Pathology of the Gallbladder

DAVID WEEDON, M.D., F.R.C.P.A.

Pathology of the Gallbladder

DAVID WEEDON, M.D., F.R.C.P.A.

Professor of Clinical Anatomical Pathology,
University of Queensland

and

The Princess Alexandra Hospital
Brisbane, Australia

MASSON Publishing USA, Inc.
New York • Paris • Barcelona • Milan • Mexico City • Rio de Janeiro

Library of Congress Cataloging in Publication Data

Weedon, David.
Pathology of the gallbladder.

(Masson monographs in diagnostic pathology; 8)
Bibliography: p.
Includes index.
1. Gall-bladder—Diseases—Diagnosis. 2. Histology, Pathological. I. Title. II. Series. [DNLM: 1. Gall-bladder diseases—Pathology. W1 MA9309S v.8 / WI 750 W394p]
RC849.W35 1984 616.3'6507 84-3873
ISBN 0-89352-219-8

ISBN 0-89352-219-8

Library of Congress Catalog Card Number: 84-3873

Printed in the United States of America

Masson Monographs in Diagnostic Pathology

Series Editor: **Stephen S. Sternberg, M.D.**

1. *Tumors and Proliferation of Adipose Tissue: A Clinicopathologic Approach*

By Philip W. Allen (1981)

2. *Diagnostic Immunohistochemistry*

Edited by Ronald A. DeLellis (1981)

3. *Diagnostic Transmission Electron Microscopy of Human Tumors*

By Robert A. Erlandson (1981)

4. *Meningiomas: Biology, Pathology, and Differential Diagnosis*

By John J. Kepes (1982)

5. *Pathology and Clinical Features of Parasitic Diseases*

By Tsieh Sun (1982)

6. *Pathology of Radiation Injury*

By Luis F. Fajardo (1982)

7. *Advances in Immunohistochemistry*

Edited by Ronald A. DeLellis (1984)

8. *Pathology of the Gallbladder*

By David Weedon (1984)

9. *The Pathology of Bone Marrow Transplantation*

Edited by George E. Sale and Howard M. Shulman (1984)

Preface

Now that tissue audits are commonplace in many parts of the world, gallbladders are being forwarded in increasing numbers for histopathologic examination. While the majority can usually be signed out as variants of cholecystitis, or sometimes cholesterolosis, there is much more to gallbladder pathology than these two diagnoses. Previous books about the gallbladder have usually focused on clinical, surgical, or radiologic aspects without specific emphasis on the pathology. The majority of journal articles discussing diseases of this organ are to be found in the surgical literature. As a result, they are not usually perused by the busy surgical pathologist.

This monograph is designed as a reference book for pathologists and other physicians interested in gallbladder pathology. It contains descriptions of the pathology of rare and unusual lesions as well as the more common disease processes. To keep the references in this monograph as current as possible, articles that have become available after the completion of a particular section have been inserted into the text in such a way as to avoid renumbering of the other references which would cause delay in publication.

I am grateful to my many colleagues who have shared their interesting cases with me. To my secretary, Mrs. Pat Forbes, and the departmental secretary, Ms. Shirley Sargeant, I offer my sincerest thanks for typing and checking the manuscript. The assistance of Ms. Glenda Gobé in preparing the photographs is also gratefully acknowledged.

DAVID WEEDON

Contents

CHAPTER 1

The Normal Gallbladder

ANATOMY

The gallbladder is a pear-shaped hollow sac closely attached to the liver and covered to a variable extent by peritoneum reflected off the liver. It measures approximately 10 cm in length and 4 cm in width. The gallbladder has a capacity of about 50 ml but as a result of the compliance of the wall, this may increase at times to 100 ml or more.[1] Volume changes in response to the infusion of cholecystokinin have recently been reported.[2] Ultrasound examination has been used to document the dimensions of the normal gallbladder in the growing child.[3] Variations in the size, shape, position and morphology of the gallbladder are considered in Chapter 2.

The gallbladder consists of a blindly-ending fundus, a body, and a neck which leads into the cystic duct. Hartmann's pouch, a dilatation in the region of the neck of the gallbladder, is considered to be a pathologic change and not a normal anatomic variation.[4] The mucosa of the cystic duct, near its junction with the neck of the gallbladder, is thrown into folds which project into the lumen, constituting the spiral valves of Heister. These appear to act as splints preventing unusual distention or collapse of the cystic duct, thus enabling the free flow of bile to occur when the duct is subjected to sudden changes of pressure.[5]

