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Hepatic Sphincters

Brief Summary of Present-Day Knowledge

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Studies of normal and pathologic circulatory physiology sometimes are carried out without taking into account (i) the blood-cell-reservoir function of the spleen, and (ii) the blood-reservoir function of the liver and portal vein bed. For instance, some of the recent reviews of the factors which affect and limit cardiac output in health and disease have paid but scant attention to the accumulated knowledge of the structure and reservoir functioning of the spleen, portal vein bed, and liver (*1*). The purposes of this article (*2*) are to give adequate leads to the earlier fundamental literature and to present a brief summation of the recent and growing knowledge in this field. The references to the basic older literature are particularly important because they come from at least two specialized fields of study: anatomy and normal circulatory physiology. Specialists in other fields of biology, medicine, and surgery are often unaware of this basic literature.

A blood reservoir may be defined as a region of the vascular apparatus of variable capacity, in which controlled amounts of blood can be stored and from which controlled amounts can be released. A necessary part of a reservoir system is physical apparatus that is capable of controlling the outflow of blood from the reservoir. The stored blood is not necessarily in the reservoir because the tissues of the reservoir are acting upon it in any special way or because the stored blood is necessary for the use of the reservoir apparatus itself. The stored blood may sometimes be stationary or moving, or various amounts may be accepted by the reservoir while other amounts are being released. Ordinary arteries cannot be considered significant as blood reservoirs because of their low capacity.

Spleen

The spleens of mammals are sometimes said to "store blood." This statement is inaccurate and misleading. The spleens of mammals, including man, store and release highly concentrated blood cells. Yang (*3*) and Yang and Chang (*4*) found that *human* spleens can store and, upon adequate stimulus, eject concentrated blood cells. This storage-and-release acts to increase or decrease the circulating red cell count, and thereby acts toward maintaining the count constant. Obviously, this also affects circulating blood volume.

Robert M. Berne has prepared a 16-millimeter motion picture which records a large volume change in the spleen of the dog. The film not only presents concrete evidence for scientists but also is ideal for classroom presentation. It can be borrowed for study (*5*). (For the older, basic literature and summary of the evidence that the spleens of mammals store and release concentrated blood cells, rather than whole blood, see *6, 7.*)

Liver and Portal Vein Bed

There is a rather large literature dealing with the blood-reservoir functions of the liver and of portal vein bed, beginning with Stolnikow in 1882 (*8–13*). A detailed analysis and summary of the fundamental knowledge was given by Knisely, Bloch, and Warner in 1948 (*7*). Descriptions of a few critical experiments follow.

Johansson and Tigerstedt (*14*) found that when saline or defibrinated blood was transfused into rabbits, large quantities of blood were stored in the liver. They say (translated): "The second fact to which we would draw attention is the great distention of the liver which we have observed in all our transfusion experiments and which has also been noted by earlier workers. After the injection of large quantities of fluid the liver becomes almost as hard as a board. If after the death of the animal the liver is cut out, fluid streams from it in great quantities. We see that a considerable quantity of fluid is taken up by the liver and thus withdrawn from the general circulation."

Krogh and Lindhard (*15*) and Krogh (*16*) clearly demonstrated by experiments performed on young, healthy, normal, unanesthetized, untraumatized, unfrightened men—namely, themselves—that the human liver and portal vein bed can store large amounts of blood, and that the rate at which such stored blood is poured into the inferior vena cava is a mathematical determinant of the amount of blood delivered to the heart. This means that the control of the outflow of blood from the livers of healthy human beings is a major factor in the control of cardiac output. These experiments did not make it possible to locate the anatomical structures that control the outflow from the liver and portal vein bed.

Jarisch and Ludwig (*17*), working with rabbits and cats, demonstrated that the veins of the intestines (which are tributaries of the portal vein) are a blood reservoir. Following even small injections of saline or blood into the animal's jugular vein, the volume of the intestinal vessels rose promptly and sharply. The vessels of the animal's legs did not make this response. The ability of the intestinal vessels to store blood was immediately abolished in all cases in which the innervation of the liver was destroyed. It must therefore be concluded that the storing of blood in in-

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testinal vessels is dependent on blood-flow control mechanisms within the liver.

Grab, Janssen, and Rein (*18*) found in 44 experiments on dogs that it was possible, following the administration of different doses of adrenalin, to cause the liver to eject a volume of blood equivalent to as much as 59 percent of the weight of the emptied organ.

Storage Control Mechanisms

Bauer, Dale, Poulsson, and Richards (*19*) found that in dogs the contraction of the large hepatic veins is a mechanism which can initiate the storage of blood in the liver. They also found that in their preparations small doses of adrenalin caused the outflow control mechanisms to relax.

