# INTRAVENOUS NUTRITION in the HIGH RISK INFANT

Edited by

Robert W. Winters, M. D.

& Eileen G. Hasselmeyer. Ph. D.

# INTRAVENOUS NUTRITION IN THE HIGH RISK INFANT

#### Editors

ROBERT W. WINTERS, M.D.

Professor of Pediatrics Columbia University College of Physicians and Surgeons New York, New York

#### EILEEN G. HASSELMEYER, Ph.D., R.N.

Director, Perinatal Biology and Infant Mortality Branch National Institute of Child Health and Human Development Bethesda, Maryland

A WILEY BIOMEDICAL-HEALTH PUBLICATION

JOHN WILEY & SONS, New York • London • Sydney • Toronto Copyright © 1975, by John Wiley & Sons, Inc.

All rights reserved. Published simultaneously in Canada.

No part of this book may be reproduced by any means, nor transmitted, nor translated into a machine language without the written permission of the publisher.

## Library of Congress Cataloging in Publication Data Main entry under title:

Intravenous nutrition in the high risk infant.

(Clinical pediatrics, maternal, and child health)

"A Wiley biomedical-health publication."
Includes bibliographical references and index.

1. Infants-Diseases-Congresses. 2. Parenteral

- therapy-Congresses. 3. Pediatric pharmacology-Congresses.
- I. Winters, Robert Wayne, 1926-
- II. Hasselmeyer, Eileen G., ed. III. United States.National Institute of Child Health and Human Development.

Perinatal Biology and Infant Mortality Branch.

[DNLM: 1. Infant, Newborn, Diseases-Congresses.

2. Parenteral feeding—In infancy and childhood—Congresses. WS420 I63 1971-72]

RJ53.F5I56 615'.5 74-26712 ISBN 0-471-95500-0

Printed in the United States of America

10 9 8 7 6 5 4 3 2 1

#### **Participants**

October 26-29, 1971 Conference Elkridge, Maryland

Peter A. J. Adam, M.D.
Assistant Professor of Pediatrics
Case Western Reserve University School of Medicine
Director, Pediatric Metabolism
Cleveland Metropolitan General Hospital
Cleveland, Ohio

Jo Anne Brasel, M.D. Associate Professor of Pediatrics Division of Growth and Development Cornell University Medical College New York, New York

Graham W. Chance, M.B., M.R.C.P.(London), D.C.H. Associate Professor of Pediatrics Faculty of Medicine University of Toronto Associate Director, Perinatal Division, The Hospital for Sick Children Toronto, Canada

Halvo: N. Christensen, Ph.D. Processor of Biological Chemistry University of Michigan Ann Arbor, Michigan Arnold G. Coran, M.D.
Chief of Pediatric Surgery
Los Angeles County Hospital
Professor of Surgery
University of Southern California Medical School
Los Angeles, California

John B. Das, M.B., Ph.D., F.R.C.S. Lecturer on Surgery Harvard Medical School Research Associate in Surgery Children's Hospital Medical Center Boston, Massachusetts

John M. Driscoll, Jr., M.D.
Assistant Professor of Pediatrics
Columbia University College of Physicians and Surgeons
Assistant Attending Pediatrician
Babies Hospital
Columbia-Presbyterian Medical Center
New York, New York

Stanley J. Dudrick, M.D.
Associate Professor of Surgery
University of Pennsylvania School of Medicine
Attending Surgeon
University of Pennsylvania Hospital
Philadelphia, Pennsylvania

L. J. Filer, Jr., M.D., Ph.D. Professor of Pediatrics University of Iowa College of Medicine Iowa City, Iowa

Robert M. Filler, M.D. Associate Professor of Surgery at the Children's Hospital Medical Center Harvard Medical School Chief of Clinical Surgery Children's Hospital Medical Center Boston, Massachusetts

Harry L. Greene, Maj. MC, M.D.
Metabolic Division of USA Medical Research and Nutrition Laboratory
Fitzsimons General Hospital
Assistant Clinical Professor of Pediatrics
University of Colorado Medical Center
Denver, Colorado

