THE CIBA COLLECTION OF MEDICAL ILLUSTRATIONS

VOLUME 3

DIGESTIVE SYSTEM

PART III

LIVER, BILIARY TRACT AND PANCREAS

FRANK H. NETTER, M.D.

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VOLUME 3

A Compilation of Paintings on the
Normal and Pathologic Anatomy of the

DIGESTIVE SYSTEM

PART III

LIVER, BILIARY TRACT AND PANCREAS

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INTRODUCTION

If the number of newly published books on a particular medical topic may be taken as an index of the interest of the profession in such a subject, the diseases of the liver would assuredly belong among those that stand at the top of the list. No less than eight monographs on the liver and/or biliary system have appeared in the last 2 years. This interest was also evidenced in some 7,000 answers CIBA received several years ago to an inquiry as to which subject would be the most desirable for the continuation of the series of medical illustrations, which had been published and distributed over a period of 10 years. At that time the central nervous system held first position, and the anatomy and pathology of the liver was a very close second. Yielding to the wishes of a small majority, Volume 1 of THE CIBA COLLECTION OF MEDICAL ILLUSTRATIONS, *Nervous System,* was published in 1953. With the present book we hope to satisfy the demands for an illustrated description of the anatomy and pathology of the liver and biliary system. In line with the over-all plan of this series of books, according to which a separate volume is devoted to each single system of the human organism (see Preface to Volume 1), the bile-producing and -transporting organs, as well as the pancreas, must be included in Volume 3, designed to cover the digestive system.

To offer the illustrations of the whole digestive system in one single book, as we did with the reproductive system, was considered too impractical. Such an attempt would not only have meant a long wait for a new volume after the appearance of the last one but would also have resulted in a rather voluminous, unwieldy and very expensive tome. The separation of Volume 3 into three parts — each a single book containing from 140 to 160 plates, issued at intervals as short as possible — seemed, therefore, to serve best the needs which this COLLECTION aims to meet. We started with the preparation of the pictures of the "large glands" of the digestive apparatus, essentially in order to comply with the incoming suggestions and requests. For the sake of a rational arrangement and in accordance with the customary and traditional order in which the digestive system is described in all textbooks, whether they pertain to anatomy, physiology, medicine or surgery, the present book had to rank as Part III, in spite of its being published first. Part I of Volume 3 will contain illustrations and discussions of the anatomy, pathology and some functional aspects of the upper alimentary tract (from mouth to duodenum, Sections I to VIII), while Part II will consummate the digestive tract, with pictures of the small and large intestines, including paintings concerned with the wall and cavity of the abdomen (Sections IX to XIV). Work on Part I has progressed while this book is going to press, so that we have valid reasons to believe that it will be ready in a short time.

The attempt to interpret the anatomic and pathologic features of the liver with pencil and colors and in words, the number of which is restricted to fit into a relatively small space, led to numerous problems for the artist and consultants alike, problems of a kind we had not met in previous volumes. New concepts of the liver structure, new insights into the pathogenesis of hepatic and pancreatic diseases, a new store of knowledge of the functional aspects and their relation to morphologic characteristics and refined discriminations of disease entities necessitated novel forms and approaches to the lucid two-dimensional visual demonstrations, more frequent conferences between the artist and the consultants, more time-consuming studies and more elaborate planning for the presentation of all the important macro- and microscopic, etiologic, functional, etc., facets. Obviously, in spite of the amazing progress medical science has made in this field, numerous problems remain unsolved and not a few differences of opinion await reconciliation by future investigation. In the pictorial part of the present book, controversial issues or claims not definitely established have been circumvented, except in very few instances, in which, however, a question mark indicates a point of view which is not generally accepted. In the text, the problematic aspects or uncertainties of specific allegations are clearly specified as such. Nevertheless, we are aware of the strong possibility that a variety of statements or opinions, though carefully formulated by our consultants, may have to be revised in a relatively short time. Such revisions had to be incorporated in pictures and texts that were prepared during the early period of work on this book (1954). In any event, we have made every possible effort to have this book reflect in all respects the status of the knowledge in this field at the time of going to press (September, 1956).

One of our great problems has been, again as in Volume 2 which deals with the reproductive system, to remain within the limits of the not easily definable "desirable details", with which the scope of this COLLECTION was described in a programmatic fashion at the time the series was launched with Volume 1. Completeness is not our aim, and it seems appropriate to emphasize again that this Part III of Volume 3 (as is the case with the previously published books) does not, and has not been set up to, substitute for a single one of the many available textbooks and monographs on the subject of diseases of the liver, extrahepatic biliary tract and pancreas. As stated before: "The principle that guided each of our consultants, as well as the artist, was to supplement rather than to replace the standard reference works in the physician's library".

With regard to the liver and biliary tract, we have attempted to cover the essential anatomic, functional and pathologic features as completely as possible within the scope indicated above. The same holds true for the pancreas, except for its endocrine aspects, which have been reserved for that volume of this COLLECTION which will illustrate the endocrine system (hypophysis, thyroid, parathyroid, adrenal, thymus and pancreas). A clear-cut separation of the exocrine and endocrine functions of a single gland is, of course, not possible; therefore, some overlapping of features shown in this book and in the future volume will be inevitable. The islet cell tumors, in spite of their obvious involvement with the hormonal situation of the organism, had to be considered together with the pictures on the tumors of the pancreas.

Some readers will observe a few inconsistencies with respect to the terminology for certain anatomic entities. We have adopted wherever possible the terms in common usage, which are in almost every case identical with the descriptive names employed in the standard American textbooks on anatomy. On the other hand, we have also tried to reconcile classical terms with the results of recent investigations and with the new list of *Nomina Anatomica* as revised by the International Nomenclature Committee and accepted by the Sixth International Congress of Anatomists (Paris, July, 1955). The *Nomina Anatomica,* which is supposed to take the place of the first international nomenclature, the famous *Basle Nomina Anatomica* (BNA) of 1895, lists the anatomic terms only in the Latin language. These had to be Anglicized to harmonize with the English names used in this book. While the preparation of this book was in progress, two meetings were held, in which specially appointed committees discussed the nomenclature of liver structures and diseases. We have also accepted terms suggested by these committees whenever they were unanimously recommended by the committee members and when they seemed to clarify the corresponding anatomic, pathologic or pathogenetic situations.

We have adhered to the principle that remarks about therapy remain restricted to a minimum of general directions.

Diagnostic procedures and functional aspects are presented in one special section (XVI). A great number of page references have been entered in the texts to all the plates, and the index has been prepared in such a fashion as to make easy the correlation between the various sections of the book. Italics within the texts that discuss the paintings have been used not exactly to emphasize certain words or terms but to make the reader aware of the fact that he will find such particular items illustrated in the accompanying plate. This technique was innovated in Volume 2, and it seems to have fulfilled the purpose for which it was contrived.

One new feature has been added. Following the suggestion of a few reviewers of Volume 2, we have prepared a record of those books and journal articles that have served as sources for the artist, as references for the editorial work and which the consultants suggested as particularly suitable to support the commentaries and discussions of the most recent developments. Needless to say, this bibliography is not at all complete, because its only aim is to offer a convenience for those interested in checking or following up certain novel or complex points or affairs which, owing to the restricted space available for the text, had to be discussed in a very concise manner. Should the list of special references prove insufficient in any particular case, it will not be difficult to find more bibliographic details in one of the monographs cited under "General References".

No words can express our gratitude to each one of our consultants. The unwavering spirit they exhibited during the many months of work on this book and their unselfish devotion to the task of making this collection of illustrations a didactically valuable contribution have been for us a provocative and at times even reviving stimulus. As indicated above, we faced problems and encountered obstacles, particularly with the series of pictures on the liver, which were not anticipated and were not encountered with the topics in the previous volumes. Dr. Popper's contagious enthusiasm, his indefatigable work power and his stimulating and persuasive personality produced a continuous challenge for us to tackle the difficulties and to surmount the many technical hindrances. Admittedly, when we approached him requesting his co-operation, because of his well-known contributions in the field, we did not realize what we were asking of him, particularly with regard to the time necessary for the many conferences, the assemblage of material, the discussions of the sketches and final paintings and, last but not least, the preparation of the texts. We profited from his knowledge, from his collection of slides and reprints, from his life-long study of the liver and its diseases and from his experience as a teacher and as author of a major monograph, *The Liver; Its Structure and Function,* a book which, fortunately for the present COLLECTION, was just moving toward its final stage when the work on the pictures for this book started. Dr. Popper's remarkable flair for the best didactic arrangement and most instructive demonstration was of indispensable help in presenting the infinite complexities of the structure and pathology of the liver.

In preparing the plates concerned with the structural pattern of the liver (Section XV, Plates 7 to 10), it was our great privilege to have the co-operation of Dr. Hans Elias, whose prudent counseling, skillful suggestions and constructive criticism were of inestimable value. For the solution of a multitude of problems in connection with the effort to demonstrate biochemical features two-dimensionally, we received most effective assistance and guidance from Dr. J. de la Huerga, who graciously and generously gave us not only much of his time but many original ideas and practical answers to some harassing questions. In other parts of the book, we have been supported by the competent advice, discriminating comments and clarifying information received from Dr. J. E. Healey, Jr. (Section XV, Plates 8 and 11), Dr. J. Higginson (Section XVII, Plate 16) and Dr. A. Grossman (pages 119 and 120). Dr. F. Schaffner showed and maintained a constant and most active interest during all the months we worked on Sections XV, XVI and XVII, liberally giving us his time and experience. Dr. R. M. Terry guided the preparation of Plate 11 in Section XVI. Most sincerely we gratefully acknowledge the help we obtained from all these gentlemen.