The wall of the gallbladder has several layers.[5] The *mucosa* is thrown into numerous folds although these are much less prominent in the distended gallbladder. The mucosa is lined by tall columnar cells which have an oval nucleus towards the base of the cell. On electron microscopy four cell types have been recognized in the surface epithelium.[6] These include: 1) ordinary epithelial cells, as already described; 2) pencil-shaped cells which are rare cells found mainly in the body of the gallbladder.[6] They have a much darker cytoplasm on electron microscopy as a result of the abundant organelles. There is controversy surrounding their function; 3) cask-shaped cells which may also be seen by light microscopy. These are also rare cells; and 4) small basal cells which are in contact with the basement membrane. On electron microscopy, the ordinary columnar cells are noted to have a microvillous border which varies in height and density. They also have a prominent Golgi apparatus and a variety of granules and discrete vesicles in the cytoplasm.[6] In addition, there is stratification of the organelles. Beneath the epithelial basement membrane is the lamina propria, composed of loose connective tissue and containing small blood vessels and lymphatics. Small tubuloalveolar glands may be found in the lamina propria and occasionally the adventitia in the region of the neck of the gallbladder (Fig. 1.1), but they are not a normal constituent when found elsewhere in the mucosa of the gallbladder. Ultrastructurally, the normal glands of the neck region differ from the metaplastic antral-type glands found in the body and fundus of many chronically inflamed gallbladders.[7] Outpouchings of the mucosa, the Rokitansky-Aschoff sinuses are acquired structures and will be considered further in Chapter 22.

The gallbladder has no muscularis mucosae, with the result that the lamina propria abuts directly onto the *muscular layer*. This consists of bundles of smooth muscle arranged in various planes, admixed with a small amount of collagen, reticulin, and elastic fibers. The thickness of the muscular layer varies somewhat in different parts of the gallbladder.

Beyond the muscular layer is the *perimuscular connective tissue layer*, sometimes called the adventitia or subserosa. This layer surrounds the

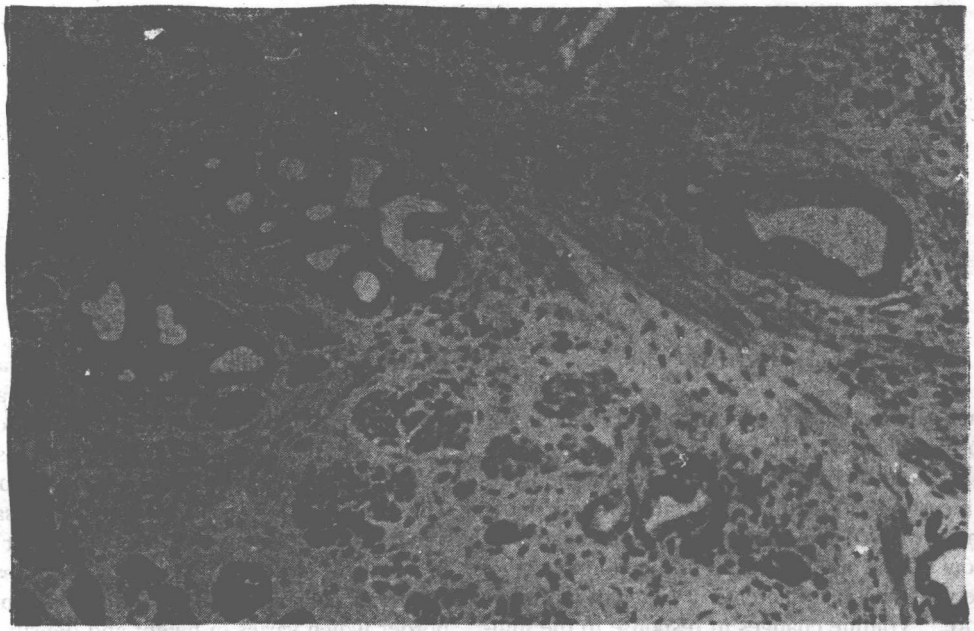

Figure 1.1 Gallbladder neck showing mucous glands in the wall.

gallbladder and is composed of loosely arranged collagen and elastic tissue with variable amounts of fat.[5] Blood vessels, nerves, and lymphatics are also present, as well as a few macrophages and scattered lymphocytes. That part of the gallbladder not attached to the liver, usually about 60% of the surface area, is covered with peritoneum. The connective tissue of the adventitia on the side in contact with the liver is in places continuous with the interlobular connective tissue of the liver.[5] Small ducts resembling hepatic bile ducts are sometimes found in this region of the adventitia (Fig. 1.2). These Luschka's ducts occur singly or in groups and are surrounded by concentrically arranged connective tissue.[8] These ducts can open into the liver, but no definite communication with the lumen of the gallbladder has been demonstrated in most studies.[8] However, Beilby examined serial sections in one case and found a communication between a Luschka's duct and the lumen of the gallbladder in the region of the neck.[9] They form an anastamosing system of ducts which frequently run beside blood vessels. Luschka's ducts are assumed to be the consequence of disturbed embryogenesis, although their exact function is uncertain.[8]

The *cystic duct* is variable in its length, course, and site of termination. Its anatomical length averages 2.5 cm, but because of its tortuous course its surgical length is approximately 1.5 cm.[10] Its length will depend on the method of its termination.[4] In nearly 70% of cases, the cystic and common hepatic ducts unite at an acute angle to form the common duct. In about 25%, the cystic and hepatic ducts run a parallel course for a variable distance of 1–7 cm before joining. They may be lightly adherent by connective tissue or more firmly fused, sharing a seromuscular coat before they join. In a small percentage of cases, the cystic duct does not enter on the right side of the common hepatic duct but spirals over or under the duct to reach its posterior or left side.[4] The cystic duct consists in the main of fibrous tissue and scanty elastic fibers and is devoid of smooth muscle.[9]

