
Gary Gitnick

**Diseases of
the Liver
and Biliary Tract**

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Diseases of the Liver and Biliary Tract

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With 193 illustrations

 **Mosby
Year Book**

St. Louis Baltimore Boston Chicago London Philadelphia Sydney Toronto



Dedicated to Publishing Excellence

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Printed in the United States of America

Mosby–Year Book, Inc.

11830 Westline Industrial Drive

St. Louis, Missouri 63146

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Library of Congress Cataloging-in-Publication Data

Diseases of the liver and biliary tract / [edited by] Gary

Gitnick, Douglas R. LaBrecque, Frank G. Moody.

p. cm.

Includes bibliographical references and index.

ISBN 0-8016-6075-0

1. Liver—Diseases. 2. Biliary tract—Diseases. I. Gitnick Gary II. LaBrecque, Douglas R. III. Moody, Frank G.

[DNLM: 1. Biliary Tract Diseases—physiopathology. 2. Liver Diseases—physiopathology. WI 700 D6115]

RC845.D56 1991

616.3'62—dc20

DNLM/DLC

for Library of Congress

91-18453

CIP

C/MV/MV 9 8 7 6 5 4 3 2 1

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*This book is dedicated to my wife, **Cherna**,
who has consistently put up with my frequent absences,
and to my children, **Neil, Kim, Jill**, and **Tracy**,
from whom I took the time to develop this and other texts.
It is also dedicated to my brother, **Jerry**, his wife, **Saranne**,
their children, **Andrea** and **Nan Marie**,
and to my mother, **Ann**, who made it all possible.*

Preface

In our own clinical practice of hepatology and in our teaching of students and house staff, the associate editors of this text and I saw a need for yet another textbook of liver disease. Although many comprehensive and excellent books are available, few of our students and colleagues were able to devote the time to reading these encyclopedic texts. Thus we perceived the need for a practical, clinically oriented text that was comprehensive and yet concise. To accomplish this seemingly impossible task, we chose to concentrate on facts and avoid the exposition of opinions or unproven concepts. Thus, although we cover pathophysiology throughout the book, we concentrate on only those areas that have been firmly established. The text is oriented to the needs of the clinician. However, it does provide an authoritative discussion of pathophysiology of each of the disease processes discussed and an understanding of liver function. The laboratory and clinical manifestations of liver disease are discussed, and diagnostic and treatment strategies are documented. In many areas, controversies persist regarding the appropriateness of diagnostic procedures and the applications of therapies. These controversies are discussed frankly, and the reader is allowed to make his or her own determinations. It is our hope that this text will serve to stimulate readers to expand their knowledge of the increasing spectrum of diseases of the liver. I am indebted to my associate editors, Douglas R. LaBrecque, M.D., and Frank G. Moody, M.D., for their exceptional efforts in developing a text that is streamlined to the needs of the clinician. I am also indebted to Susan Dashe, who diligently worked to bring together this text in a timely and efficient manner.

Gary Gitnick

Diseases of the Liver and Biliary Tract

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SECTION ONE

Basic Concepts

1 Introduction

Gary Gitnick

The design of the liver enables this complex organ to respond to unique functional demands. Comprising approximately 2.5% of total body weight, the liver metabolizes amino acids, carbohydrates, lipids, and vitamins. It also filters foreign substances and handles the products of heme metabolism. Intestinal substrates are taken up and stored, metabolized, and distributed to bile and to blood. Transformation in bile of drugs, toxins, and endogenous metabolites is another one of the liver's major functions. The liver distributes various substances, many of which are metabolites, to a variety of organs. Immune complexes enter the liver from the lymphatic system and from the spleen, and endotoxins enter from the intestine (where they are produced by bacterial flora). The sinusoidal lining cells of the liver are potent sources of phagocytosis and endocytosis. Finally, the liver participates in the regulation of blood volume and blood flow.

The organization of the vascular elements and parenchymal cells of the liver is specifically designed to interact with the digestive tract and other organ systems. This interaction is demonstrated by the liver's handling of amino acids, carbohy-

drates, lipids, vitamins, and a variety of pollutants that enter the body during ingestion of water or food. The uptake of substrates from the intestine and their subsequent storage, metabolism, and distribution by blood and bile are essential functions of the liver. The transformation of drugs, pollutants, and metabolites by complex biochemical mechanisms is an equally important function. These are simply examples of the many metabolic functions of the liver, all of which are affected by regulatory factors. The liver is an effective source of phagocytosis of materials, such as bacteria. It possesses certain unique features and functions.

The liver harbors exocrine and metabolic functions in the same cell. It has a double blood supply from the hepatic arterial and the portal systems. It also has a unique enterohepatic circulation, in which biliary solutes are reabsorbed in the intestine and then recirculated. The unique arrangement of cells facilitates the exchange between blood and liver cells. Vast biochemical activities between liver cells and the membranes of other cells regulate specific functions of the liver.

Disease states produce varying demands on the liver and may actually alter

its structure. The process of tissue repair, involving regeneration of liver cells or formation of nodules, is well documented. Cirrhosis is characterized not only by these features but also by abnormal communication between the afferent and efferent blood supply. Cholestasis alters the relationship between the parasinusoidal spaces and the canaliculi, thereby altering bile flow. Thus structural and functional interrelationships exist in health and in disease. These interrelationships help to develop the important physiologic and biologic alterations that occur in both the normal and the diseased liver. These alterations are explained in greater depth in the chapters that follow.

This fascinating and complex organ is subject to a great variety of disease states. This text integrates a background in hepatic structure and function with an understanding of disease pathophysiology, diagnosis, and treatment. Advances in our understanding of liver disease have irrevocably changed previously held concepts. Among these advances has been the discovery of viruses associated with many forms of hepatitis. Viruses were initially implicated as causes of hepatitis A and hepatitis B and have now been documented as causes of hepatitis C, hepatitis D, and hepatitis E. It is likely that one or more additional hepatitis viruses also exists. We have witnessed the development of hepatitis vaccines and observed the relationship between chronic viral hepatitis and the development of chronic hepatitis and the subsequent development of cirrhosis and hepatocellular carcinoma. We have also found that interferon can improve symptoms and biochemical test results.

Primary sclerosing cholangitis has increased in incidence; fortunately there are

new tools for its management, including ursodeoxycholic acid. Using new serologic assays, we can detect primary biliary cirrhosis at an earlier stage than before. New approaches to treatment include ursodeoxycholic acid, cyclosporine, and other, more controversial, approaches. We have seen the rapid development of hepatobiliary imaging and the usefulness of endoscopic diagnostic techniques, including endoscopic ultrasound. We have also extended endoscopy into the treatment arena with endoscopic sphincterotomy and extraction of common duct stones. Biliary manometry has assumed an important new role. We have new methods of lithotripsy and medical dissolution of gallstones. All of these advancements have provided new insights and new challenges.

In the case of ascites, new diuretics are more effective. Medical treatment of pyogenic liver abscesses has become possible, and hepatic transplantation has virtually revolutionized our approach to treatment of severe liver disease. Many other advances will be described in the chapters that follow.

These remarkable accomplishments in science and technology are outweighed by the continuing necessity to promote effective doctor-patient relationships. Advances only help patients who feel comfortable enough with their physicians to comply with treatment. The symptoms of the physical disease are only a small part of what patients with chronic diseases suffer. Nowhere in medicine is it more important for a physician to be both understanding and compassionate than in management of chronic liver disease. Most of our patients have diseases that last throughout their lives, which are likely to be shortened as a result of their