For his meticulous attention and expert counsel in the preparation of three decidedly clinical topics concerned with the liver, we tender our hearty thanks to Dr. Victor M. Sborov, who also has dedicated many years to the better understanding of hepatic diseases. We regret that our association with him was only relatively short and sincerely hope that future volumes will give us the opportunity to benefit from his sound scientific and practical guidance.

For the presentation of the facial expressions and other features in hepatic coma (Section XVII, Plate 11) we had the good fortune to be able to study leisurely a motion picture made by Dr. W. H. J. Summerskill (Thorndike Memorial Hospital, Boston University) of patients under the care and observation of Dr. S. Sherlock (Department of Medicine, University of London, England). The film, with Dr. Summerskill's permission, was obligingly placed at our disposal by Dr. L. W. White (Stanford Medical School).

Working on the section on Diseases of the Biliary Tract, we enjoyed the co-operation of Dr. Donald D. Kozoll, a former co-worker of Dr. Popper. Though an exhausting surgical practice laid claim to his time, we found him on all occasions willing to help, to advise us with the selection of topics and to suggest improvements after seeing the preliminary sketches or final pictures.

The pictures on the various aspects of the pancreas (with the exception of Plates 23 and 24 in Section XV) were prepared under the counselorship of Dr. Oscar Bodansky and Dr. Eugene E. Cliffton, both well-known experts in the field. The resumption of former friendly relations with Dr. Bodansky, as a result of our requesting and receiving his co-operation, gave us a personal and heartfelt satisfaction. His experience as a teacher and author in the field of biochemistry, his insistence on simple and instructive presentations, avoiding all speculative concepts, we consider to have been a great advantage for the book. Similarly, we hold in esteem Dr. Cliffton's sincerity in guiding us through the complexities of pancreatic diseases and their anatomic background. The pictures, as they appear in Sections XV and XIX, owe their reliability to his convincing judgment of the things we know and the things of which we are ignorant. Always willing to give his valuable time to this enterprise, he went out of his way in order to provide the necessary material. In his careful selection of the microscopic pictures to be shown, Dr. Cliffton was effectively supported by Dr. J. Ellis. To both gentlemen we extend our sincere thanks.

Without the tireless co-operation of Mrs. L. A. Oppenheim, serving as assistant to the editor and as organizational center between artist, consultants, editor, engraver and printer, the development of Part III of Volume 3 would have taken far longer than it did. The unstinting efforts and gracious devotion to the project of Mrs. Vera Stetson, assistant to Dr. Netter, contributed much to ease and expedite the task. To them and to Mrs. Hans Popper, who voluntarily took over the work of providing us, with the least delay, the 96 typescripts of her husband's descriptive texts, go our special thanks. We acknowledge finally the concurrent efforts of Messrs. A. W. Custer and Felton Davis, Jr., of the CIBA staff, Wallace and Anne Clark of Buttzville, N. J., as literary consultants, and the staffs of Embassy Photo Engraving Co., Inc., and Colorpress.

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Section XV

NORMAL ANATOMY OF THE LIVER, BILIARY TRACT AND PANCREAS

by

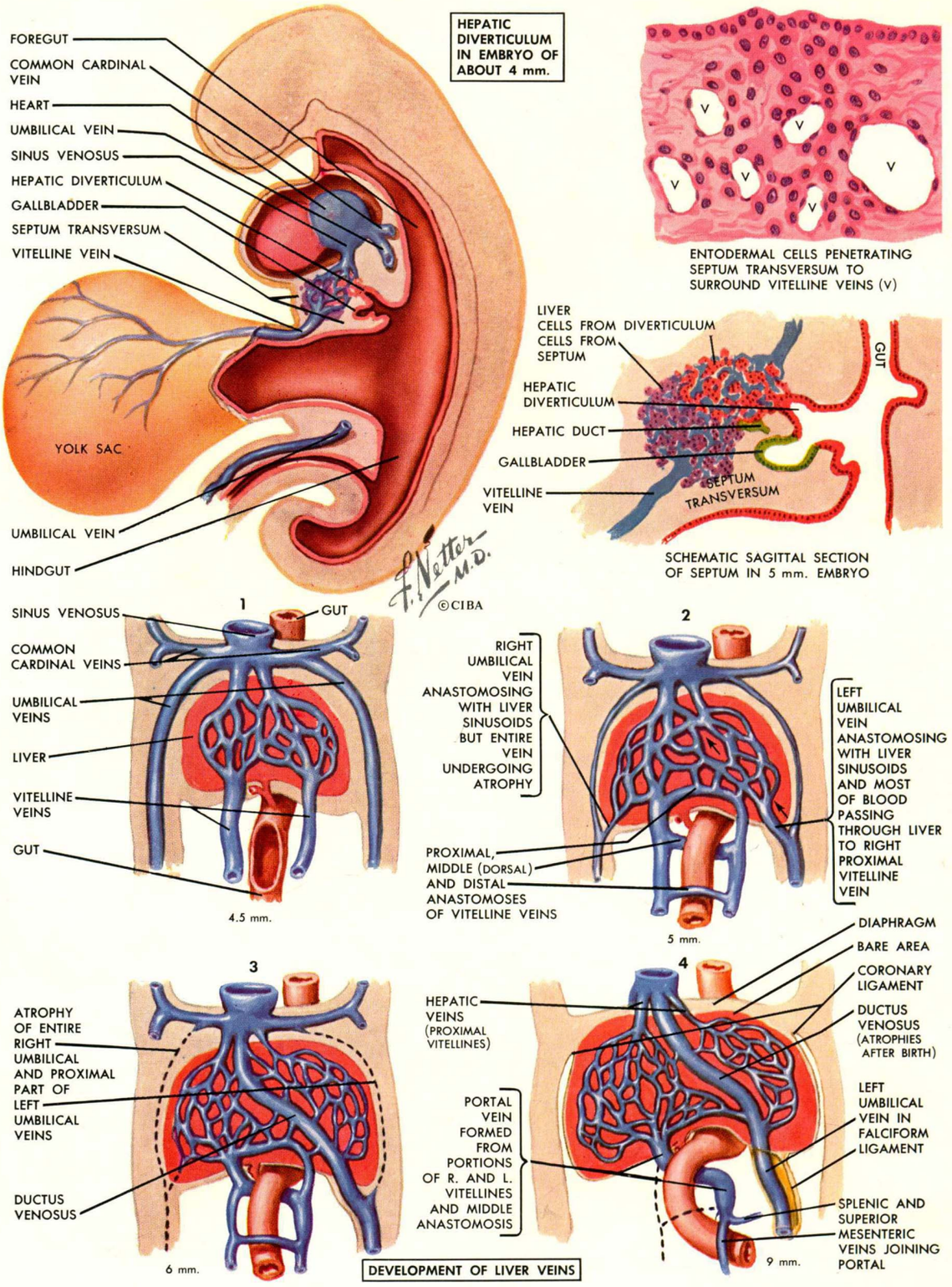
FRANK H. NETTER, M.D.

