The Clinician's Guide to Pancreaticobiliary Disorders
The Clinician’s Guide to
Pancreaticobiliary Disorders

Gregory G. Ginsberg, MD
University of Pennsylvania
Philadelphia, Pennsylvania

Nuzhat A. Ahmad, MD
University of Pennsylvania
Philadelphia, Pennsylvania

Slack Incorporated
An innovative information, education, and management company
6900 Grove Road • Thorofare, NJ 08086
DEDICATION

I dedicate this book to my mother Geraldine McDonnell Ginsberg, always a lady, who schooled me in humor and humility. In her personal struggle with chronic illness she exemplified strong will, perseverance, and grace.

G.G.G.

Dedicated to Professor Abdus Salam: Pakistani Nobel Laureate in Physics 1979— for leading by example.

N.A.A.
CONTENTS

Dedication ............................................................................................................................ v
Acknowledgements ............................................................................................................... ix
About the Editors ................................................................................................................ xi
Contributing Authors ......................................................................................................... xiii
Preface .................................................................................................................................................... xv

Chapter 1: Development and Function of the Pancreas, Bile Duct, and Gallbladder .......................................................................................................................... 1
Binita M. Kamath, MBChir; Raman R. Sreedharan, MD; Petar Mamula, MD

Chapter 2: Gallstones and Gallbladder Disorders ....................................................................... 21
Ann Marie Joyce, MD; William B. Long, MD

Chapter 3: Choledocholithiasis .................................................................................................... 47
Eric Goldberg, MD; Peter Darwin, MD

Chapter 4: Bile Duct Injuries ..................................................................................................... 69
Janak N. Shah, MD

Chapter 5: Ampullary Disorders .................................................................................................. 91
William B. Silverman, MD, FACG

Chapter 6: Cholangiocarcinoma .................................................................................................. 103
Patrick R. Pfau, MD

Chapter 7: Infections of the Biliary System ............................................................................... 121
Faten N. Aberra, MD, MSCE

Chapter 8: Acute Pancreatitis .................................................................................................. 147
John Horwhat, MD; Paul Jowell, MD

Chapter 9: Chronic Pancreatitis ................................................................................................ 179
Tyler Stevens, MD; Darwin L. Conwell, MD

Chapter 10: Pancreatic Ductal Complications .......................................................................... 217
Ali Fazel, MD

Chapter 11: Solid Pancreatic Tumor .......................................................................................... 239
Shyam Varadarajulu, MD; Mohamad A. Eloubeidi, MD, MHS, FACP, FACG

Color Atlas

Chapter 12: Pancreatic Cystic Lesions ..................................................................................... 257
David G. Forcione, MD; Brenna C. Bounds, MD
Chapter 13: Surgical Approaches to Pancreatic Cancer
Giorgos C. Karakousis, MD; Francis R. Spitz, MD

287

Chapter 14: Biliary Tract Surgery
Rachel Rapaport Kelz, MD, MSCE; Jon B. Morris, MD

297

Chapter 15: Imaging of the Pancreatobiliary System Using
Endoscopic Ultrasound
Nuzhat A. Ahmad, MD

311

Chapter 16: Magnetic Resonance Imaging/Magnetic Resonance
Cholangiopancreatography of the Pancreatobiliary System
Wendy C. Hsu, MD; Evan S. Siegelman, MD

327

Chapter 17: Pancreaticobiliary Diseases: The Role of the Interventional
Radiologist
Richard Shlansky-Goldberg, MD; Aalpen Patel, MD

353

Index
367
ACKNOWLEDGMENTS

For their support and inspiration we wish to acknowledge our parents and teachers, our respective spouses and kids, colleagues and students, and most certainly our patients. We are grateful to the contributing authors for their time and dedication devoted to developing a text that will benefit countless clinicians and patients.
ABOUT THE EDITORS

Gregory G. Ginsberg, MD is Professor of Medicine at the University of Pennsylvania School of Medicine, Gastroenterology Division, and Executive Director of Endoscopic Services at the University of Pennsylvania Health Systems. A graduate of Lafayette College, Easton, PA and Jefferson Medical College of Thomas Jefferson University, Philadelphia, PA, he completed Internal Medicine and Gastroenterology training at Georgetown University Medical Center, Washington, DC. Dr. Ginsberg’s clinical practice and research have focused on the development of new techniques and the evaluation of new technologies as they apply to endoluminal management disorders of the digestive system. Outside of his professional activity, he finds fulfillment with his wife, Jane, and four daughters, Jenny, Kathleen, Elizabeth, and Meg.