The *common duct* is formed by the union of the common hepatic and cystic ducts. Its length depends on the type of cystic duct entry, but averages 5–8 cm in length. The diameter of its lumen measures up to 10 or 12 mm. The duct passes behind the first part of the duodenum and the pancreas, usually lying in a deep groove on the posterior aspect of the pancreas, although it may be entirely extrapancreatic.[4] The lumen,

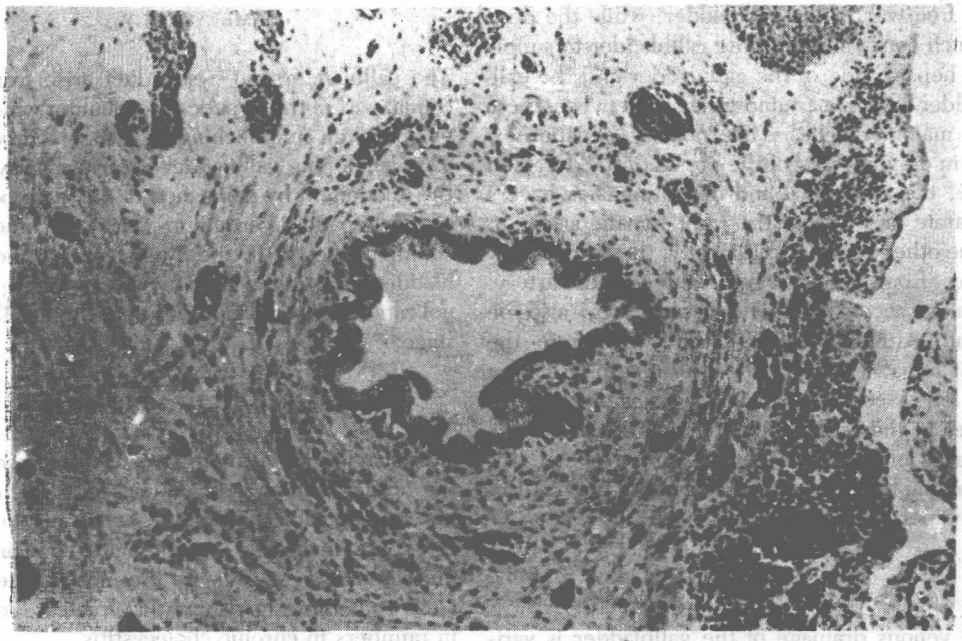

Figure 1.2 Luschka's duct in the adventitia. Note the concentric fibrosis surrounding it.

on radiologic examination, tapers just before it enters the duodenal wall. This apparently results from thickening of the wall of the lower segment of the duct due to the addition of muscle fibers. The pancreatic duct approaches the common duct at about this level and both share a muscular and connective tissue sheath as they pass obliquely through the wall of the posteromedial side of the second part of the duodenum.[4] With use of operative cholangiography, it was noted in one report that the common duct terminated at an anomalous site in the duodenum in 23% of the 120 patients who were undergoing radiologic investigations for suspected biliary tract disease.[11] In about 60–80% of cases,[4,10] the lumina of the common and pancreatic ducts fuse in the submucosa of the duodenum to form a common channel which opens into the duodenum at the papilla of Vater. Because of the arrangement of the sphincter, a physiologic common channel, as distinct from an anatomic one, is thought to occur in a small percentage of cases only. Separate terminal openings of these ducts occur in about 15–25% of cases. In the remaining small number of cases, the duct of Wirsung is not patent and the pancreatic drainage passes through the duct of Santorini.[4] Excellent reviews of the choledochoduodenal region and the anatomy and pathology of the ampulla of Vater have been published by Hand,[12] Flodisch,[13] Sterling,[14] and Newman et al.[15]

The mucosa of the common duct is grayish in color, with minute flecks along its course corresponding with the orifices of the intramural glands.[10] The cystic and common ducts are lined with tall columnar epithelium, with the nucleus at the base of the cell. The cells desquamate very quickly following death. The epithelium dips into the wall for varying distances, forming small diverticula. The wall is composed of loose connective tissue containing collagen, elastic tissue, and mucus glands.[4,10] There is only a small amount of smooth muscle present, and this has largely a longitudinal orientation. Muscle fibers increase considerably in the intraduodenal portion of the common duct.

ARTERIAL SUPPLY

The gallbladder is supplied by the cystic artery, which usually arises from the right hepatic artery in Calot's triangle.[4,16] At the neck of the gallbladder, the cystic artery bifurcates into a superficial and deep branch. The superficial branch supplies

the free wall of the gallbladder, while the deep branch courses behind the gallbladder to supply the hepatic side of the gallbladder and the gallbladder bed. Anastamoses exist between these two major branches. This "normal" situation exists in only 50–60% of the population.[4] In about 25%, the superficial and deep branches have a separate origin from the right hepatic artery or some other vessel. Occasionally, the cystic artery arises from an aberrant right hepatic artery. Smaller accessory cystic vessels may also be found. Although these usually arise from the right hepatic artery, they may take origin from the left or common hepatic arteries or other arteries in the region. A discussion of the various arterial anomalies is beyond the scope of this monograph. An excellent account is provided in the paper by Michels.[16]

VENOUS DRAINAGE

The venous drainage of the gallbladder is variable, but many of the veins pass directly into the liver. Sometimes there is a well-formed cystic vein which empties into the portal vein.