in collaboration with

EUGENE E. CLIFFTON, M.D.
Plates 25-29

HANS POPPER, M.D.
Plates 1-24

Development of Liver and Its Venous System

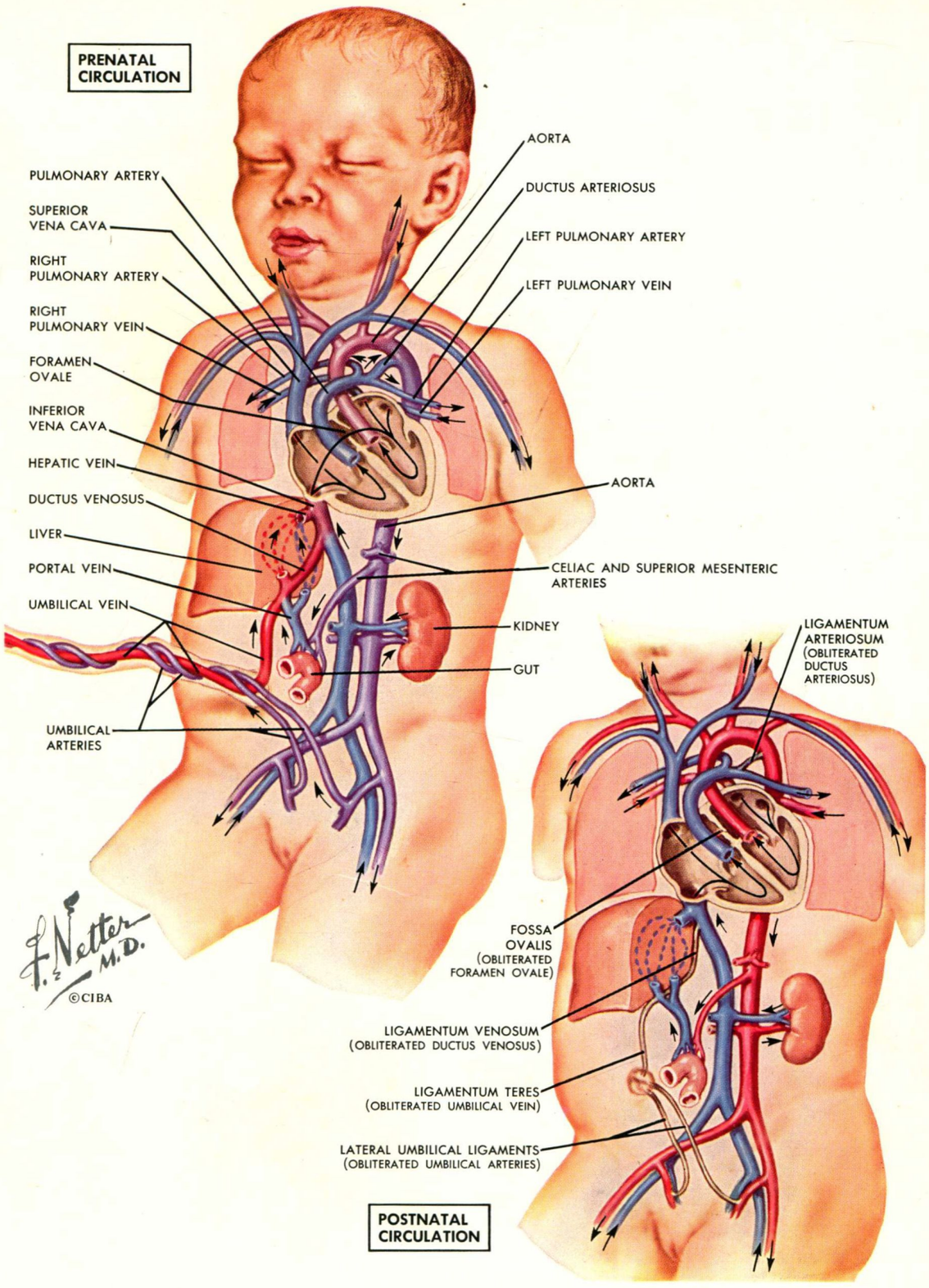


The liver develops from a *diverticulum,* which sprouts in close relation to the *vitelline veins* from the ventral floor of the endodermal foregut at a site corresponding to the future duodenum. The caudate portion of the diverticulum is the origin of the bile ducts and the *gallbladder*. The cephalad portion splits up into cellular masses which extend ventrally into the splanchnic mesoderm in the *septum transversum*. Part of this septum subsequently becomes the diaphragm, while the lower portion serves as the site for the liver formation. A vascular plexus branching out from the *vitelline veins* becomes surrounded by the irregularly arranged endodermal cells, which, apparently as a result of mutual stimulation, differentiate into liver cells, originally in several-cell-thick plates and later in one-cell-thick plates. The endothelial cells of the plexus become the Kupffer cells. The mesenchyma provides also the connective tissue for the capsule and the portal tracts. At 10-mm. embryonal length, bile capillaries, as well as intrahepatic bile ducts and cholangioles (ductules), develop between the liver cell plates. In contrast to previous belief, the epithelium of the cholangioles, and probably also of the bile ducts, derives from the liver cells rather than vice versa. This would explain the formation of cholangioles from liver cells during regeneration (see page 63). The intrahepatic bile ducts connect subsequently with the *extrahepatic bile ducts* which come into existence from the caudate part of the hepatic diverticulum.

At an early stage the pairs of vitelline veins split into a *plexus within the liver*. Uniting again behind the plexus into pairs, these veins enter into the *sinus venosus* of the heart together with the *umbilical veins* coming from the placenta and with the common *cardinal veins*. Subsequently, the pairs of vitelline veins form more anastomoses, the proximal of them lying within the liver, a middle and distal one extending dorsally and ventrally around the duodenum, so that a vascular ring is formed, part of which obliterates together with the distal portion of the vitelline veins. The remaining venous trunk becomes the *portal vein* which is joined by the *superior mesenteric* and *splenic veins*. The proximal portions of the paired vitelline veins between the plexus and the sinus venosus become the *hepatic veins,* the left of which atrophies, so that the blood of the left half of the liver drains into the right vitelline vein. The umbilical veins also find contact with the hepatic sinusoidal system, but later the entire right umbilical vein and the part of the left vein proximal to the anastomosis with the hepatic sinusoids atrophy and disappear. For a time the venous blood from the placenta passes through the liver to the right vitelline vein. Eventually, a large venous trunk develops and separates from the hepatic sinusoids to carry as *ductus venosus* pure oxygenated blood directly to the heart. At this stage approximately half of the blood from the umbilical vein goes through the ductus, while the rest passes through the liver.

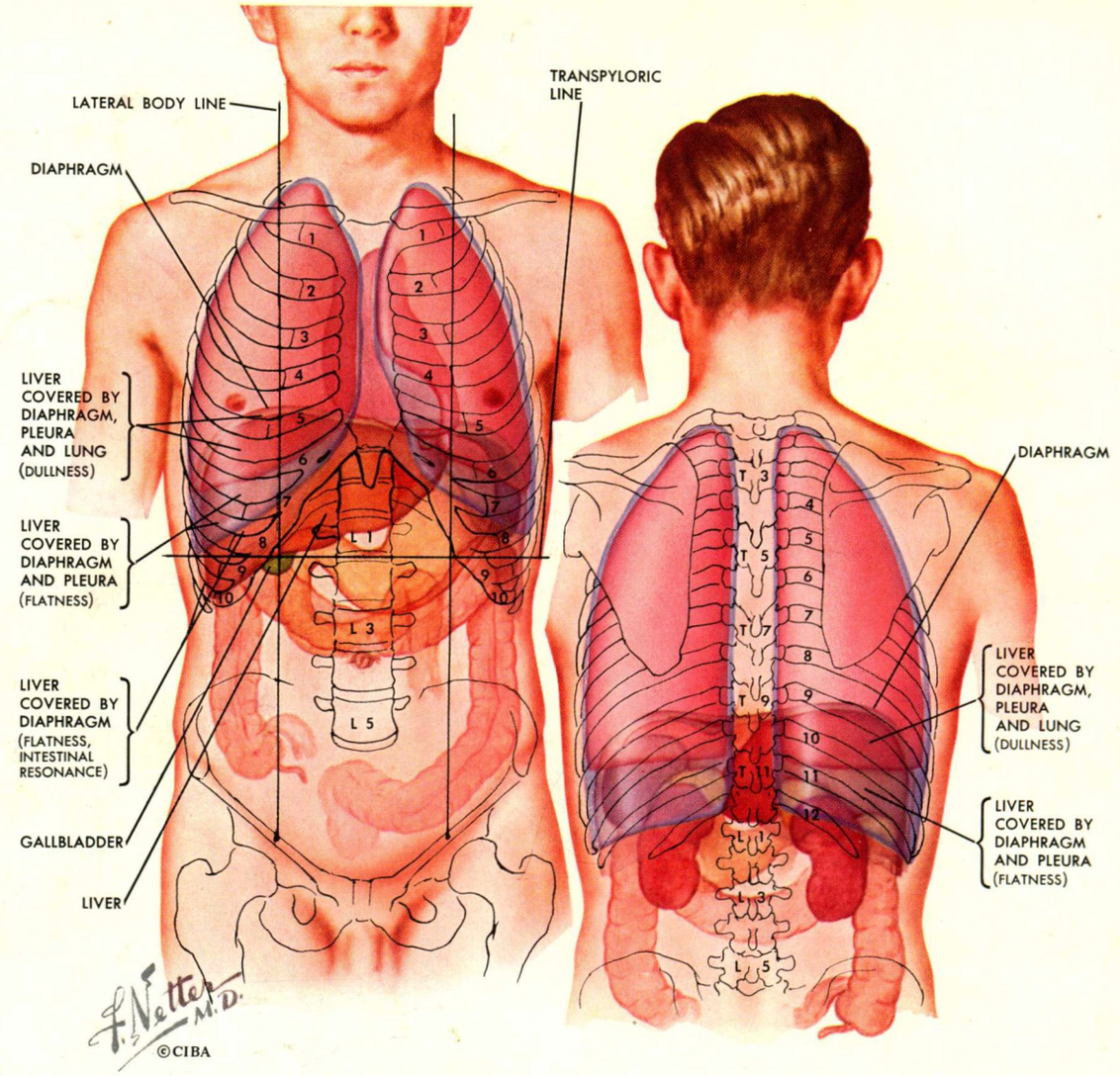
As the liver protrudes into the abdominal cavity, it remains in contact with the *diaphragm* in the *bare area;* and the attachment to the septum transversum becomes the *coronary ligament*. At the same time the umbilical vein becomes included as ligamentum teres into the *falciform ligament*.

