THE PATHOGENESIS OF POLYCYSTIC LIVERS

Reconstructions of Cystic Elements in Two Cases *

Robert F. Norris, M.D.,† and Ralph M. Tyson, M.D.
(From the Ayer Clinical Laboratory and the Pediatric Service, Pennsylvania Hospital, Philadelphia, Pa.)

The occurrence of congenital polycystic disease of the liver has been known and studied for a long time and the cause of the lesions has been the subject of much speculation. In addition to numerous case reports, reviews of the literature and discussions of the problem of etiology may be found in the papers of Kahlden,[1] Still,[2] Moschcowitz,[3] Bunting,[4] Vorpahl,[5] Meyenburg,[6,7] Sears,[8] Teuscher,[9] Wackerle,[10] Delore and Croizat,[11, 12] Rümler,[13] Lutembacher,[14] Baccarini,[15] and Monserrat and Latienda.[16]

In those papers, it is clear that the cystic lesions have been thoroughly studied microscopically, often in serial sections, but they have not been evaluated by means of reconstructions. However, since it may rightly be assumed that the origin and mode of development of cystic lesions in all organs are governed by the same principles and since studies of models from polycystic kidneys have been made, the theories which have been proposed for the etiology of polycystic kidneys have been applied to polycystic disease of the liver. The kidney, furthermore, is probably the organ best suited for the study of this disease, since it is formed from two separated anlagen which subsequently unite and the individual nephrons are composed of elements from both anlagen. In the kidney, therefore, the character of developmental defects and the time of their occurrence should be much more easily demonstrated than in organs such as the liver, pancreas, and lungs, in which the proper formation of individual epithelial elements is not dependent upon the union of different anlagen. Nevertheless, information on these points has been only slowly accumulated. Consequently, the problem of polycystic disease of the liver will be more easily understood if the theories of origin of polycystic kidneys are briefly reviewed.

At first it was thought by Virchow,[17, 18] and others that inflammatory lesions of the fetal kidney might disturb the developing nephrons sufficiently to cause obstruction and cystic dilatation. This theory at present is not in favor since inflammatory lesions are not always present and could scarcely be hereditary. Later it was suggested by

* Aided by a grant from Mead Johnson & Co.
Received for publication, March 4, 1946.

† Now at the William Pepper Laboratory of Clinical Medicine of the University of Pennsylvania, Thirty-sixth and Spruce Streets, Philadelphia 4, Pa.

Mutach,[19] Ribbert,[20] and others that failure of union of the two anlagen might explain these lesions. Although attractive by virtue of its simplicity, this theory is untenable since it does not explain why polycystic disease occurs in organs in which the union of two separate anlagen does not occur and since it has been shown recently [21, 22] that the two anlagen in all probability do unite. Because of the large size of many cysts and the occasional finding of undifferentiated masses of epithelial cells, it was proposed by Brigidi and Severi,[23] and others that the lesions were truly neoplastic. There seems little basis for this argument since the cysts show no evidence of rapid proliferation and the great majority are lined by only a single layer of epithelium. Much more logically, Albrecht [24] suggested the term "Hamartome" for these lesions, which impressed him as being an improper proliferation of tissue as a consequence of faulty development. However, recently, doubt has been cast upon the fundamental importance of excessive proliferation of epithelium,[22] since in one case segmentation of nephrons occurred without excessive dilatation or proliferation of epithelium. Important contributions to the subject recently were made by Kampmeier,[25-28] and McKenna and Kampmeier,[29,30] These workers demonstrated that the first generations of nephrons in the metanephros are normally provisional and often persist for short periods in fetal life as small, isolated cysts. They concluded that persistence of these segments as cysts might explain the occurrence of polycystic disease. More recently, however, Norris and Herman [22] found in one of their cases that virtually all of the nephrons were segmented and cystic and that the total number of nephrons was approximately normal for a newborn child. By means of serial sections and reconstructions, 4 cases were studied, 2 of which were newborn infants and 2 adults. In the 2 infants, normally formed but isolated glomeruli without marked capsular dilatation were found in the cortex, and blindly-ending but undilated collecting ducts emptying into the calyces were found in the papillae. Between the two zones were cysts and undilated segments of nephrons. It was concluded, first, that for the glomeruli to be so perfectly formed, continuity between the nephrogenic anlage and ureteric anlage must first have been established and have been followed by segmentation and cystic dilatation of the detached elements and, second, that excessive epithelial proliferation was not necessarily responsible for the lesions. It was also pointed out from the literature that the mesonephros normally degenerates by a process of segmentation as do the early generations of nephrons in the metanephros. It was suggested, therefore, that polycystic disease of the kidneys is in reality an extension of this normal process of degeneration to include some or all of the later generations of nephrons.

To determine whether this last theory is also applicable to polycystic disease in general, study of other cystic organs is essential. For this purpose, we are reporting descriptions of cystic livers, together with reconstructions of some of the lesions, from the 2 infants previously reported by Norris and Herman.[22]

Materials and Methods

Case numbers 1 and 2 of the present report correspond to the case numbers given before by Norris and Herman.[22] Briefly, case 1 was that of a full-term male infant in whom greatly enlarged polycystic kidneys and liver so embarrassed respirations that he died 20 minutes after birth. Case 2 was that of a full-term female infant who developed a hemorrhagic diathesis, jaundice, and evidence of renal insufficiency and died 24 days after birth. Following delivery, sixth digits of both hands were amputated. Relatively undilated cystic lesions of the kidneys, liver, and pancreas were found at autopsy. Since in the previous paper the clinical histories, anatomic diagnoses, and detailed findings in the kidneys were presented, only the gross and microscopic lesions of the livers will be described at this time.

