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Diagnosis of Liver Disease

Second Edition

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Preface

Our book is a primer that should guide practitioners, internists, gastroenterologists, and hepatologists in the assessment of patients with liver problems and is instructive for undergraduates and graduates in studying practical applications for diagnosis and treatment of liver diseases. Clinical manifestations, image analysis, and liver biopsy are essential for diagnosis and are combined throughout this book to assist clinicians in formulating differential diagnosis and treatment plan. Liver biopsy with or without peritoneoscopy is being replaced by noninvasive modalities for diagnosis. However, liver biopsy is still the "gold standard" for accurate diagnosis, and there is a significant emphasis on the role of macro- and microscopic pathology in elucidating pathogenesis as well as identifying confounding features of image findings in patients with liver disease that may lead to a more elaborate differential diagnosis. If appropriate, the role of light and electron microscopic examination—as well as the role of specific stains and molecular techniques—is illustrated.

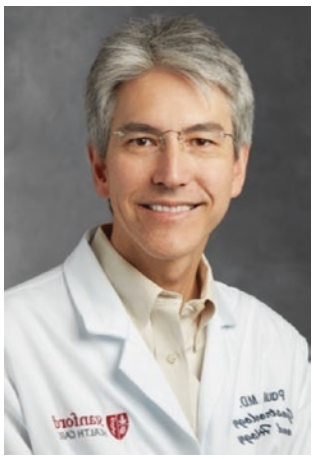
Progress in diagnostic and therapeutic aspects of liver disease has been impressive, and our second book is edited by Professor Paul Y. Kwo, Professor Arief A. Suriawinata, Director Wilson M. S. Tsui, and Professor Etsuko Hashimoto as well as myself, and they also participate in authorship for their individual specialized chapters. We can also welcome Professor Takashi Kojima (anatomy and function), Associate Professor Yoshio Sumida (laboratory tests in liver disease), Associate Professor Yoshinori Harada (acute hepatitis), Professor Akio Ido (acute liver failure), Associate Professor Terumi Takahara (liver cirrhosis), Professor Mikio Zeniya (autoimmune liver diseases), Director Masahiko Koda (vascular and granulomatous liver diseases), Professor Toshinori Kamisako (hyperbilirubinemia), Associate Professor Naoshi Nishida (malignant liver tumors), and Professor Hironori Haga (liver pathology in transplantation) as authors. They describe essential and most current information for diagnosis of and therapy for liver diseases. Concepts related to each liver disease including the pathogenesis are summarized, and the diagnosis and therapy are presented in helpful tables. Concise, accurate, and up-to-date data on various diseases are provided in all chapters, and unresolved problems in diagnosis, treatment, and pathogenesis are clearly described. Thus, this book can be used as a textbook of clinical hepatology and can also be useful for gastroenterologists and hepatologists or researchers to explore topics and themes in the clinical field which should be scientifically investigated.

Practitioners, internists, gastroenterologists, and hepatologists encountering a patient with clinical manifestations of possible liver disease are often challenged when deciding how to reach a diagnosis for therapy by integrating clinical information, imaging studies, and potential liver biopsy. The latter may be accompanied simultaneously by peritoneoscopy showing macroscopic changes of the liver as well as image analysis to add accurate information for understanding the pathogenesis and generating a differential diagnosis. The findings should guide further management and assist in the final diagnosis of the liver disease and its treatment. The approach in this book is a practical one with a focus on the evaluation of representative cases, simultaneously illustrated with cross-sectional images (ultrasonography, computed tomography, magnetic resonance imaging, and angiography),

pathological findings, and peritoneoscopic images. Our second book is cooperatively edited by specialists in hepatology and pathology and with the authors comprising experts from the United States, Europe, Asia, and Japan. This book should serve as a useful source of information for physicians, internists, hepatologists, gastroenterologists, radiologists, and pathologists worldwide.

