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THE ISOLATION, SHAPE, SIZE, AND NUMBER OF THE LOBULES OF THE PIG'S LIVER

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TWELVE FIGURES (TWO PLATES)

INTRODUCTION

The following description of the lobules of the pig's liver is based on a study of lobules that were isolated from one another by means of an acid macerating fluid. This method of isolation is invaluable in giving one a correct idea of the shape and size of the hepatic lobule, and in addition, affords a good means of approximately estimating the total number of lobules in the liver. If the maceration is stopped at just the right point, the method permits the easy dissection of blocks of liver tissue. Dissections of injected livers made in this manner, with the blood vessels and bile ducts as little disturbed as possible, give one a clearer understanding of liver structure than can be obtained by any other method.

A survey of the literature shows that to Wepfer belongs the credit of discovery of the lobule of the liver. In a letter to Paulli (1665) signed by Wepfer, 1664, the substance of the liver was described as follows:

> Examine carefully boiled pig's liver; remove the external membrane and you will find the whole large mass a combination, as it were, of innumerable small glands. Concerning the livers of other animals, I confess, I have not yet made investigations. But upon thoroughly boiling a piece of pig's liver, I have seen small glands, quadrangular and other forms.

In 1666, Malpighi, unaware of Wepfer's discovery, described the lobular nature of the liver in molluscs, the lizard, ferret, mouse, squirrel, ox and man. Concerning those of man, he states:

Finally, in the human body if one will take the care to wash out the blood which is found in the liver by the injection of water, one will observe all the substance of the liver tissue to be composed of a number of small lobes, which resemble, as in other animals, a bunch of grapes.

The lobules were again described by Malpighi in 1683 and in his Opera Posthuma (1698), he accredited Wepfer with the priority of discovery.

A most noteworthy and often cited contribution to the subject of liver lobules is that of Kiernan, 1833. He states:

> The form of the liver lobules will be now easily understood: their dimensions are known to all anatomists. They are small bodies arranged in close contact around the sub-lobular-hepatic veins, each presenting two surfaces. One surface of every lobule, which may be called its base, rests upon a sublobular vein, to which it is connected by an intralobular vein running through its center, the base of the lobule thus entering into the formation of a canal in which the sublobular vein is contained. The canal containing the hepatic veins may be called the hepatic-venous canals or surfaces; and as the base of a lobule rests on the sublobular vein, it is evident that the canals containing these veins are formed by the bases of all the lobules of the liver. The external or capsular surface of every lobule is covered by an expansion of Glisson's capsule, by which it is connected to and separated from the contiguous lobules, and in which the branches of the hepatic duct, portal vein and hepatic artery ramify. All the lobules resemble each other in their general form, and they are all of nearly equal dimensions, they appear larger when the section is made in the direction of the hepatic vein, and smaller when in the transverse direction.

Although in few details the above description is incorrect, on the whole it gives one a clear idea of the arrangement of liver lobules. Kiernan's whole paper is full of splendid observations, and one may truthfully say, serves as the basis of our present knowledge of the liver. His figures illustrating the liver lobules, very probably taken from the liver of the pig, have found their way into numerous textbooks of anatomy.

In 1842, Weber called attention to the fact that the lobules of the human liver are not separated from one another as in the pig, and that while lobules are indicated, the parenchyma forms a continuous mass throughout.

The work of Theile, 1884, (cited from Mall, '06) in which are described 'pseudo lobules,' gave rise to a new conception of the

structural arrangement of the liver, although Kiernan in 1833 made the statement that "the essential part of the gland is undoubtedly its duct; vessels it possesses in common with every other organ; and it may be thought that in the above description too much importance is attached to the hepatic veins." We owe to Sabourin ('82, '88) however, the discovery of the true significance of this newly recognized unit of the liver, the unit which is built around the portal canal. This unit, with its imaginary boundaries, has been discussed in recent years by Berdal ('94), Mall ('00 and '06) and Lewis ('04), and has been variously named the biliary lobule, portal lobule, secreting lobule and structural unit by different writers. The value of this latter concept of liver structure is no longer questioned; considered from physiological or morphological view points it stands out as the true unit of the liver. The connective tissue septa dividing the liver into hepatic lobules must be considered secondary both in point of development and importance. Yet in most animals it is the hepatic lobule which appears to be the more definite anatomical structure, and its study is essential to a clear understanding of the portal lobule. With this in mind, and without any intent to emphasize the morphological value of the hepatic lobule, the present study has been made.