All tissue was fixed either in Kaiserling's or Regaud's solutions. Blocks were embedded in paraffin and sections were stained with Delafield's hematoxylin and eosin. Sections for ordinary study were cut at 5 μ. From each liver, several hundred serial sections, 15 μ in thickness, were cut from each of four blocks about 2 cm. on a side. The cystic lesions and distorted bile ducts were traced and studied microscopically through these sections. Reconstructions were accomplished by the method previously described.[21]

Observations

Case 1

Gross Examination. The liver of case 1 weighed 270 gm. and, in spite of the enlargement, had distinctly normal contours. There were distinct right and left lobes. The gallbladder was partially distended with thick, dark green bile and, except for post-mortem changes of the mucosa, was normal. The cystic duct, extrahepatic bile ducts, and common duct were also patent and normal. On section, the parenchyma was bloody throughout. The lobular architecture was evident but was not as distinct as is normal. In the periphery of the lobules highly irregular cystic dilatations were seen averaging about 3 mm. in diameter. There were no large cysts nor any focal lesions.

Microscopic Examination. The lobular architecture of the liver was not distorted and branches of the hepatic veins were situated normally in the center of each lobule. The parenchymal liver cells showed no

lesions, but the sinusoids were slightly dilated and large areas of erythropoiesis and myelopoiesis were present. The periportal areas, however, were greatly distorted by marked cystic dilatations of the intrahepatic bile ducts which, as seen in low-power fields (Fig. 3), completely encircled cords of loose connective tissue containing branches of the hepatic artery and portal vein. These cysts were lined by single layers of cuboidal or low-columnar epithelium. The cytoplasm of these cells was usually clear and the nuclei were vesicular. There was no evidence of active proliferation. Under higher power, about the periphery of these cystic areas were seen numerous highly distorted bile ducts, lined by epithelium of similar character, which were not markedly dilated (Fig. 4). These, also, had a conspicuous tendency to encircle the branches of the portal vein and hepatic artery. The connective tissue surrounding these ducts was loose and in many areas cellular elements of the foci of hematopoiesis were migrating through the epithelium to the lumina of the ducts. Nearly all of the cystic bile ducts contained erythrocytes and casts of both hemoglobin and bile. The small bile canaliculi, however, were not dilated and did not contain casts.

In serial sections, as can be seen in the model (Fig. 1), the encirclement of the hepatic arteries and portal veins by the greatly dilated bile ducts was also readily demonstrated. The cystic ducts were highly irregular in contour and there were numerous large outpocketings. Anastomoses were numerous and, in many places, undilated but distorted ducts formed continuations and branches of the cystic ducts. Although many of the outpocketings or branches were blindly-ending, it was not demonstrated that any of the large dilated ducts were completely isolated as cysts. The courses of the hepatic arteries and portal veins were generally straight and uninterrupted although there was considerable irregularity of the contours of these vessels.

Case 2

Gross Examination. The liver of case 2, which weighed 220 gm., was normally formed and had distinct right and left lobes. The gallbladder contained a small amount of yellow bile and, except for post-mortem changes of the mucosa, was normal. The cystic duct, extrahepatic bile ducts, and common duct were likewise patent and normal. On section, the lobular architecture of the liver was grossly normal, the intrahepatic bile ducts were not dilated, and no focal lesions were seen.

Microscopic Examination. In low-power fields, the lobules of the liver were generally normal in contour. The central veins were not

remarkable and the parenchymal cells and sinusoids showed no lesions. Many of the branches of the portal vein, however, appeared dilated and were surrounded by larger numbers of bile ducts than is normal (Fig. 5). Under higher power, these ducts, although not conspicuously dilated, were highly irregular in contour, appeared more numerous than is normal and were grouped around the branches of the portal vein and hepatic artery (Fig. 6). They resembled the nondilated ducts in case 1 (Fig. 4). Individually, the lining cells were low-columnar or cuboidal. The cytoplasm was clear and colorless and the nuclei were vesicular. There was no evidence of rapid cellular proliferation. Many of the small bile canaliculi and some of the small bile ducts were slightly distended with casts of inspissated bile. There was no extramedullary hematopoiesis.

In serial sections, irregularity and distortion of individual bile ducts were marked. As can be seen in the reconstruction (Fig. 2), the ducts sometimes were narrow and sometimes were focally dilated. Small and large segments of ducts were often isolated as cystic structures without significant enlargement or dilatation when compared with the adjacent unsegmented ducts. Many of these isolated segments were in a direct line with branches of biliary ducts which were not segmented. This observation suggests that these segments were previously in continuity with the bile ducts and secondarily became isolated as nondilated cysts. Although the branches of the hepatic artery were generally straight, the branches of the portal vein were often distorted. No isolated segments of veins were identified.

