

# SHERLOCK'S DISEASES OF THE LIVER AND BILIARY SYSTEM

12TH  
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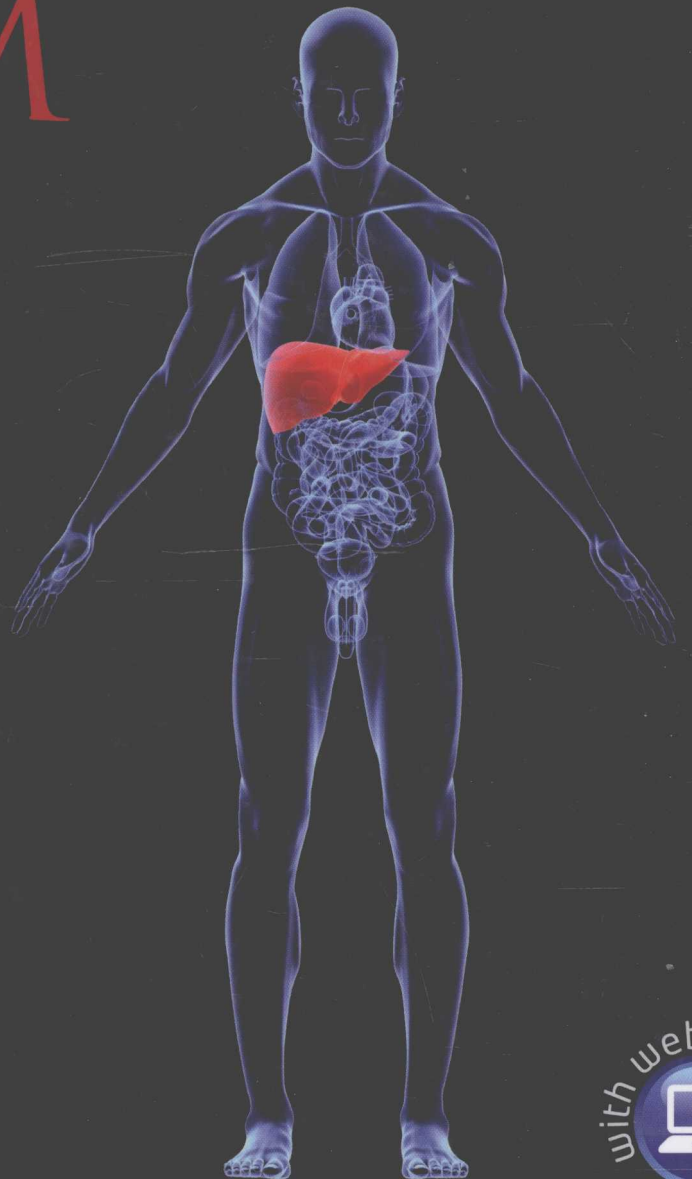
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 WILEY-BLACKWELL



# Sherlock's Diseases of the Liver and Biliary System

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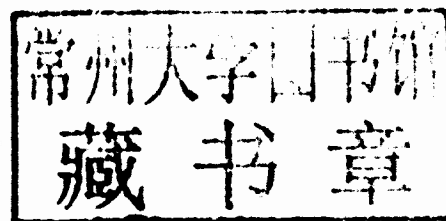
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# Preface to the Twelfth Edition

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The 11<sup>th</sup> edition marked the end of an era. Professor Dame Sheila Sherlock died in December 2001, having a month before seen and enjoyed an advanced copy of her latest textbook. Her journey in Hepatology began in the 1940s, and she was instrumental in its development and recognition as a major specialty. In 1955 she published the first edition of what was to become a classic textbook. Single handed she updated the script on a regular basis and it became an influential instrument for the development of Hepatology. There were many translations of the editions over subsequent 50 years. Recognising the growth and complexity of the subject, she involved a co-author from 1993. Many attribute their career in liver disease to reading and enjoying her approach to Hepatology through her book.

The question of a 12<sup>th</sup> edition was raised on several occasions over the subsequent years. Although some wondered whether it should cease with her passing, many others constantly asked when the next edition would be—a reflection of the special content, presentation and readability—an accessible source to relevant information for student to specialist physician.

Continuing a two author book was not thought practicable. The growth of Hepatology as a speciality demanded a greater pool of expertise, in viral, immune and genetic diseases, as well as the management of the complications of acute and chronic liver disease, and of course, liver transplantation.

Dame Sheila always promoted the internationalism of Hepatology and therefore it was a short step to draw together editors and contributors from the UK, Europe and North America. The challenge—apart from updating the previous edition with pertinent data—was to keep the ethos of the book. The style of English, the lay out of text and the clarity of figures and tables were hallmarks. With this in mind contributors were approached with expertise in particular areas; most had trained or worked with Dame Sheila. It is a tribute to her influence that the resultant text comes from such an international community, many of whom had close links with her.