THE ISOLATION OF LIVER LOBULES

The method of isolation which I first employed (Johnson, '17), that is, macerating small blocks of formalin fixed liver in 20 per cent nitric acid, I find less satisfactory than the hydrochloric acid macerating fluid used by Huber ('11) in the isolation of kidney tubules. The best method which I have evolved from a number of trials is as follows: Blocks of liver tissue, 1 cm. in thickness, are thoroughly hardened in 10 per cent formalin. They are then placed in 50 to 75 per cent hydrochloric acid and left standing in it at room temperature over night. Next they are placed in an oven (still in the acid) at a temperature of 50° to 60°C. In about two to four hours, depending upon the strength of the acid and the temperature of the oven, the lobules begin to fall apart. The maceration should be stopped when

the lobules separate by gentle shaking. Care should be taken not to allow the maceration to proceed too far, yet it should not be stopped before all the connective tissue is destroyed. The blocks can be tested from time to time by gently pressing them with a dissecting needle. When the maceration is complete, the acid should be diluted four or five times with cold water and the lobules studied in this solution. (When placed in either water or alcohol the lobules disintegrate inside of a day or two.) If dissections of the liver lobules and vessels are desired, such as are shown in figures 11 and 12, maceration should be stopped when the lobules can be torn apart easily with dissecting needles. I have been unable to obtain good results in the isolation of lobules following hardening in either Zenker's or Bouin's fluid or in alcohol, and have been entirely unsuccessful in macerating fresh unfixed liver.

THE SHAPE OF THE LIVER LOBULES

The form of liver lobules is so variable that it is impossible to describe them in terms of any familiar solid. In general, it may be said that they are irregular polyhedrons of a varying number of sides, borders and angles. The surfaces may be plane, convex or concave, and may vary from as few as four or five in some of the smaller lobules to fifteen or more in some of the larger ones. The borders may be either sharply marked or rounded, while the angles formed by the union of the borders may vary from sharply acute to greatly obtuse.

So far as shape alone is concerned I have found no way of determining on which surface the hepatic vein leaves the lobule, the surface which Kiernan ('33) describes as the base. Its point of exit may be either a small or large surface, plane, convex or concave, or it may even proceed from one of the borders or angles of the lobule (figs. 5, 6, 9 and 10).

The surface lobules (figs. 1, 5, 9 and 11) are in many instances distinguishable from the deeper lobules in that they are often irregularly prismatic in shape, their external surfaces are usually slightly convex and the shape of a four, five or six-sided polygon; the sides are plane or only slightly curving and more or less rec-

tangular. The deeper ends of these lobules are usually irregular in shape and quite often larger or smaller than the surface ends. Occasionally are to be seen lobules which are markedly pyramidal in shape, the apices of which may be directed either toward or away from the surface of the liver.

The fact that the lobules of the liver are closely packed solids leads to the question whether or not they resemble any of the regular geometrical solids which fill space. Of such solids, in addition to three, four and six-sided prisms, may be mentioned the tetrahedron, hexahedron, dodekahedron and the tetrakaidekahedron. The surface lobules, as stated above, tend to be prismatic, but I have found but few of the deeper lobules which approach in form any of the above named geometrical solids. Occasionally, however, one may be found which meets the requirements of one of these solids when viewed from one side, but fails when viewed from the other. Several such lobules are shown in figures 1, 2 and 6. If there is any attempt in development to cut the liver up in similarly shaped units, the adult condition does not show it. It should be further pointed out that the lobules in young stages of the pig, amongst them stages in which the lobules are just beginning to be marked off from one another, likewise show but very few regularly-shaped lobules. Among the factors which might tend to break up any uniformity in the shape of the lobules may be mentioned the splitting up of the lobules to form additional ones (Johnson, '17) the unequal growth and size of the various lobules, and the presence of the portal and hepatic canals.

