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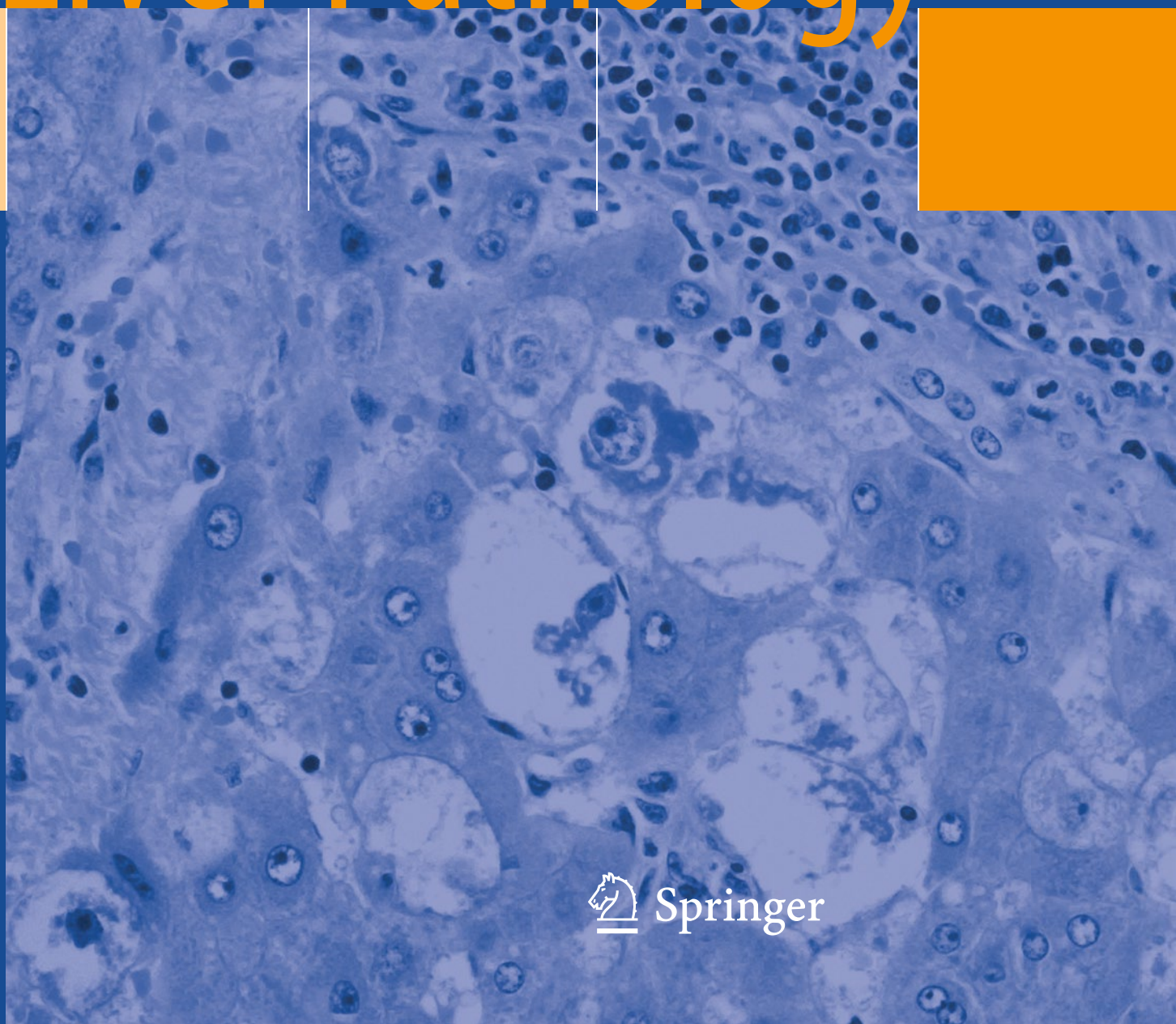
Atlas of Liver Pathology