Nuzhat A. Ahmad, MD is an Assistant Professor of Medicine at the University of Pennsylvania School of Medicine, Gastroenterology Division, and Associate Director of Endoscopic Services at the University of Pennsylvania Health Systems. She is also the chief of Gastroenterology at the Philadelphia VA Medical Center.
CONTRIBUTING AUTHORS

Faten Aberra, MD, MSCE
Instructor of Medicine
Division of Gastroenterology
Hospital of the University of Pennsylvania
Philadelphia, PA

Brenna Casey Bounds, MD
Instructor in Medicine
Harvard Medical School
Director of Endoscopic Training
Massachusetts General Hospital
Boston, MA

Darwin L. Conwell, MD
Department of Gastroenterology and Hepatology
The Cleveland Clinic Foundation
Cleveland, OH

Peter Darwin, MD
Associate Professor of Medicine
Director of Gastrointestinal Endoscopy
University of Maryland Medical School
Baltimore, MD

Mohamad A. Eloubeidi, MD, MHS, FACP, FACG
Associate Professor of Medicine and Pathology
Director, Endoscopic Ultrasound Program
Co-Director, Pancreatice-biliary Center
University of Alabama at Birmingham
Birmingham, AL

Ali Fazel, MD
Assistant Professor of Medicine
Co-Director, Center for Endoscopic Ultrasound
Division of Gastroenterology, Hepatology and Nutrition
Department of Medicine
University of Florida
Gainesville, FL

David G. Forcione, MD
Assistant Physician
Gastrointestinal Unit
Massachusetts General Hospital
Instructor of Medicine
Harvard Medical School
Boston, MA

Eric Goldberg, MD
Assistant Professor of Medicine
University of Maryland Medical School
Baltimore, MD

John Horwhat, MD
Duke University
Durham, NC

Wendy C. Hsu, MD
Hospital of the University of Pennsylvania
Philadelphia, PA

Paul Jowell, MD
Associate Professor of Medicine
Division of Gastroenterology
Duke University Medical Center
Durham, NC

Ann Marie Joyce, MD
Instructor of Medicine
Hospital of the University of Pennsylvania
Philadelphia, PA

Binita M. Kamath, MBBChir
Division of GI & Nutrition
The Children’s Hospital of Philadelphia
Philadelphia, PA

Giorgos C. Karakousis, MD
Resident in General Surgery
Department of Surgery
Hospital of the University of Pennsylvania
Philadelphia, PA
Contributing Authors

William B. Long, MD
Associate Professor of Medicine
Hospital of the University of Pennsylvania
Philadelphia, PA

Petar Mamula, MD
Division of GI & Nutrition
The Children's Hospital of Philadelphia
Philadelphia, PA

Jon B. Morris, MD
Associate Professor of Surgery
Program Director for General Surgery
Division of GI Surgery
Department of Surgery
Hospital of the University of Pennsylvania
Philadelphia, PA

Aalpen Patel, MD
Department of Radiology
Division of Interventional Radiology
Hospital of the University of Pennsylvania
Philadelphia, PA

Patrick R. Pfau, MD
Assistant Professor of Medicine
Director of Gastrointestinal Endoscopy
University of Wisconsin Medical School
Madison, WI

Rachel Rapaport Kelz, MD, MSCE
Assistant Professor of Clinical Surgery
Hospital of the University of Pennsylvania
Philadelphia, PA

Janak N. Shah, MD
Director of Therapeutic Endoscopy
San Francisco Veterans Medical Center
Assistant Clinical Professor of Medicine
University of California
San Francisco, CA

Richard Shlansky-Goldberg, MD
Department of Radiology
Division of Interventional Radiology
Hospital of the University of Pennsylvania
Philadelphia, PA

Evan S. Siegelman, MD
Associate Professor of Radiology
Department of Diagnostic Radiology
Hospital of the University of Pennsylvania
Philadelphia, PA

William B. Silverman, MD, FACG
Professor of Medicine
Division of GI/Hepatology
Department of Internal Medicine
University of Iowa Hospitals & Clinics
Iowa City, IA

Tyler Stevens, MD
Department of Gastroenterology and Hepatology
The Cleveland Clinic Foundation
Cleveland, OH

Francis Spitz, MD
Assistant Professor of Surgery
Department of Surgery
Hospital of the University of Pennsylvania
Philadelphia, PA

Raman R. Sreedharan, MD
Division of GI & Nutrition
AI DuPont Hospital for Children
Wilmington, DE

Shyam Varadarajulu, MD
Assistant Professor of Medicine
Division of Gastroenterology-Hepatology
University of Alabama at Birmingham School of Medicine
Birmingham, AL
PREFACE

This book was developed as part of the popular *Clinician's Guide* series and focuses on the understanding, diagnosis, and management of disorders of the pancreas and biliary systems. Chapters are clear and concise and written in a uniform manner. The multidisciplinary effort provides a broad and complete treatment of the topic. Images, artwork, graphics, and tables provide a visually appealing complement to the robust text. We think clinicians will find this to be a ready and reliable resource when encountering patients with pancreaticobiliary disorders.
Introduction