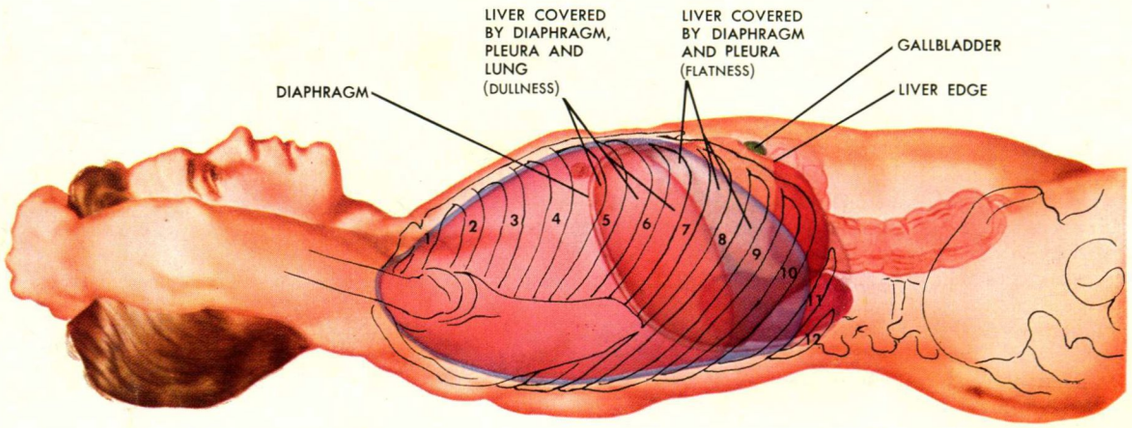
Prenatal and Postnatal Circulation



In intra-uterine life the fetus receives blood carrying oxygen and nutrients obtained by contact with maternal blood in the placenta (see THE CIBA COLLECTION, Volume 2, page 219) through the *umbilical vein,* except during the very early stages when the yolk sac and vitelline veins still function. While the vitelline veins are transformed (see page 2), the umbilical vein makes contact with the vitelline plexus and anastomoses, so that at one stage (6 mm. fetal length) the entire blood of the umbilical vein passes through the primitive hepatic sinusoids. At the same time, the right umbilical vein branch and the proximal portion of the left undergo atrophy, while subsequently the enlarged distal part of the left umbilical vein courses diagonally through the liver in a channel, the *ductus venosus,* which has formed by rearrangement of early hepatic sinusoids. With the growing of the liver lobes, the ductus venosus comes to lie outside the liver and joins the *inferior vena cava,* in which the small amount of venous blood from the caudate fetal portions is mixed with the oxygen-rich blood coming through the ductus venosus. This blood stream, entering the right atrium, hits the interatrial membrane (septum secundum) and is directed through the *foramen ovale* into the *left atrium* and thus keeps the foramen open. In the left atrium the blood mixes with some nonoxygenated blood from the pulmonary veins and passes through the left ventricle into the ascending aorta, whence mixed blood provides the coronary artery, the head, neck and upper extremities. A small amount of blood from the vena cava inferior, together with the inflow from the superior caval vein, is diverted into the *pulmonary artery* supplying the lungs. The greater part of the blood from this artery, however, owing to a higher resistance in the pulmonary vascular tree, is shunted through the *ductus arteriosus* directly into the *aorta descendens,* where it joins the blood ejected from the left ventricle. This vascular organization is instrumental in providing heart and brain with blood of higher oxygen content than is supplied to other organs less sensitive to hypoxia.

After birth, probably because of a sphincter mechanism at its origin, the ductus venosus closes rapidly. It soon obliterates and is transformed into the *ligamentum venosum,* which connects with the *ligamentum teres* or round ligament, where the obliterated umbilical vein is lodged. The ligamentum teres (see page 5) terminates at the umbilicus, from where also the lateral umbilical ligaments containing the remnants of the *umbilical arteries* spread in the interior abdominal wall to the hypogastric arteries. With the closure of the ductus venosus, oxygenated blood no longer reaches the inferior vena cava, and the liver from birth on is provided with oxygen-rich blood only via the hepatic artery. With the first respiration the resistance in the pulmonary vascular tree diminishes, and this pressure change leads immediately to a shift of the current in the right and left atria, so that no blood passes through the foramen ovale, which, within 1 year, closes in 75 per cent of newborns by fusion of the atrial septa. A *fossa ovalis* indicates in adult life the former site of the foramen. In the remaining 25 per cent of infants, an oblique communication persists between right and left atria, which may be demonstrated anatomically but only in rare cases is patent enough to have functional consequences. The ductus arteriosus closes with breathing, apparently by muscular contraction, and is obliterated gradually by intima proliferation, so that within 3 months after birth only a connective tissue band, the *ligamentum arteriosum,* remains, except in a small percentage of cases wherein a patent ductus arteriosus persists.





Topography of Liver

The liver (hepar) is located in the upper part of the abdomen, where it occupies the right hypochondriac and the greater part of the epigastric regions. With its left lobe the liver extends, to an individually varying degree, into the left hypochondrium. The liver, the largest organ of the body, weighs from 1400 to 1600 gm. in the adult male and from 1200 to 1400 in the female. In normal, healthy individuals, the *liver margin* extending below the thoracic cage is smooth and offers little resistance to the palpating finger. Downward displacement, enlargement, hardening and formation of nodes or cysts produce impressive palpatory findings. Using percussion, one must consider that the lungs overlay the upper portion of the liver and that the liver, in turn, overlaps the intestines and the stomach.

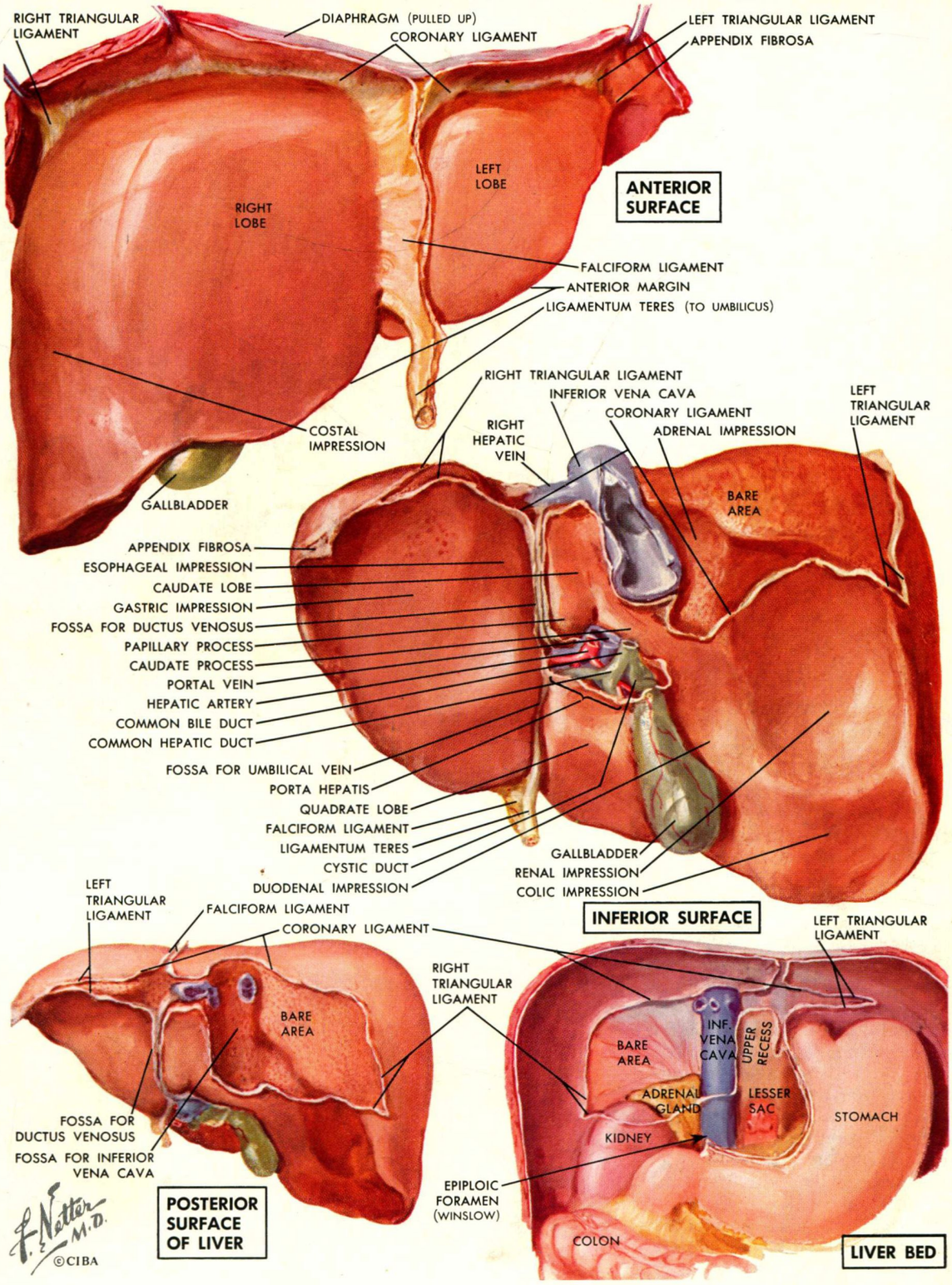
The *projections of the liver on the body surface* have acquired added significance in the performance of liver biopsy (see page 46). The projections vary, depending upon the position of the individual as well as the body build, especially upon the configuration of the thorax. The liver lies close to the diaphragm, and the upper pole of the right lobe projects as far as the level of the fourth intercostal space or the fifth rib, the highest point being 1 cm. below the nipple near the lateral body line. The upper limit of the left lobe projects to the upper border of the sixth rib. Here, the left tip of the liver is close to the diaphragm.