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Atlas of Anatomic Pathology

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Atlas of Liver Pathology

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Series Preface

One Picture Is Worth Ten Thousand Words

– Frederick Barnard, 1927

Remarkable progress has been made in anatomic and surgical pathology during the last 10 years. The ability of surgical pathologists to reach a definite diagnosis is now enhanced by immunohistochemical and molecular techniques. Many new clinically important histopathologic entities and variants have been described using these techniques. Established diagnostic entities are more fully defined for virtually every organ system. The emergence of personalized medicine has also created a paradigm shift in surgical pathology. Both promptness and precision are required of modern pathologists. Newer diagnostic tests in anatomic pathology, however, cannot benefit the patient unless the pathologist recognizes the lesion and requests the necessary special studies. An up-to-date Atlas encompassing the full spectrum of benign and malignant lesions, their variants, and evidence-based diagnostic criteria for each organ system is needed. This Atlas is not intended as a comprehensive source of detailed clinical information concerning the entities shown. Clinical and therapeutic guidelines are served admirably by a large number of excellent textbooks. This Atlas, however, is intended as a "first knowledge base" in the quest for definitive and efficient diagnosis of both usual and unusual diseases.

The *Atlas of Anatomic Pathology* is presented to the reader as a quick reference guide for diagnosis and classification of benign, congenital, inflammatory, nonneoplastic, and neoplastic lesions organized by organ systems. Normal and variations of "normal" histology are illustrated for each organ. The Atlas focuses on visual diagnostic criteria and differential diagnosis. The organization is intended to provide quick access to images and confirmatory tests for each specific organ or site. The Atlas adopts the well-known and widely accepted terminology, nomenclature, classification schemes, and staging algorithms.

This book Series is intended chiefly for use by pathologists in training and practicing surgical pathologists in their daily practice. It is also a useful resource for medical students, cytotechnologists, pathologist assistants, and other medical professionals with special interest in anatomic pathology. We hope that our trainees, students, and readers at all levels of expertise will learn, understand, and gain insight into the pathophysiology of disease processes through this comprehensive resource. Macroscopic and histological images are aesthetically pleasing in many ways. We hope that the new Series will serve as a virtual pathology museum for the edification of our readers.

Liang Cheng, MD, Series Editor

Preface

This atlas is designed to be a primer for students and residents and for general pathologists in the interpretation of liver biopsy histology. The liver is subjected to a wide range of insults but has a relatively limited repertoire of histopathological changes. Optimal interpretation of liver biopsy specimens requires accurate recognition of the morphological abnormalities and an ability to put these into the appropriate clinical context.

We have deliberately not tried to be comprehensive in this atlas but rather sought to cover an approach to the most common forms of liver disease in which biopsy interpretation remains an important part of the diagnostic workup or indeed in prognostication. We set the scene with the first two chapters by covering normal liver and variants and basic patterns of injury. This forms a basis for a greater understanding of the impact of different disease processes on liver microarchitecture described in the remaining chapters.

All four of the authors remain fascinated by the changes that can be seen by microscopy in liver tissues; we hope that our enthusiasm for the subject will rub off on those who read and use this book. We are each indebted to our respective mentors and to histopathological and hepatological colleagues who continue to share their interesting and challenging cases with us. Finally all four authors would like to acknowledge the incredible support of their respective families during the preparation of this atlas.

Hong Kong — Anthony W.H. Chan
London — Alberto Quaglia
Newcastle — Beate Haugk
Adelaide — Alastair Burt

Contents

Normal, Variants, and Methods

1

A sound knowledge of normal liver microscopic anatomy is essential for the correct interpretation of pathological changes. The severity and the progression of acute and chronic liver injury often are defined on the basis of how the injury affects the lobular architecture and the normal anatomic vascular relationships. The classical models of the Kiernan lobule and Rappaport acinus commonly are used to describe the distribution, extent, and possible causes of some types of liver injury. The appearance of some normal components varies according to the location (e.g., the connective tissue of small and large portal tracts) and age (e.g., periportal accumulation of iron and copper in neonates). A sound knowledge of liver biopsy techniques, specimen processing, and staining helps in evaluating the adequacy of a biopsy sample, recognising artefacts, and choosing the most appropriate set of histochemical and immunohistochemical stains to answer specific clinical questions. This chapter covers all these aspects, illustrating the normal liver architecture and its variants, common technical artefacts, sampling size variation in relation to biopsy technique, and the application of the common histochemical and immunohistochemical stainings.