Discussion

In the cases presented, the conspicuous lesions were those of the small intrahepatic bile ducts. The ducts in both cases were highly irregular in contour and diameter and did not conform to a regular pattern. The number of ducts in the periportal areas appeared to be greater than is normal. This was especially true in case 2, as can be seen in the model (Fig. 2). Anastomoses in both cases were numerous. In case 1, many of the ducts were not dilated, but in nearly all of the periportal areas there were large cystic ducts which in places completely encircled the hepatic artery and portal vein. None of these, however, were demonstrated as being isolated, blindly-ending cysts. By contrast, in case 2 none of the ducts were greatly dilated but many small and large segments were isolated and were blindly-ending in both directions. That the flow of bile, elaborated by the parenchymal epithelial cells, was obstructed in many places was shown by jaundice and by bile casts in the canaliculi. In case 1, however, there was no jaundice and the

canaliculi did not contain bile casts, so that biliary obstruction was not demonstrated.

It is surprising that in case 1 the large cystic ducts were not found isolated as cysts. If these ducts were not segmented, as the lack of obstructive jaundice also indicates, then it may be argued that cystic dilatation may occur before segmentation and isolation of these elements as cysts. In case 2, by contrast, segmentation occurred without cystic dilatation. On the other hand, in the kidneys of case 1 similar large cystic dilatations were shown definitely to be isolated as cysts. In the latter, there were also numerous anastomoses. It is quite possible, therefore, that similar anastomoses in the liver obscured a previous tendency to segmentation and isolation of cysts.

In the kidneys, although the method for estimating the number of nephrons was admittedly crude, it was not demonstrated that there was an overproduction of elements. In the livers, more than the usual number of bile ducts appeared to be present in the periportal areas. Theoretically, an excessive production of elements persisting until birth can occur, since early generations of nephrons are normally provisional as are many of the small intrahepatic bile ducts. The association of polydactylism with polycystic disease also suggests this possibility. That an overproduction of elements is significant in the pathogenesis of polycystic disease has been previously suggested and has been used as the basis for the assumption that abnormal proliferation of epithelial elements is the fundamental lesion of the disease.[13,23,24] However, the liver differs from the kidney in that bile ducts can regenerate in various diseases whereas nephrons, after birth, at least, do not have this potentiality. Moreover, anastomoses among small bile ducts are the rule but do not occur normally among nephrons. Consequently, so far as the present cases are concerned, preceding abnormalities of the developing bile ducts might stimulate the production of excessive numbers of elements. The apparent overproduction of bile ducts would then be the result of the lesions rather than the cause of them.

Before discussing further the significance of the cystic lesions which have been described and illustrated in these cases, it is important to review the normal development of the liver. According to Lewis,[31] the anlage of the liver is a median ventral outgrowth of the entodermal tube. Cords of epithelial cells proliferate distally and are later separated from the gut by a short, solid stem. Eventually this stem becomes canalized to form the common bile duct. Meanwhile the trabeculae and cords of proliferating epithelial cells indent the lumina of the omphalomesenteric veins which grow out between the cords to invest

and surround them with endothelium. The right omphalomesenteric vein later becomes the portal vein and the hepatic vein is essentially the persistent outlet of this right omphalomesenteric vein. The left umbilical vein also sends branches to the liver and becomes the round ligament after birth. For a period in embryonic development, the hepatic vein is connected with the portal and umbilical veins by a large blood sinus within the liver, the ductus venosus, which disappears before birth by subdividing into the sinusoidal circulation. Meanwhile, branches of the hepatic artery are proliferating along branches of the hepatic ducts which are developing in continuity with the common duct. The intrahepatic ducts, however, do not proliferate extensively until after branches of the portal vein are formed and generally follow the course of these branches. Between the embryonic stages of 10 and 23 mm., segments of blindly-ending ducts may be observed. These blend with the hepatic trabeculae, and it is not until the stage of about 23 mm. that proliferation of the duct system is active. These ducts form a plexus in the periportal mesenchyma. Anastomoses which are numerous at first are fewer at the time of birth, although fluid injected into one hepatic duct will be returned by way of the other.

From these facts concerning the development of the normal liver it is possible to date roughly the origin of the lesions in the present cases. Since intrahepatic bile ducts do not appear until the embryo is 10 mm. in length and do not proliferate actively until about 23 mm., 10 to 23 mm. is the earliest stage at which the lesions of the ducts could begin. By this time, however, the lobules are beginning to differentiate and branches of the portal vein and hepatic artery are already appearing in the perilobular mesenchyma. It is quite possible, therefore, that pathologic changes of the ducts did commence at this stage. The encirclement of branches of the portal vein and hepatic artery by dilated ducts in case 1 indicates progressive enlargement of the ducts after this initial stage and it is altogether likely that the development of the lesions in both cases was continuous but gradual.

The gross structure of the livers in both of the present cases was remarkably normal. The gallbladders were normally formed and there was no dilatation or atresia of the common bile ducts. Both grossly and microscopically, the lobular pattern was normal. The central veins, sinusoids, and parenchymal epithelial cells showed no lesions. Although there was some distortion and irregularity of the branches of the portal vein and hepatic artery, they were normally situated in the perilobular connective tissue. In both cases, therefore, the principal lesions were confined to the small intrahepatic bile ducts and were of such a nature that the normal development of the other elements of

the liver and biliary system was not prevented or significantly altered. This observation is also in agreement with the fact that the structural development of the cystic kidneys in those cases was likewise normal.