LYMPHATIC DRAINAGE

The gallbladder has a rich supply of lymphatic channels which are found in the lamina propria of the mucosa and the adventitia. Those from the left side of the gallbladder drain into the cystic gland while those from the right side enter the superior pancreaticoduodenal gland.[4] Lymphatic drainage from these nodes eventually reaches the cisterna chyli.

INNERVATION

The gallbladder and bile ducts receive both sympathetic and parasympathetic innervation. The sympathetic nerves are represented by postganglionic fibers, mainly emerging from the celiac ganglia, while the parasympathetic nerves are branches of the vagus nerve.[17] The gallbladder has subserosal, intramuscular and submucosal ganglion cells which form plexuses within each of these layers.[10] Paraganglia have also been reported in the perimuscular connective tissue.[17,18]

EMBRYOLOGY

The gallbladder and cystic duct arise from the caudal part of the hepatic diverticulum which develops as an outpouching of the gut entoderm. The developing gallbladder is carried away from the duodenum by elongation of the main portion of the hepatic diverticulum which becomes the common duct.[19] In the 5-mm embryo, the gallbladder anlagen is a solid cylinder which by vacuolization again develops a lumen by the 15-mm stage.[20]

OTHER ASPECTS OF MORPHOLOGY

Immunoglobulin-containing cells are present in the normal human gallbladder,[21] although they are rather sparsely distributed. In the mucosa, IgA-containing cells predominate, but in the muscle layer IgM cells are the more numerous. Cells containing IgA show the greatest increase in numbers in chronic cholecystitis.

A glycoprotein antigen which is apparently specific for the gallbladder has been isolated from mucosal extracts of gallbladders and from bile. It resembled sulfoglycoprotein.[22] In addition, three other gastrointestinal antigens were found in gallbladder mucosa in this same study. Two of these were gastric antigens and the third was intestinal in type.[22]

References

1. Schoetz, D.J., Jr., La Morte, W.W., Wise, W.E., Birkett, D.H., and Williams, L.F., Jr.: Gallbladder compliance: A significant physiologic and pathophysiologic concept. *Curr Surg 37: 204–208, 1980.*
2. Lilja, P., Fagan, C.J., Wiener, I., Inoue, K., Watson, L.C., et al.: Infusion of pure cholecystokinin in humans. Correlation between plasma concentrations of cholecystokinin and gallbladder size. *Gastroenterology 83: 256–261, 1982.*
3. McGahan, J.P., Phillips, H.E., and Cox, K.L.: Sonography of the normal pediatric gallbladder and biliary tract. *Radiology 144: 873–875, 1982.*
4. Hand, B.H.: Anatomy and function of the extrahepatic biliary system. *Clin Gastroenterol 2: 3–29, 1973.*
5. Maximow, A.A., and Bloom, W.: *A Textbook of Histology,* (7th ed.), W.B. Saunders Company, Philadelphia, 1957, pp. 412–418.
6. Evett, R.D., Higgins, J.A., and Brown, A.L., Jr.: The fine structure of normal mucosa in human gall bladder. *Gastroenterology 47: 49–60, 1964.*
7. Laitio, M., and Nevalainen, T.: Gland ultrastructure

in human gall bladder. *J Anat 120: 105–112, 1975.*

8. Elfving, G.: Crypts and ducts in the gallbladder wall. *Acta Pathol Microbiol Scand* [A] *49 (Suppl 135): 1–45, 1960.*
9. Beilby, J.O.W.: Diverticulosis of the gall bladder. *Br J Exp Pathol 48: 455–461, 1967.*
10. Sterling, J.A.: *The Biliary Tract.* Williams & Wilkins Company, Baltimore, 1955, pp. 12–56.
11. Keddie, N.C., Taylor, A.W., and Sykes, P.A.: The termination of the common bile duct. *Br J Surg 61: 623–625, 1974.*
12. Hand, B.H.: An anatomical study of the choledochoduodenal area. *Br J Surg 50: 486–494, 1963.*
13. Flodisch, H.: [Histological studies on normal and pathological Vater's ampulla]. *Norm Pathol Anat (Stuttg) 24: 1–58, 1972.*
14. Sterling, J.A.: The common channel for bile and pancreatic ducts. *Surg Gynecol Obstet 98: 420–424, 1954.*
15. Newman, H.F., Weinberg, S.B., Newman, E.B., and Northup, J.D.: The papilla of Vater and distal portions of the common bile duct and duct of Wirsung. *Surg Gynecol Obstet 106: 687–694, 1958.*
16. Michels, N.A.: Variational anatomy of the hepatic, cystic, and retroduodenal arteries. *Arch Surg 66: 20–32, 1953.*
17. Kuo, T., Anderson, C.B., and Rosai, J.: Normal paraganglia in the human gallbladder. *Arch Pathol 97: 46–47, 1974.*
18. Fine, G., and Raju, U.B.: Paraganglia in the human gallbladder. *Arch Pathol Lab Med 104: 265–268, 1980.*
19. Arey, L.B.: *Developmental Anatomy,* (6th ed.), W.B. Saunders Company, Philadelphia, 1954, pp. 254–259.
20. Nelson, W., Hatch, F.F., and Jackson, H.M.: Congenital absence of the gall bladder. *Surgery 25: 916–923, 1949.*
21. Green, F.H.Y, and Fox, H.: An immunofluorescent study of the distribution of immunoglobulin-containing cells in the normal and the inflamed human gall bladder. *Gut 13: 379–384, 1972.*
22. Hakkinen, I., and Laitio, M.: Epithelial glycoproteins of human gallbladder. Immunological characterization. *Arch Pathol 90: 137–142, 1970.*