1.1 Normal Liver Landmarks

Recognition of normal liver landmarks helps in the assessment of the integrity of the overall hepatic architecture and the distribution of pathologic changes, and hence in the formulation of histopathologic diagnoses (Figs. 1.1 to 1.10).

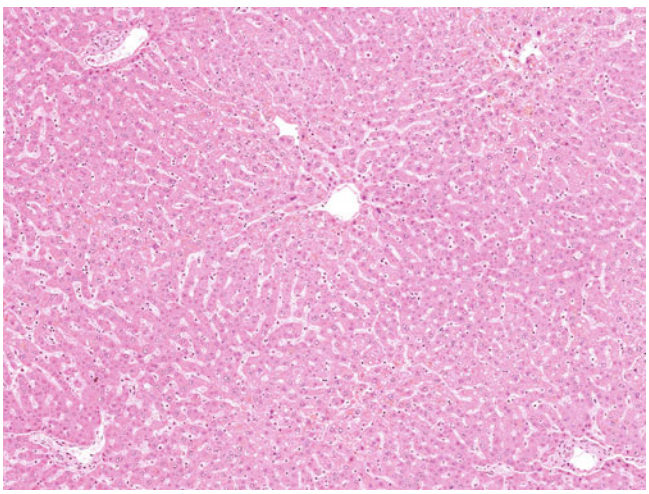

Fig. 1.1 Normal histology; low-power view of normal liver parenchyma. Two terminal hepatic venules (central veins) are located in the centre and at the right-hand side of the image. Three portal tracts also are seen; each one is separated from the others by a similar distance. The overall hepatic architecture is best assessed under low magnification. An even distribution of portal tracts and terminal hepatic venules indicates preserved hepatic architecture. The normal distance between portal tract and terminal hepatic venule is approximately 0.5 mm (0.4–0.75 mm). Distortion of hepatic architecture can be manifest by approximation of the portal tract and terminal hepatic venules (indicating parenchymal collapse), the absence of portal tracts or terminal hepatic venules, or the presence of fibrosis.

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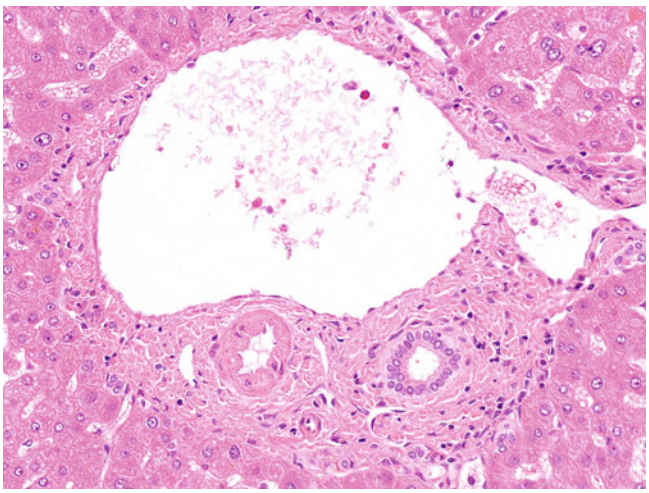

Fig. 1.2 Normal portal tract. A normal portal tract contains a portal venule, a hepatic arteriole, and an interlobular bile duct, which collectively are called a portal triad. A few lymphocytes and macrophages frequently are present in normal portal tracts. Not all portal tracts contain all three components of the portal triad. One recent study demonstrated that 6.2%, 10.2%, and 9.2% of portal tracts do not contain a bile duct, hepatic artery, or portal vein, respectively. The hepatic artery is accompanied by a nearby (within a distance two to three times that of its diameter) interlobular bile duct of similar diameter in >90% of portal tracts. This so-called parallelism of hepatic arteries and bile ducts is the basis of recently proposed criteria for ductopaenia.