Apart from updating the previous chapters, there have been other changes. New chapters have been com-

missioned including those on fibrogenesis, non alcoholic fatty liver disease, HIV and the liver, and transplantation in patients with hepatitis B, C or HIV infection. Some previous chapters, which have stood the test of time on their own, have been removed or combined with others. Thus Budd Chiari syndrome joins the portal hypertension chapter, and biliary imaging that on gallstones and benign bile duct diseases.

The 12<sup>th</sup> edition contains more than 2240 new references and over 130 new figures. Each chapter begins with learning points. The previous artwork has been reformatted, alongside the new figures and tables. As before the book is intended for a wide readership across students, trainees, general and specialist physicians.

We are most grateful to the production team at Wiley Blackwell, in particular Rebecca Huxley (whose 3rd edition this is). Anne Bassett and Annette Abel have enthusiastically taken on the challenge of collecting manuscripts and proofs and chasing the large number of contributors, working beyond the call of duty to produce the book rapidly. We are grateful to Jane Fallows for the new artwork and reworking of the old. As before the publishers have allowed the latest important publications to be included at the proofing stage.

We dedicate this edition to the memory of Sheila Sherlock and to Geraint James, her husband of 50 years who died in October 2010. He knew of the development of the new edition and took pleasure in its anticipation. We hope that their two daughters, Amanda and Auriole, always referenced in previous prefaces with their life stories, will take pleasure from seeing the legacy of their mother's exceptional life preserved in this textbook.

The science and practice of Hepatology continue to move on at breathtaking speed. This progress is reflected in the 12<sup>th</sup> edition of *Sherlock's Diseases of the Liver and Biliary System*, in a manner which we hope will continue to enthuse its readers.

James S. Dooley  
Anna S.F. Lok  
Andrew K. Burroughs  
E. Jenny Heathcote  
March 2011

# Preface to the First Edition

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My aim in writing this book has been to present a comprehensive and up-to-date account of diseases of the liver and biliary system, which I hope will be of value to physicians, surgeons and pathologists and also a reference book for the clinical student. The modern literature has been reviewed with special reference to articles of general interest. Many older more specialized classical contributions have therefore inevitably been excluded.

Disorders of the liver and biliary system may be classified under the traditional concept of individual diseases. Alternatively, as I have endeavoured in this book, they may be described by the functional and morphological changes which they produce. In the clinical management of a patient with liver disease, it is important to assess the degree of disturbance of four functional and morphological components of the liver—hepatic cells, vascular system (portal vein, hepatic artery and hepatic veins), bile ducts and reticulo-endothelial system. The typical reaction pattern is thus sought and recognized before attempting to diagnose the causative insult. Clinical and laboratory methods of assessing each of these components are therefore considered early in the book. Descriptions of individual diseases follow as illustrative examples. It will be seen that the features of hepatocellular failure and portal hypertension are described in general terms as a foundation for subsequent discussion of virus hepatitis, nutrition liver disease and the cirrhoses. Similarly blood diseases and infections of the liver are included with the reticulo-endothelial system, and disorders of the biliary tract follow descriptions of acute and chronic bile duct obstruction.

I would like to acknowledge my indebtedness to my teachers, the late Professor J. Henry Dible, the late Professor Sir James Learmonth and Professor Sir John McMichael, who stimulated my interest in hepatic disease, and to my colleagues at the Postgraduate Medical School and elsewhere who have generously invited me to see patients under their care. I am grateful to Dr A. G. Bearn for criticizing part of the typescript and to Dr A. Paton for his criticisms and careful proof reading. Miss D. F. Atkins gave much assistance with proof reading and with the bibliography. Mr Per

Saugman and Mrs J. M. Green of Blackwell Scientific Publications have co-operated enthusiastically in the production of this book.

The photomicrographs were taken by Mr E. V. Willmott, FRPS, and Mr C. A. P. Graham from section prepared by Mr J. G. Griffin and the histology staff of the Postgraduate Medical School. Clinical photographs are the work of Mr C. R. Brecknell and his assistants. The black and white drawings were made by Mrs H. M. G. Wilson and Mr D. Simmonds. I am indebted to them all for their patience and skill.

