Problems in Intrahepatic Cholestasis

Second International Symposium on Intrahepatic Cholestasis
Florence, October 13-14,1978

Problems in
Intrahepatic Cholestasis

Editors
Paolo Gentilini, Florence; Hans Popper, New York, N.Y.,
Sheila Sherlock, London, and Ugo Teodori, Florence

66 figures and 29 tables, 1979

S. Karger Basel München Paris London New York Sydney

The Second International Symposium on Intrahepatic Cholestasis was organized
by the Postgraduate School of Gastroenterology, University of Florence (Director:
Prof. Paolo Gentilini), and the International Menarini Foundation (President:
Dr. Sergio Gorini). Secretariat: Prof. Calogero Surrenti, Prof. Giampiero Buzzelli,
Dr. Carlo Smorlesi and Dr. Adolfo Arcangeli.

National Library of Medicine Cataloging in Publication
International Symposium on Intrahepatic Cholestasis, 2d, Florence, 1978
Problems in intrahepatic cholestasis
Organized by the Postgraduate School of Gastroenterology, University of Florence
and the International Menarini Foundation.
Proceedings of the 1st congress (unnumbered and lacking congress name) entered
under title: Intrahepatic cholestasis.
1. Cholestasis - congresses I. Gentilini, Paolo, ed. II. Université degli studi di
Firenze. Postgraduate School of Gastroenterology III. International Menarini
Foundation IV. Title: Intrahepatic cholestasis V. Title
W3 IN919FH 2d 1978p/WI 703 157 1978p
ISBN 3-8055-3009-9

All rights reserved.
No part of this publication may be translated into other languages, reproduced or
utilized in any form or by any means, electronic or mechanical, including photocopying,
recording, microcopying, or by any information storage and retrieval
system, without permission in writing from the publisher.
Contents

Foreword VIII

Introductory Remarks

Gentilini, P. (Florence): Problems in Drug-Induced Cholestasis 8

Pathogenesis of Intrahepatic Cholestasis
Chairmen: S. Sherlock, London, and M. Coppo, Modena

Desmet, V. J. (Leuven): Morphological Features of Intrahepatic Cholestasis 11
Phillips, M. J. (Toronto, Ont.): Electron Microscopic Findings in Intrahepatic Cholestasis 19
Simon, F.R.; Sutherland, E., and Davis, R.A. (Denver, Colo.): Studies of the Liver Surface Membrane in the Pathogenesis of Intrahepatic Cholestasis. Possible Role of Alterations in (Na-K)ATPase and Lipid Structure in Estrogen-Induced Bile Secretory Failure 30
Zimmon, D.S. (New York, N.Y.): Mechanical Factors in Intrahepatic Cholestasis: Reversible and Irreversible 42
Tygstrup, N.; Petersen, P., and Bremmelgaard, A. (Copenhagen): Ultrastructural Findings and Bile Acid Patterns in Idiopathic Intermittent Intrahepatic Cholestasis 47
Martini, G.A. (Marburg): Cholestasis in Alcohol-Induced Liver Disease 53

Modification of Bile Flow and Related Alterations
Chairmen: N. Tygstrup, Copenhagen, and N. Dioguardi, Milan

Schmid, R. (San Francisco, Calif.): Metabolism and Excretion of Bile Pigments 60
Schemen, T. (Göteborg): Modification of Bile Acid Dependent and Independent Fractions of Bile Flow during Cholestasis 64
Stiehl, A.; Czygan, P., and Götz, R. (Heidelberg): Bile Acid Metabolism in Cholestasis 70
Matern, S. and Gerok, W. (Freiburg i.Br.): Bile Acids in Intrahepatic Cholestasis 75
Bode, J. C. ; Zelder, O., and Bode, C. (Marburg/Lahn) : Qualitative and Quantitative Alterations of Hepatic Bile Flow during Recovery from Extrahepatic Cholestasis 83
Barbara, L.; Roda, ; Roda, ; Aldini, R.; Mazzella, G.; Santa, C; Festi, D.; Bazzoli, F., and Morselli, A.M. (Bologna): Circadian Rhythm of Bile Acids in Intrahepatic Cholestasis 88
Fleischmann, R. and Remmer, H. (Tübingen): The Action of Estrogens on the Activity of Drug-Metabolizing Enzymes in Human Liver and Its Possible Relation to Cholestasis and Liver Tumors 93
Tiribelli, C; Lunazzi, G.C.; Luciani, M.; Gazzin, B., andsottocasa, G.L. (Trieste): Carriers and Specific Hepatocellular Receptors for Endogenous and Exogenous Anions 111

Clinical and Biological Conditions Related to Intrahepatic Cholestasis
Chairmen: F.Schaffner, New York, N.Y., and F. De Rids, Naples