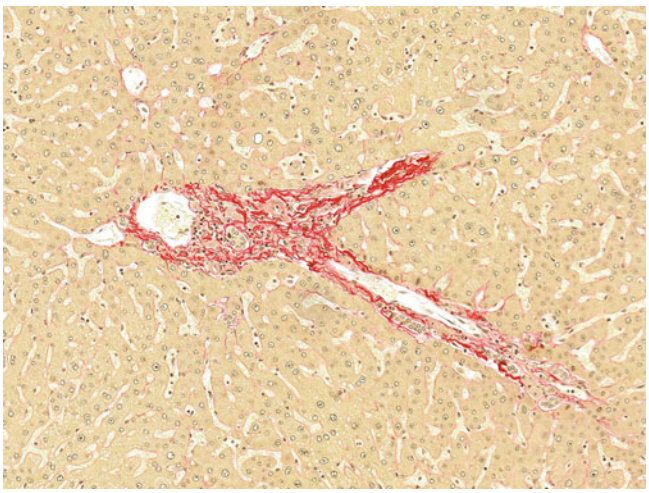

Fig. 1.4 Normal portal tract (picrosirius red stain); normal branching small-sized portal tract. A portal venule and interlobular bile duct are present in the branching connective tissue stroma. One of the pitfalls in assessing fibrosis is misinterpretation of branching or tangentially cut portal tracts as periportal or even bridging fibrosis. Branching or tangentially cut portal tracts can be recognized correctly by the presence of vessels and/or bile ducts travelling along thin fibrous "septa."

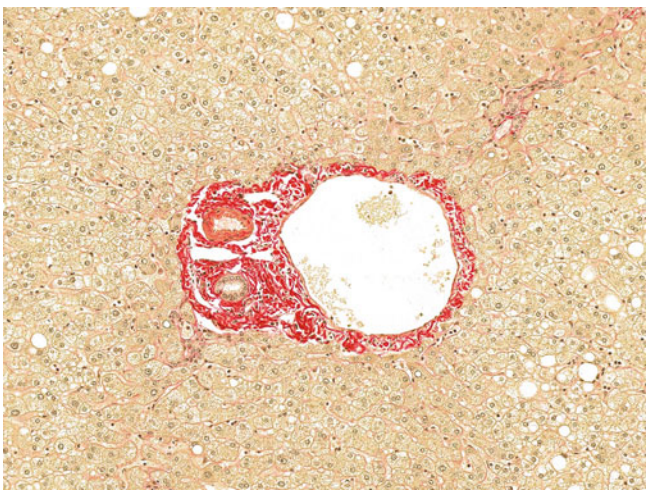

Fig. 1.3 Normal portal tract (picrosirius red stain). A normal medium-sized portal tract contains a portal vein branch, a hepatic arteriole, and an interlobular bile duct. Normal portal tracts contain a certain amount of connective tissue to support their constituent structures. The amount of connective tissue is proportional to the size of the vascular and biliary components and, hence, the size of the portal tract. An appreciation of normal amounts of portal connective tissue is crucial in being able to assess abnormal excessive deposition of connective tissue (i.e., fibrosis). Portal tracts in older people may contain more connective tissue, slightly more lymphocytes and macrophages, and/or hyalinised arterioles.