Alfred E. Harper, Ph.D.
Professor of Biochemistry and Nutritional Science
University of Wisconsin
Madison, Wisconsin

Eileen G. Hasselmeyer, R.N., Ph.D.
Director, Perinatal Biology & Infant Mortality Program
National Institute of Child Health and Human Development
Bethesda, Maryland

William C. Heird, M.D.
Assistant Professor of Pediatrics
Columbia University College of Physicians and Surgeons
Assistant Attending Pediatrician Babies Hospital
Columbia-Presbyterian Medical Center
New York, New York

Malcolm A. Holliday, M.D. Professor of Pediatrics University of California School of Medicine San Francisco, California

James P. Keating, M.D.
Assistant Professor of Pediatrics
Washington University School of Medicine
Pediatric Gastroenterologist
St. Louis Children's Hospital
St. Louis, Missouri

Poul Kilderberg, M.D.
Professor of Pediatrics
University of Odense School of Medicine
Odense, Denmark

John C. Sinclair, M.D.
Professor of Pediatrics
McMaster University School of Medicine
Hamilton, Ontario, Canada

Selma E. Snyderman, M.D.
Professor of Pediatrics
New York University School of Medicine
Visiting Physician
Bellevue Hospital
Attending Pediatrician
University Hospital
New York, New York

Mildred T. Stahlman, M.D.
Professor of Pediatrics
Vanderbilt University School of Medicine
Nashville, Tennessee

Lewis D. Stegink, Ph.D.
Associate Professor of Pediatrics and Biochemistry
University of Iowa College of Medicine
Iowa City, Iowa

Paul R. Swyer, M.B., M.R.C.P.
Associate Professor of Pediatrics Faculty of Medicine
University of Toronto
Director, Perinatal Division
The Hospital for Sick Children
Toronto, Canada

Lars H. Victorin, M.D.
Assistant Professor of Pediatrics
University of Göteborg School of Medicine
Director of Neonatal Service
East Hospital, Göteborg, Sweden

Robert W. Winters, M.D.
Professor of Pediatrics
Columbia University College of Physicians and Surgeons
Attending Pediatrician
Babies Hospital
Columbia-Presbyterian Medical Center
New York, New York

#### **Participants**

Washington D. C. Conference May 24, 1972

Stanley J. Dudrick, M.D.
Associate Professor of Surgery
University of Pennsylvania School of Medicine
Attending Surgeon
University of Pennsylvania Hospital
Chief of Surgery,
Philadelphia,
Veterans Administration Hospital
Philadelphia, Pennsylvania

Harry L. Greene, Maj. MC, M.D.
Metabolic Division of USA Medical
Research and Nutrition Laboratory
Fitzsimons General Hospital
Assistant Clinical Professor of Pediatrics
University of Colorado Medical Center
Denver, Colorado

Alfred E. Harper, Ph.D.
Professor of Biochemistry and Nutritional Sciences
University of Wisconsin
Madison, Wisconsin

Eileen G. Hasselmeyer, R.N., Ph.D.
Director, Perinatal Biology and Infant Mortality Program
National Institute of Child Health and Human Development
Bethesda, Maryland

William C. Heird, M.D.
Assistant Professor of Pediatrics
Columbia University College of Physicians and Surgeons
Assistant Attending Pediatrician Babies Hospital
Columbia-Presbyterian Medical Center
New York, New York

James P. Keating, M.D.
Assistant Professor of Pediatrics
Washington University School of Medicine
Pediatric Gastroenterologist
St. Louis Children's Hospital
St. Louis, Missouri

George R. Kerr, M.D.
Associate Professor of Nutrition
School of Public Health
Harvard Medical School
Boston, Massachusetts

Hamish N. Munro, M.D., D.Sc. Professor of Nutritional Science Massachusetts Institute of Technology Cambridge, Massachusetts

John F. Nicholson, M.D.
Associate Professor of Pediatrics
Columbia University College of Physicians and Surgeons
Associate Attending Pediatrician Babies Hospital
Columbia-Presbyterian Medical Center
New York, New York

Merrill S. Read, Ph.D. Director, Growth and Development Program National Institute of Child Health and Human Development Bethesda, Maryland