If these lesions were caused by inflammation, of which there was no evidence, or by an unrestrained proliferation of the bile ducts, it is difficult to understand how the rest of the liver could be so normal. Likewise, since so many of the ducts were distorted or segmented, the occurrence of the lesions can hardly be explained by the persistence of the few normally provisional bile ducts in accordance with Kampmeier's theory that persistence of normally provisional nephrons accounts for the polycystic lesions of the kidney.

In view of these various considerations, therefore, it is proposed that, as for the kidneys, differentiation of the hepatic anlage was at first normal. Only after the appearance of the small intrahepatic bile ducts did cystic lesions begin. Whether the apparent overproduction of the bile ducts was primary or secondary is immaterial. Distortion, segmentation, and cystic dilatation of these elements occurred progressively while the normal differentiation of the rest of the liver was proceeding uninterruptedly. Fundamentally, this is a process of degeneration and is analogous to the sequence of anatomic changes which have been demonstrated in the kidneys. As segmentation of elements is the initial stage of resorption in the mesonephros and in the first generations of nephrons in the metanephros, so the early generations of bile ducts normally segment before complete degeneration and resorption. Consequently, it is believed that in polycystic disease of the liver many more of the small intrahepatic bile ducts than is normal are provisional and that persistence of these segments, which may progressively become dilated as cysts, explains the polycystic disease of the adult. The evidence presented confirms the previous hypothesis that polycystic disease in general is occasioned by an abnormal extension of a normal process of degeneration. The lesions may or may not be accompanied by an overproduction of elements and cystic dilatation may occur before or after segmentation. The familial incidence of the disease strongly suggests a hereditary defect.

Summary and Conclusions

As part of a study of the polycystic lesions in the livers of 2 infants, three-dimensional reconstructions of some of the elements were prepared.

The lesions, confined exclusively to the intrahepatic bile ducts, consisted of distortion, segmentation, and dilatation.

The normal development and differentiation of the rest of the liver and biliary tract was not prevented or significantly altered.

As is the case in polycystic kidneys, it was concluded that the lesions in the livers are essentially degenerative and are an abnormal extension of the process of resorption which occurs normally in the first generations of bile ducts.

REFERENCES

1. Kahlden, C. Ueber die Genese der multiloculären Cystenniere und der Cystenleber. *Beitr. f. path. Anat. u. z. allg. Path.*, 1893, **13**, 291–308.
2. Still, G. F. Congenital cystic liver with cystic kidney. *Tr. Path. Soc. London*, 1897–98, **49**, 155–165.
3. Moschcowitz, E. Non-parasitic cysts (congenital) of the liver, with a study of aberrant bile ducts. *Am. J. M. Sc.*, 1906, **131**, 674–699.
4. Bunting, C. H. Congenital cystic kidney and liver with family tendency. *J. Exper. Med.*, 1906, **8**, 271–288.
5. Vorpahl, F. Über einen Fall von kongenitaler Cystenleber und Cystenniere mit Übergang in riesenhafte Kystombildung. *Beitr. z. path. Anat. u. z. allg. Path.*, 1912, **53**, 477–490.
6. Meyenburg, H. v. Über Atresie der grossen Gallenwege. *Virchows Arch. f. path. Anat.*, 1916, **221**, 352–366.
7. Meyenburg, H. v. Über die Cystenleber. *Beitr. z. path. Anat. u. z. allg. Path.*, 1917–18, **64**, 477–532.
8. Sears, W. G. Congenital cystic disease of the kidneys, liver, and pancreas. *Guy's Hosp. Rep.*, 1926, **76**, 31–52.
9. Teuscher, M. Über die kongenitale Cystenleber mit Cystennieren und Cystenpankreas. *Beitr. z. path. Anat. u. z. allg. Path.*, 1926, **75**, 459–485.
10. Wackerle, L. Zur Frage der Cystenleber. *Virchows Arch. f. path. Anat.*, 1926, **262**, 508–530.
11. Delore, P., and Croizat. Contribution à l'étude de la maladie polykystique. Un cas de maladie polykystique du foie et des reins avec porencéphalie et hémiplégie infantile. *Arch. franco-belges de chir.*, 1928, **31**, 177–185.
12. Delore, P., and Croizat. Un caso di malattia policistica del fegato e dei reni con poroencefalia ed emiplegia infantile. (Contributo allo studio della malattia policistica.) *Rinasc. med.*, 1929, **6**, 158–161.
13. Rümler, E. Die polycystische Entwicklungsstörung im Pankreas, zugleich ein Beitrag zur Frage der Cystenleber und der Cystennieren. *Virchows Arch. f. path. Anat.*, 1934, **292**, 151–165.
14. Lutembacher, R. Reins polykystiques congénitaux à kystes miliaires. *Ann. de méd.*, 1936, **39**, 440–448.
15. Baccarini, L. Contributo allo studio della patogenesi del "fegato policistico." *Arch. ital. di chir.*, 1936, **43**, 92–114.
16. Monserrat, J. L., and Latienda, R. I. Riñon e hígado micropoliquístico (disembrioplasia micropoliquística hepato-renal). *Arch. Soc. argent. de anat. norm. y. pat.*, 1942, **4**, 88–94.
17. Virchow, R. Über Hydrops renum cysticus congenitus. *Virchows Arch. f. path. Anat.*, 1869, **46**, 506–507.
18. Virchow, R. Verhandlungen ärztlicher Gesellschaften. *Klin. Wchnschr.*, 1892, **29**, 104–107.
19. Mutach, A. v. Beitrag zur Genese der congenitalen Cystennieren. *Virchows Arch. f. path. Anat.*, 1895, **142**, 46–86.