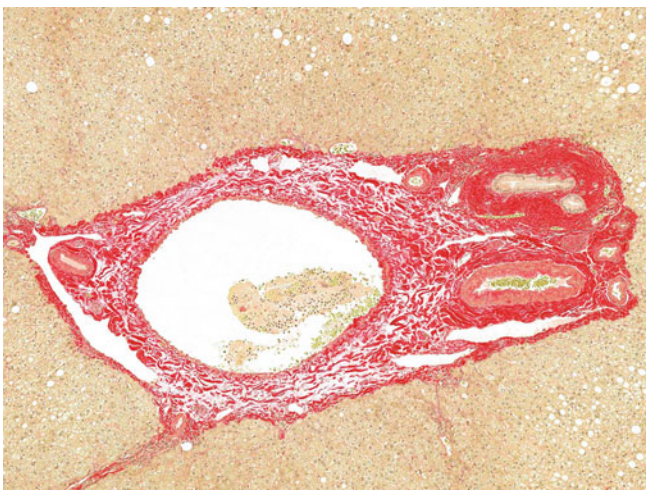

Fig. 1.5 Normal portal tract (picrosirius red stain); normal large-sized portal tract containing a portal vein branch, hepatic artery, and septal bile duct, which are embedded in a normal amount of connective tissue. Another pitfall in the assessment of fibrosis is misinterpretation of normal large-sized portal tracts as portal fibrosis. Identification of larger vessels or septal bile ducts may clarify this potentially misleading appearance. A further problem is that septal bile ducts normally are surrounded by denser connective tissue than are smaller ducts, and this may be mistaken for periductal fibrosis.

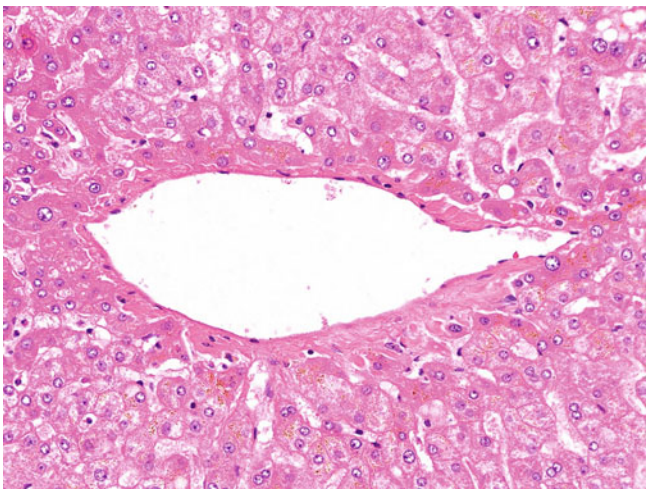

Fig. 1.6 Normal perivenular region. A normal terminal hepatic venule (central vein) is shown. The hepatocytes surrounding the venule contain some golden-yellow fine granular pigment (lipofuscin) in their cytoplasm. Identification of lipofuscin might be useful in the identification of perivenular regions. The distinction between perivenular and periportal areas sometimes may be problematic in small biopsies in which there are ductopaenic conditions (especially chronic allograft rejection in which hepatic arteries may also be lost) and confluent necrosis associated with ductular reaction. Immunostaining for glutamine synthetase, however, serves as a better tool for highlighting perivenular hepatocytes in such conditions.

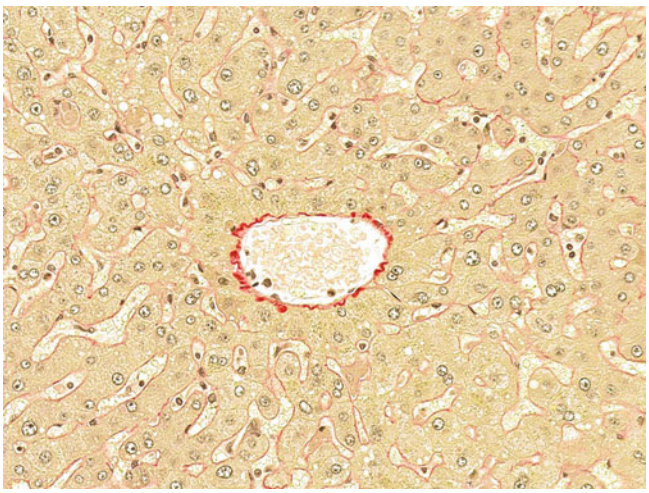

Fig. 1.7 Normal terminal hepatic venule (picrosirius red stain). A normal small-sized terminal hepatic venule is surrounded by a thin rim of connective tissue. Some irregularity of perivenular fibrous tissue is a normal finding and should not be mistaken for perivenular fibrosis. The absence of thick perivenular fibrous tissue and/or pericellular scarring may avoid overestimation of perivenular fibrosis.