The statement that the lobules of the pig's liver are completely separated from one another by connective tissue septa is prevalent in anatomical literature. While this is true of the majority of lobules, it will not hold for a large number of them. If a block of liver tissue is macerated in hydrochloric acid there will be seen amongst the completely separated lobules a number which cling together in small clumps of from 2 to 6 lobules each, figures 7, 8 and 10. The individual lobules of these clumps cannot be isolated by shaking or gentle teasing, and a definite tearing of the liver parenchyma is necessary in order to divide them.

The clumps, therefore, must be considered as "compound lobules" (Kiernan) and are due to incomplete connective tissue septa. They undoubtedly are the result of the failure of the septa to grow completely across the lobules in the developing liver, at the time when the lobules are dividing to form additional ones. The evidence of incomplete septa can often be seen in ordinary sections of the adult pig's liver.

THE SIZE AND NUMBER OF THE LIVER LOBULES

The size of the lobule of the adult pig's liver is very variable, great differences existing within any individual liver. The smallest lobules may be no larger than 0.5 mm. in diameter; the largest ones may be 2 mm. or over. Assuming that the shapes of the large and small lobules are approximately similar, it is evident that the largest lobules must be as much as 64 times greater by volume than the smallest ones.

The average volume of the liver lobule is dependent to a certain degree upon the size of the liver, thus in small livers the average volume is less than in large ones. This is shown in the accompanying table.

The total number of lobules in the pig's liver is also quite variable. This can be readily observed with the naked eye when examining isolated lobules of different livers of approximately the same weight—in some the majority of lobules are large while in others they are decidedly smaller.

The method of calculating the average size and number of hepatic lobules, which I have found most satisfactory, is as follows: Rectangular blocks of formalin-fixed liver, with dimensions between 1 and 2 cm., were taken from a liver of known weight. Each block was carefully weighed, placed in a separate dish in 50 per cent hydrochloric acid over night, and then in an oven at a temperature of from 50° to 60°C. After about an hour the surface lobules become swollen and each projects slightly from the surface. The surface lobules now being definitely marked off from one another, were counted under a hand-lens, care being taken not to count twice those lobules on the borders and corners of the block. The block was again placed in the oven and

maceraton allowed to proceed until the lobules separated. The lobules were then counted under a hand-lens, a few being taken out at a time with a pipette and removed to a watch glass. In counting, the individual parts of compound lobules were considered as separate lobules; so also were the cut portions of the lobules which came from the cut surfaces of the block. This number was reduced by one-half the number of surface lobules counted, since I assumed that in slicing a piece of liver, the sum of the cut lobules on one side equals the sum of those on the other. Dividing the number of lobules obtained in this way into the weight of the block gives the weight per lobule, and the weight per lobule into the weight of the liver gives the total number of lobules. The average of a number of counts on nine different livers are given in the table below. The average weight per lobule obtained is 2.41 milligrams and the average number of lobules 702,000. The latter number is somewhat higher than that (480,000) obtained by Mall as the average number of lobules in the dog's liver.

TABLE 1

WEIGHT OF LIVER	AVERAGE WEIGHT PER LOBULE[1]	NUMBER OF LOBULES
grams	*mgm.*	
1132	1.95	570,000
1203	1.40	859,000
1418	2.62	541,000
1658	1.95	850,000
1658	2.21	750,000
1786	2.36	757,000
1886	3.99	472,000
1927	2.98	647,000
1942	2.22	874,000
Average.....	2.41	702,000

[1] The "average weight per lobule" was obtained from calculations based on counts from several blocks taken from each liver.