The hepatic outflow control mechanisms have received several names, such as *sluice valves, sluice channels, throttle veins* and, in German, *Drosselvenen.* These terms have developed in general as a result of experiments using the methods of gross physiology. For the most part, the terms designate function and not specific, identified portions of anatomy. For a summary of the older anatomical knowledge of *Drosselvenen,* see Benninghof (*9*), Franklin (*10*), and Arey *et al.* (*12*).

Within recent years, knowledge of the specific anatomical locations of the contractile outflow control mechanisms has been growing. Four, perhaps five, separate sets of mechanisms are now known which can control the outflow of blood from the portal vein bed and liver.

Contractile hepatic veins. In dogs, long stretches of whole hepatic veins can dilate widely or contract so tightly shut that the available blood pressure cannot force them open (*12, 13, 19, 20*). Arey *et al.* (*12*), using wax plate reconstruction methods, have provided precise descriptions of the arrangements of stainable smooth muscles in hepatic venules of various sizes in the dog, raccoon, and fur seal.

According to Testut and Latarjet (*21*) (translated): ". . . the hepatic veins differ from the portal vein branches by the quite special development of their muscular fibers, which form a real tunic around their whole circumference and over their whole extent. This muscular tunic . . . consists of an internal layer of circular fibers and an external layer of longitudinal fibers. It is rather thin in man but very thick in some animals: thus, it reaches a thickness of 4 mm. in the ox and in the horse."

Contractile sublobular veins. Deysach (*22*) presented pharmacologic and histologic evidences that the sublobular veins are powerfully contractile in the cat, rabbit, raccoon, Virginia opossum, grizzly bear, coati mundi, white-tailed deer, "and others." (Deysach received his rare animals from a zoo.)

Deysach "small sluice channel." A fairly large number of hepatic sinusoids come together into a single channel which enters either a central or sublobular venule through a single contractile sphincter, which is the "small sluice channel." Deysach (*22*) first described these channels and demonstrated their presence mainly in adult cats and rabbits. Harding (*23*) saw Deysach small sluice channels in the living livers of frogs, mice, rats, hamsters, guinea pigs, rabbits, cats, dogs, and rhesus monkeys. The small sluice channels are greatly outnumbered by the fourth type of outflow control mechanism.

Sinusoid outlet sphincters. Each hepatic sinusoid or small group of sinusoids drains through a single outlet sphincter into a central or small sublobular venule (see Fig. 1). When one sinusoid outlet sphincter remains open, and those on each side of it shut off tightly, the blood from several of the neighboring, branching, and anastomosing sinusoids passes out through the single open-outlet sphincter. It is often difficult or impossible to know whether a given Deysach small sluice channel definitely is an anatomical structure, or whether the arrangement observed is a result of the aforementioned physiologic activities of the tissues at the moment.

Possible fifth mechanism. The arrangement of the smooth muscle fibers of the wall of the vena cava, arching around the outlet orifices of the large hepatic veins may, in some species, be a hepatic outflow control mechanism (see, for instance, the suggestive figure presented by R. Spanner, *24*). Both Arey *et al.* (*12*) and Franklin (*10*) provide reviews of older, relevant anatomical knowledge, mainly concerning possible throttle-valve mechanisms in aquatic diving mammals.

Sphincters of the Liver Lobule

Knisely, Bloch, and Warner (*7*) presented a diagram showing the parts of the liver lobule of frogs, based on microscopic study of the quartz-rod transilluminated living livers of 3500 animals (for anatomical orientation, see Fig. 1). The purpose of their study was to learn the structure and visible mechanical functioning of the parts of the liver lobule of one species thoroughly; it would then be possible to see which structures and functions of the liver lobules of other species are like those of frogs, and which differ, and how they differ. These investigators also reported the presence of inlet and outlet sphincters, which were observed in the lobules of one rhesus monkey.

Since then, Seneviratne (*25*) has studied living frog, mouse, and rat livers and reported that he could not see sphincter valves in any of these species. However, his Figs. 7, 9, and 10 show sinusoids ending blindly, leaving a clear space between the ends of the sinusoids and the adjacent larger vessel. This is the exact appearance of rows of sphincters when they are contracted tightly shut.

Both inlet and outlet sphincters have been observed by Irwin and Macdonald (*26*) in living guinea pigs; by Bloch (*27*) in 6000 living animals (frogs, rats, mice, bats, guinea pigs, rabbits, and rhesus monkeys); by Rappaport (*28*) in living weanling white rats. Outlet sphincters were seen by Harding (*23*) in living frogs, mice, rats, hamsters, guinea pigs, rabbits, cats, dogs, and in one rhesus monkey. Inlet sphincters have been seen during the past 5 years in our laboratory in living frogs, mice, rats, cats, hamsters, and dogs.

In summation, both inlet and outlet sphincters have now been seen in the livers of living frogs, mice, rats, guinea pigs, rabbits, hamsters, bats, cats, dogs, and rhesus monkeys.