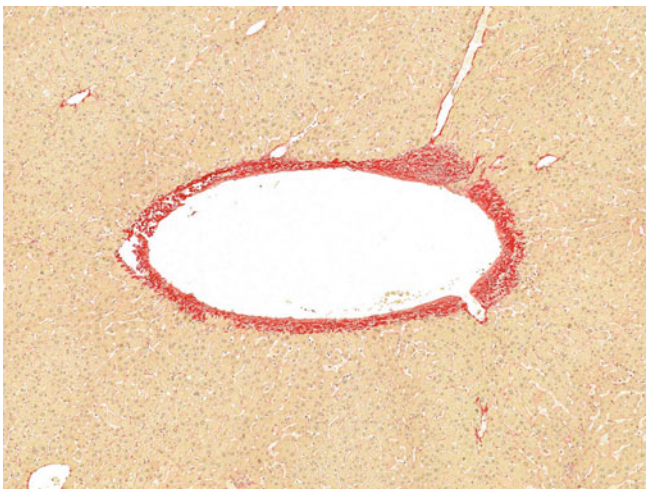

Fig. 1.8 Normal hepatic vein (picrosirius red stain). A normal large-sized hepatic vein is surrounded by a thicker rim of connective tissue. Similar to portal tracts, the amount of connective tissue surrounding the hepatic vein correlates with the size of the vein. A large hepatic vein sometimes may be mistaken for perivenular fibrosis.

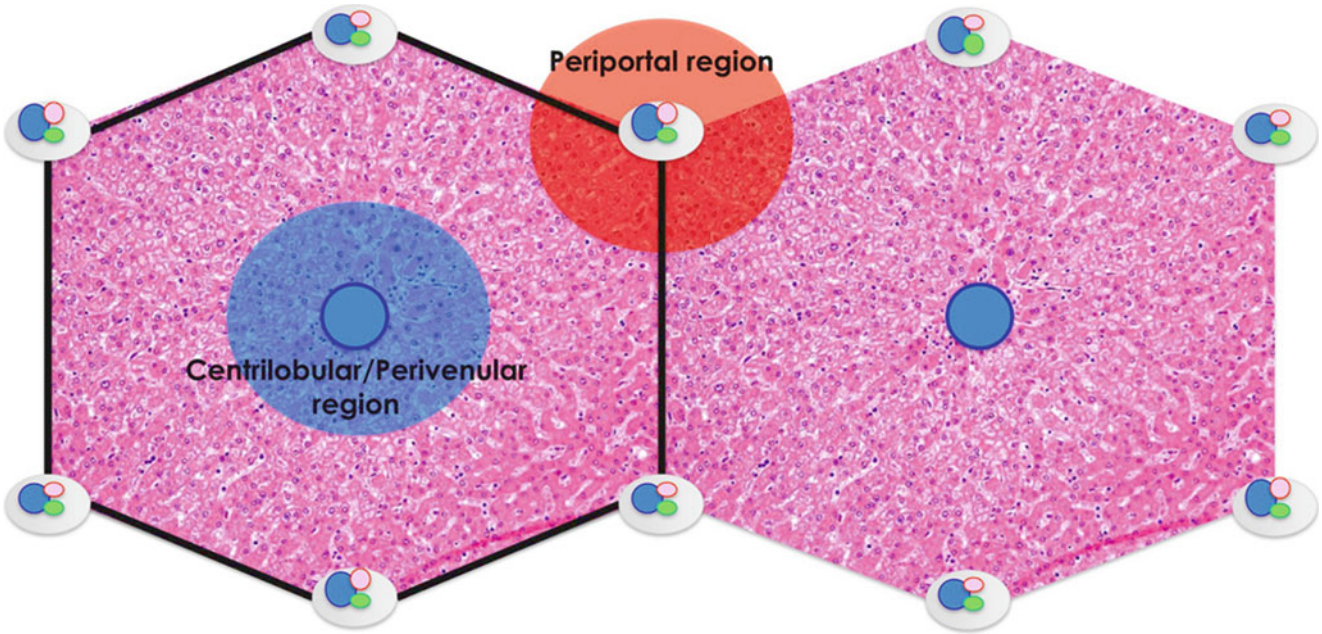

Fig. 1.9 Classic lobular architecture. The classic lobule was described by Kiernan in 1833. A hepatic lobule is a roughly hexagonal structure containing a central vein (terminal hepatic venule) at its core with plates of hepatocytes radiating centrifugally towards portal tracts (three to six) at the corners. The lobule is divided into three regions: a centrilobular/perivenular region around the central vein, a periportal region around the portal tract, and a midlobular region situated in between. This concept is easy to understand, and the microanatomy of the liver is easy to appreciate under the microscope. It still is very common for pathologists to use the terminology of this lobular concept to describe the distribution of pathologic changes.