Masaki Iwai, MD, PhD

Editors



Professor Paul Y. Kwo, MD

Professor Arief A. Suriawinata, MD

Director Masaki Iwai, MD, PhD

Director Wilson M. S. Tsui, MD, FRCPath

Professor Etsuko Hashimoto, MD, PhD

Acknowledgments I

The second edition of our book was supported by many doctors, whose contributions and warm assistance I hereby acknowledge: I am very happy to publish the second edition of Diagnosis of Liver Disease based upon the first edition for medical or graduate students, practitioners, hepatologists or gastroenterologists, radiologists, and clinical pathologists who want to study liver diseases. I expect that this book will be used for studying not only clinical manifestations, image analysis, and pathological features in liver diseases but also their pathogenesis. We were helped by contributions of Professors Alex Y. Chang, Dirk J. van Leeuwen, Paul Y. Kwo, Arief A. Suriawinata, and Director Wilson M. S. Tsui to the first edition preceding the second edition, and we acknowledge in the second edition all colleagues in the Department of Molecular Gastroenterology and Hepatology, Kyoto Prefectural University Graduate School of Medical Science, Otsu Municipal Hospital, Kyoto First Red Cross Hospital, North Medical Center Kyoto Prefectural University of Medicine, Kyoto Municipal Hospital, Kyoto Mitsubishi Hospital, Osaka Railway General Hospital, Kyoto Kizugawa Hospital, Kanagawa Prefectural Ashigarakami Hospital, Faculty of Medicine Tottori University, Tokyo Women's Medical University, and Caritas Medical Centre for presenting various kinds of liver diseases. I was much encouraged by editors and many authors to publish the second edition, and this textbook is dedicated not only to all colleagues working with us but also to medical students, internists, practitioners, gastroenterologists, hepatologists, radiologists, pathologists, and investigators who are studying liver diseases. I am also grateful to Springer Nature, Thieme Medical Publishers, Wiley, Wolters Kluwer, Japanese Society of Gastroenterology, Gastroenterological Endoscopy or Hepatology, and Kyoto Prefectural University of Medicine for kind permission to reproduce illustrations from their publications. Finally, I express my thanks to Subramaniam Vinodhini, a project manager and Sasirekka Nijanthan, a project coordinator in SPi Global, and Sachiko Hayakawa, an editor in Springer, for their continuous encouragement and kind support at all times in the publication of our second edition.

Masaki Iwai, MD, PhD

Acknowledgments II

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Editors

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Anatomy and Function

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Masaki Iwai, Takashi Kojima, and Arief A. Suriawinata

Contents

Abbreviations

AFP	Alpha fetoprotein
cAMP	cyclic adenosine 3′,5′-monophosphate
cGMP	cyclic guanosine 3′,5′-monophosphate
Cx	Connexin
EGFR	Epidermal growth factor receptor
GVHD	Graft-versus-host disease
HCV	Hepatitis C virus
IL-6	Interleukin-6
JAMs	Junctional adhesion molecules
PDZ	Postsynaptic density 95; Discs large, zonula occludens
PKC	Protein kinase C
PSC	Primary sclerosing cholangitis
SR-BI	Scavenger receptor BI
TNF	Tumor necrosis factor
ZO	Zonula occludens

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1.1 Anatomy of the Liver

The liver weighing 1200–1500 g is the largest organ in the human adult and occupies about 2% of body weight. There are two anatomical lobes in the liver, right and left, with the right lobe six times in volume than the left lobe. The right and left lobes are separated anteriorly by the falciform ligament, posteriorly by ligamentum venosum, and inferiorly by ligamentum teres. The Couinaud classification [1] defines eight segments of the liver, and the Bismuth classification [2] divides it into four sectors; they are subdivided into right anterior (V and VIII), right posterior (VI and VII), left medial (IV), or left lateral (II and III) segment and caudate lobe (I) (Fig. 1.1).

The liver receives double blood supply from the portal vein and hepatic artery. The portal vein brings about 65% of hepatic blood flow to the liver from the intestine and spleen, while the hepatic artery brings the remainder 35% from the celiac axis. These vessels enter the liver through the porta hepatis. Inside

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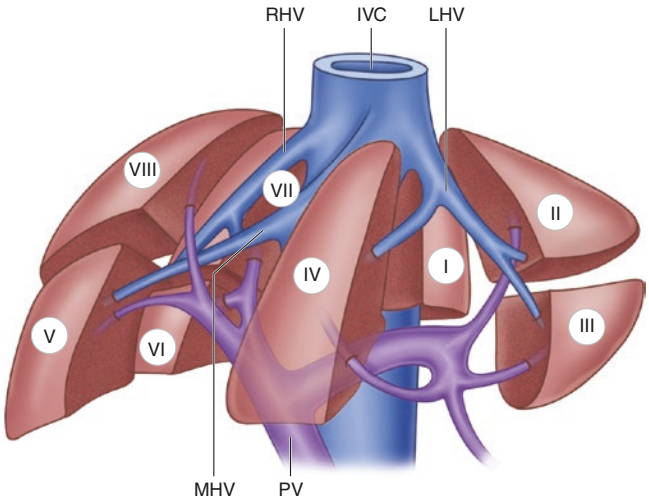

Fig. 1.1 Schematic demonstration of the vascular relations with the segments of the liver (Bismuth classification). The right anterior sector contains segments V and VIII; right posterior sector, segments VI and VII; left medial sector, segment IV; left lateral sector, segments II and III; caudate lobe, segment I. *IVC* inferior vena cava, *LHV* left hepatic vein, *MHV* middle hepatic vein, *RHV* right hepatic vein, *PV* portal vein

the porta hepatis, the portal vein and hepatic artery branch into the right and left lobes. Venous blood from the liver drains into the right and left hepatic veins and enters the inferior vena cava very near to the entry of the right atrium. Lymphatic channels are divided into deep and superficial networks. The former runs parallel to the branches of the portal vessels and hepatic veins, while the latter is found in the capsule, with numerous anastomoses among these networks. The right and left hepatic bile ducts join to form the common hepatic duct. The hepatic nerve plexus contains fiber from the synaptic ganglia, and it accompanies the hepatic artery and bile ducts in the portal tracts. A few fibers enter at the porta hepatis, and arteries are innervated by sympathetic fibers. The bile ducts are innervated by both sympathetic and parasympathetic fibers (Fig. 1.2a). Nerve fibers are present in the portal tract (Fig. 1.2b), and these unmyelinated sympathetic fibers innervate the hepatic parenchyma. Most hepatic nerve fibers are aminergic or peptidergic. Vasoactive intestinal peptide, neuropeptide Y, glucagon, somatostatin, neurotensin, and calcitonin gene-related peptide are present in hepatic nerve fibers (Fig. 1.2c) [3].

