Diseases of the Liver and Biliary System

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Preface to the Eleventh Edition

The eleventh edition welcomes the new Millenium. Progress in basic and clinical hepatology remains exponential. Since 1997, the advances have been wide-ranging, with those in molecular and cellular biology, and in diagnosis and treatment, leading the way. In a world in which information technology gives all too ready access to individual publications, the eleventh edition sets the new within established knowledge and practice.

Viral hepatitis remains the worldwide hepatological challenge. This is reflected in a change in format with separate chapters on hepatitis B and C. Molecular virology continues to expose the inner workings of all the viruses. New therapeutic approaches are proving more effective against hepatitis C. Molecular and cellular biologists are showing us the importance of apoptosis and the intricate regulation of fibrosis. Mutation analysis for diagnosis of genetic haemochromatosis is routine, while the identification of the haemochromatosis gene has led to a surge of exploration in iron metabolism. Canalicular transporters have been cloned and linked to cholestatic syndromes, giving a new perspective to the bile plug seen under the microscope. Advances in imaging, particularly magnetic resonance, continue to reduce the need for invasive techniques. Patients needing transplantation benefit from improvements in immunosuppression and surgical techniques, while there is steady progress in the management of complications of cirrhosis.

This edition contains more than 1000 new references and 100 new figures. Developments in publishing allow a more colourful format, but care has been taken to preserve clarity. Experience has shown that students, interns, postgraduate trainees as well as generalists and specialist clinicians have found previous editions useful. The goal of the book remains unchanged: a textbook of manageable size, critical and current.

We are indebted to many colleagues for their generous contributions to this edition including in particular Professor Peter Scheuer, Professor Amar Dhillon and Dr Susan Davies for histological material, and Dr Robert Dick, Dr Tony Watkinson and Dr Jon Tibballs for radiological images. We would also like to express our great thanks to Dr Leslie Berger, Dr Andrew Burroughs, Dr John Buscombe, Dr Martyn Caplin, Professor Geoffrey Dusheiko, Dr David Harry, Dr Andrew Hilson, Professor Humphrey Hodgson, Professor Neil McIntyre, Dr Kevin Moore, Dr Marsha Morgan, Dr Chris Kibbler and Dr David Patch for their help in the preparation of this edition.

Miss Aileen Duggan and Miss Karma Raines have assisted tirelessly with their meticulous secretarial support. The clarity and style of figures preserved from previous editions owes much to the artistry of Miss Janice Cox over many years.

We are grateful to Blackwell Publishing and, in particular, Rebecca Huxley for her tireless help with both manuscript and proofs, and for responding without a murmur to demands within a tight schedule. We also thank Jane Fallows who has reformatted and coloured all the previous line drawings as well as creating the many new and visually inviting figures for the eleventh edition.

The preface to the first edition which was published in 1955 refers to daughters Amanda and Auriole. Amanda is now an ordained Minister in the Baptist Church, and Auriole is working with Kent Police. Grandchildren have arrived, including Alice aged 9 and Emily aged 6.

On the 13th July 2001, the senior author was elected a Fellow of the Royal Society in its 341st year, a Society founded to improve natural knowledge. This honour was achieved because of the support of all the clinicians and scientists who have contributed to the Liver Unit and its associated departments at The Royal Free. The new Millenium is indeed an exciting time for all those working to solve the puzzles within hepato-biliary disease.

SHEILA SHERLOCK
JAMES DOOLEY
November 2001

Preface to the First Edition

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

Chapter 1
Anatomy and Function

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 bile ducts join to form the common hepatic duct. The *hepatic nerve plexus* contains fibres from the sympathetic ganglia

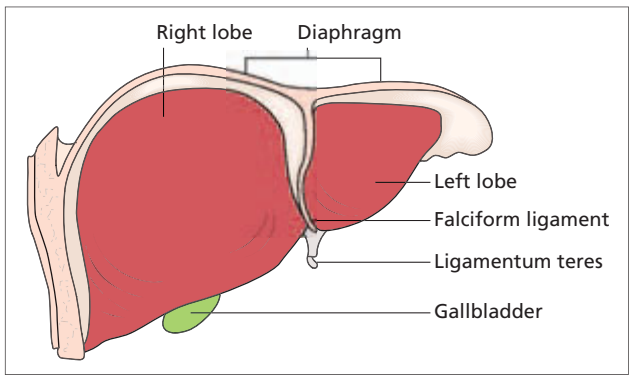

Fig. 1.1. Anterior view of the liver.

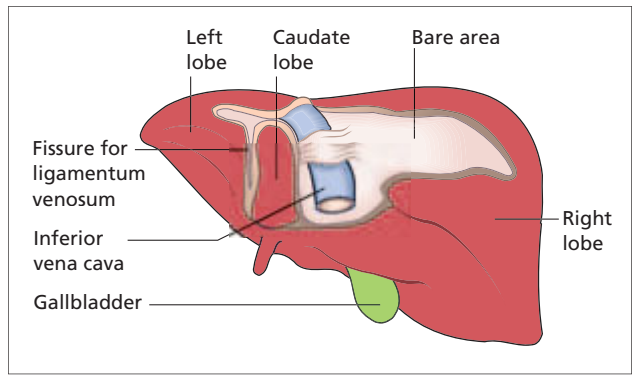

Fig. 1.2. Posterior view of the liver.