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PLATE 1

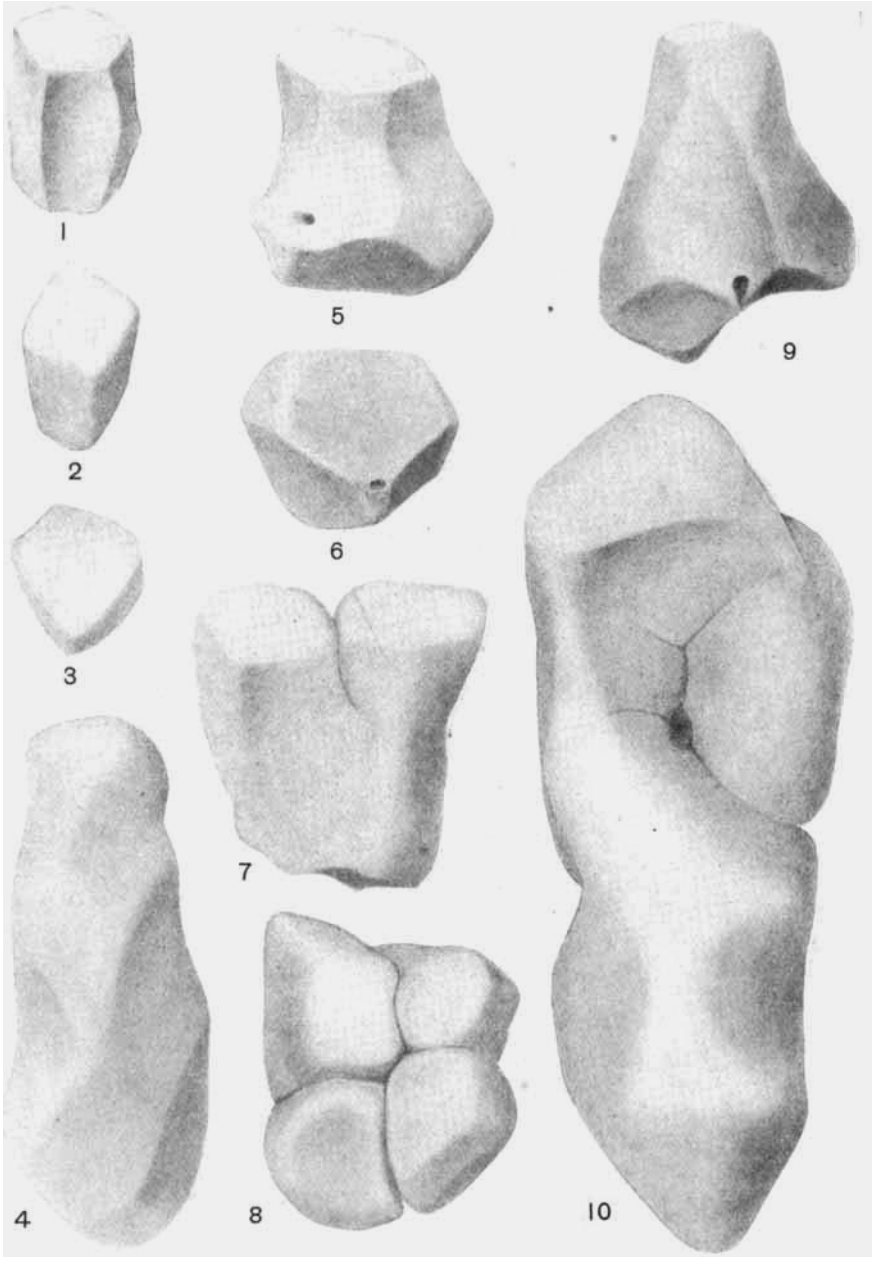
EXPLANATION OF FIGURES

Isolated liver lobules drawn at a magnification of 12.5 diameters. The greatest extremes in sizes are not shown.

1, 5, 9 Surface lobules

1, 2, 6 Geometrical forms.

7, 8, 10 Compound lobules.