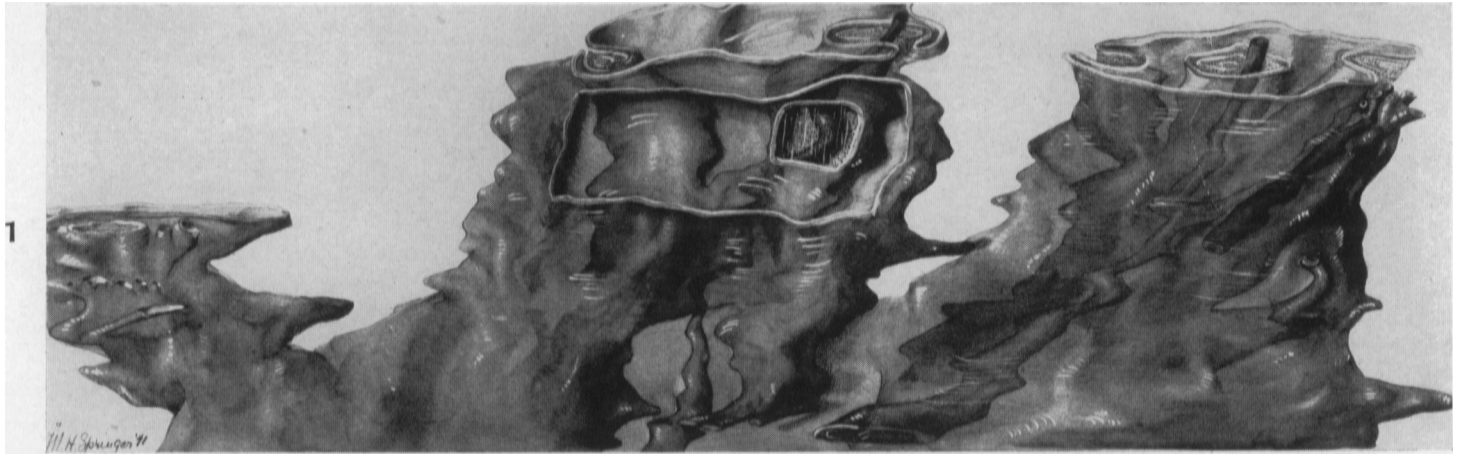
20. Ribbert, H. Ueber die Entwicklung der bleibenden Niere und über die Entstehung der Cystenniere. *Verhandl. d. deutsch. path. Gesellsch.*, 1899, **2**, 187–203.
21. Norris, R. F., and Herman, L. Observations on the anatomic basis of congenital polycystic kidneys. *Tr. Am. A. Genito-Urin. Surgeons*, 1938, **31**, 41–57.
22. Norris, R. F., and Herman, L. The pathogenesis of polycystic kidneys: Reconstruction of cystic elements in four cases. *J. Urol.*, 1941, **46**, 147–176.
23. Brigidi, V., and Severi, A. Contributo alla patogenesi delle cisti renali. *Sperimentale, Arch. di biol.*, 1880, **46**, 1–25.
24. Albrecht. Ueber Hamartome. *Verhandl. d. deutsch. path. Gesellsch.*, 1904, **7**, 153–157.
25. Kampmeier, O. F. Über das Schicksal der erstgeformten Harnkanälchen der bleibenden Niere beim Menschen. *Arch. f. Anat. u. Physiol., anat. Abteil.*, 1919, 204–226.
26. Kampmeier, O. F. A hitherto unrecognized mode of origin of congenital renal cysts. *Surg., Gynec. and Obst.*, 1923, **36**, 208–216.
27. Kampmeier, O. F. Weitere Studien über die Entwicklungsgeschichte der bleibenden Niere beim Menschen. *Ztschr. f. Anat. u. Entwcklngsgesch.*, 1924, **73**, 459–500.
28. Kampmeier, O. F. The metanephros or so-called permanent kidney in part provisional and vestigial. *Anat. Rec.*, 1926, **33**, 115–120.
29. McKenna, C. M., and Kampmeier, O. F. A consideration of the development of polycystic kidney. *Tr. Am. A. Genito-Urin. Surgeons*, 1933, **26**, 377–383.
30. McKenna, C. M., and Kampmeier, O. F. A consideration of the development of polycystic kidney. *J. Urol.*, 1934, **32**, 37–43.
31. Lewis, F. T. The Development of the Liver. In: Keibel, F., and Mall, F. P. (eds.) Manual of Human Embryology. J. B. Lippincott Co., Philadelphia, 1912, **2**, 403–428.