Charles R. Scriver, M.D.
Professor of Pediatrics
Associate Professor of Biology
McGill University School of Medicine
Attending Physician
Montreal Children's Hospital
Montreal, Canada

Sydney Segal, M.D.
Professor of Peadiatrics
Assistant Professor of Obstetrics and Gynaecology
University of British Columbia School of Medicine
Director of the Division of Neonatology
Vancouver General Hospital
Vancouver, Canada

Selma E. Snyderman, M.D.
Professor of Pediatrics
New York University School of Medicine
Visting Physician
Bellevue Hospital
Attending Physician
New York University Hospital
New York, New York

Mildred T. Stahlman, M.D.
Professor of Pediatrics
Vanderbilt University School of Medicine
Nashville, Tennessee

Lewis D. Stegink, Ph.D.
Associate Professor of Pediatrics and Biochemistry
University of Iowa College of Medicine
Iowa, City, Iowa

Robert W. Winters, M.D.
Professor of Pediatrics,
Columbia University College of Physicians and Surgeons
Attending Pediatrician
Babies Hospital
Columbia-Presbyterian Medical Center
New York, New York

#### **Foreword**

This book resulted from two interdisciplinary conferences concerned with total parenteral nutrition and sponsored by the Perinatal Biology and Infant Mortality Branch of the National Institute of Child Health and Human Development. These conferences are part of a series of meetings that pertain to research issues concerned with various facets of maternal and infant health.

Its subject, "Intravenous Nutrition in the High Risk Infant," is an extremely timely topic. Despite its relatively short history, total parenteral nutrition appears to have achieved an important place in contemporary therapeutics, particularly in infants. Yet a great deal remains to be learned about the potential benefits of this technique as well as its hazards. Answers to the many questions posed by its use will come only from an interdisciplinary approach and, accordingly, such a group was assembled for these conferences.

It is my hope that the timeliness of these conferences as well as the expertise of the participants, will expedite the exchange of new knowledge and stimulate new research in this important field.

GERALD D. LAVECK. M.D. Director, National Institute of Child Health and Human Development

Bethesda, Maryland August 1974

xiii

#### **Preface**

Total parenteral nutrition, or so-called hyperalimentation, represents an important recent development in the field of pediatrics in general and in neonatal medicine in particular. There is little doubt that this technique has already saved the lives of many infants; but there is also little doubt that its use has raised a series of new and important questions.

One group of such questions concerns the metabolic consequences of bypassing the liver and gastrointestinal tract. Other questions involve the types of hazards that attend the long-term presence of a catheter in a central vein, the means by which such hazards can be minimized, the definition of indications, nonindications, and contraindications for the use of the technique in different patient groups, and, finally, the possible beneficial or adverse long-term effects of early total intravenous nutrition on the mental and neurological status of low birth weight infants.

In order to frame these questions in a more definite form, two conferences were held, the first at Belmont, the Smithsonian Institute Conference Center, Elkridge, Maryland, on October 26 to 29, 1971 and a second in Washington, D.C., on May 24, 1972.

The first conference, the proceedings of which comprise Parts I through V of this volume, was attended by 25 biomedical scientists drawn from diverse fields. These experts presented data and provided much needed interdisciplinary discussion of the general questions concerning intravenous nutrition alluded to above. It is the editors' hope that the papers and discussions of this conference will stimulate the biomedical community to further research in this complex area.

A second purpose of this conference was to develop some practical guidelines, based on current knowledge, for implementation of this technique in infants. A preliminary draft of such guidelines was prepared by Robert W. Winters, then circulated to approximately 40 neonatologists for further refinements and

xvi Preface

suggestions. A revised draft, presented to the conference, was discussed extensively and further revisions were made. The final draft is included in these proceedings. We are grateful to all who helped in the various stages of the preparation of these guidelines, and hope they will be useful to the pediatric community in representing a distillate of expert opinion as to the current status of practice of intravenous alimentation of infants.

