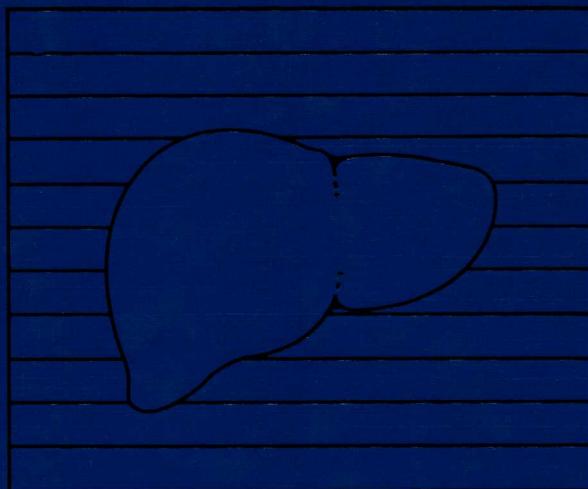


# TEXTBOOK OF PEDIATRIC HEPATOLOGY

A. R. Colón



Second Edition

# Textbook of Pediatric Hepatology

Second Edition

A. R. COLÓN, M.D.

*Professor and Chief*

*Pediatric Gastroenterology and Nutrition*

*Georgetown University's Children's Medical Center*

*Washington, D.C.*



NOT FOR RESALE



YEAR BOOK MEDICAL PUBLISHERS, INC.

CHICAGO • LONDON • BOCA RATON • LITTLETON, MASS.

# Textbook of Pediatric Hepatology

Second Edition

A. R. COLÓN, M.D.

Pediatric Gastroenterology and Nutrition  
Georgetown University Children's Medical Center  
Washington, D.C.

Copyright ©1990 by Year Book Medical Publishers, Inc. All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means—electronic, mechanical, photocopying, recording, or otherwise—without prior written permission from the publisher. Printed in the United States of America.

1 2 3 4 5 6 7 8 9 0 94 93 92 91 90

## Library of Congress Cataloging-in-Publication Data

Colón, A. R.

Textbook of pediatric hepatology / A. R. Colón.—2nd ed.

p. cm.

Rev. ed. of: Pediatric hepatology. 1983.

Includes bibliographies and index.

ISBN 0-8151-1818-X

1. Liver—Diseases. 2. Pediatric gastroenterology. I. Colón, A.

R. Pediatric hepatology. II. Title

[DNLM: 1. Liver Diseases—diagnosis. 2. Liver Diseases—in infancy & childhood. 3. Liver Diseases—therapy. WS 310 C719t]

RJ456.L5C64 1990

618.92'362—dc20

DNLM/DLC

for Library of Congress

89-14667

CIP

Sponsoring Editor: Nancy E. Chorpenning

Assistant Director, Manuscript Services: Frances M. Perveiler

Proofroom Supervisor: Barbara M. Kelly

---

# TEXTBOOK OF PEDIATRIC HEPATOLOGY

Second Edition

A. R. COLON, M.D.

*Professor and Chief*

*Pediatric Gastroenterology and Nutrition*

*Georgetown University Children's Medical Center*

*Washington, D.C.*



YEAR BOOK MEDICAL PUBLISHERS, INC.  
CHICAGO • LONDON • BOCA RATON • LYNN, MASS.



*You know, if Patricia Ann hadn't taken over most of the nuts and \_\_\_\_\_ bolts of everyday living, I wouldn't have had the time to do the first edition, nevermind the second. For Pat, with love.*

A. R. COLÓN, M.D.  
Professor and Chief  
Pediatric Gastroenterology and Nutrition  
Georgetown University's Children's  
Medical Center  
Washington, D.C.

CLIFTON A. LEFRIDGE, M.D.  
Associate Professor  
Pediatric Radiology  
Georgetown University's Children's  
Medical Center  
Washington, D.C.

JOAN S. DIPALMA, M.D.  
Assistant Professor  
Pediatric Gastroenterology  
Georgetown University's Children's  
Medical Center  
Washington, D.C.

IAN H. LETSOWITZ, M.D.  
Instructor, Pediatric Gastroenterology  
Georgetown University's Children's  
Medical Center  
Washington, D.C.