DESCRIPTION OF PLATES

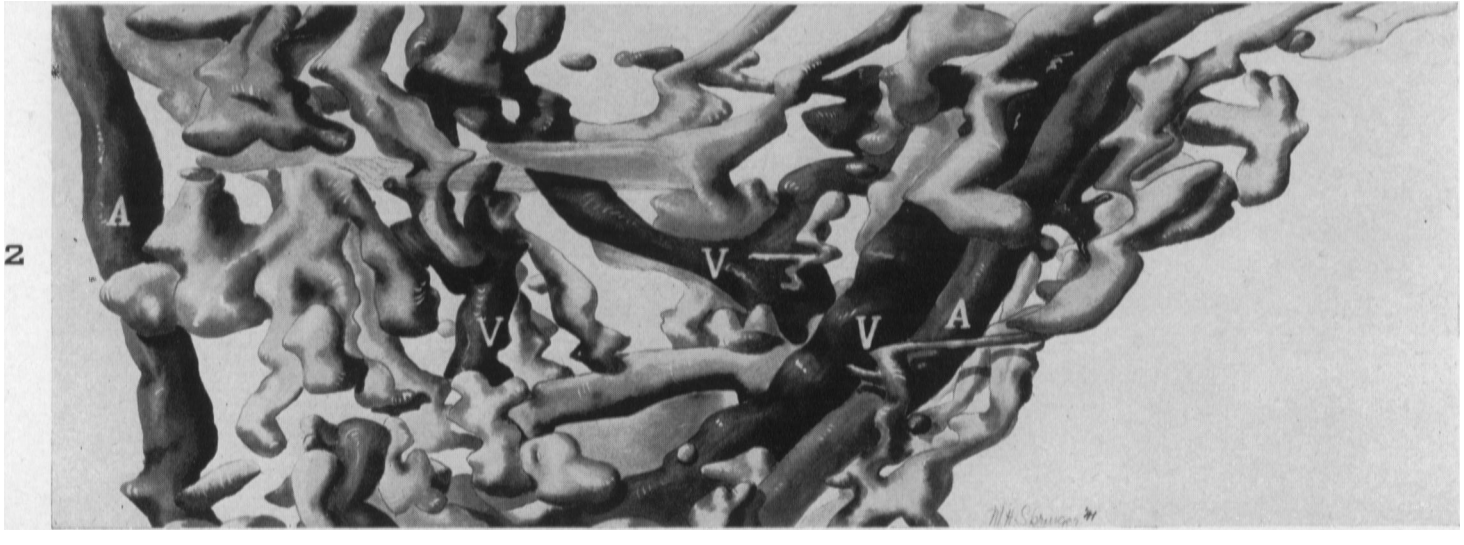
PLATE 36

FIG. 1. Case 1. Model of dilated cystic bile ducts. Anastomoses and blindly-ending projections are numerous. At the extreme left of the model, relatively nondilated branches of the duct are seen in cross section. At the extreme right, the dark tubular structures are branches of the portal vein which in this instance lie outside the duct. Encompassed by the two large cystic ducts are branches of the hepatic artery which are also tubular and less darkly shaded. In the center of the model, windows have been cut to illustrate the cystic folds of the duct and the interior location of the artery. The approximate vertical extent of the reconstruction in the liver was 0.64 cm.

FIG. 2. Case 2. Model of reconstructed elements. Branches of the hepatic artery (A) and portal vein (V) are generally straight but are intimately associated and frequently surrounded by the numerous, more lightly shaded bile ducts. The ducts show considerable variation in diameter and lack a regular pattern. Many branches end blindly. In the lower half of the model are several completely isolated globular segments of ducts as well as a minute circular segment overlying the vein. Just to the right of center, also overlying a vein, is a highly irregular, nondilated segment of duct. Elsewhere there are several more isolated minute segments. Many of the isolated segments appear to be detached continuations of nearby ducts. The approximate vertical extent of the reconstruction in the liver was 0.14 cm.