The text includes part of unpublished material included in a thesis submitted in 1944 to the University of Edinburgh for the degree of MD, and part of an essay awarded the Buckston-Browne prize of the Harveian Society of London in 1953. Colleagues have allowed me to include published work of which they are jointly responsible. Dr Patricia P. Franklyn and Dr R. E. Steiner have kindly loaned me radiographs. Many authors have given me permission to reproduce illustrations and detailed acknowledgments are given in the text. I wish also to thank the editors of the following journals for permission to include illustrations: *American Journal of Medicine*, *Archives of Pathology*, *British Heart Journal*, *Circulation*, *Clinical Science*, *Edinburgh Medical Journal*, *Journal of Clinical Investigation*, *Journal of Laboratory and Clinical Investigation*, *Journal of Pathology and Bacteriology*, *Lancet*, *Postgraduate Medical Journal*, *Proceedings of the Staff Meetings of the Mayo Clinic*, *Quarterly Journal of Medicine*, *Thorax* and also the following publishers: Butterworth's Medical Publications, J. & A. Churchill Ltd, The Josiah Macy Junior Foundation and G. D. Searle & Co.

Finally I must thank my husband, Dr D. Geraint James, who, at considerable personal inconvenience, encouraged me to undertake the writing of this book and also criticized and rewrote most of it. He will not allow me to dedicate it to him.

SHEILA SHERLOCK

1955

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with:

- All 700 figures and captions in the book as Powerpoints for downloading

# CHAPTER 1

## Anatomy and Function

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### Learning points

- The liver is derived from a foregut endodermal bud which develops in the third week of gestation and divides into two parts: hepatic and biliary.
- The Couinaud classification subdivides the liver into eight segments (segments I–IV in the left lobe, segments V–VIII in the right lobe) based on vascular and biliary anatomical landmarks.
- The lobule described by Kiernan is the most widely used unit of liver microanatomy, consisting of a hexagon-like region of liver parenchyma with a central vein as its hub and portal tracts located in the periphery of the hexagon.
- Hepatocytes are functionally heterogeneous within the lobular parenchyma, whereby centrilobular cells subserve different functions (e.g. drug metabolism) from periportal cells (e.g. bile salt-dependent bile formation).
- Uncomplicated regeneration of hepatocytes and/or bile duct epithelium usually occurs by cell division of the indigenous cells; however, when normal regenerative capacity is overwhelmed there may be activation of progenitors cells located in the region of the canals of Hering.

### Development of the liver and bile ducts

The liver begins as a hollow endodermal bud from the foregut (duodenum) during the third week of gestation. The bud separates into two parts—hepatic and biliary. The *hepatic* part contains bipotential progenitor cells that differentiate into hepatocytes or ductal cells, which form the early primitive bile duct structures (bile duct plates). Differentiation is accompanied by changes in cytokeratin type within the cell [1]. Normally, this collection of rapidly proliferating cells penetrates adjacent mesodermal tissue (the septum transversum) and is met by ingrowing capillary plexuses from the vitelline and umbilical veins, which will form the sinusoids. The connection between this proliferating mass of cells and the

foregut, the *biliary* part of the endodermal bud, will form the gallbladder and extrahepatic bile ducts. Bile begins to flow at about the 12th week. Connective tissue cells of portal tracts are derived from the mesoderm of the septum transversum. Kupffer cells derive from circulating monocytes and possibly yolk sac macrophages. Hepatic stellate cells appear to be mesodermal derivatives from submesothelial cells located beneath the surface of the developing liver [2]. The fetal liver is the main site of haemopoiesis by the 12th week; this subsides in the fifth month coincident with the onset of bone marrow haemopoietic activity, so that only a few haemopoietic cells remain at birth.

### Anatomy of the liver

The liver, the largest organ in the body, weighs 1200–1500 g and comprises one-fiftieth of the total adult body weight. It is relatively larger in infancy, comprising one-eighteenth of the birth weight. This is mainly due to a large left lobe.

Sheltered by the ribs in the right upper quadrant, the upper border lies approximately at the level of the nipples. There are two anatomical lobes, the right being about six times the size of the left (Figs 1.1–1.3). Lesser segments of the right lobe are the *caudate lobe* on the posterior surface and the *quadrate lobe* on the inferior surface. The right and left lobes are separated anteriorly by a fold of peritoneum called the falciform ligament, posteriorly by the fissure for the ligamentum venosum and inferiorly by the fissure for the ligamentum teres.

The liver has a double blood supply. The *portal vein* brings venous blood from the intestines and spleen and the *hepatic artery*, coming from the coeliac axis, supplies the liver with arterial blood. These vessels enter the liver through a fissure, the *porta hepatis*, which lies far back on the inferior surface of the right lobe. Inside the porta, the portal vein and hepatic artery divide into branches to the right and left lobes, and the right and left hepatic



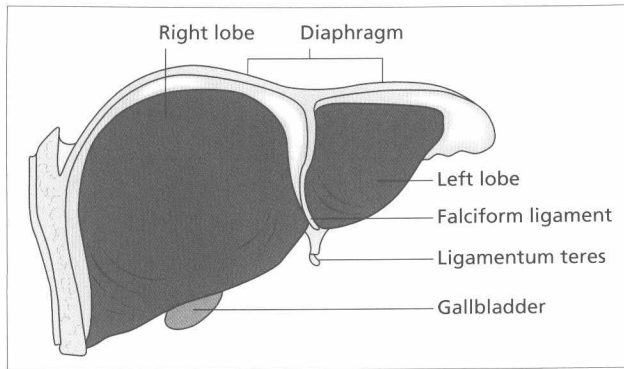


Fig. 1.1. Anterior view of the liver.