CHAPTER 2

Congenital Anomalies

Although congenital anomalies of the gallbladder are relatively uncommon, there is a voluminous literature in this area. This, in part, reflects the diagnostic problems often raised by patients in this group both for the surgeon and radiologist. The pathologist may also be confronted with these abnormalities, not only in surgically-resected material but also at autopsy, often as an incidental finding. Major reviews of the various congenital anomalies were published by Gross in 1936[1] and by Flannery and Caster in 1956.[2]

Traditionally this subject has been discussed under the following headings:

A. Anomalies in the shape and form of the gallbladder
B. Anomalies in number
C. Anomalies in position

This will be used as the basis for a more detailed classification which appears in Table 1. The various heterotopic tissues so far described in the gallbladder will be considered in Chapter 3. Congenital anomalies of the common bile duct will be discussed in Chapter 31.

ANOMALIES IN SHAPE AND FORM

Some of the alterations in the shape and form of the gallbladder to be discussed below should probably be regarded as variations in the normal anatomy rather than true congenital abnormalities. For convenience, they will be discussed under the following headings:

1. Shape and size
2. Phrygian cap
3. Diverticula
4. Cysts
5. Multiseptate gallbladder
6. Hourglass deformity
7. Cholecystocele

Septate gallbladders are sometimes included with this group but it seems more rational to consider them in association with duplications as all gradations from septate gallbladder to bilobed or fully duplicated structures have been described.

Shape and size

The gallbladder is usually described as being pearshaped, although it may vary from pyriform to a modified cylindrical form. The relationship between the shape of the gallbladder and the body habitus has been controversial.[3] In hypersthenics, the gallbladder may show some shortening and widening, producing an ovoid shape, contrasting with the narrow and ptotic type seen in some asthenics.[4] Spherical gallbladders have been described as an uncommon variant in shape, but they do not appear to correlate with body habitus.[3]

The term syphonopathy has been used for what is probably a normal constitutional variation in the shape of the gallbladder.[4] It is characterized by an acute angle between the infundibulum and neck and the neck and cystic duct, producing a syphonlike configuration on cholecystograms.

Acquired alterations in the shape of the gallbladder are also found. These result from the pressure of adjacent masses such as polycystic livers,[5,6] hydatid cysts,[7] liver tumors, both primary and secondary,[8,9] large lymph nodes,[9] and hepar lobatum.[9]

It is sometimes difficult to be certain whether an abnormality in the size of the gallbladder is the result of a congenital anomaly or is secondary to some disease process. Congenital hypoplasias will be discussed in conjunction with agenesis of the gallbladder. Large gallbladders may be found as an acquired phenomenon in patients with obstruction of the common bile duct,[10] or in diabetes,[11–13] acromegaly,[14] parenteral hyperali-

Table 1.
Congenital Anomalies of the Gallbladder and Cystic Duct

A. Anomalies in shape and form
  (1) Variations in shape and size (excluding hypoplasia)
  (2) Phrygian cap
  (3) Diverticula
  (4) Cysts
  (5) Multiseptate gallbladder
  (6) Hourglass deformity
  (7) Cholecystocele
B. Agenesis and hypoplasia
  (1) Agenesis
  (2) Hypoplasia
C. Duplications
  (1) Septate
    (a) Longitudinal
    (b) Transverse
  (2) Bilobed
  (3) Duplication of the gallbladder
    (a) with a common cystic duct (Y-type)
    (b) with the cystic ducts entering the common bile duct separately (H-type)
    (c) with the accessory cystic duct entering the right hepatic duct or branch thereof
    (d) with the accessory cystic duct entering the left hepatic duct or branch and the accessory gallbladder towards the left side
    (e) with the accessory cystic duct entering the duodenum
    (f) with duplication of the liver and biliary system
D. Triplications
E. Anomalies of position
  (1) Left-sided
    (a) Isolated
    (b) With *situs inversus*
  (2) Intrahepatic
  (3) Retroplacement
  (4) Suprahepatic
  (5) Falciform ligament
  (6) Lesser sac
  (7) Abdominal wall
  (8) Transverse position
  (9) Wandering (floating)
F. Anomalies of the cystic duct
  (1) Absence
    (a) with absent gallbladder
    (b) isolated
  (2) Duplication
    (a) with duplication of gallbladder
    (b) isolated
  (3) Anomalies of drainage
G. Miscellaneous anomalies
  (1) Anomalies of the hepatic duct
  (2) Accessory bile ducts
  (3) Tracheocholedochal duct
  (4) Pancreatic bladder

mentation, or after truncal vagotomy (see Chapter 21). A so-called "giant" gallbladder measuring 14 × 5.5 cm has been described in a transverse position in the upper abdomen extending across the midline to the left upper quadrant.[15] It showed acute cholecystitis with early gangrenous change. The unusual position of the gallbladder is some support for this being a congenital enlargement, although the author made no claim in this regard. The large gallbladder described recently from Japan was attributed to a congenital anomaly.[16] It measured 18 cm in length and 4 cm in maximum diameter. An extremely long cystic duct was also noted.