One of the most important contributions of the first conference was the realization that one of the primary challenges posed by the technique of intravenous nutrition concerns the specific pattern and amount of amino acids to be delivered to an infant by the parenteral route. Because of the press of time, this important subject was not fully discussed at that conference. Accordingly, a second conference, entitled "Amino Acid Requirements for Total Intravenous Nutrition in Infants," was held on May 24, 1972 in Washington, D.C. Scientists with special knowledge in the area were invited to submit recommendations; which were circulated prior to the meeting. The deliberations of this group of experts along with comments from other observers concerning these recommendations are presented in Part VI. From these discussions a consensus of expert opinion appears' to have been achieved concerning the composition of the "ideal" amino acid solution for parenteral nutrition in infants. It is our hope and belief that this second conference will be of interest to the scientific community involved with this problem and to the pharmaceutical industry with whom they must necessarily work closely to bring about the most effective nitrogen sources for total parenteral feeding of the pediatric patient.

We wish to acknowledge the services of Mrs. Anne M. Schmid for technical editing, Ms. Agnete Thomsen for artwork, and Mr. Herbert Mason for photography. Special acknowledgement is made to Mrs. Maureen L. Mayser who served as editorial assistant in the preparation of the entire manuscript.

ROBERT W. WINTERS EILEEN G. HASSELMEYER

New York, New York Bethesda, Maryland August 1974

## Intravenous Nutrition in the High Risk Infant

### **Contents**

i INTRODUCTION	
Introduction to the Conference,	3
ROBERT W. WINTERS	
Historical Considerations of Intravenous Hyperalimentation	7
STANLEY J. DUDRICK	
II CLINICAL RESULTS	33
Intravenous Alimentation	
PAUL R. SWYER	3:
Very Low Birth Weight Infants (< 1300 gm birth weight)	
GRAHAM W. CHANCE	39
A Preliminary Study of Total Intravenous Alimentation in Low Birth Weig	ght Infant
JOHN M. DRISCOLL, JR.	5
Alimentation and Growth Patterns in Small Prematures and in Infan Hyaline Membrane Disease	ts with
MILDRED T. STAHLMAN	65

xvii

xviii Contents

Cell Growth Parameters During Malnutrition	
JO ANNE BRASEL	75
Caloric Equivalent of Weight Gain in the Low Birth Weight Infant: Contribution of Minimal Metabolic Rate and Thermal Environment	
JOHN C. SINCLAIR	91
Discussion of Prematures	97
Results in Surgical Neonates	
ROBERT M. FILLER	103
Discussion of Surgical Neonates	113
Parenteral Nutrition in Infants with Malabsorption	
JAMES P. KEATING	117
Gastrointestinal Enzymes and Malabsorption	
HARRY L. GREENE	127
Discussion of Infants with Malabsorption	133
III METABOLIC STUDIES AND COMPLICATIONS	139
Glucose and Fat Metabolism in the Newborn Infant of Low Birth W	eight
PETER A.J. ADAM	141
Studies of Glucose Assimilation and Insulin Secretion in Very Low Birth Infants	Weight
GRAHAM W. CHANCE	163
Glucose Utilization in Surgical Neonates	
JOHN B. DAS	169
Discussion of Glucose Metabolism	173
Amino Acid Metabolism	
LEWIS D. STEGINK	181

Contents	xix
Amino Acid Requirements	
SELMA E. SNYDERMAN	205
Amino Acid Imbalance	
ALFRED E. HARPER	215
Studies of Amino Acid Metabolism in Infants	
JOHN B. DAS	229
Factors that Should Be Considered for the Improvement of Amino Acid Solutions for Intravenous Nutrition	
HALVOR N. CHRISTENSEN	237
Discussion of Amino Acid Metabolism	245
Disorders of Calcium and Phosphorus Metabolism	
WILLIAM C. HEIRD	249
Discussion of Calcium and Phosphorus Metabolism	253
Disorders of Acid-Base Metabolism	
WILLIAM C. HEIRD	257
Acid-Base Considerations in Intravenous Nutrition	
POUL KILDEBERG	263
Discussion of Acid-Base Metabolism	271
Trace Elements and Vitamins	
HARRY L. GREENE	273
Discussion of Trace Elements and Vitamins	283
Essential Fatty Acids	
STANLEY J. DUDRICK	285
Discussion of Essential Fatty Acids	291