TECHNICAL PAPERS

The Liver Cord Concept after One Hundred Years[1, 2]

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One hundred years have passed since Gerlach (*5*) stated that the liver parenchyma consists of hepatic cells in linear arrangement. This concept has been developed, chiefly by Beale (*1*), and Pflüger (*9*), into the theory of the hepatic cord, almost universally accepted by the authors of modern textbooks. Accidentally, in the last year of its first century of existence, the validity of the liver cord theory came to be questioned.

A film strip on the histology of the liver for use in medical schools was prepared according to the description found in standard textbooks. This film strip consisted of stereograms, and presented the liver as composed of cords of cells (Fig. 1), surrounded by blood spaces called sinusoids. The liver cord is a double row of cells, as all textbooks agree (except Sharpey-Schafer's [*10*]). A bile capillary runs between the cells through the center of the cord. The textbooks have also agreed that these cell cords, columns, or trabeculae anastomose with one another and are in essence arranged radially around the central vein of each liver lobule (Fig. 2). The film strip was prepared according to these conceptions.

After completion of the stereograms for the film strip, it seemed essential to supplement the view diagrammatically presented by means of wax plate reconstructions and photomicrographs. It seemed easy to find longitudinal sections of cords (Figs. 3 and 4) in sections perpendicular to central veins. But the long rows of cells seen invariably in such sections are all too numerous. If tortuous but linear columns did exist in radial arrangement about the central vein, the chances of cutting them lengthwise with the microtome for any considerable distance are very slight. There should not be more than one longitudinal section of cord per microscopic field at high power, even in sections perpendicular to a central vein. The majority of sections of cords, if they did exist, should be oblique, i.e., about three to four cells long. While it had been suspiciously easy to find apparently longitudinal sections of cords, it was practically impossible to find cross sections of cords, despite the fact

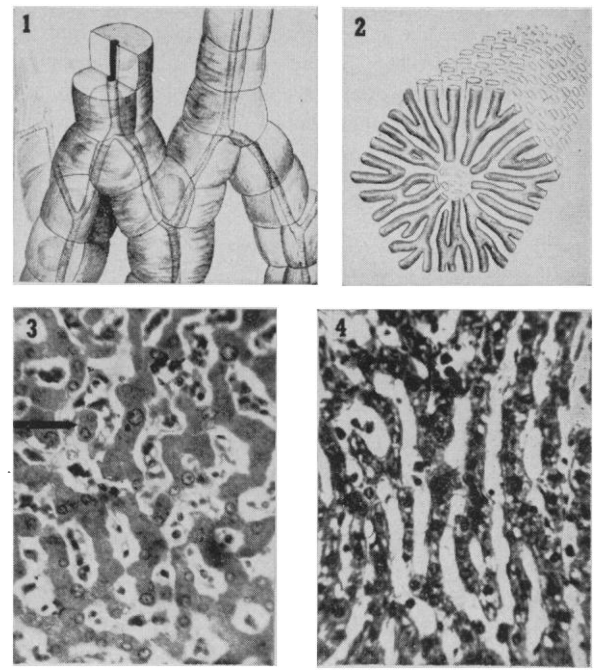


FIG. 1. Stereogram of the conventional concept of anastomosing liver cords, containing axial bile canaliculi.

FIG. 2. Conventional interpretation of the structure of an hepatic lobule.

FIG. 3. Section of human liver lobule perpendicular to central vein. The arrow points to a cross section of an interlaminary bridge.

FIG. 4. Section of liver lobule of horse, perpendicular to central vein. This, as well as the preceding section, consists of long rows of cells, one cell wide.

that they should be very numerous in tangential sections of a lobule (see Fig. 2). In man (Fig. 5) and the cat, sections parallel to the central vein showed long rows of cells simulating cords.

In whatever direction we may cut a human or cat liver lobule, we always obtain long linear rows of cells. And at widely scattered places we find isolated patches of hepatic cells in an epithelial arrangement (Fig. 6).

The liver of man and the cat, hence, can *not* consist of cords or columns. It must be fashioned of structures which will show, in almost whatever direction they are sectioned, long rows of cells one cell wide, and which at a few places may give sections appearing as larger epithelial masses. Clearly, the formations that can yield these sections cannot be anything but curved plates, sheets, or laminae, one cell thick.

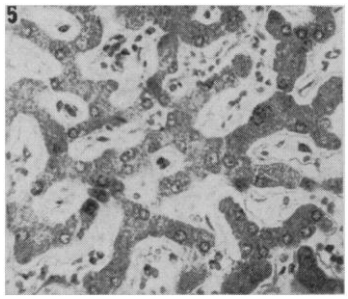
This logical conclusion can easily be verified by means of wax plate reconstructions and also by examining thick, unstained sections mounted in glycerin. Fig. 7 shows a group of hepatic plates drawn with the camera lucida from a section perpendicular to a central vein and 30 μ thick. The plates are curved, frequently perforated, and

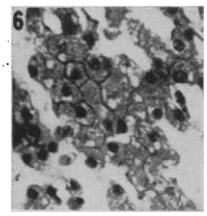
[1] The contents of this report are being described and discussed more thoroughly in the *American Journal of Anatomy*. The paper was read before the American Association of Anatomists, April 23, 1948, and abstracted in *Anat. Rec.*, 1948, **100**, 23.