DEVELOPMENT AND FUNCTION OF THE PANCREAS

The pancreas makes its appearance in the fetal embryo as early as the 4th week of gestation. The development of pancreas starts as a dorsal and a ventral outpouching from the endodermal lining of the primitive duodenum (Figure 1-1). The dorsal anlage appears earlier than the ventral anlage and eventually forms the neck, body, tail, and superior part of the head of the pancreas. The ventral anlage appears more caudally and is closely related to the bile duct and hepatic diverticulum and develops into the inferior part of the head and uncinate process of the pancreas. The two parts of the pancreas are brought into apposition by the partial rotation of the duodenum by 7 weeks of gestation, and they eventually fuse together. Each part of the primitive pancreas has an axial duct—the dorsal duct (duct of Santorini) arising directly from the duodenal wall and the ventral duct (duct of Wirsung) arising from the common bile duct. At the time of the fusion of the dorsal and ventral parts of the pancreas, the ducts fuse at the junction of the head and body of the pancreas to form the main pancreatic duct. In the majority of individuals, the ventral duct (duct of Wirsung) becomes the main excretory duct and opens into the major papilla along with the common bile duct. The proximal part of the dorsal duct (duct of Santorini) becomes the accessory duct and is patent in 70% of individuals. A wide variety of anatomic variations exist in relation to the fusion and openings of the dorsal and ventral ducts.

Both exocrine and endocrine cells originate from a common pluripotent progenitor under the influence of multiple transcription factors\(^1\). Distinct pathways like Hedgehog, Notch, and TGF-\(\beta\) signaling promote or restrict cell differentiation and morphogenesis. Disruptions in these pathways may lead to development of various congenital anomalies (Table 1-1).
Chapter 1

The pancreas has an exocrine and an endocrine function. The exocrine function consists of production of various digestive enzymes such as lipase, amylase, proteases, and nuclease by acinar cells. The endocrine function unit are islets of Langerhans composed of four different types of cells: a type secreting glucagon, d type secreting somatostatin, PP cells secreting pancreatic polypeptide, and ß secreting insulin.

**Table 1-1**

<table>
<thead>
<tr>
<th>Congenital Anomalies of the Pancreas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pancreas divisum</td>
</tr>
<tr>
<td>Pancreas annulare</td>
</tr>
<tr>
<td>Heterotopic pancreas</td>
</tr>
<tr>
<td>Aplasia</td>
</tr>
<tr>
<td>Hypoplasia</td>
</tr>
<tr>
<td>Dysplasia</td>
</tr>
<tr>
<td>Ductal anomalies</td>
</tr>
</tbody>
</table>

The pancreas has an exocrine and an endocrine function. The exocrine function consists of production of various digestive enzymes such as lipase, amylase, proteases, and nuclease by acinar cells. The endocrine function unit are islets of Langerhans composed of four different types of cells: a type secreting glucagon, d type secreting somatostatin, PP cells secreting pancreatic polypeptide, and ß secreting insulin.

**Development of the Biliary Tract and the Gallbladder**

The liver primordium appears as a thickening of the ventral midline endoderm (the hepatic plate) by day 22 of development (see Figure 1-1). The cells in the hepatic plate proliferate to form the hepatic diverticulum that projects into the septum transversum. The proliferating endodermal cells of the hepatic diverticulum invade the septum...
Development and Function of the Pancreas, Bile Duct

transversum, forming cords of hepatoblasts. These hepatoblasts give rise to the intra- and extrahepatic biliary system as well as the parenchymal elements of the liver.

The intrahepatic bile ducts develop primarily by a process of differentiation from the hepatocytes at the margins of the portal tracts. This differentiation results in the formation of the so-called ductal plate, a single layer or sleeve of cells surrounding a portal vein. The ductal plate becomes a double layer of cells around 7 weeks of gestation. Through a process termed as remodeling, tubular structures form between the two cell layers of the ductal plate. These developing bile ductules express cytokeratins consistent with differentiated biliary epithelium. After completion of remodeling, the nontubular elements of the ductal plate involute, leaving only the centrally located, highly differentiated interlobular duct. Maturation of the intrahepatic biliary tree progresses from the hilum of the liver outwards to the periphery beginning at approximately 11 weeks gestational age and continues for several months after birth. The physiologic and biochemical factors governing the differentiation and remodeling of the ductal plate are essentially unknown at present, though the role of ductal-vascular interactions is increasingly being recognized.

The extrahepatic bile ducts and gallbladder develop from the caudal portion or pars cystica of the hepatic diverticulum before the 4th week of gestation. The pars cystica originates from the anterior side of the duodenum but assumes the definitive position of the common bile duct following rotation of the duodenum. The cystic portion of the hepatic diverticulum is initially hollow but the lumen is obliterated by proliferation of epithelial cells. The early gallbladder and extrahepatic biliary tree therefore consist of solid cords of epithelial cells in the 5th week of gestation. Subsequent vacuolization results in the formation of a lumen in the common bile duct by week 6 and this is fol-

Figure 1-2. Morphogenesis of the intrahepatic ducts in mouse. At embryonic (E) day 15.5 the biliary precursor cells form a single-layered ring called ductal plate, which over the next two days becomes bilayered with focal dilations between the layers. These dilations give rise to the bile ducts, while the rest of the ductal plate regresses. (Adapted from Lemaigre F. Development of the biliary tract. Mechanisms of development. 2003;120:81-87, with permission from Elsevier.)