Jain, S. (Birmingham): Copper Metabolism and Primary Biliary Cirrhosis 121
Gentilini, P.; Laffi, G.; Buzzelli, G.; Cappelli, G.; Stefani, P.; Smorlesi, C; La Villa, G., and Mazzanti, R. (Firenze): Functional Renal Alterations in Intrahepatic Cholestasis 125
Rodés, J.; Parés, ; Rimola, , and Bruguera, M. (Barcelona): Renal Tubular Function in Chronic Cholestasis 132
Surrenti, C; Casini, , and Ramarli, D. (Firenze): Serum Inhibitory Activity on Cell-Mediated Immunity in Patients with Cholestasis 137
Stefanini, G.F.; Facchini, ; Miglio, F.; Mariant, E.; Bernardi, M.; Gasbarrini, G., andLabó, G. (Bologna): In vitro Lymphocytotoxicity in Intrahepatic Cholestasis 145
Sherlock, S. (London): The Immunology of Cholestasis 157

Diagnosis and Treatment of Intrahepatic Cholestasis
Chairmen: H.Popper, New York, N.Y., and P.Gentilini, Florence

Schaffner, F. (New York, N. Y.) : Cholestasis in Pregnancy, after Oral Contraceptives, and as an Idiopathic Condition 166

Contents VII

Ventura, E.; Rocchi, ; Balli, F.; Gibertini, P.; Santunione, V., and Zeneroli, M.L.
(Modena): Fecal and Urinary Coproporphyrin Isomers in the Diagnosis of Biliary Atresia 172
Husen, . van; Safrany, L., and Kautz, G. (Münster i.W.): Differential Diagnosis of Intrahepatic Cholestasis by Endoscopic Retrograde Cholangiography 184
Tittobello, .; Testoni, P.A.; Evangelista, ., and Ballarin, E. (Milano): Diagnostic Value of Endoscopic Retrograde Cholangiography and Pancreatography in Comparison with Percutaneous Transhepatic Cholangiography 191
Alagille, D. (Bicêtre): Diagnosis and Treatment of Neonatal Cholestasis 204

Free Communications

Doss, M.; Look, D., and Henning, H. (Marburg): Coproporphyrin Isomer Composition in Urine in Liver Disease with Intrahepatic Cholestasis 220
Schwenk, M.; López del Pino, V.; Bolt, H; Schwarz, L.R., and Remmer, H. (Tübingen): Transport and Disposition of Cholestatic Agents in Isolated Liver Cells 221
Hoensch, H. and Heinrich, R. (Tübingen): Longstanding Intrahepatic Cholestasis with Liver Cell Adenoma 222
Findor, J.; Bruch, I.E.; Domecq, R.B.; Fay, O.; Tanno, H; Jorge, ., and Ron-coroni, M. (Buenos Aires): HBsAg and HBeAg in Primary Biliary Cirrhosis 225
Tanikawa, K. and Abe, H. (Kurume): Effects of Phénobarbital and Corticosteroid on Intrahepatic Cholestasis 226


Author Index 240
Subject Index 242

Foreword
International medical symposia serve various purposes. These include the review of information from different countries. They may thus consist of presentations of facts well known to the experienced physician and resemble postgraduate courses, or they may present sophisticated specific information known only to specialists and result in a mutual exchange of information and stimulation for further research. Another form, however, is the symposium where the meeting of scientists working on the same questions from different viewpoints may result, in workshop fashion, in development of new concepts and better understanding of a well-defined problem. The Symposium on Intrahepatic Cholestasis recorded here was conceived as belonging into the last type. This explains the repeated assembly of in part the same, and in part different investigators, at variable intervals, to attempt to resolve one of the difficult clinical problems in liver disease, which has not only conceptional and academic but, even more so, diagnostic and therapeutic implications. Therefore, this book contains by necessity a progress report of the state of the art rather than a presentation of definitive information. Clinical medicine has to take its cue quite often from data not fully established, and may thus be based on implications rather than on hard facts. It is hoped that clinicians, as well as basic scientists, may learn from reading these papers. By the same token, the editors are aware of then-obligation to clearly separate hypotheses and implications from established facts. Since shortage of space prevents the recording of the animated discussions of the symposium, the Concluding Remarks attempt to bring some of the information presented in the discussions. At this point, gratitude should be expressed to those who made this Symposium possible: for sponsorship as well as for the financial support, to the International Menarini Foundation, and to the organizers, who assembled an array of distinguished speakers from all over the world. Thanks are also due to the speakers, who travelled, often from far away, to offer their data, and prepared manuscripts on a tight schedule. The participants, who not only listened to lengthy sessions, but provided thoughtful questions and comments, also deserve recognition, as does the publisher, who made speedy publication possible, which is essential in a rapidly moving field. The reader will decide whether the effort was worthwhile.

The Editors