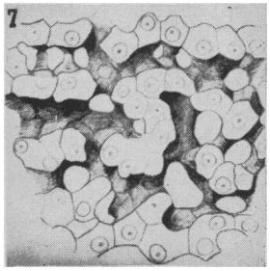
[2] A preliminary report.

[3] From Production Division, Atlanta, Georgia.

wherever they are cut the section is a row of cells one cell wide. It is clear that sections cutting these sheets in other directions will appear as single rows of cells. But it will also be possible, if the level and angle of cutting is favorable, to obtain tangential sections of these laminae, such as the section shown in Fig. 6. In the upper left-hand corner of Fig. 7, unicellular bridges can be seen connecting neighboring plates. Such unicellular and sometimes bicellular bridges account for the occasional occurrence of apparent cross sections of cords, as seen at the tip of the arrow in Fig. 3.







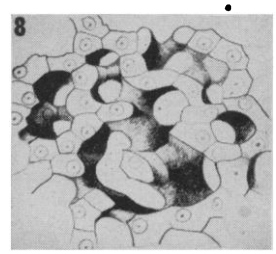


FIG. 5. Section of human liver lobule parallel to central vein. Also in this direction, long rows of cells, one cell wide, are seen. Note the incompatibility of this as well as of the succeeding section with Figs. 1 and 2.

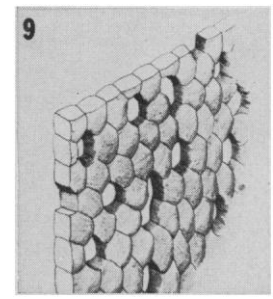
FIG. 6. Tangential section of liver plate (lamina hepatica) of cat.

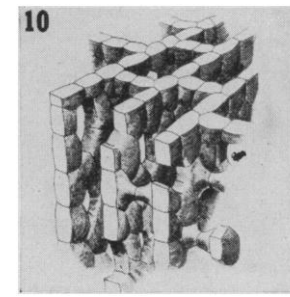
FIG. 7. Liver of cat, showing anastomosing, cribriform, curved, hepatic plates. The spaces which they surround are irregular in shape. Camera lucida drawing of frozen section, 30 μ thick, cut perpendicularly to central vein, not stained, mounted in glycerin.

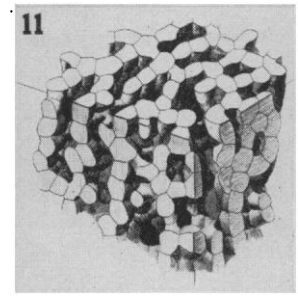
FIG. 8. Liver of cat, showing anastomoses of hepatic plates, saccular shape of hepatic lacunae, interlaminary bridges (upper left), perforations of laminae. Technique as in Fig. 7, sectioned parallel to central vein.

Fig. 8 shows a 30-μ-thick section parallel to a central vein, from the same cat's liver as seen in the preceding figure. It shows that the tortuous laminae anastomose with one another and form wide tubes with irregularly curved, and undoubtedly flexible, walls.[4] We are looking into these saccular lacunae which run toward the central vein. But we are following their course for a distance of only 30 μ. Wax plate models showing the same arrangement were obtained by taking serial, optical sections with the motion picture camera, moving the microscope's fine adjustment from frame to frame for 1 μ.

For the conventional idea of the hepatic cord, consisting of a double row of cells (Fig. 1), there must, therefore, be substituted the concept of the hepatic lamina (Fig. 9) which is one cell thick and frequently perforated to permit the passage of sinusoids. However, hepatic sheets are not straight and they never occur isolated. They form a continuous tissue of connected walls which enclose between them the spaces in which the sinusoids run. This arrangement is shown schematically in Fig. 10. In reality, the plates are curved as seen in Fig. 11. The liver of man and the cat may tentatively be called the saccular type of liver, since the spaces between the plates have the character of long sacs.







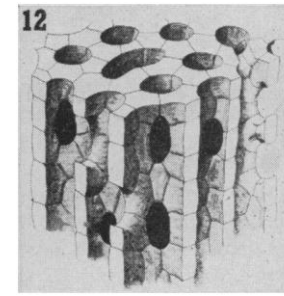


FIG. 9. Schematic stereogram of hepatic plate.

FIG. 10. Schematic stereogram of the saccular liver. Note interlaminary bridges.

FIG. 11. Semidiagrammatic stereogram of the human liver (hepar sacculare).