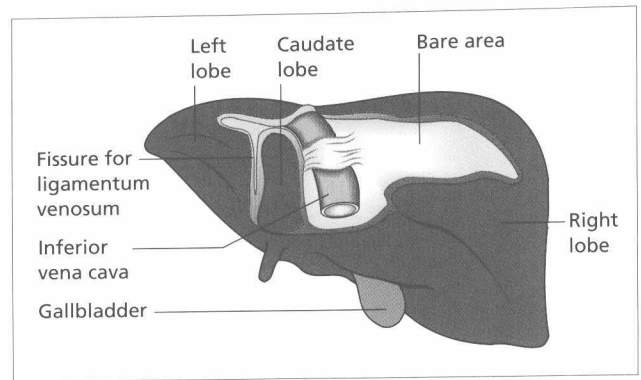


Fig. 1.2. Posterior view of the liver.

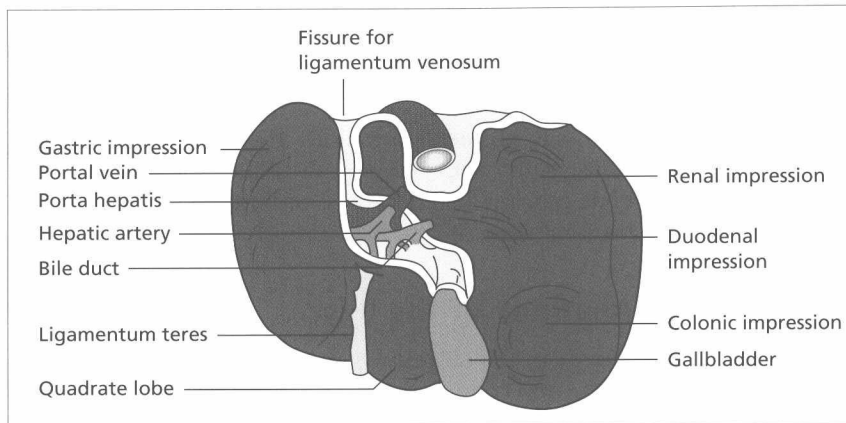


Fig. 1.3. Inferior view of the liver.

bile ducts join to form the common hepatic duct. The *hepatic nerve plexus* contains fibres from the sympathetic ganglia T7–T10, which synapse in the coeliac plexus, the right and left vagi and the right phrenic nerve. It accompanies the hepatic artery and bile ducts into their finest ramifications, even to the portal tracts and hepatic parenchyma [3].

The *ligamentum venosum*, a slender remnant of the ductus venosus of the fetus, arises from the left branch of the portal vein and fuses with the inferior vena cava at the entrance of the left hepatic vein. The *ligamentum teres*, a remnant of the umbilical vein of the fetus, runs in the free edge of the falciform ligament from the umbilicus to the inferior border of the liver and joins the left branch of the portal vein. Small veins accompanying it connect the portal vein with veins around the umbilicus. These become prominent when the portal venous system is obstructed inside the liver.

The venous drainage from the liver is into the *right and left hepatic veins* which emerge from the back of the liver and at once enter the inferior vena cava very near its point of entry into the right atrium.

*Lymphatic vessels* terminate in small groups of glands around the porta hepatis. Efferent vessels drain into glands around the coeliac axis. Some superficial hepatic lymphatics pass through the diaphragm in the falciform ligament and finally reach the mediastinal glands. Another group accompanies the inferior vena cava into the thorax and ends in a few small glands around the intrathoracic portion of the inferior vena cava.

The *inferior vena cava* makes a deep groove to the right of the caudate lobe about 2 cm from the midline.

The *gallbladder* lies in a fossa extending from the inferior border of the liver to the right end of the porta hepatis.

The liver is completely covered with peritoneum, except in three places. It comes into direct contact with the diaphragm through the bare area which lies to the right of the fossa for the inferior vena cava. The other areas without peritoneal covering are the fossae for the inferior vena cava and gallbladder.

The liver is kept in position by peritoneal ligaments and by the intra-abdominal pressure transmitted by the tone of the muscles of the abdominal wall.