# CONTRIBUTORS

---

A. R. COLÓN, M.D.  
*Professor and Chief*  
*Pediatric Gastroenterology and Nutrition*  
*Georgetown University's Children's*  
*Medical Center*  
*Washington, D.C.*

JOAN S. DiPALMA, M.D.  
*Assistant Professor*  
*Pediatric Gastroenterology*  
*Georgetown University's Children's*  
*Medical Center*  
*Washington, D.C.*

CLIFTON A. LEFRIDGE, M.D.  
*Associate Professor*  
*Pediatric Radiology*  
*Georgetown University's Children's*  
*Medical Center*  
*Washington, D.C.*

IAN H. LEIBOWITZ, M.D.  
*Instructor, Pediatric Gastroenterology*  
*Georgetown University's Children's*  
*Medical Center*  
*Washington, D.C.*



A. R. Colón

# PREFACE TO THE SECOND EDITION —

New ideas as well as new understanding and refinement of past concepts have prompted a virtually complete rewriting of *Pediatric Hepatology*. This second edition includes new chapters on nutrition, hepatic imaging, and transplantation. The original chapter on hepatitis has been expanded to three—on viral, nonviral, and chronic hepatitis. A chapter on specific care protocols has been written with the many general gastroenterologists in mind who treat children and youth. There are seven new chapters in all, and all of the extant chapters have received extensive revision. The bibliography is current and comprehensive. The pathology mini-atlas of the first edition has been replaced by pertinent histopathologic figures interspersed throughout the text.

A pathophysiologic approach to liver disease invites a degree of overlap inasmuch as some diseases have variable mechanisms of action. Several entities therefore appear in more than one chapter. For example, total parenteral nutrition is examined with respect to both hyperbilirubinemia and cirrhosis. Similarly, ammonia metabolism is discussed in chapters that focus on steatosis and encephalopathy. The overlap is minimal, and should reinforce pathophysiologic concepts.

I have touched on tropical liver diseases in my desire to be all inclusive, and with hope that my comments will be of some use to those pediatricians and gastroenterologists who care for children globally, especially those friends and colleagues in Central and South America, Pacific Asia, and Africa.

The task of rewriting the text has reaffirmed the enjoyment and satisfaction I derive from work in my chosen field. My intentions and hope in writing and revising this book are to provide a service to my colleagues who have dedicated their professional lives to the care of sick children throughout the world. Given the opportunity, I will in the future continue this endeavor.

I would like to acknowledge the assistance of Gail Williams. I thank Pat Colón for her constructive suggestions and a patient reading of the text. As always, I acknowledge the children who have taught me compassion and a sense of humor.

A. R. Colón

# PREFACE TO THE FIRST EDITION \_\_\_\_\_

This text is intended for students, pediatric residents, practicing pediatricians, and any busy physician wanting basic core information about childhood liver disease in a concise outline form. Full references are provided for more detail, or for those who learn better by traditional narrative form. But for those whose minds flow algorithmically, outlines, diagrams, tables, and algorithms form the core of the text. All microphotographs are gathered into an appendix as a mini-atlas of pathology. This atlas is intended to aid in the visualization and conceptualization of pathologic processes, not to identify specific diseases. In short, the text is designed to be practical and brief.

Acknowledgments are warmly given to: Gunnar Stickler, M.D., who put me onto pediatric gastroenterology; Douglas Sandberg, M.D., who, during my fellowship, encouraged me quietly but firmly; and Philip Calcagno, M.D., who put the original pediatric “bug” in my head. I am beholden to them and to my other good teachers, and to all of my students and residents who relentlessly probe, question, and teach. Many thanks.

Some of the histopathologic materials were kindly provided by Roma Chandra, M.D. The marvelous drawings are from the talented hands of Peter Stone. The typing, typing, and retyping was done ungrudgingly by Barbara Runner.

Finally, for all her pushing, intellectual prodding, and tireless scrutiny of this manuscript, I thank my friend, critic, and companion, P. A. Colón.

