

*Clinical and Biochemical Aspects of Lactic Acidosis*

by Robert D. Cohen and H. Frank Woods

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xii + 276 pages. £10.50

The current interest in lactic acidosis as an important component of a wide range of clinical disorders is indicated by the appearance of several recent reviews including an article on this topic in the first volume of the new series 'Essays in Medical Biochemistry'. In their introduction to this volume, the authors state that 'the time appears ripe to attempt to marry together the relevant (sic) clinical, biochemical and physiological information'. 'Clinical and Biochemical Aspects of Lactic Acidosis' is presumably therefore another child of such a tripartite union.

In reviewing a book of this type, one should perhaps ask two major questions. Firstly, do the contents adequately cover present knowledge of the condition under consideration from all three aspects? And, secondly, have the authors succeeded in arranging a marriage of this knowledge such that their offspring is a source of enlightenment to readers seeking a deeper understanding of the topic? The objective of assembling most of the information relevant to lactic acidosis at the biochemical and physiological levels certainly has been achieved. I wonder, in fact, whether the desire for completeness has in some instances led to the inclusion of information which is of marginal relevance to the main theme of the book. The section (admittedly brief) on the metabolism of D-lactic acid is one example. Although inclusion of such peripheral material is not inherently a serious defect, it does cause further fragmentation of a text which is already extensively sub-divided and difficult to follow. Furthermore, some of the biochemical information appears a little out-of-date. The discussion of the mechanisms responsible for regulation of glycolytic and gluconeogenic flux appears to represent the euphoric vintage of 1968 rather than the more critical atmosphere of 1976, while certain of the factual information does not reflect recent developments. For example, it is now generally accepted that

in mammals and birds pyruvate carboxylase is located in the mitochondrial matrix and a satisfactory explanation has been provided for data which were inconsistent with this view. The tissue location of this enzyme is also not as restricted as would be suggested by table 2.9, since significant levels of activity are found in both heart and brain while adipose tissue and the adrenal gland contain levels comparable with those found in the kidney.

It would be presumptuous for a biochemist to pass judgement on the adequacy and coverage of the clinical aspects of lactic acidosis and its treatment. However, as a non-specialist reading these sections, I was also impressed with the extent of detail rather than with the clarity of organisation and presentation. Considerable stress is laid on the question of classification of lactic acidoses. The authors proposed a scheme of classification which differs from that due to Huckabee and in which the crucial distinction rests on whether or not the lactic acidosis can be attributed to a patent inadequacy in tissue oxygen supply. Although superficially attractive, I wonder whether in the long term such a distinction will prove useful since it has no obvious conceptual basis. If classification is of value, might not it have been approached more profitably on the basis of whether the acidosis is primarily due to overproduction or under-utilisation of lactate?

The marriage achieved between the biochemical, physiological and clinical information appears generally less satisfactory possibly because certain simple basic concepts are not clearly established. For example, many biochemists (and possibly clinicians too) focus on the carbon, oxygen (and nitrogen) balance of metabolic pathways and pay little attention to the hydrogen ion balance. Yet it is exactly this feature which is crucial to an understanding of lactic acidosis (or any metabolic pH disorder for that matter), and which comes across very clearly in the review by Krebs et al. in *Essays in Medical Biochemistry*. It is

missing here (possibly because of partial common authorship with this latter review). This apart, the most satisfactory integrative section is the discussion of the modes of failure of lactate removal mechanisms which constitutes the bulk of chapter 6. It is notable that this is also one of the longest coherent sections in the book.

In sum, therefore, this volume is, so far as I am competent to judge, an excellent compendium of

information, which will be of much use to research workers and clinicians with interests in lactate metabolism and lactic acidosis, and to those who teach in this field. It is certainly not easy reading, and one feels that the deeper understanding which might have been achieved has been a casualty of the thoroughness of the treatment.

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*Use of Isolated Liver Cells and Kidney Tubules in Metabolic Studies*

Edited by J. M. Tager, H. D. Söling, J. R. Williamson

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One of the most important recent developments in studies in metabolism has been the description and increasing use of isolated cell preparations. The current interest in these preparations was recognised in the organisation of a FEBS advanced course on this topic in July 1975 and it is the proceedings of this course together with those of a companion symposium on 'Mitochondrial-Cytosolic Interactions in Cell Metabolism' which make up this volume. In some respects, the title of the book is therefore somewhat misleading, since although studies using isolated liver cell preparations receive considerable emphasis especially in the proceedings of the advanced course, the presentation and discussions are by no means restricted to data obtained using these preparations. Furthermore, possibly in reflection to the current state of the art with these two isolated cell preparations, considerably more attention is paid to the liver cell. Thus, those with a particular interest in isolated kidney tubules may find directly relevant information is somewhat sparse. In the initial section which contains the proceedings of the symposium on mitochondrial-cytosolic interrelationships, most of the major presentations focus on various aspects of metabolite distributions between the mitochondrial and cytosolic compartments including recent direct experimental approaches to the measurement of concentrations in

these sub-cellular fractions. As is clearly stated by Sir Hans Krebs in his introduction, the articles in this section will be best appreciated by those who already possess a good basic understanding of the field. They provide an excellent summary of current developments and problems in this important area. It is however rather unfortunate that no summaries of discussions appear in this section. It is hard to imagine that a symposium of this type did not include discussion between participants, especially in view of the controversial material presented. This apparent omission results in some anomalies. For example, consideration of the article on the source of ammonia for urea synthesis in liver and the role of glutamate dehydrogenase (Chappell) in the Symposium is deferred to a panel discussion following the section on Regulation of Ureogenesis in the proceedings of the Advanced Course. Although it was clearly desirable to have a unified treatment of the present controversy in this area, no acceptable rationale appears to underly the placing of Chappell's article in this volume in relationship to the relevant discussion.

In contrast, the extensive reports of both the specific and general discussions are one of the best features of the sections derived from the proceedings of the Advanced Course. I was particularly impressed with the quality of the general discussions which took up