Advances in Hepatic Encephalopathy and Urea Cycle Diseases

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Advances in Hepatic Encephalopathy and Urea Cycle Diseases

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Drug Dosage
The authors and the publisher have exerted every effort to ensure that drug selection and dosage set forth in this text are in accord with current recommendations and practice at the time of publication. However, in view of ongoing research, changes in government regulations, and the constant flow of information relating to drug therapy and drug reactions, the reader is urged to check the package insert for each drug for any change in indications and dosage and for added warnings and precautions. This is particularly important when the recommended agent is a new and/or infrequently employed drug.
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Preface
This volume contains the papers presented at the 5th International Symposium on Ammonia, held in Semmering, Austria, May 16-19, 1984 and covers a wide spectrum of research activities conducted to uncover the mystery of hepatic encephalopathy. The contributions include various topics such as metabolism, endocrinology, neuro chemistry, electrophysiology, nutrition etc., reflecting the enormous increase in knowledge of many aspects of liver failure.

The possible metabolic derangements in liver failure are not a simple consequence of the breakdown of several functions of the liver but of a series of interactions of almost any organ in the body. Against this background it was not surprising that many different hypotheses of the pathogenesis of hepatic encephalopathy have been promoted and that still the right solution is lacking. This development in research was evident when Dr. I. Szam (Budapest, Hungary) the president of the 1st International Symposium on Ammonia, reviewed the past symposia and their highlights.

The position of ammonia as "frontrunner" and candidate toxin for the mediation of hepatic encephalopathy was strengthened in this symposium. Important interactions between ammonia and the metabolism of branched chain amino acids (BCAA), the permeability of the blood brain barrier and the altered neurotransmission in hepatic encephalopathy have been presented and hence, ammonia could serve as an important link to other hypotheses. The liver plays an even more complex role in ammonia metabolism then recognized before. The landmark work to this topic by Dr. D. Häussinger (Freiburg, FRG) on "New Concepts in Hepatic Ammonia Metabolism and pH Regulation" was awarded with the Friedrich Wewalka Award 1984.

Therapeutic strategies to lower blood ammonia concentration in urea cycle diseases have been considerably improved and may also provide a new approach to the treatment of hepatic encephalopathy. The "false neurotransmitter" hypothesis of the pathogenesis of hepatic encephalopathy by Fischer and Baldessarini lead to trials to treat hepatic encephalopathy with BCAA alone or with BCAA enriched amino acid solutions. After a period of great enthusiasm about the possible therapeutic values on intravenous BCAA, first controlled studies have tempered our hopes.

Therefore, these proceedings start with the panel about the "Future Clinical Trials in Treatment of Acute Hepatic Encephalopathy" which was excellently chaired and edited by Dr. N. Tygstrup from Copenhagen. Undoubtedly the
highly qualified panelists and the competent discussants in the auditorium made this panel to one of the most exciting events of the symposium. The new concepts of receptor mediated changes as causal pathogenic factor of HE included not only the "classical" neurotransmitters serotonin, dopamine and noradrenaline but also an altered amino acidergic neurotransmission was presented, stressing the role of the major inhibitory neurotransmitter of the mammalian brain, gamma-aminobutyric-acid (GABA), in the pathogenesis of hepatic encephalopathy. In addition the possible role of alterations of the blood brain barrier in liver failure was discussed in detail by well recognized experts in this field. However, it became clear that the different animal models used to study the effects of liver failure and the different methods used to detect and to quantitate possible changes yielded different and even contradictory results. Future studies of brain function in hepatic encephalopathy may clarify many issues and new facilities may result in a better understanding of events mediating hepatic encephalopathy. We like to express our gratitude to all participants of the symposium for contributing their efforts and for their cooperation. Our special thanks are due to Mrs. Reingard Kleinberger for her secretarial work and to Karger, Munich, especially H. Rupprecht and W. Kunz for providing the rapid publication of this volume. Furthermore we are extremly thankful to the numerous sponsors of this conference, without which we not have had the possibility to organize and publish this conference for the scientific community.

Vienna, October 1984

Gunter Kleinberger
Peter Ferenczi
Peter Riederer
Heribert Thaler