The *ribs cover* the greater part of the liver's right lobe, while a small part of its anterior surface is in contact with the anterior abdominal wall. In the *erect position* the liver extends downward to the tenth or eleventh rib in the right midaxillary line. Here, the pleura projects downward to the tenth rib, and the lung to the eighth. The anterior margin of the liver crosses the costal arch in the right lateral body line approximately on the level of the pylorus (*transpyloric line*). In the epigastrium the liver is not covered by the thoracic cage and extends about three fingers below the base of the xyphoid process in the midline. Part of the left lobe is covered again by the rib cage.

Over the upper third of the right half of the liver, percussion gives a *dull zone,* since here diaphragm, pleura and lung overlay the liver. Over the middle portion *flat percussion* is obtained. Over the lowest third of the liver, usually a flat percussion tone is heard, except that sometimes *intestinal resonance* is produced by gas-filled intestinal loops. The border between dullness and flatness moves on respiration and is altered by enlargement or displacement of the liver, and also by conditions within the thoracic cage which change the percussion qualities of the thoracic organs.

In the *horizontal position* the projection of the liver moves a little upward, and the area of flatness appears slightly enlarged. The portion of the flat sound, best percussed in the horizontal position, permits information about the size of the organ.

The projections of the liver are altered in some diseases of the liver, such as tumor infiltration, cirrhosis or syphilitic hepar lobatum, and are changed by displacements of the organ or more often by thoracic conditions pushing the liver downward. Subphrenic abscesses, depending upon location and size, also displace the liver downward. Ascites, excessive dilation of the colon or abdominal tumors may push the liver upward, and retroperitoneal tumors may move it forward. Kyphoscoliosis or a barrel shape of the chest alters the position of the liver. Sometimes the liver is abnormally movable (hepatoptosis), causing peculiar palpatory findings.



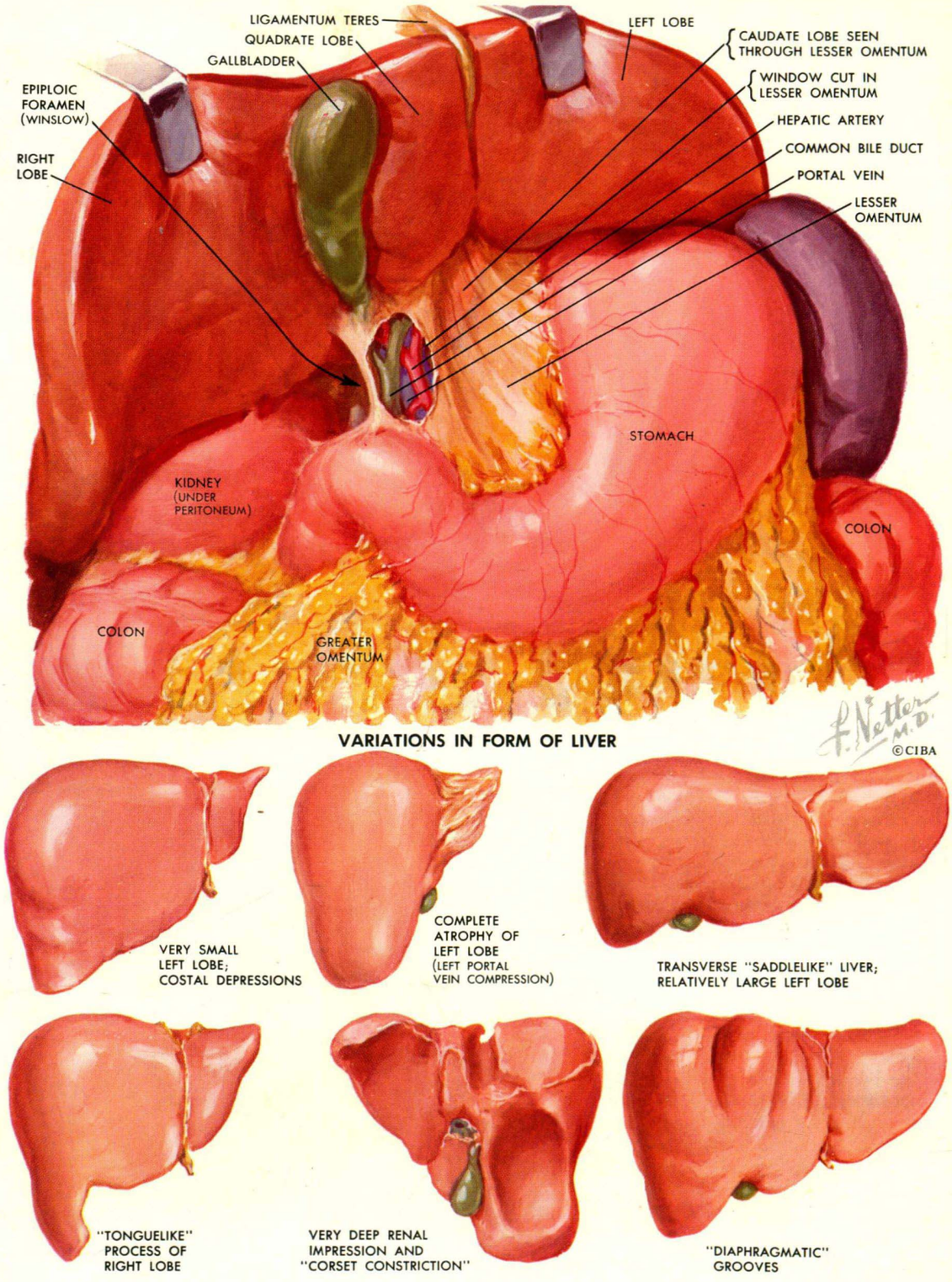
Surfaces and Bed of Liver

The liver has the shape of a triangular pyramid, the apex being formed by the thin, flattened left extremity of the left lobe. The base is represented by the right lateral surface, which rests on the diaphragm and the right thoracic cage, which produces the *costal impressions* on this surface. The sides of the pyramid are formed by the *anterior, posterior* and *inferior surfaces*. The border between the anterior and inferior surfaces is the *anterior margin*. Its consistency, sharpness of edge, smoothness of surface and movement upon respiration provide clinical information. On laparotomy the anterior margin and the anterior surface are first exposed. Otherwise, the hepatic surfaces are not separated by distinct margins.

The liver is covered by peritoneum, except for the gallbladder bed, the hilus, adjacent parts surrounding the inferior vena cava, and a space to the right of the vena cava inferior called *"bare area"*, which is in contact with the right adrenal gland (*adrenal impression*) and the right kidney (*renal impression*). The peritoneal duplications, which extend from the anterior abdominal wall and from the diaphragm to the organ, form the ligaments of the liver, which, formerly, were thought to maintain the liver in its position but probably add little to its fixation. It is now held that the liver is kept in place by intra-abdominal pressure. The horizontal peritoneal duplication is the *coronary ligament*, the upper layer of which is exposed if the liver is pulled away from the diaphragm. The right free lateral margin of the coronary ligament forms the *right triangular ligament*, whereas the *left triangular ligament* surrounds and merges with the left tip of the liver, the *appendix fibrosa hepatis*. Over the right lobe the space between the upper and lower layers of the coronary ligament is filled with areolar connective tissue. Below the insertion of the lower layer of the right coronary ligament, the hepatorenal space extends behind the liver.

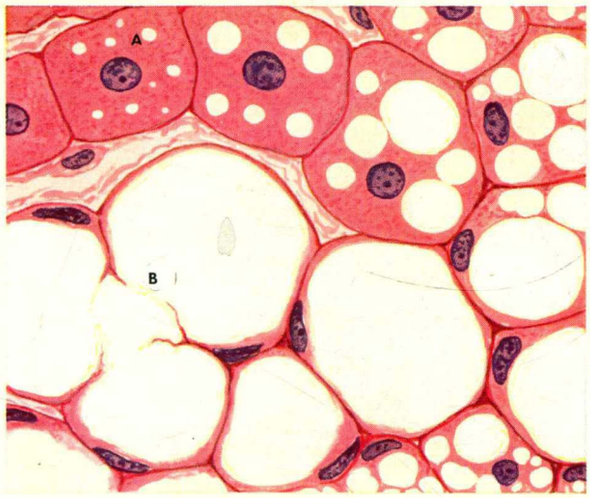
From the middle portion of the coronary ligament originates another peritoneal duplication, the *falciform ligament*, which extends from the liver to the anterior abdominal wall between the diaphragm and the umbilicus. Its insertion on the liver divides the organ into a *right* and *left lobe*. The inferior edge of this ligament is enforced to form the *round ligamentum teres*, which extends to a point where the longitudinal fissure of the liver crosses over the inferior surface. With its anterior part this fissure separates the *quadrate lobe* and the left lobe (tuber omentale) and forms a *fossa for the umbilical vein* or its remnant. The fissure proceeds toward the posterior surface, creating the *fossa for the ductus venosus* (ligamentum venosum in adult life). The two fossae may be regarded as the right limb of an H-shaped pattern characteristic of the inferior surface of the liver. The left limb is formed by the *gallbladder bed* and the fossa for the *vena cava inferior*. The horizontal limb is marked by the *porta hepatis*, which contains the *common hepatic duct, hepatic artery, portal vein,* lymphatics and nerves. The *quadrate lobe*, between the gallbladder and the fossa for the umbilical vein, is in contact with the pylorus and the first portion of the duodenum (*duodenal impression*). On the inferior and posterior surfaces lies the *caudate lobe* between the fossa for the ligamentum venosum and the vena cava inferior, its anterior projection being the *papillary process*. The inferior surface of the liver reveals further impressions of the organs with which it is in contact: the *impressions for the colon and the right kidney*, and on the left lobe the *impressions for the esophagus and the stomach*. The superior surface is related to the diaphragm and forms the domes of the liver.