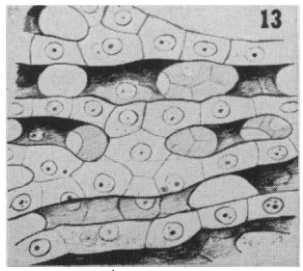
FIG. 12. Stereogram of the equine liver (hepar tubulare).

A second type of liver is to be found in the horse and in the rabbit. This is the tubular liver, one in which the spaces between the hepatic laminae or walls are narrow and cylindrical. Fig. 13 shows some of these tubes from a horse, cut longitudinally, that is, perpendicularly to the central vein of the lobule. Fig. 13 is also a 30-μ-thick section, unstained, and mounted in glycerine. As Fig. 4 shows, this tubular type of liver also yields, in thin sections, long single rows of cells. Fig. 12 is a stereogram of the tubular liver.

The knowledge of the laminary liver structure makes it much easier to understand the existence of the well-known polygonal meshwork of bile capillaries. These polygonal networks, which are so easily demonstrated with Golgi's silver method or with Chrzonszczewsky's indigocarmine method, do not fit at all into the conven-

[4] The flexibility of the hepatic laminae becomes obvious in sections of livers from which the blood has been drained, after severe hemorrhages. In this case the lacunae become collapsed.

tional picture of columnar liver structure. The bile capillaries run, in the majority of cases, between the cells and form hexagonal, intercellular, and pericellular networks within the liver plates.



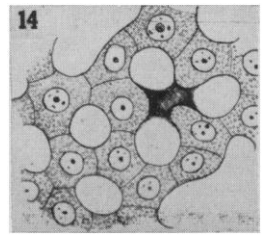


FIG. 13. Liver of horse, showing the tubular character of the lacunae, technique as in Figs. 7 and 8, perpendicular to central vein.

FIG. 14. Same as Fig. 13, but cut parallel to central vein.

From a historical point of view these observations are very interesting. The earliest account of the intimate structure of the liver was given by Gerlach in 1849 and upheld by Beale in 1856 (*1*). Beale described the liver as consisting of membranous tubes which contained rows of liver cells. Basically, this is the conception of modern textbooks. A cell cord surrounded by a network of lattice fibers is essentially the same as a row of cells contained in a noncellular tube.

In 1859, Budge (*4*) raised doubts. He objected to the inadequate methods Beale had used (maceration for days in water, not even in saline, at room temperature; teasing; no use of sections), but he did not find the correct solution.

In 1866, Hering (*6*) analyzed and described, in all correctness and exactly as outlined in this paper, the tubular type of liver (not using this expression) in the rabbit.

In 1867, Kölliker (*8*) described the human liver as a network of tender leaves and strings. Thus, he took a position intermediate between Beale and the view presented in this paper.

In 1869, Pflüger (*9*) ridiculed Hering and upheld the opinion of Gerlach and Beale. Both Beale and Pflüger were prominent men; hence their view was almost universally accepted. Pflüger ignored Kölliker's findings.

Once more, in 1872, Hering (*7*) asserted his viewpoint, bringing more evidence and considering very carefully the geometrical, three-dimensional aspect of the subject. However, his opinion was not accepted.

As late as 1889, Beale (*2*) restated and tried to prove his original concept by obsolete methods; washing the liver through the portal vein with water (not saline), then letting it soak for some time in soda water before beginning to inject his material and observe it with the teasing method. Inadequate as his methods were, Beale nevertheless prevailed, and the most modern textbooks presented the mammalian liver as made of cell columns ensheathed in an argyrophil network.

There are two exceptions to the majority of opinions in textbooks: Braus (*3*) found plates in the liver of man. These are, however, according to him, two cells thick and occur simultaneously with cords which are also two cells thick. The other exception is Sharpey-Schafer (*10*), who described the liver as a parenchyma pervaded by cylindrical sinusoids. This is almost in accordance with Hering, from whom a figure is reproduced. But Sharpey-Schafer does not mention the fact that the walls separating the sinusoids are only one cell thick.

All other textbooks have accepted without question the statements of Beale and Pflüger and perpetuated for 99 years a fundamental misconception of this important organ.

It was the problem of stereographic screen projection of liver anatomy which stimulated a re-examination of the architecture of this organ.

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Perchloric Acid in the Cytochemistry of Pentose Nucleic Acid[1]

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Cytochemical methods for demonstrating pentose nucleic acid (PNA)in tissue sections are based on the removal by ribonuclease of the ability of certain cell constituents to be stained by basic dyes, such as pyronin in Unna's pyronin-methyl green mixture (*1*), methylene blue (*3*), and toluidine blue (*4*). Parallel sections, treated and not treated with ribonuclease, are stained simultaneously and compared. The specificity of the demonstration, of course, depends upon the freedom of the enzyme preparation from proteolytic activity.

Analytical work in this laboratory (*5*, *6*) on root tip homogenates has led to a method for the differential acid extraction of the constituents of PNA and desoxypentose nucleic acid (DNA) into separate fractions, which may

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