Phrygian cap

The Phrygian cap or folded fundus is an angulation of the distal portion of the fundus of the gallbladder.[17–19] The name was coined by Bartel in 1916 because of the resemblance of this deformity to the hats worn by the people of Phrygia, an ancient country of Asia Minor.[20] The Phrygian cap does not appear to be the result or cause of disease.[17] It is of no clinical importance except that it may simulate a stone or other pathology on radiologic examination. The anomaly has been regarded as congenital by some, while others believe it is an acquired characteristic.[18] The Phrygian cap has been found in 4% of routine cholecystograms and in 6% of a series of gallbladders removed at operation.[17]

Boyden suggested that there were two distinct types: a serosal type in which the peritoneum follows the bend in the fundus and which is then reflected on itself as the fundus rests on the body of the gallbladder, and a retroserosal or concealed type in which there is a mucosal fold projecting into the lumen.[18] The usual methods of handling the gallbladder will fail to show this septum unless the specimen is fixed in the distended state and sections taken longitudinally. Histologic examination will then show a small fold of the mucosa with some alteration in the arrangement of the muscle bundles in the underlying muscularis.

Diverticula

Diverticula are protuberances of the wall of the gallbladder which are found anywhere along the surface from the fundus to the neck.[21] They vary greatly in size, ranging from 0.6 cm to 8 cm or more.[21,22] The larger diverticula may cause pressure on surrounding structures such as the duodenum,[23] or undergo perforation. Diverticula are usually single, but multiple protuberances can occur (Fig. 2.1).

Clinically diverticula are usually silent but they may contain stones [22], or become in-

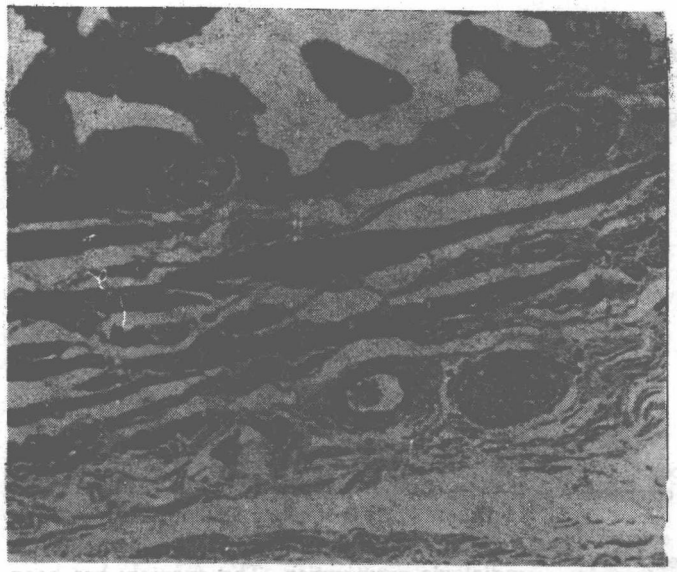

Figure 2.1 Diverticulum of the gallbladder. The wall is thin.

fected.[23,23a] It seems that they can become separated from the rest of the gallbladder, giving rise to fundal cysts having no apparent communication with the gallbladder itself.[24,25] Calcification of such cysts has been reported.[25]

Congenital diverticula are thought to arise as a result of incomplete resolution of the solid stage. Those near the neck of the gallbladder may represent persistent cyst–hepatic ducts.[26] Acquired diverticula can develop following traction from adhesions, partial healing of fistulas, and from erosions of the wall by stones producing pseudodiverticular outpouchings. Using strict criteria, Castro accepted only three of the 68 diverticula he analysed at the Mayo Clinic as being congenital in nature.[27]

On histologic examination, congenital diverticula contain all the elements of the normal gallbladder wall,[28] whereas acquired diverticula, with the exception of the traction type, usually have little or no smooth muscle in their wall.[29] Occasionally an incomplete membrane or diaphragm may be found at the mouth of the diverticulum. Cholesterolosis has been noted in the mucosa of the diverticulum.[30] Congenital diverticula will usually function normally on radiologic examination of the gallbladder.

Cysts

There have been several reports of fundal cysts occurring in the gallbladder.[24,25] These have been referred to above. One of these cysts measured 16 cm in diameter,[24] while the other was smaller with calcification of its wall.[25] In both cases, the authors assumed that they had arisen by occlusion of the communication into a fundal diverticulum.