Lesser Omentum, Variations in Form of Liver

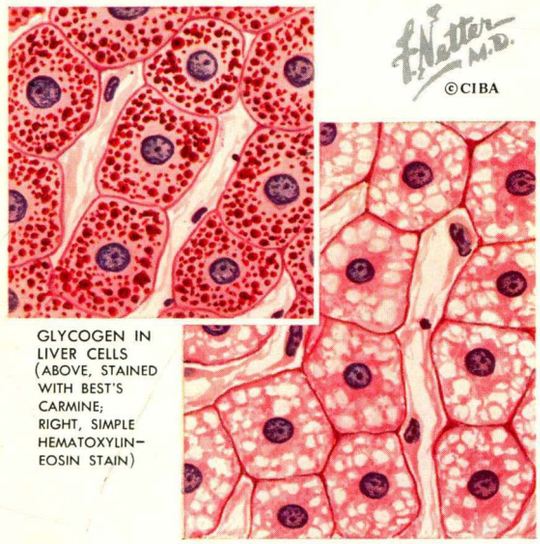


If the anterior margin of the liver is lifted, the *lesser omentum* is exposed. It represents a peritoneal fold, which extends from the first portion of the duodenum and the lesser curvature of the stomach and the diaphragm to the liver, where it is inserted at the fossa of the ligamentum venosum and continues to the porta hepatis. Here, the layers are separated to accommodate the structures running to and from the hilus of the liver. On the free right edge of the lesser omentum, the reunited peritoneal layers are enforced to form the hepatoduodenal ligament. It is the anterior boundary of the *epiploic foramen of Winslow,* which is the entrance to the lesser abdominal cavity. The posterior wall of this cavity is formed by the *vena cava inferior* and the caudate lobe of the liver (see page 5). Near the right margin of the lesser omentum is found the *common bile duct* dividing into the cystic and common hepatic ducts. To its left lies the *hepatic artery* and behind both, the *portal vein.* The nerves (see page 21) and the lymph vessels (see page 20) of the liver accompany these structures. The hilus of the liver is anteriorly limited by the *quadrate* and posteriorly by the caudate (see page 5) lobes. On the right side of the hilus, the right and left hepatic ducts branch from the main hepatic duct and enter the liver. To the left of them, the hepatic artery (see page 14) enters the liver behind the ductal branches. The forking portal vein enters posteriorly to the ductal and arterial ramifications.

The shape of the liver varies. Its great regenerative ability, as well as the plasticity of the liver tissue, permits a wide variety of forms, which depend in part upon pressure exerted by neighboring organs and in part upon disease processes or vascular alteration. A *greatly reduced left lobe* is compensated by enlargement of the right lobe, which reveals very conspicuous and deep costal impressions. Occasionally, the *left lobe* is completely *atrophic,* with a wrinkled and thickened capsule and, microscopically, an impressive approximation of the portal triads (see page 11), with hardly any lobular parenchyma between them. In the majority of such cases, vascular aberrations have been demonstrated, such as partial obstruction of the lumen of the left branch of the portal vein by a dilated left hepatic duct or obstruction of the bile ducts. Therefore, this lesion has been considered the effect of a local nutritional deficiency, especially since the nutritional condition of the left lobe is poor to begin with (see page 18). In other instances, associated with a transverse position of the organ, the left lobe is unduly large. Formerly, disfiguration of the liver frequently resulted from laced corsets or from tight belts or straps. Such physical forces may flatten and elongate the liver from above downward, with reduction of the superior diaphragmatic surface and sometimes with peculiar *tonguelike extension of the right lobe.* In other instances the *"corset liver"* is displaced, and the *renal impression* is exaggerated. Clinical symptoms (dyspepsia, cholelithiasis, chlorosis) were ascribed to the "corset liver", but it is questionable whether the "corset liver" actually leads to clinical manifestations other than peculiar findings on palpation. Indentations on the liver are normally produced by the ribs, by diaphragmatic insertions and by the costal arch. In kyphoscoliosis the rib insertions may become very prominent. Parallel sagittal furrows on the hepatic convexity have been designated as *"diaphragmatic" grooves.* Functionally, none of the described variations are today considered significant.



LIVER CELLS WITH VARIOUS DEGREES OF FAT ACCUMULATION RANGING FROM FINE DROPLETS (A) TO LARGE FATTY CYSTS (B)



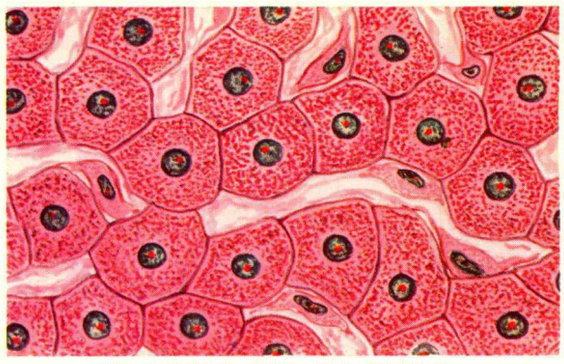
GLYCOGEN IN LIVER CELLS (ABOVE, STAINED WITH BEST'S CARMINE; RIGHT, SIMPLE HEMATOXYLIN–EOSIN STAIN)

Cellular Elements of Liver

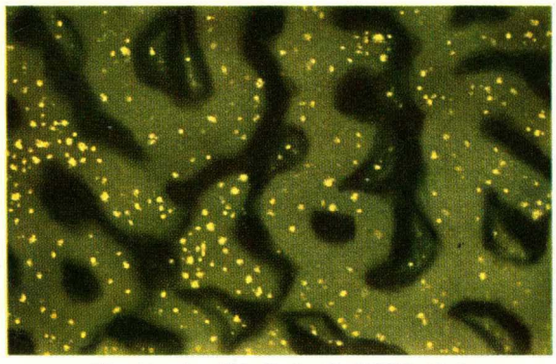
The cytoplasm of the liver cells normally contains various defined particles which can be visualized by histochemical methods. Neutral fat is found in the form of droplets, which are stainable in frozen sections by fat stains but appear as vacuoles after dissolution of fat with the routine use of organic solvents in histologic techniques. The *fat droplets* or *vacuoles* in normal liver cells do not exceed 4 microns in diameter. They usually line up on the free margin of the cells, like pearls on a string. Enlargement of the fat droplets (fatty metamorphosis) is the result of an imbalance between the transport of fat to the liver from either the intestine or the peripheral tissue, or of its formation or catabolism within the liver (see pages 36 and 37). The imbalance in fat metabolism may be focal, then mainly resulting from disturbances of the blood flow and local anoxia, or may be diffuse (fatty liver, see pages 78 and 79). The fat droplets become gradually larger until the liver cell cytoplasm is studded with droplets of different size, the nucleus, however, still remaining in the center. Subsequently, the droplets merge, and one large drop pushes the nucleus to the side. Eventually, large drops of neighboring liver cells coalesce to form *fatty cysts,* in which the fat is actually extracellular and the remnants of several cells line the cyst (Hartroft).

Glycogen, if previously precipitated by alcohol fixation, appears as fine red particles in the cytoplasm after staining with Best's carmine or periodic acid and Schiff's reagent. In routinely fixed and stained sections or biopsy specimens of normal liver, the dissolved glycogen produces a fine, granulated and vacuolated appearance of the cytoplasm. In severe disease of any kind, particularly in the agonal period, the glycogen content becomes markedly reduced, so that, as a rule, in autopsy specimens little glycogen is found. The glycogen content of the liver cells is an index of its functional status.

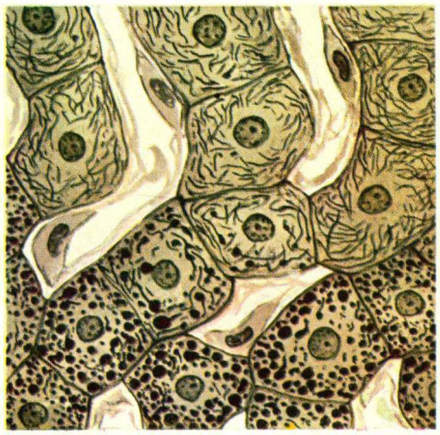
The cytoplasm of the normal cell contains many fine basophilic granules which, in *methyl green-pyronine stain,* appear distinctly red, as does the nucleolus. This reaction is caused by pentose nucleic acids in contrast to the desoxypentose nucleic acids in the nuclear chromatin, which stain green. The specificity of the reactions requires further confirmation. The cytoplasmic pentose nucleic acids have been tentatively associated with protein formation, and attention has been drawn to a parallelism between cytoplasmic basophilia of the liver cells and their capacity to form proteins (see page 39).