1
5
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4
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10

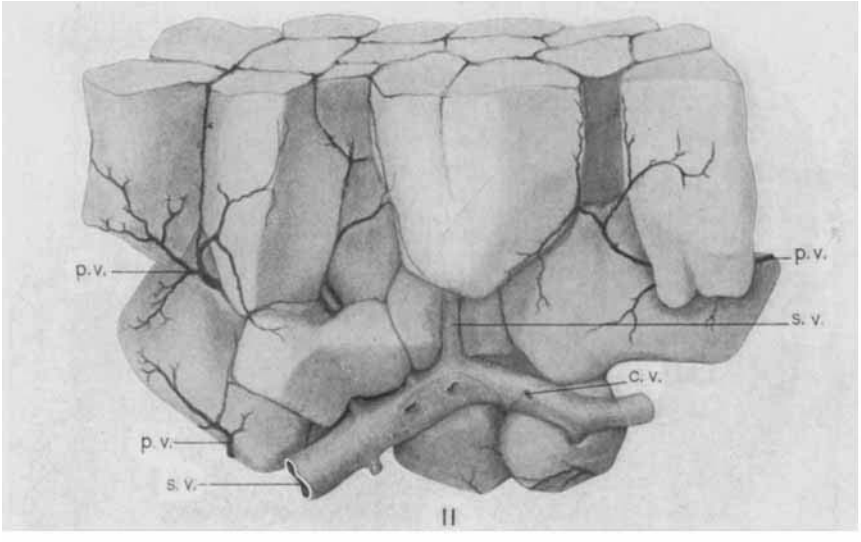
PLATE 2

EXPLANATION OF FIGURES

Dissections of liver lobules to show their arrangement.

11 A group of surface lobules. Bile ducts and branches of the hepatic artery have been omitted.

12 A group of lobules situated deep in the substance of the liver. On the left is seen a large portal canal with bile duct, hepatic artery, and portal vein. The branches of these vessels were worked out as far as possible. Undoubtedly some of them were torn away in lifting off the lobules in dissecting, so that all the branches ramifying over the surfaces of the lobules are not shown. *p.v.*, portal vein; *s.v.*, sublobular (hepatic) vein; *c.v.*, central (hepatic) vein; *b.d.*, bile duct; *h.a.*, hepatic artery.


p.v.
p.v.
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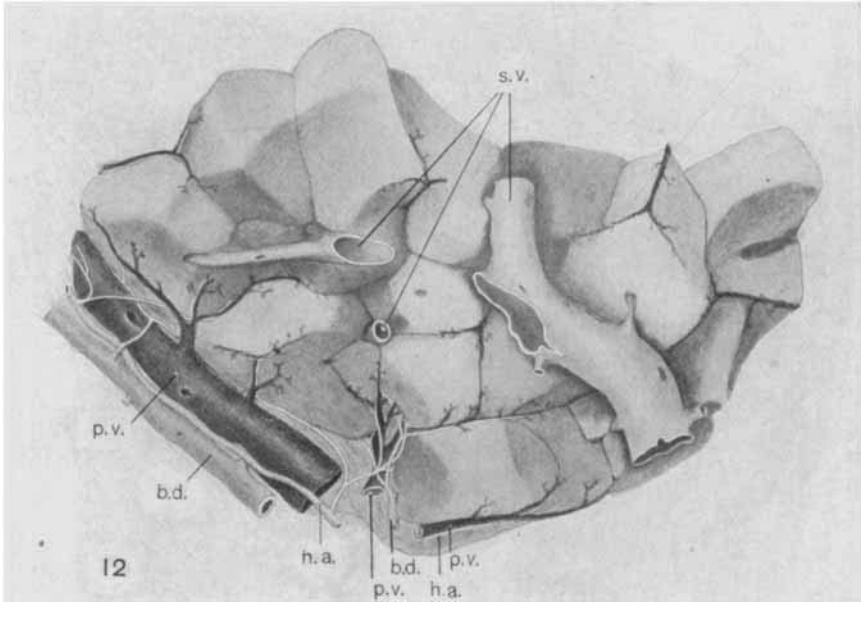
s.v.
11


s.v.
p.v.
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