Furnival has described a cyst, 1 cm in diameter, lined by flattened epithelium beneath the mucosa at the fundus of the gallbladder.[32] The multilocular cyst lying between the liver and gallbladder reported by Cureton and Newcombe was lined by columnar epithelium.[33] These two cases were thought to have arisen from Luschka's ducts.

Multiseptate gallbladder

Multiseptate gallbladder is a rare congenital anomaly in which the organ is divided into a variable number of communicating chambers by multiple thin septa.[34–40] This abnormality has been attributed to incomplete resolution of the solid stage of development or to irregular plication of the gallbladder anlage prior to the vacuolization of the solid bud.[34,38]

Patients with this abnormality usually present in their third or fourth decade with recurrent abdominal pain. Stones have not been present in most of the cases reported to date. The gallbladder may be of normal size, slightly enlarged, or even hypoplastic.[37,39]

The multiseptate gallbladder usually feels

spongy to palpation. The external surface is essentially smooth, although some irregularities may be visible. The number of compartments varies from three to 10 or more. On microscopic examination the septa are lined by epithelium, usually tall columnar in type. There is an underlying muscular layer continuous with that of the outer wall. However, smooth muscle is sometimes absent from the very thin septa.[40] The changes of mild chronic cholecystitis may be present.[34]

Hourglass gallbladder

In the hourglass or "dumb-bell" gallbladder, a zone of narrowing or constriction divides the lumen into a proximal and distal cavity. An hourglass appearance may not be evident on the external surface.[41] In most cases this is an acquired deformity, and the annulus dividing the gallbladder into the two compartments shows adenomyomatosis or inflamed fibrous tissue.[42,43] The congenital hourglass deformity is closely related to the septate gallbladders of transverse type and their separation in somewhat arbitrary.[44]

Either or both compartments may be inflamed or contain stones, but there is a predisposition for these changes to be limited to the distal cavity.[45] There is usually an abrupt transition from a normal thin wall of the proximal compartment to a thickened and inflamed distal chamber. Torsion of the distal segment has also been noted.[46] Like the septate gallbladder, the hourglass deformity is thought to arise as a result of a defect in the period of recanalization of the solid stage. Extrinsic pressure during development has also been suggested.[41]

Cholecystocele

The term, cholecystocele, has been used for an abnormality of the gallbladder similar in nature and origin to the choledochal cyst.[47] It consists of a large cystic structure in continuity with the gallbladder lumen such that the gallbladder appears to be a diverticulum of the large cyst. In the one case so far described, the wall was composed of dense fibrous tissue with no epithelial lining. Numerous bile canaliculi were described in the wall. Variations of this condition have probably been described in the past.[48]

AGENESIS AND HYPOPLASIA

Agenesis

Over 200 cases of gallbladder agenesis have now been reported. The incidence of this congenital anomaly is difficult to assess with accuracy, as in many of the earlier cases reported no attempt was made to exclude an ectopic gallbladder within the substance of the liver or the falciform ligament. Tallmadge[49] found 18 cases of agenesis in 18,350 autopsies, while McIlrath and colleagues[50] at the Mayo Clinic reported 10 cases in 26,531 routine autopsies. Monroe,[51] on the basis of a questionnaire sent to pathologists, collected 181 cases from a total of 1,352,000 autopsies, an incidence of 1:7,500. In surgical material, agenesis of the gallbladder and cystic duct was noted in three cases out of 2451 cholecystectomies and cholecystostomies in one series,[52] but in only four of 21,525 similar operations at the Mayo Clinic.[53] The gallbladder is absent from various species of herbivorous mammals as well as some fish and birds. The published cases of agenesis of the gallbladder have been reviewed at various times.[1, 54–62]

In surgical material, the diagnosis of agenesis has usually been made late in the fifth decade of life. Although there has been an equal sex incidence of this abnormality in autopsy material, females have predominated in some of the surgical series. Clinical symptoms may mimic those of cholecystitis or cholangitis.[63,64] Jaundice has been noted in a significant percentage of patients. In some cases, there has been no biliary tract pathology other than agenesis to explain the symptoms.[65,66]

The cystic duct is usually absent as well, although in a few cases a vestigial stump of the cystic duct has been present. The gallbladder fossa is often absent on the undersurface of the liver, and this may be associated with poor delineation of the quadrate lobe.

Agenesis of the gallbladder is thought to result from a failure of development of the ventrocaudal sacculation of the hepatic diverticulum. A vestigial or hypoplastic structure may result if the gallbladder anlage fails to recanalize after the solid phase. There have been several reports suggesting an hereditary basis in some cases.[67–70]

Agenesis of the gallbladder and cystic duct can

occur as an isolated phenomenon[71–73] or be associated with other congenital anomalies or with pathologic processes involving the biliary tract. The most common associated pathology is choledocholithiasis which has been described in from 10 to 50% of cases.[74–81] Dilatation of the common bile duct is often present in these patients, but acalculus dilatation may also occur. The pathogenesis of the dilated common bile duct in these circumstances is uncertain. The stones may form in the common duct or migrate from the hepatic ducts or their branches. Despite the reports quoted above there are some authors who maintain that agenesis of the gallbladder does not increase the tendency to biliary tract disease.[81,82]