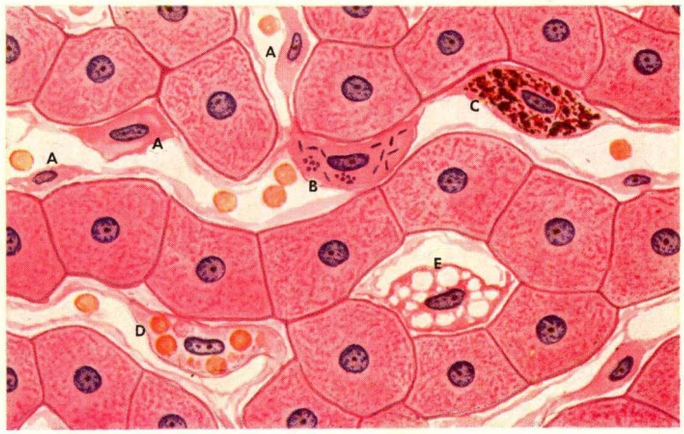
LIVER CELLS WITH METHYL GREEN–PYRONINE STAIN (METHYL GREEN STAINS CHROMATIN; PYRONINE STAINS CYTOPLASMIC INCLUSIONS AND NUCLEOLUS)



VITAMIN A IN LIVER CELLS AND KUPFFER CELLS MADE VISIBLE BY FLUORESCENCE



VARIFORM MITOCHONDRIA IN LIVER CELLS REFLECTING DIFFERENCES IN FUNCTIONAL ACTIVITY (JANUS GREEN STAIN)

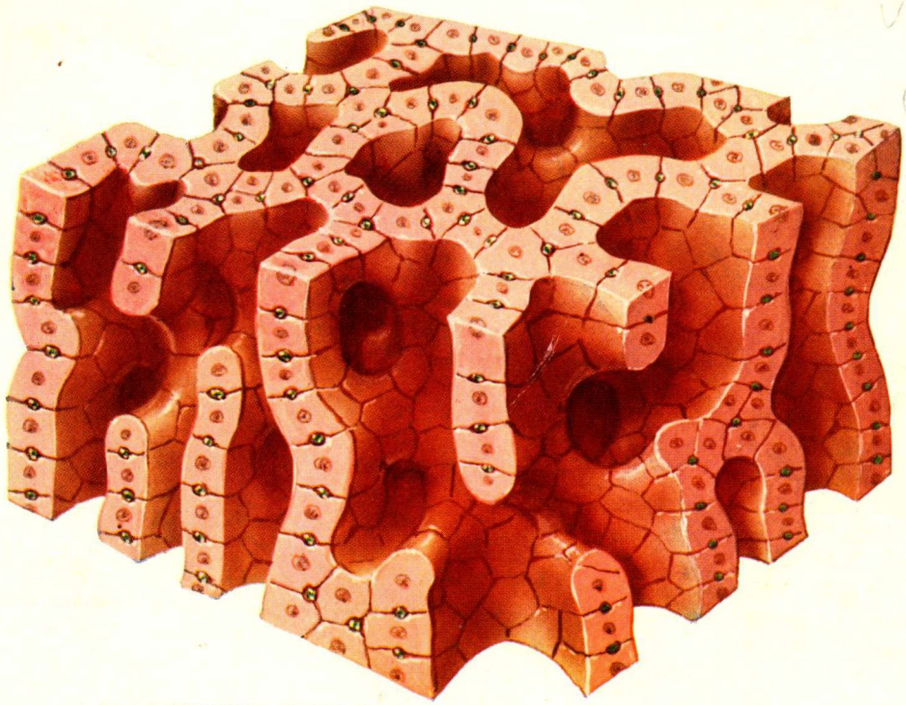


KUPFFER CELLS IN VARIOUS STAGES— (A) IN RESTING STAGE; (B) CONTAINING BACTERIA; (C) CONTAINING PIGMENT; (D) CONTAINING RED BLOOD CELLS; (E) CONTAINING FAT DROPLETS

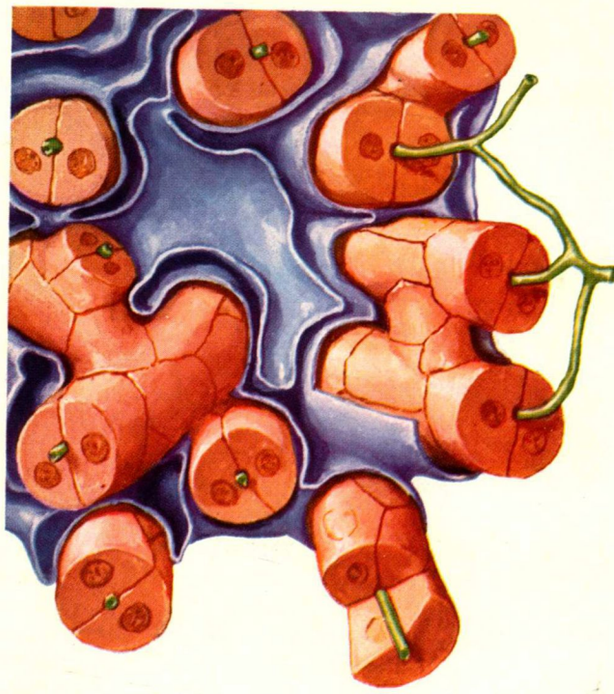
Under the fluorescence microscope in frozen section, a rapidly fading yellow-green fluorescence of the cytoplasm of liver and Kupffer cells is caused by *vitamin A,* mainly in fat droplets. This fluorescence decreases in malnutrition and increases upon the administration of large amounts of vitamin A. In liver damage the distribution of the fluorescence, never quite regular, becomes patchy and more irregular.

The *mitochondria,* stainable, for instance, supravitally with Janus green, are globular elements in the center and rod-shaped in the periphery of the lobule. They contain, as in all cells of the body, phospholipids and a great number of enzyme systems.

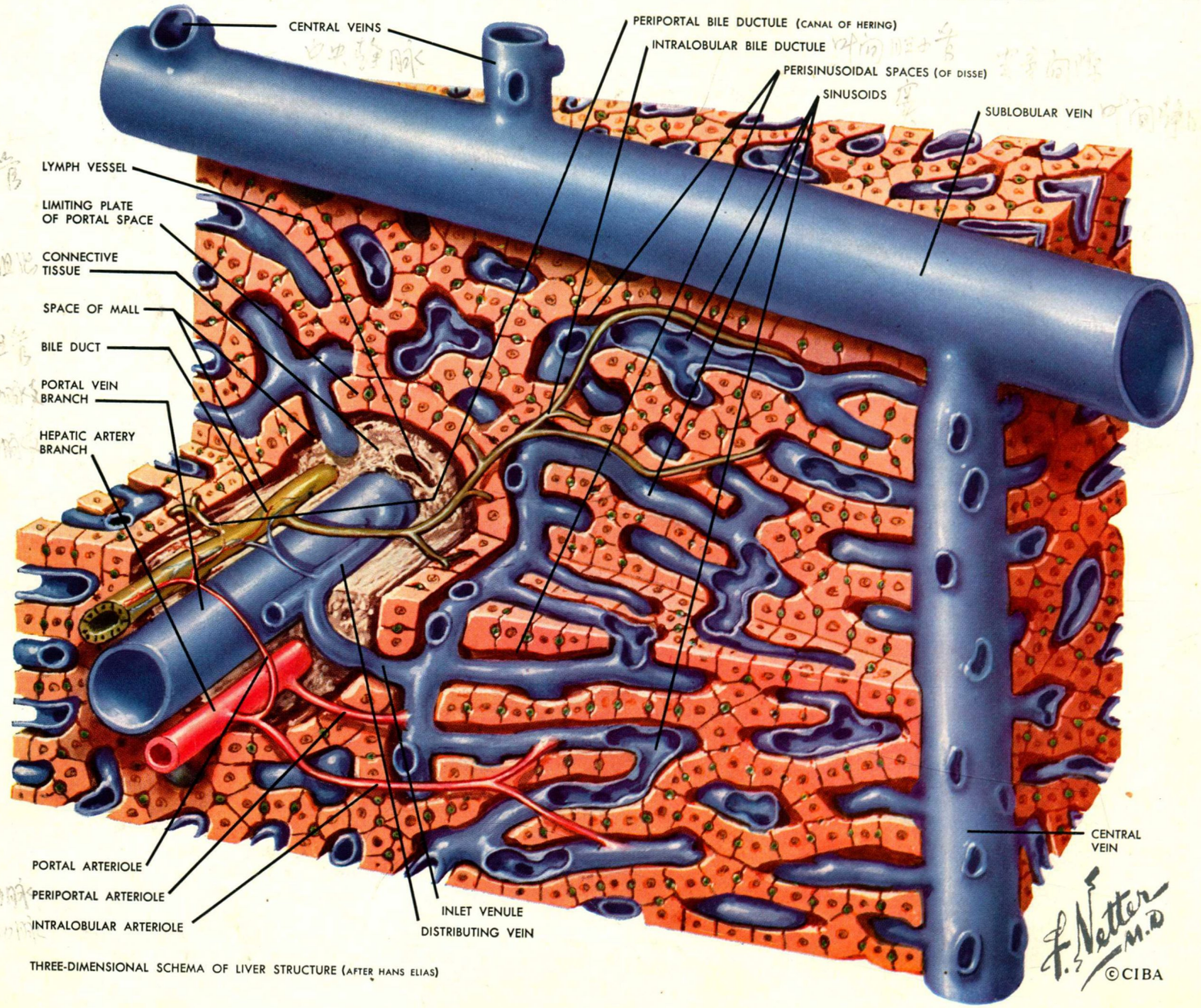
The *Kupffer cells* assume in the normal liver a great variety of shapes as an expression of different activity stages, primarily phagocytosis. Some of them are flat, similar to endothelial cells in other organs. Others have a large cytoplasm which contains various inclusions, not necessarily an expression of disease. Some of these inclusions are *bacteria,* other *pigments, red cells* or *fat droplets.* In various abnormal conditions, the phagocytosis is exaggerated. Vital microscopic studies have demonstrated that a resting endothelial-like Kupffer cell can very rapidly change into the large phagocytic type.