A. R. Colón, M.D.



# CONTENTS

|                                      |           |
|--------------------------------------|-----------|
| <i>Preface to the Second Edition</i> | <b>ix</b> |
| <i>Preface to the First Edition</i>  | <b>xi</b> |

|   |           |
|---|-----------|
| <b>1 / Pediatric Hepatology-A Historic Overview</b> | <b>1</b>  |
| <b>2 / General Considerations</b>                   | <b>6</b>  |
| Embryology and Growth                               | 6         |
| Anatomy   | 7         |
| Metabolic Overview                                  | 11        |
| <b>3 / Signs and Symptoms</b>                       | <b>16</b> |
| Jaundice  | 16        |
| Ascites   | 19        |
| Hepatosplenomegaly                                  | 23        |
| Hematologic Abnormalities                           | 24        |
| Other Signs and Symptoms                            | 25        |
| <b>4 / Diagnostic Aids</b>                          | <b>30</b> |
| Proteins  | 30        |
| Lipids  | 33        |
| Enzymes   | 34        |
| Pigments  | 36        |
| Bile Acids  | 38        |
| Vitamins  | 38        |
| Dyes  | 39        |
| Immunoproteins                                      | 39        |
| Liver Biopsy  | 44        |
| <b>5 / Hepatobiliary Imaging</b>                    | <b>48</b> |
| <i>by Clifton A. Leftridge and A. R. Colón</i>      |           |
| Plain-Film Radiography of the Liver and Gallbladder | 48        |
| Ultrasound  | 49        |
| Computed Tomography                                 | 51        |
| Radionuclide Methodology                            | 52        |
| Angiography   | 54        |
| Cholangiography                                     | 56        |
| Magnetic Resonance Imaging                          | 59        |

|   |            |     |
|---|------------|-----|
| <b>6 / Hepatotoxicity</b>                                     | <b>65</b>  |     |
| Detoxification  | 65         |     |
| Natural Substances as Toxins (Noninfectious "Food Poisoning") |            | 66  |
| Chemicals as Toxins   | 69         |     |
| Mineral Toxicity  | 70         |     |
| Therapeutic Substances as Toxins                              |            | 71  |
| <b>7 / Viral Hepatitis</b>                                    | <b>78</b>  |     |
| Hepatitis A   | 78         |     |
| Hepatitis B   | 81         |     |
| Non-A, Non-B Hepatitis  |            | 90  |
| Hepatitis D   | 92         |     |
| Rubella   | 93         |     |
| Rubeola   | 94         |     |
| Cytomegalovirus   |            | 94  |
| Varicella   | 96         |     |
| Herpes Simplex  | 98         |     |
| Epstein-Barr Virus  | 99         |     |
| Coxsackie B Virus   | 100        |     |
| Enteric Cytopathic Human Orphan Virus                         |            | 100 |
| Adenovirus  | 101        |     |
| Reovirus  | 102        |     |
| Flaviviruses  | 102        |     |
| Other Viruses   | 103        |     |
| <b>8 / Non-viral Hepatitis</b>                                | <b>110</b> |     |
| Bacterial Hepatitis   | 110        |     |
| Rickettsial Hepatitis   | 123        |     |
| Fungal Hepatitis  | 124        |     |
| Parasitic Hepatitis   | 127        |     |
| <b>9 / Chronic Hepatitis</b>                                  | <b>135</b> |     |
| Chronic Persistent Hepatitis                                  |            | 135 |
| Chronic Active Hepatitis                                      |            | 136 |
| Liver-Kidney-Microsomal Syndrome                              |            | 142 |
| <b>10 / Fatty Liver Syndromes</b>                             | <b>146</b> |     |
| General Pathophysiology                                       | 146        |     |
| Causes of Fatty Liver   | 149        |     |
| <b>11 / Hyperbilirubinemia Syndromes</b>                      | <b>171</b> |     |
| Syndromes of Unconjugated Hyperbilirubinemia                  |            | 171 |
| Syndromes of Conjugated Hyperbilirubinemia                    |            | 174 |
| <b>12 / Biliary Tract and Gallbladder</b>                     | <b>182</b> |     |
| Biliary Atresia   | 182        |     |
| Gallbladder Disease   | 195        |     |
| <b>13 / Cirrhosis and Fibrosis</b>                            | <b>208</b> |     |
| Cirrhosis   | 208        |     |
| Fibrosis  | 222        |     |