Primary adenocarcinoma of the common duct has been described in three patients with agenesis of the gallbladder.[83–85] Calculi were absent in all three cases. Sclerosing cholangitis has also been reported in a patient with absent gallbladder.[86]

Other congenital abnormalities have been present in some patients with gallbladder agenesis. These have included absence of the ascending colon,[87] polycystic kidneys,[57,88] tracheo-esophageal fistula,[57] cardiac defects,[57,88a] imperforate anus,[57] other gastrointestinal abnormalities,[89,90] annular pancreas,[91] the Klippel-Feil syndrome[91a] congenital lumbar hernia[92] and horseshoe kidney combined with malrotation of the gut.[93] Stolkind has reviewed several other abnormalities reported in the older literature.[94]

Hypoplasia

Congenital hypoplasia of the gallbladder[94–98] has been described, although its differentiation from postinflammatory shrinkage can be difficult to establish. It is characterized by a fibrotic bulb attached to the cystic duct or an unusually small gallbladder with a narrow lumen. Stolkind distinguished three types of related anomalies: absent gallbladder, the fibrous cord type of hypoplastic gallbladder, and the rudimentary organ,[94] the latter being less than 3 cm in length. A hypoplastic gallbladder may be situated in its usual fossa beneath the liver or be found as a rudimentary tube beside the common duct and within the same sheath.[97] In most, a lumen lined by columnar epithelium is present, with a fibromuscular wall (Fig. 2.2). As mentioned earlier, hypoplastic gallbladders probably arise as a result of failure of recanalization of the solid tube or incomplete development of the gallbladder bud.

Figure 2.2 Hypoplastic gallbladder. There is no well-defined muscle layer.

A hypoplastic gallbladder may be found in association with congenital biliary atresia and in mucoviscidosis.[99] This will be considered in other chapters.

DUPLICATIONS

Duplications of the gallbladder are quite common in certain domestic and wild animals.[100] Although much less common in man, over 200 reports have now appeared in the world literature. Septate and bilobed gallbladders have been classified by some with anomalies in the form of the organ.[101] They will be considered here with the duplications. The classification used below, and outlined in Table 1, is modified from one suggested by Harlaftis and colleagues.[102]

Septate gallbladders

Septate gallbladders have a longitudinal or transverse septum dividing the gallbladder into two chambers. In those cases with a longitudinal septum,[103–106] the external appearance is usually normal, but sometimes a small cleft is present at the fundus. Septate gallbladders were included with the bilobed structures by Boyden[100] and some subsequent writers.[104–107] The two cavities in this condition are drained by a single cystic duct. The longitudinal septum is of variable length, producing chambers that are usually of equal size. The incidence of cholecystitis is probably higher in this deformity than in the normal structure, although the number of cases reported is small. Stones may be present in one or both of the chambers. A septate gallbladder with an attached mesentery has been reported, as has a longitudinal cystic duplication lined in part by ciliated epithelium.[108]

There are only several reports discussing transverse septa in the gallbladder.[44,109–112] The distinction between this group and the hourglass deformity is not always clear cut.[45] Beilby studied transverse strictures in the gallbladders of adults and neonates and reached the conclusion that the strictures seen in adults were also congenital in origin.[44]

Obstructive symptoms can be quite marked in patients with a transverse septum. This has been attributed to contraction of the distal gallbladder against the resistance of the septum or the pooled bile in its cavity. The distal compartment frequently contains calculi and often shows the changes of chronic cholecystitis or cholecystitis glandularis proliferans. Beilby has shown that this comes about by progressive crypt formation and muscular hypertrophy distal to the point of narrowing.[44] In two of the cases reported, duodenal bands have also been present.[111]

Histologic examination of the septa shows them to be lined by epithelium, usually columnar in type. There is an underlying loose connective tissue stroma and a central layer of smooth muscle. The well-developed septa considered here should not be confused with the small mucosal folds up to several millimeters high that may be found within the gallbladder, particularly at the junction between the various anatomical regions.[4]

Septa are thought to result from incomplete resolution of the solid stage of gallbladder development. A longitudinal septum could also be the result of failure of refusion of paired buds of the gallbladder primordium.

Bilobed gallbladder

In bilobed gallbladders, there are two separate fundic cavities united at their neck and drained by a single cystic duct. The individual lobes may be of the same or unequal size. Stones may be present in one or both lobes. In most of the cases reported, chronic cholecystitis has also been present.[106] One case has been associated with duodenal atresia.[113] Bilobed gallbladders are thought to arise on a similar basis as the septate type.

Duplication of gallbladder

The most common type of duplicated gallbladder occurs when the cystic duct and the accessory cystic duct enter the common bile duct separately (H-type).[102] This anomaly accounts for approximately half of the duplicated gallbladders. The second most common subgroup is the so-called Y-type in which the individual cystic ducts unite to form a common cystic duct which then drains into the common bile duct (Fig. 2.3).[114]

When duplicated gallbladders are contiguous, they often share a common peritoneal investment, giving them the appearance of a single structure on external examination.[115] In such cases, both organs are usually involved when an inflammatory process is present. When the gall-