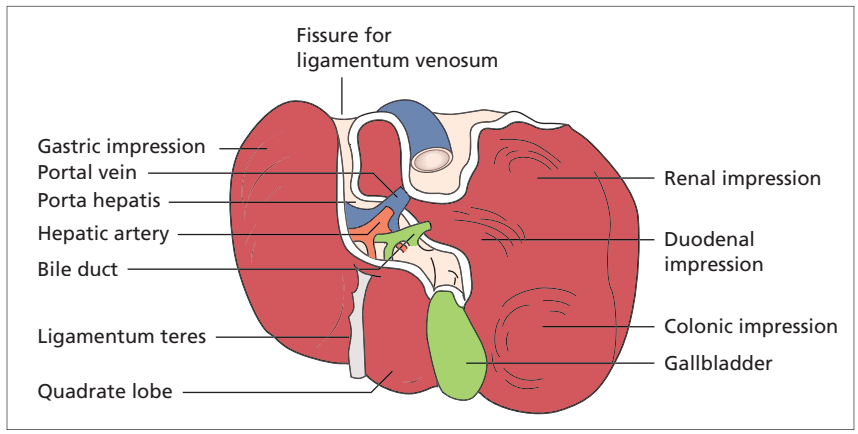

Fig. 1.3. Inferior view of the liver.

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 [4].

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 mid-line.

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.

Functional anatomy: sectors and segments

Based on the external appearances described above, the liver has a right and left lobe separated along the line of insertion of the falciform ligament. This separation, however, does not correlate with blood supply or biliary drainage. A *functional anatomy* is now recognized based upon studies of vascular and biliary casts made by injecting vinyl into the vessels and bile ducts. This classification correlates with that seen by imaging techniques.

The main portal vein divides into right and left branches and each of these supplies two further subunits (variously called sectors). The sectors on the right side are anterior and posterior and, in the left lobe, medial and lateral—giving a total of four sectors (fig. 1.4). Using this definition, the right and left side of the liver are divided not along the line of the falciform ligament, but along a slightly oblique line to the right of this, drawn from the inferior vena cava above to the gallbladder bed below. The right and left side are independent with regard to portal and arterial blood supply, and bile drainage. Three plains separate the four sectors and contain the three major hepatic vein branches.

Closer analysis of these four hepatic sectors produces a further subdivision into segments (fig. 1.5). The right anterior sector contains segments V and VIII; right posterior sector, VI and VII; left medial sector, IV; left lateral sector, segments II and III. There is no vascular anastomosis between the macroscopic vessels of the segments but communications exist at sinusoidal level. Segment I, the equivalent of the caudate lobe, is separate from the other segments and does not derive blood directly from the major portal branches or drain by any of the three major hepatic veins.

This functional anatomical classification allows interpretation of radiological data and is of importance to the

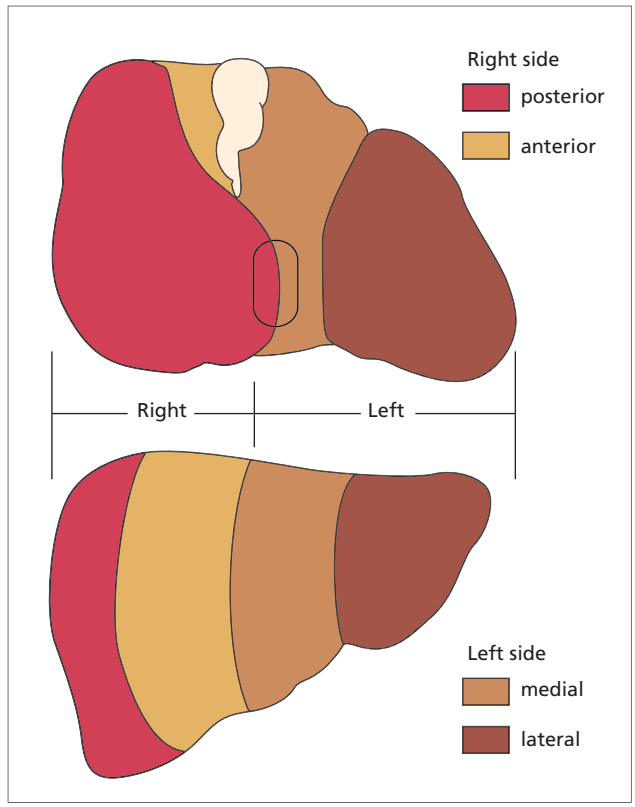

Fig. 1.4. The sectors of the human liver.