|   |            |
|---|------------|
| <b>14 / Hepatic Encephalopathy</b>          | <b>233</b> |
| Definitions                                 | 233        |
| Pathogenesis                                | 234        |
| Ammonia Intoxication                        | 234        |
| False Neurochemical Transmitters            | 235        |
| Short-Chain Fatty Acids                     | 236        |
| Amino Acids                                 | 236        |
| Other Metabolic Abnormalities               | 236        |
| Treatment                                   | 237        |
| Prognosis                                   | 240        |
| <b>15 / Portal Hypertension</b>             | <b>243</b> |
| Definitions                                 | 243        |
| Signs and Symptoms                          | 246        |
| Prehepatic Portal Hypertension              | 247        |
| Hepatic Portal Hypertension                 | 247        |
| Laboratory Aids                             | 249        |
| Treatment                                   | 249        |
| <b>16 / Hepatic Abscess and Infestation</b> | <b>254</b> |
| Pyogenic Liver Abscess                      | 254        |
| Amebic Abscess                              | 255        |
| Helminthic Infections                       | 256        |
| Schistosomiasis (Bilharziasis)              | 258        |
| Flukes                                      | 259        |
| Trichinosis                                 | 260        |
| <b>17 / The Liver in Other Disorders</b>    | <b>262</b> |
| Immunopathic Disorders                      | 262        |
| Pregnancy                                   | 266        |
| Gastrointestinal Disorders                  | 267        |
| Renal Disorders                             | 269        |
| Collagen Vascular Diseases                  | 270        |
| Neurologic Disorders                        | 270        |
| Peroxisomal Diseases                        | 271        |
| Metabolic Disorders                         | 271        |
| Hematologic Disorders                       | 276        |
| Cardiovascular Disorders                    | 277        |
| Miscellaneous Disorders                     | 279        |
| <b>18 / Hepatic Tumors and Trauma</b>       | <b>288</b> |
| Hepatic Tumors                              | 288        |
| Hepatic Trauma                              | 296        |
| <b>19 / Liver Transplantation</b>           | <b>301</b> |
| by Joan S. DiPalma and A. R. Colón          |            |
| Indications                                 | 301        |
| Evaluation                                  | 304        |
| Patient Selection                           | 306        |
| Preoperative Preparation                    | 307        |

|  |            |  |
|--|------------|--|
| Graft Procurement                          | 308        |  |
| Surgery                                    | 309        |  |
| Postoperative Care                         | 310        |  |
| Rejection                                  | 310        |  |
| Immunosuppression                          | 311        |  |
| Surgical Complications                     | 316        |  |
| Outcome                                    | 319        |  |
| Financial Considerations                   | 320        |  |
| Donor Availability                         | 320        |  |
| Summary                                    | 321        |  |
| <b>20 / Liver Disease and Nutrition</b>    | <b>326</b> |  |
| <i>by Ian H. Leibowitz and A. R. Colón</i> |            |  |
| Galactosemia                               | 326        |  |
| Tyrosinemia                                | 327        |  |
| Copper Excess                              | 327        |  |
| Glycogen Storage Diseases                  | 328        |  |
| Hereditary Fructose Intolerance            | 328        |  |
| Infantile Cholestasis                      | 329        |  |
| Cirrhosis                                  | 331        |  |
| Acute Viral Hepatitis                      | 333        |  |
| <b>21 / Specific Care Protocols</b>        | <b>337</b> |  |
| Chronic Liver Disease Protocol             | 337        |  |
| Liver Failure Protocol                     | 338        |  |
| Post-Transplant Protocol                   | 339        |  |
| <b>Index</b>                               | <b>340</b> |  |



# Chapter 1



## Pediatric Hepatology—A Historic Overview

Prior to and throughout the 1st and early 2nd millennia, the medical literature made no reference whatsoever to diseases of the liver in children<sup>1</sup> (Table 1–1). Jaundice in the adult, to be sure, was noted even in ancient writings, and several terms were used to describe the condition, including *icterus*, *aurigo*, *morbus regius*, and *morbus arquatus*.<sup>2</sup> It was not, however, until the 15th century that even passing mention was made of this most obvious reflection of liver dysfunction in children. In 1473, Bartholomaeus Metlinger wrote in *Ein Regiment der Jungen Kinder* (Fig 1–1) that:

Jaundice comes of coarse thick milk of the nursing woman through which the passages of the liver and bile become stopped up. The nursing woman should avoid pastry, fish, and cheese. . . .<sup>3</sup>

No clinical significance was attributed to the condition. Two centuries later, Michael Ettmuller (1644–1683) wrote about jaundice in the newborn in *De Infantum Morbis* and suggested that it be treated with saffron.<sup>4</sup> In 1742, John Burton published *A Full View of All the*

*Disease Incident to Children*. His observations of benign, physiologic jaundice astutely noted the response to mobilized enterohepatic metabolism through the universal “physik”<sup>5</sup>:

. . . at birth or soon after, Children are often observed to have the Jaundice . . . [which] generally yields to any gentle Purgative, and very often is carried away by any medicine that increases the Contraction of the Gut. . . .

The first reference to a congenital and malignant form of jaundice appeared in 1784 in Michael Underwood’s *Treatise on Diseases of Children*. He described a mother of 11 children, ten of whom had died after jaundice appeared days to weeks after their births. Underwood conducted an autopsy on that last child and found “a livid liver with permeable ducts.”<sup>6</sup>

The distinction between benign and malignant jaundice, however, was not made until William Dewees published his *Treatise on the Physical and Medical Treatment of Children* in 1825. Dewees thoroughly described physi-

**TABLE 1-1.**

Chronology of Adult Hepatology: To 1900

| To the Early 19th Century     |  |
|-------------------------------|--|
| Hippocrates (?460–377? BC)    | Recognized infectious hepatitis, hydatid cysts; refined palpation                                  |
| Erasistratos (300–250 BC)     | Tapped ascites; coined term parenchyma   |
| Galien (130–200)              | Distinguished hemolytic from obstructive jaundice  |
| Leonardo DaVinci (1452–1519)  | Described cirrhosis  |
| Andreas Versalius (1514–1564) | Defined hepatic anatomy  |
| Thomas Bartholin (1616–1680)  | Ascribed the liver as the “body’s master cook and engineer”  |
| Francois Glisson (1597–1677)  | Described liver capsule and blood supply   |
| Marc. Malpighi (1628–1694)    | Ascribed glandular bile production to the liver  |
| Johann Wepfer (1620–1695)     | Defined the lobule   |
| Thomas Sydenham (1624–1689)   | Conducted studies of epidemic hepatitis  |
| John Browne (1642–1700?)      | Gave first good description of cirrhosis   |
| Fred. Ruysch (1638–1731)      | Described hydatid liver  |
| Alb. von Haller (1708–1777)   | Described liver anatomy in detail  |
| Giov. Morgagni (1682–1771)    | Described hepatic necrosis and cirrhosis   |
| William Heberden (1710–1801)  | Emphasized alcoholic cirrhosis   |
| Thomas Coe (1704–1761)        | Wrote a text on gallstones   |
| Gaspard Bayle (1774–1816)     | Described fatty liver  |
| Sam. Soemmerring (1755–1830)  | Detailed study of gallstones   |
| Francis Kiernan (1800–1874)   | Described lobule microscopy  |
| Michael Chevreul (1786–1889)  | Studied bile composition   |
| Rene Laennec (1781–1826)      | Defined macroscopic cirrhosis  |
| Thomas Williams (1819–1865)   | Studied microscopy of acute necrosis   |
| Carl Rokitsansky (1804–1878)  | Coined “acute yellow atrophy”  |
| Richard Bright (1789–1858)    | Discussed hepatic coma   |
| George Budd (1808–1882)       | Discussed liver coma and congestion  |
| William Bowman (1816–1892)    | Performed microscopy of fatty liver  |
| To the Late 19th Century      |  |
| Hans Chiari (1851–1916)       | Endarteritis and thrombosis of the liver   |
| Luigi Lucatello (1863–1926)   | Puncture biopsy of the liver   |
| Claude Bernard (1813–1878)    | Opened the door to biochemical study of the liver with <i>De la Presence du Sucre dans le Foie</i> |
| Theodor Frerichs (1819–1885)  | Wrote <i>A Clinical Treatise on Diseases of the Liver</i> (1860)                                   |
| von Libermeister (1833–1901)  | Separated portal from biliary cirrhosis  |
| Victor Hanot (1844–1896)      | Refined the description of biliary cirrhosis   |
| vonRecklinghausen (1833–1910) | Described liver hemochromatosis  |
| Paul Ehrlich (1854–1915)      | Performed blind liver biopsy   |
| Carl Langerbuch (1846–1901)   | Performed the first cholecystectomy  |
| Louis Courvoisier (1843–1918) | Popularized cholecystectomy  |
| Friedel Pick (1867–1926)      | Described pseudocirrhosis of pericarditis  |