1

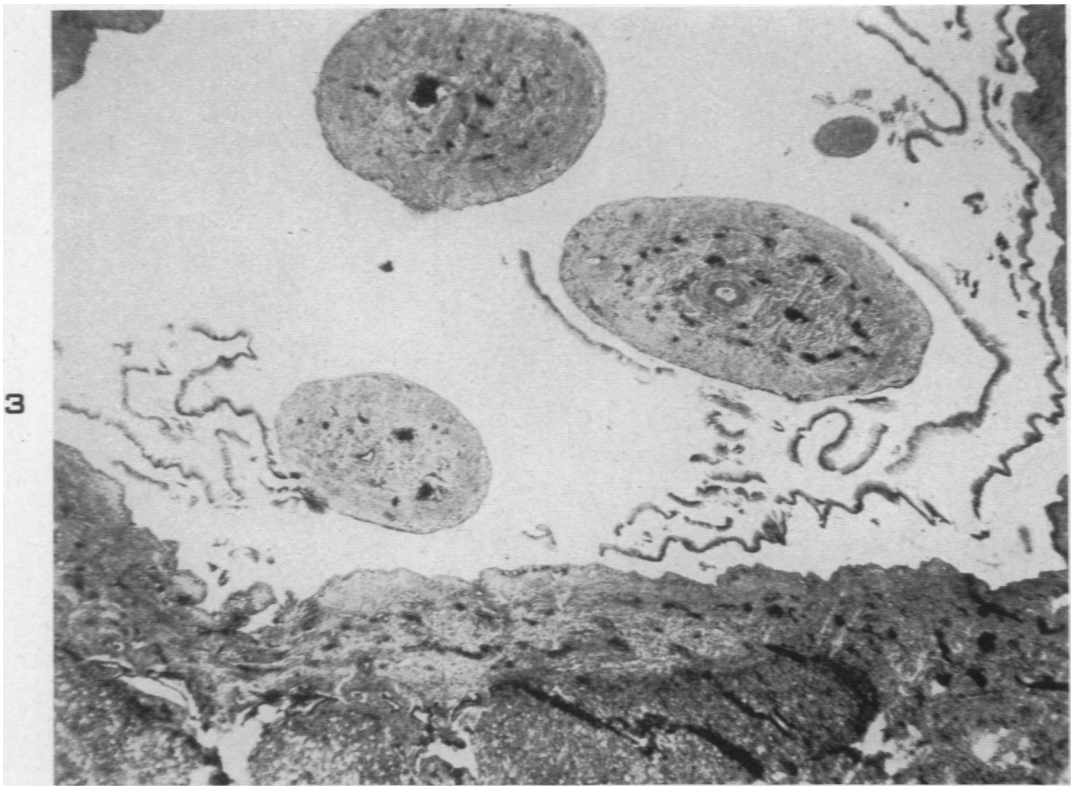


2

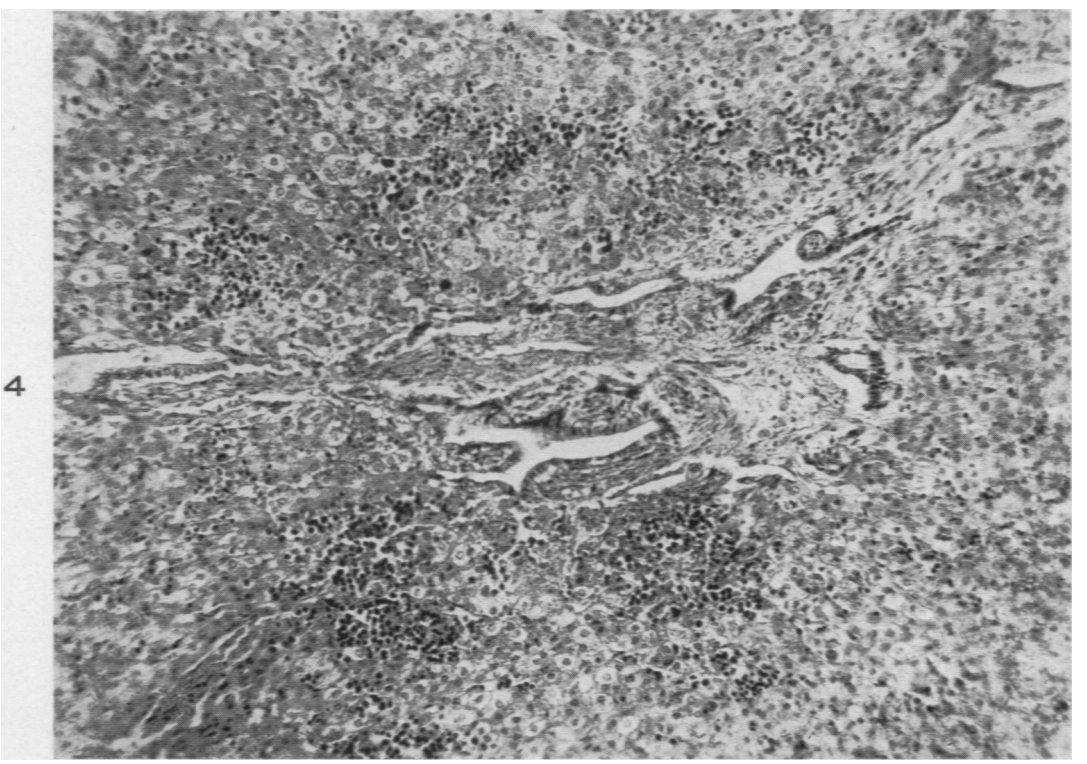
PLATE 37

FIG. 3. Case 1. Low-power photomicrograph showing a large cyst which is a cross section of a dilated bile duct. The lining columnar epithelium is generally detached. The circular cores of solid tissue within the lumen of the cyst are cross sections of trabeculae composed of periportal connective tissue which have been completely encircled and invested by the dilated duct. Embedded in the fibrous stroma are branches of the hepatic artery and portal vein. Hematoxylin and eosin stain. × 45.

FIG. 4. Case 1. Higher-power illustration of the relatively nondilated but highly irregular and distorted bile ducts about the periphery of one of the dilated cystic lesions. The number of ducts is greater than is normal. Small branches of the hepatic artery and vein lie between the ducts in the center. Foci of hematopoiesis are evident among the cords of parenchymal epithelial cells. Hematoxylin and eosin stain. × 190.