STEREOGRAM OF LIVER CELL PLATES AFTER REMOVAL OF DUCTS, VESSELS AND CONNECTIVE TISSUE (ACCORDING TO CONCEPT OF HANS ELIAS)



FORMER CONCEPT OF LIVER STRUCTURE AS COMPOSED OF CELL CORDS



THREE-DIMENSIONAL SCHEMA OF LIVER STRUCTURE (AFTER HANS ELIAS)

F. Netter M.D.

Intrahepatic Structures

Liver Cell Arrangement

Until about 10 years ago the standard description of the pattern of liver cell arrangement, as presented in all textbooks, was considered securely settled. The *liver cells* were supposed to *form cords* composed of opposing cells which were thought to be arranged on either equal or alternate levels. The cords were believed to extend in an irregular and frequently crooked and angular fashion from the periphery of the lobule (marked by the final termination of the portal vein) toward the central vein. The existence of many communications between the various cords as well as their corresponding central bile capillaries had to be assumed. These cords were considered to be surrounded by the blood sinusoids, which thus were visualized as forming a large pool around the liver cell cords. Few investigators dissented from the "cord theory", but it is noteworthy that Hering, for instance, almost 100 years ago described the rabbit liver as a continuous cellular mass traversed by blood capillaries. A few years ago Elias challenged the cord theory as a result of his attempt to draw, in three-dimensional fashion, the structure of the liver, especially as it would appear to a microorganism inhabiting the liver. He was unable to conceive a pattern which would agree with the standard description of the liver and at the same time conform to its appearance in histologic slides and, especially, to three-dimensional reconstructions made from serial sections. He realized that if the cord theory were correct the histologic sections, representing a cross section through the liver, should exhibit, mainly, isolated groups of two cells with a central bile capillary between them. Where the cords were cut obliquely, short rows of cells up to three and four in number should be seen. Actual observation, however, revealed, generally, long rows of cells almost always in single file, with an occasional multicellular group. The appreciation of these pictures, well known to any anatomist or pathologist, prompted Elias to statistical geometrical analysis, as well as to reconstructions of liver tissue. As a result of his studies, he proposed the "plate theory" of the liver to replace the cord structure. This theory, to a great extent in agreement with the old concept of Hering, is also well reconciled with the histologic picture and with various older reconstruction models, such as the classical model of Braus in which the presence of both plates and cords is demonstrated.

The plate concept assumes that the mature *liver* is *composed of plates,* as a rule one cell thick, which are only in part straight but otherwise curved in all directions. An irregular wallwork comes into existence because of the many holes of various sizes in the plates and because of their fusing together at different angles. Where one or several plates meet each other, the cut surface seen in the histologic sections reveals an aggregation of several cells, whereas otherwise the liver cells appear usually as long rows of cells in single file, with the nucleus being in the center of the plate and a relatively great part of its border a free surface. As Elias has also shown, the size and the shape of the individual liver cell vary greatly, depending upon the cell's position in the plate. Cells near a hole in the plate are usually small, whereas cells at the corners, where several cells meet, are large. He even proposes that the frequently encountered presence of two or more nuclei in the normal liver cell depends upon the location of the cell and the thus determined size. Two-cell-thick plates are hardly ever found in the normal mature human liver. They are the rule in lower vertebrates and also in the embryologic stage of the human liver, when gradual maturation from several-cell-thick plates to the one-cell-thick plate takes place (see page 2). Similarly, in adult regeneration (see page 63) or tumor development (see page 113), two-and-more-cell-thick plates are found. The two-cell-thick plate is far less efficient than the one-cell-thick plate, because in the former the free surface in contact with the blood stream is much smaller, probably only one eleventh of its entire surface, whereas in the one-cell-thick plate one fifth of the total surface is free. Moreover, the one-cell-thick plate responds to stretching or other mechanical stresses with far less distortion than does the two-cell-thick plate and is, therefore, considerably more stable.

The liver is thus conceived to consist not of a communicating system of cords surrounded by the sinusoids but rather of an irregular, almost spongelike wallwork or cellular mass tunneled by a communicating system of cavities, to which the term lacunae has been applied. The diameter of these lacunae in man is usually considerably wider than the diameter of a single liver cell, and only occasionally is it found narrow and cylindrical, as seen in rodents and the horse. The lacunae contain the blood capillaries of the liver, the sinusoids, which have a basement membrane. Their endothelial lining is formed by the Kupffer cells. The sinusoids differ from capillaries elsewhere in the body by the specific functions of the Kupffer cells which may increase in size (see page 7), as well as owing to the greater permeability of their membrane for macromolecular substances, especially proteins. This faculty permits a better exchange of large-sized compounds between liver cell and sinusoid. The exchange of nutrients and waste products of large or small size takes place through a very narrow tissue space separating the sinusoidal wall from the liver cell plates. This interstice, known as Disse's space (see also page 20), has been wrongly assumed to act as a lymphatic space. It is probably correct that the tissue fluid in this space may be drained by the lymphatic vessels, especially when the blood capillaries or the liver cells are unable to absorb excessive amounts of fluid accumulating in it, which happens in hepatic edema caused, *e.g.,* by abnormal permeability of the sinusoidal wall. The tissue spaces in the human liver, examined after death, may thus appear unduly wide because of the edema developing in the agonal period (see pages 20 and 63). In vivo, therefore, under normal circumstances this space, traversed by a few reticulum fibers, is hardly existent, and, therefore, the lacunae between the liver cell plates are almost entirely filled out by the blood in the sinusoids. The arrangement of the cells in the liver cell plates is fairly fixed; however, the shape and direction of the plates are highly variable and depend, *e.g.,* on the blood stream which creates the lobular arrangement (see Plate 8, page 10).

The mass of epithelial cells is traversed by two mesenchymal tracts arranged around the vessels and bile ducts of the liver; one is the portal tract and around it the cellular mass assumes a characteristic arrangement. A *limiting plate envelops the portal tract* along its entire circumference and is perforated only where *bile ductules* enter the portal tract and where blood vessels enter the parenchyma. This plate is actually continuous throughout the liver. It is separated from the connective tissue of the portal tract by a very narrow tissue space, the *space of Mall* (see also page 20). From the limiting plate the other plates seem to originate at almost a right angle. The cells of the limiting plate differ cytologically from the cells of the other plates by being flatter, by being markedly basophilic because of the presence of pentose nucleic acids (see page 7) and by being relatively poor in glycogen. Moreover, these cells are more prone to regeneration, not only because of their cytologic characteristics but also because of their close relation to the portal vein, since portal vein blood, so important in stimulating regeneration, reaches them in highest concentration. Actually, nodular regeneration (see pages 63, 66 and 67) has a tendency to develop especially from the vicinity of the portal tract, and some evidence also exists that primary hepatic cancer (see page 112) seems to start in this location. If in the course of inflammatory and degenerative processes around the portal tracts the limiting plate is destroyed, healing is completed when a new limiting plate is formed. Around the other mesenchymal tract, the *central canal,* the liver cell plates end abruptly (frequently perpendicularly). An enveloping plate is encountered only around larger hepatic veins.

Connective Tissue, Vascular and Ductal Relations (Plate 8, page 10)

The liver is covered by thick collagenous fibers and membranes, intermixed with elastic elements which form *Glisson's capsule* (see Plate 8). Under its surface this capsule is lined by a serosal endothelium. In the deeper layers it carries a lymphatic network, a few blood vessels and nerves. Though representing vestigial structures, some aberrant bile ducts (see page 22) also found in the capsule are of clinical interest because of their becoming markedly dilated in extrahepatic biliary obstruction, so as to cause

(*Continued on page 10*)