts in blood-brain barrier research. I can heartily recommend The Blood–Brain Barrier. Cellular and Molecular Biology.

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J. Pharm. Pharmacol. 1995, 47: 974

Book Review

Applied Neuromuscular Pharmacology
Editied by B. J. Pollard
Published 1994 Oxford University Press, Oxford
xiv + 436 pages
ISBN 0 19 262148 3 £69.50

All departments of anaesthesia should have this book on their library shelves as it is an invaluable source of reference for aspects of the pharmacology and clinical use of neuromuscular blocking agents. The book is also essential to any researcher embarking on a higher degree in this branch of pharmacology.

There is a considerable amount of overlap of the information given in individual chapters. While this is a criticism if the book is taken as a whole, it is more likely that the reader will use the book to look up specific aspects of neuromuscular pharmacology. In this respect, it is an advantage that each chapter is complete in itself and the reader is not constantly referred to other chapters for essential information. The index is not as helpful as it could have been. For example, there is no obvious reference in the index to the pharmacogenetics of suxamethonium metabolism. However, reading the chapters it is clear that this aspect of pharmacology is described in more than one place.

The topics discussed in the book range from the molecular biology of the nicotinic receptor to drug interactions and the effects of disease states on the activity of drugs at the neuromuscular junction. Both pharmacokinetics and monitoring are covered. Senior anaesthetists with a pharmacological bias will be aware of much of the information supplied in this book as most of the work reported was done some years ago. The reason for this is that there has been little new, concerning this subject, reported in the more recent literature. Molecular biology may have cut its milk teeth on the nicotinic receptor but research interest have moved away from this area of pharmacology to those more trendy areas which are more likely to attract research funding. I have heard it said that anaesthetists do not kill enough people to attract adequate research funding for the pharmacology of anaesthetic drugs. While applauding the former, it is a source of regret that the basic science research into anaesthetic drugs could grind to a half.

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