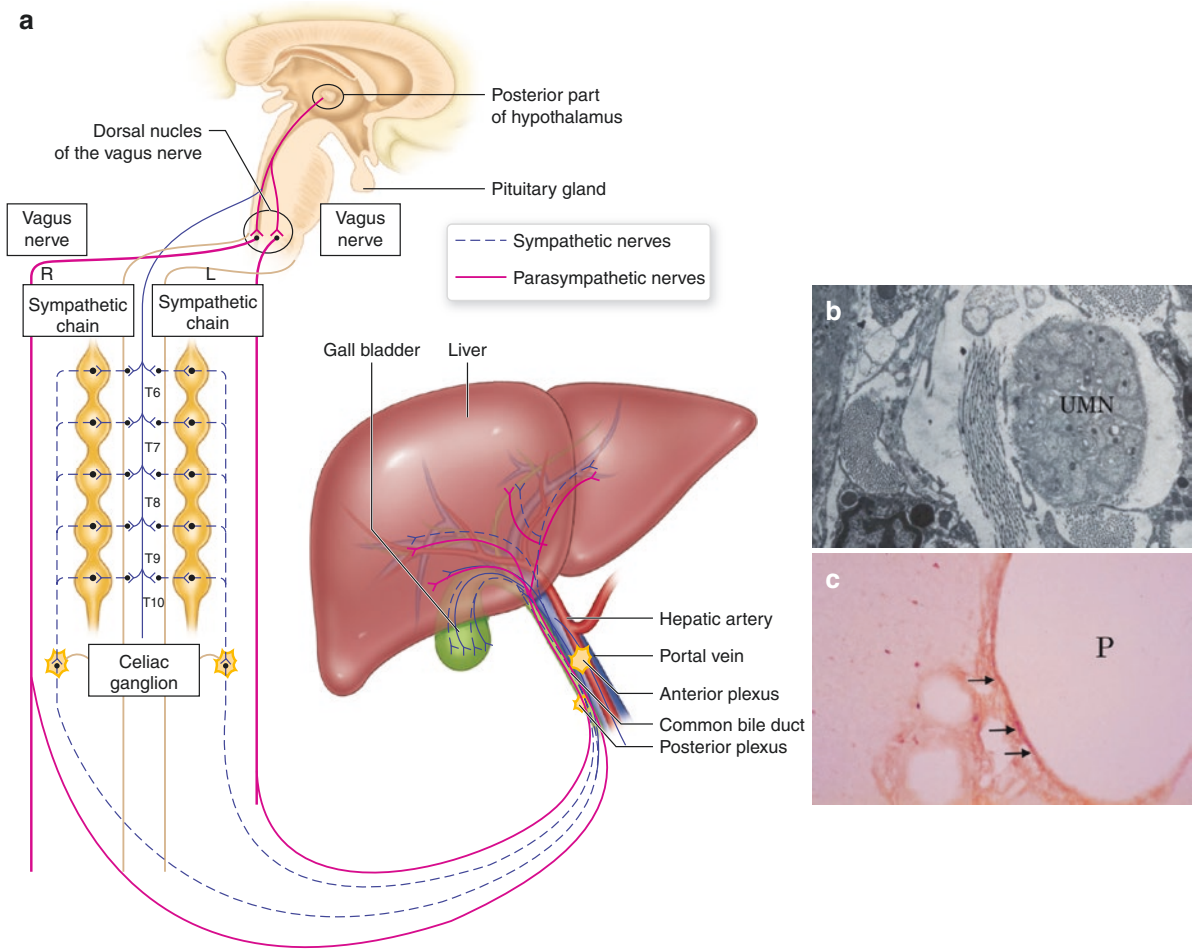

Fig. 1.2 Hepatic nerves. (**a**) Parasympathetic nerve fibers are derived from the dorsal nucleus of vagus nerve, while sympathetic nerve fibers are derived from spinal segments of T6 or 7–T10. They form intercommunicating plexuses around the hepatic artery and portal vein. (**b**) Unmyelinated nerve (UMN) bundle is seen in portal tract of rat liver. (**c**) Glucagon-immunoreactivity (arrow) is seen on nerve fibers in the wall of rat portal vein (P). (**b**, **c**); reuse of Iwai M, et al. Immunoreactive glucagon in rats with normal or regenerative livers induced by galactosamine. Biomedical Res. 1988;9:85–92, with permission of its chief editor