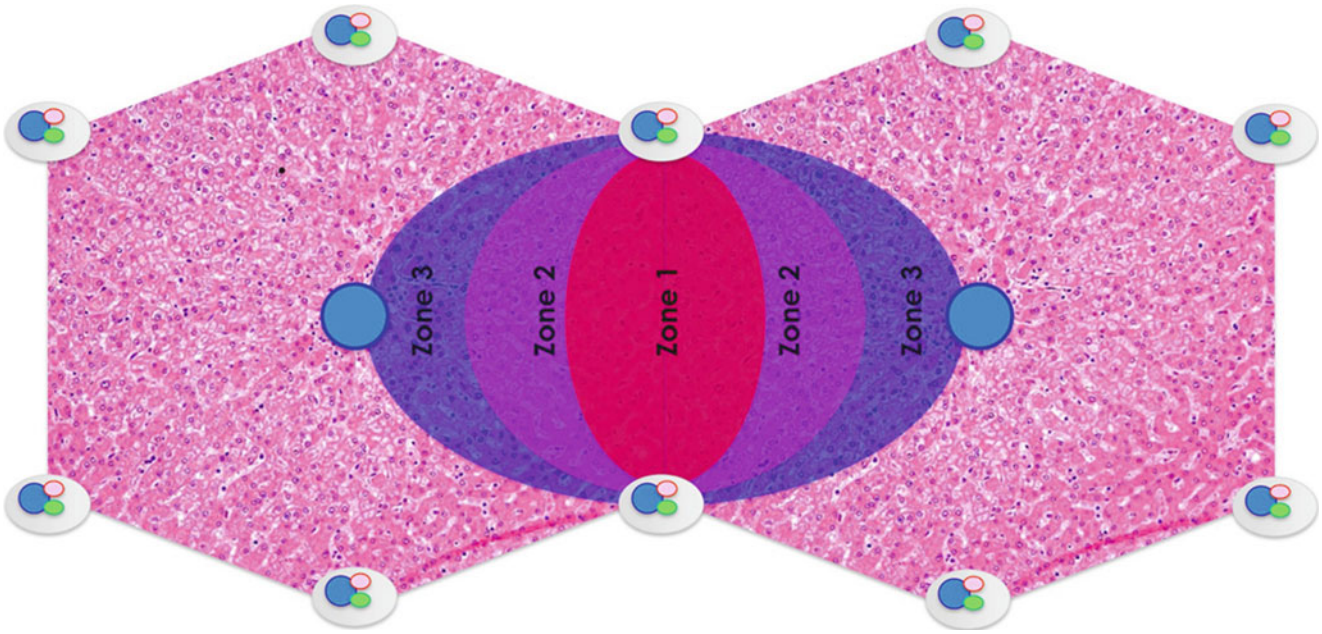

Fig. 1.10 Rappaport acinar architecture. The acinar structure was proposed by Rappaport in 1954. A simple acinus is a berry-shaped structure with a central axis formed by the terminal branches of a portal venule, a hepatic arteriole, and an interlobular bile duct. Blood from the terminal branches of portal venules and hepatic arterioles drains through the hepatic sinusoids into several terminal hepatic venules at the periphery of the acinus. The acinus is divided into three zones (zones 1, 2, and 3) according to the proximity to the terminal branches of vessels. The three zones differ in their tissue oxygenation, metabolic activity, and enzyme distribution. The acinar concept explains the zonal predilection of certain liver injuries. Portal–central and portal–portal bridging necrosis/fibrosis can be better appreciated as extensive zone 3 and zone 1 necrosis/fibrosis, respectively.