TABLE 1-1 (cont.).

Chronology of Adult Hepatology: To 1900

|                                      |   |
|--------------------------------------|---|
| Karl Wilhelm von Kupffer (1829–1902) | Described the stellate cells of the liver |
| Bernhard Riedel (1846–1916)          | Described the lobe of the liver           |

ologic jaundice, and, while admitting ignorance of its cause, emphasized its benign nature:

The skins of newly born children are frequently of a yellow colour; but this does not constitute the disease in question. The yellowness here spoken of is not of a deep tone though very generally diffused. This appearance may continue for several days, and then disappear without the aid of remedy, or without leaving any evil behind. It is difficult to say, to what this yellow tinge may be owing; certain it is, it cannot be attributed to the presence of bile, since, neither the urine, nor the whites of the eyes, assume the yellow hue.<sup>7</sup>

Understanding the significance of the color of stools in the jaundiced child, Dewees went further:

So long as the stools are dark green, or yellow, we need not give ourselves any anxiety about it. But if on the contrary, the above marks are attended by deficiency of colour in the stools . . . jaundice, in its most formidable form, is present . . . the common duct obstructed as in the jaundice of adults.

Surely this was the first reference in the medical literature to what is now known as biliary atresia “with a shrunken, shriveled duct.” He laments the inability to treat the condition:

When a genuine jaundice attacks a newborn child, it is but too often fatal, with whatever propriety or energy we may attempt to relieve it.

The distinction between a benign and malignant form of jaundice in the child marked the beginnings of pediatric hepatology as a distinct field of study and treatment. It was not, however, until 50 years later—about 1880—that authorities on the subject of childhood liver disease emerged.

Writing in John Keating’s *Cyclopedia of Diseases of Children*<sup>8</sup> (1890), H. Dwight Chapin

elaborated on *grave icterus neonatorum*, or choledochal cyst and/or biliary atresia, as distinguished from *grave icterus familiarum*, or erythroblastosis fetalis. Chapin also gave a vivid description of biliary obstruction secondary to ascariasis.

J. H. Muser combed the existing literature and compiled all the then known causes of hepatomegaly in children. He wrote:

The growth of population and the increase of special hospitals for children have made it more

# Ein regiment der jungen kinder Wie man sy halten vnd erziehen sol von trier gepurt biß sy zû jren tagen kômen.



FIG 1-1.  
Frontispiece from Metlinger’s *Ein Regiment der Jungen Kinder*, ed 4, appearing in 1497.



practicable for single observations to be made. The accumulated results of the more careful observations scattered through the literature of medicine form sufficient data for intelligent writing on any disease of the liver incident to—or, rather occurring in—childhood.<sup>8</sup>

In the same tome, Marcus Hatfield described the various causes of contractions (cirrhosis) of the liver and offered the supportive and expectant treatment modalities of the time.

Thereafter, a cascade of anatomic descriptions and clinical reports followed,<sup>9, 10</sup> culmi-

nating in the 20th century with the recognition and formalization of pediatric hepatology as a specialized field of endeavor.

I have elected to list chronologically the major contributions to pediatric hepatology (Table 1–2) in order to provide, at a glance, a capsulization of the rapid advancements and understanding in the last 100 years as compared with the antecedent millenia (Tables 1–1 and 1–3). The list is not carved in stone, and surely, with time, the import of current thought and research will amend the contents.

