

Book Reviews

From Blood Substitutes to Semiconductors and beyond

Blood Substitutes. Preparation, Physiology and Medical Applications. Edited by *K. C. Lowe*, VCH Verlagsgesellschaft, Weinheim, 1988. 187 pp., bound, DM 168.—ISBN 3-527-26556-2.

The development of a blood substitute and, more generally, an effective injectable oxygen carrier, has become a pressing but considerable challenge. Extensive progress has been achieved in recent years. It is the objective of the multiauthor book edited by *K. C. Lowe* to provide a review of the state of the art in the field. It deals with both simple plasma substitutes for volume restoration and oxygen-delivering fluids, whether the latter are based on hemoglobin or on fluorocarbons as the gas carrier.

In an easy-to-read first chapter, *E. S. Parry* sets the search for O_2 -carrying blood substitutes in a historical perspective. The chapter is mainly (ca. 85 %) devoted to a detailed up-to-date account of the vicissitudes of the hemoglobin approach since the turn of the century, and of the progress achieved in recent years, but without attempting to minimize the numerous questions and concerns which remain to be answered before human trials can be safely envisaged. The more recent fluorocarbon and synthetic chelate approaches unfortunately receive a much shorter and scantier treatment, with literature coverage up to 1982 only; this leaves out the most recent developments, but the reader will fortunately find these in subsequent chapters.

Chapter 2 by *K. Messmer* is devoted to plasma substitutes for rapid volume restoration after hemorrhage. The author discusses and compares the role, advantages, limitations and adverse effects of isotonic electrolyte solutions, plasma substitutes based on natural colloids prepared from human plasma or placenta, and artificial colloids including dextran, gelatin and hydroxyethyl starch. While plasma substitutes have been used on a routine basis for several decades now, it is shown that there is still room for improvement and that they constitute an active field of research with, for example, the successful development of hapten inhibition of dextran-induced anaphylactic reactions, and exploration of the concept of small volume resuscitation by hypertonic/hyperosmotic solutions.

In Chapter 3 *G. W. Odling-Smee* and *B. G. Wilson* discuss hemoglobin as a blood substitute, and show how successive modifications—pyridoxylation then polymerization—can improve its oxygen-delivering capacity and intravascular persistence, which are both strongly reduced when

hemoglobin is extracted from its natural environment. The authors give a brief summary of contradictory reports on the effectiveness and safety of such preparations, and end by stressing the outstanding problems, namely cardiovascular effects and effectiveness in the presence of red cells, which in the authors' opinion need to be addressed before they would recommend them for use in humans.

There follows a too-short chapter by *T. M. S. Chang* which concentrates on microencapsulation of hemoglobin as a way of preserving its oxygen-unloading characteristics, and (again) on cross-linked hemoglobins. A section on toxicity and safety expresses the author's concern about the immunogenicity of the modified crosslinked hemoglobins.

Polymerized pyridoxylated hemoglobins consist, indeed, of complex mixtures of chemically modified materials, difficult to reproduce, and each one of these more or less randomly occurring modifications can be the source of immunogenic problems. The chemist will remain unsatisfied, as none of the three chapters devoted to the modified hemoglobin approach to blood substitutes broaches the central and difficult question of the chemistry involved in these reactions. This is all the more regrettable as the lack of insight into what is really happening to the hemoglobin molecule, as well as the diversity, poor definition and poor reproducibility of the resulting preparations are probable reasons for many contradictory reports.

Turning to the fluorocarbon approach, *J. G. Riess* and *M. Le Blanc* give an authoritative and thoroughly documented account of the state of the art, including the criteria of selection, preparation procedures and properties of fluorocarbons and surfactants, formulation, preparation, characteristics and control of the emulsions. A stringent analysis of the shortcomings of the Fluosol-DA-type first generation of preparations enables them to delineate what research should be done with the aim of improving on this early emulsion. Emphasis is then laid on the advances that have already been achieved with respect to Fluosol-DA. Among these, the discovery of fluorocarbons with much shorter organ dwell time, and the preparation of five times more concentrated and room temperature stable fluid emulsions, are certainly the most remarkable breakthroughs. This strongly consolidates the potential of the fluorocarbon approach to blood substitutes, including use in case of hemorrhagic shock, where the early emulsions had only limited efficacy. Further improvement is shown to depend in large part on the synthesis and

selection of new biocompatible surfactants, more specifically designed for emulsifying fluorocarbons.