3

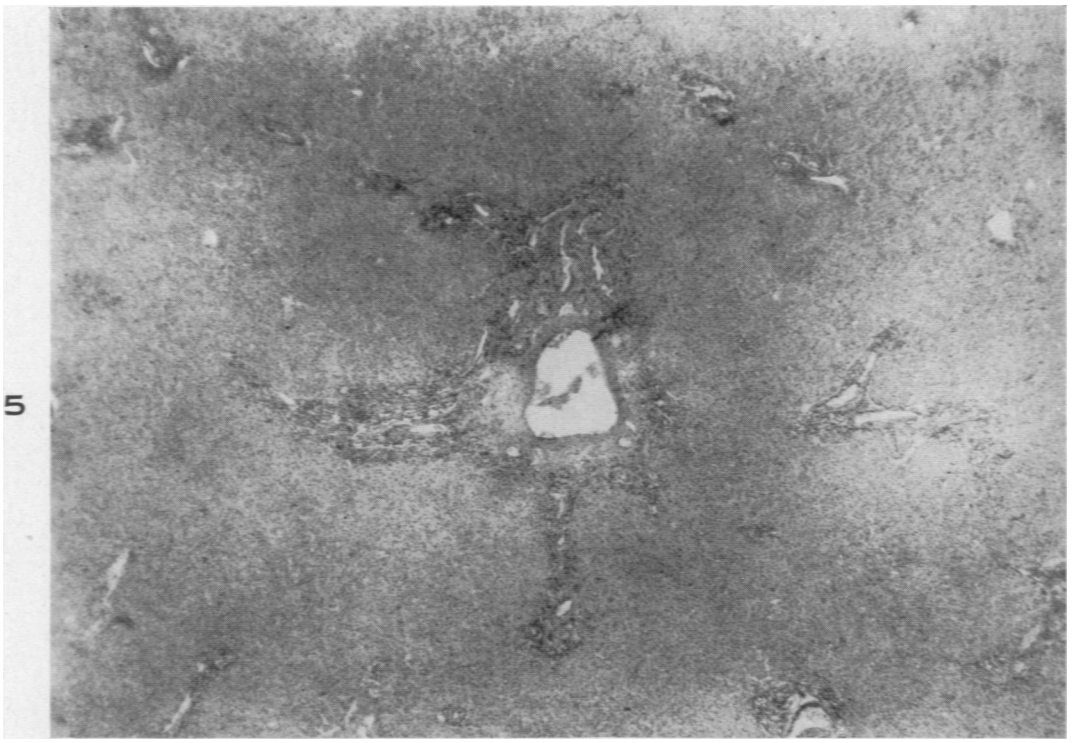


4

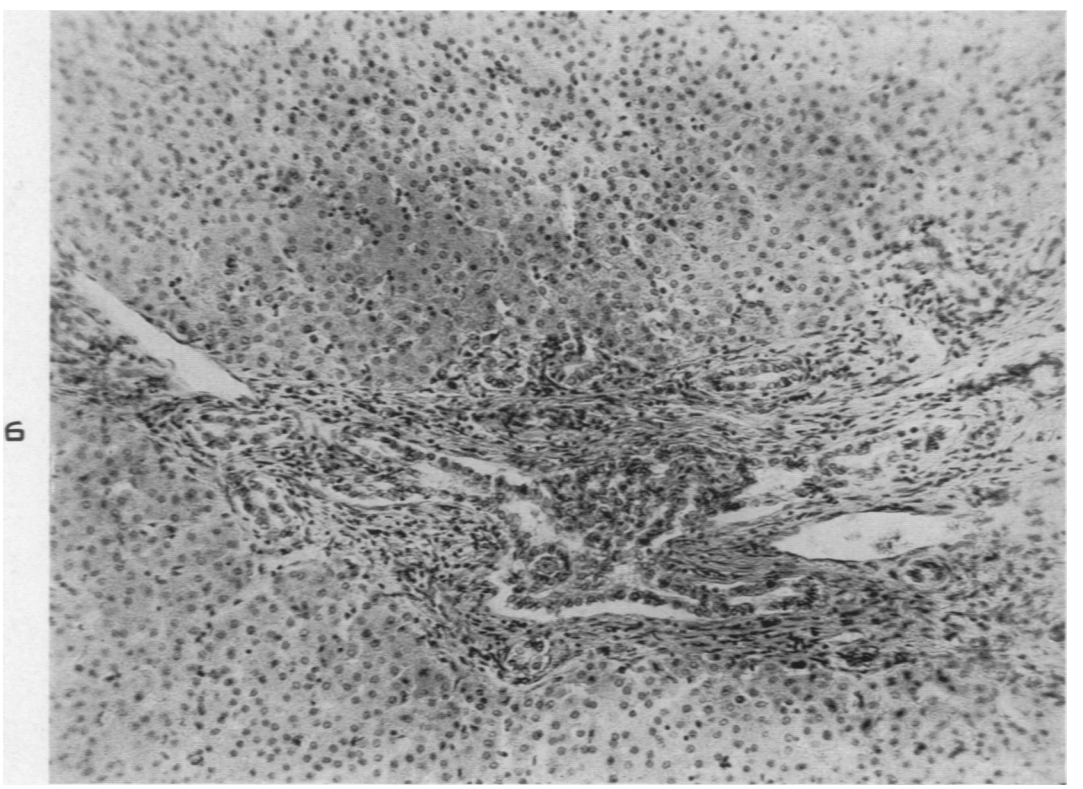
PLATE 38

FIG. 5. Case 2. Low-power photomicrograph showing a periportal space in the center and the relatively normal lobular architecture. The centrally located circular space is a branch of the portal vein. Branches of the hepatic artery are adjacent. The vessels are completely encircled by small, irregular bile ducts which appear more numerous than is normal. Hematoxylin and eosin stain. × 23.

FIG. 6. Case 2. Higher-power illustration of a periportal space. The marked distortion and irregularity without significant dilatation of the small bile ducts are evident. There are also slightly distorted branches of the portal vein. Of note is the similarity of these ducts to those in Figure 4. Hematoxylin and eosin stain. × 190.



5



6

Norris and Tyson Pathogenesis of Polycystic Livers