**TABLE 1–2.**

**Chronology of Pediatric Hepatology**

|      |                          |   |
|------|--------------------------|---|
| 1892 | Thompson                 | Published reports of 50 necropsies of biliary malformations |
| 1894 | Swaine                   | Corrected first biliary cyst                                |
| 1900 | Gilbert                  | First example of metabolic liver dysfunction                |
| 1913 | Ylppo                    | Concept of immaturity of biliary metabolism                 |
| 1927 | Ladd                     | First surgical cure of biliary atresia                      |
| 1935 | Gross                    | Described inspissated bile                                  |
| 1949 | McMahon, Taunhauser      | Described intrahepatic biliary atresia                      |
| 1952 | Illingworth, Cori, Cori  | Series of papers describing glycogen storage disease        |
| 1952 | Crigler, Najjar          | Metabolic familial jaundice                                 |
| 1953 | Cole, Lattle             | Glucuronyl transferase immaturity                           |
| 1954 | Hsia                     | Micromethod for bilirubin                                   |
| 1954 | Jelliffe                 | Veno-occlusive disease                                      |
| 1956 | Isselbacher              | Congenital galactosemia                                     |
| 1959 | Kasai                    | Biliary atresia surgery                                     |
| 1963 | Reye                     | Visceral steatosis and encephalopathy                       |
| 1963 | Starzl                   | Transplantation   |
| 1967 | Scriber, Larochelle      | Hereditary tyrosinemia                                      |
| 1968 | Sharp                    | Alpha-1-antitrypsin liver disease                           |
| 1971 | Peden                    | Total parenteral nutrition cholestasis                      |
| 1973 | Alagille-Watson          | Arteriohepatic dysplasia syndrome                           |
| 1973 | Goldfischer              | Peroxisome/mitochondrial defect                             |
| 1983 | Balistreri, Huebi, Suchy | Physiologic cholestasis concept                             |



**TABLE 1-3.**  
Adult Hepatology in the 20th Century

|      |                             |   |
|------|-----------------------------|---|
| 1916 | vandenBergh                 | Diazotized sulfanilic acid determination                        |
| 1930 | Rosenthal                   | Bromsulphalein dye excretion test                               |
| 1933 | Kalk                        | Conjoined laparoscopy and biopsy                                |
| 1937 | Eppinger                    | Wrote <i>Die Leberkrankheiten</i>                               |
| 1938 | Liverson, Roholm, Silverman | Developed needle biopsy techniques                              |
| 1955 | Karmen                      | Transaminase determination                                      |
| 1955 | Sherlock                    | <i>Diseases of the Liver and Biliary System</i> (first edition) |
| 1956 | Schmid                      | Direct hyperbilirubinemia                                       |
| 1956 | Schiff                      | <i>Diseases of the Liver</i> (first edition)                    |
| 1958 | Menghini                    | Further refined needle biopsy                                   |
| 1958 | Popper, Schaffner           | Extensive survey of liver literature                            |
| 1965 | Blumberg                    | Australia antigen   |

REFERENCES

1. Franken FH: History of hepatology, in Cso-mos G, Thaler H (eds): *Clinical Hepatology*. New York, Springer-Verlag, 1983, pp 1-15.

2. Freirichs FT: *A Clinical Treatise on Diseases of the Liver*. London, New Syndenham Soci-ety, 1860, pp 76-81.

3. Ruhrah J: *Pediatrics of the Past*. New York, Hoeber, 1925.

4. Still GF: *History of Paediatrics*. London, Ox-ford University Press, 1931.

5. Colón AR: *The Boke of Children*. Columbus, Ohio, Ross, 1987.

6. Underwood M: *Treatise on Diseases of Chil-dren*. London, J Matthews, 1784.

7. Dewees WP: *Treatise on the Physical and Medical Treatment of Children*. Philadelphia, HC Carey, 1825, pp 271-275.

8. Keating J: *Cyclopedia of Diseases of Chil-dren*. Philadelphia, JB Lippincott, 1890, vol III, pp 403-515.

9. Huard P, LaPlane R: *Histoire Illustree de la Pediatrie*. Tome I. Paris, Roger DaCosta, 1981.

10. Diamond LK: A history of jaundice in the newborn. *Birth Defects* 1970; 6:3-6.