A solid chapter by *N. S. Faithfull* discusses the potential of fluorocarbon emulsions in medicine and research. The author's reminder that it is the carrier's oxygen delivering capacity rather than its oxygen dissolving capacity which is important, is welcome. He then emphasizes that the potential of fluorocarbon emulsions goes considerably beyond that of a substitute for blood. Microcirculatory support of the myocardium and central nervous system, use in radiology or for radiosensitization of hypoxic tumors, for organ preservation or during cardiopulmonary bypass, or percutaneous transluminal coronary angioplasty, treatment of respiratory failure, and stimulation of killer macrophages are among the most promising avenues that are being explored. The reader may regret that some of these applications are not discussed in greater depth.

K. C. Lowe left for himself the difficult task of summarizing the biological assessment of fluorocarbon emulsions, which is treated in a meticulous, detailed manner. Particular consideration is given to the uptake of emulsion components into lymphoid tissues and the reticuloendothelial system, and to the consequences these may have on immune defence in the recipients. Unfortunately the greater part of the available data still concern the early fluorocarbon-poor and Pluronic F-68 containing emulsions, Fluosol-DA and Fluosol-43. It will nevertheless be of great use by providing the reader with extensive information and numerous protocols which should prove helpful for evaluating the newer emulsions. The need for improved biocompatibility with respect to Fluosol-DA is indeed highlighted.

Chapter 8, by *G. M. Vercellotti* and *D. E. Hamerschmidt*, reviews the clinical studies that have so far involved fluorocarbon emulsions. Again these studies concern *solely Fluosol-DA*; the data analyzed highlight the side effects and limitations of this particular preparation. These are by no means representative and cannot be extrapolated to other fluorocarbon emulsions. The authors then discuss the possible mechanisms for the adverse reactions noted with Fluosol-DA, and show that they can be assigned primarily to complement activation by Pluronic F-68, the main surfactant used in this preparation. As a result they call for the development of emulsions with a lower ability to activate plasma complement.

On the whole, *Lowe's* book, in spite of some omissions (the chemistry of modified hemoglobin, for example) and repetitions (the compositions of Fluosol-DA is given no less than three times), inevitable in such a multi-author enterprise, reaches its objective. It is timely and useful—useful as it summarizes a considerable amount of recent information in a relatively small, compact volume—timely in view of the increasing demand for substitutes for blood, triggered by increased difficulties of transfusion, and also because the decisive breakthroughs that have recently been achieved, especially in the fluorocarbon approach, should lead to new preparations now becoming available for research.

There are few typographical errors in the text; the same is unfortunately not true of the chemical formulas and equations, which sadly appears to be a common fault in medicaly-oriented books.

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Electrons in Solids: An Introductory Survey. By *R. H. Bube*. Academic Press Inc., San Diego 1988. xiv, 315 pp., bound, \$ 39.50.—ISBN 0-12-138552-3

The book is intended as an introductory survey for students with a background in materials science or other engineering disciplines. This is explicitly stated by the author in the preface to the first edition. The second edition has been updated in some chapters by including recent developments, and an additional chapter on "sample problems" has been included in the appendix.

The presentation is clear and supported by very good illustrations. Since the reader is not expected to have a knowledge of electrodynamics, quantum mechanics or basic solid state physics, the author has to cover a lot of ground before he can present the facts on various properties of solid state materials. In the first chapters he therefore has to give a short description of the above mentioned basic physics. After having discussed the general properties of waves in Chapters 1 and 2, he continues by describing lattice waves and light waves in Chapters 3 and 4. The usual examples of quantum mechanics are described in Chapter 5, and in the next two chapters the simplest models of solids are presented, namely the free electron model and the tight binding description. In the second half of the book we find the main topic, with chapters on optical, electrical and magnetic properties, and an additional chapter on junctions between different materials.

The treatment contains a good mixture of phenomenological descriptions, formal presentations of basic formulas, and comparison with experimental results. Nevertheless, I have the feeling that a student reading Chapter 4, for example, where on 14 pages the Maxwell equations are presented, may have difficulties in really understanding these basic equations. A good list of further references including textbooks on this subject should at least have been provided. The same problem for the reader might also arise with the topics in the other six introductory chapters.

The second half of the book discusses a quite extensive list of properties of the solid state, and again the clarity of the presentation is to be admired. The chapter on optical properties presents an overview of the various absorption processes. Unfortunately, there is no discussion on new developments, e.g. on various aspects of laser physics. The next chapter on electrical properties discusses the basic relaxation