In quartz-rod transilluminated livers, the sphincters have been observed by using high-resolving Leitz biobjective binocular dissection microscopes, which give magnifications from about 50 to 150. In our laboratory, compound binocular microscopes, provided with water-immersion objectives, have permitted observations up to ×550.

Irwin and Macdonald (*26*) made a significant contribution to the microscopic study of living structures in mammals. They adapted tracheal insufflation techniques, thereby making it possible to reduce or stop gross respiratory motions, nearly eliminating these motions from the minute structures that were being observed. Rappaport, working in our laboratory during July 1956, devised an arrangement which still further reduces the motions of mammalian structures. He arranged intra-abdominal polyethylene aprons under which Ringer's solution was run through a narrow polyethylene tube, thereby maintaining a constant intra-abdominal pressure. By using both of the aforementioned techniques simultaneously, it is now possible to focus a water-immersion lens on a single outlet sphincter and keep that structure in focus at as much as ×550 magnification for several hours at a time.

When it is properly illuminated, the sphincter material has a translucent appearance, sharply different from that of the surrounding hepatic parenchyma. With our light source (a tungsten-fila-

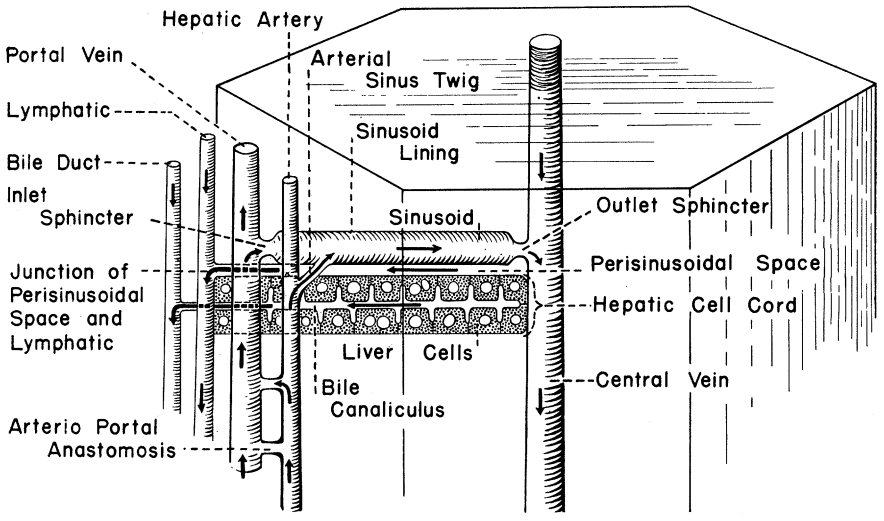

Fig. 1. Frog liver lobule. Each of the kinds of structure present in the lobule and the interrelationships between them are shown. Multiple interrelationships of items of the same kind are not shown—for instance, the well-known branching and anastomosing of sinusoids. Note the positions of (i) the inlet sphincter, at the point where the sinusoid joins the afferent intralobular portal venule, and (ii) the outlet sphincter at the junction of the efferent end of the sinusoid and the central vein of the lobule.

ment, motion-picture projection bulb operated at somewhat less than its rated 120 volts), the contractile tissue sometimes has a translucent golden color.

When illuminated by near-ultraviolet light from a General Electric Mazda A-H-5 lamp, transmitted to the liver by a quartz rod, the contractile inlet and outlet tissue of frogs fluoresces quite differently from the parenchyma. The contractile tissue becomes a greenish-gold color. (This is a "natural fluorescence"; no dye has been given the animal.)

In frogs, an injection of 0.6 milliliter of 0.5-percent trypan blue (dissolved in distilled water) into the dorsal lymph sac stains the hepatic parenchyma tissue sharply but leaves the sphincter material completely unstained.

Inlet Sphincter Function

In frogs, the inlet sphincters play a significant role in the "autotransfusion reaction." Knisely, Bloch, and Warner (7) described their observations of this reaction as follows: *"The Autotransfusion Reactions*: When a lightly anesthetized frog, which has a moderate to large percentage of its hepatic sinusoids storing blood or concentrated blood cells, has a moderately rapid hemorrhage from any part of its body, the terminals of the hepatic arterioles and portal venules and the inlet sphincters constrict tightly shut, the outlet sphincters open, the sinusoid linings constrict (often peristaltically from the periphery of the lobule toward the center), thus ejecting the contents of the sinusoids into the central veins. Thus the animal 'gives himself a blood transfusion.' The outlet sphincters then close, which prevents backflow into the sinusoids. The central and sublobular veins may also constrict somewhat (but usually not tightly shut) thus ejecting a little more blood. The whole autotransfusion is a precisely coordinated reaction of the individual structures which participate. In well nourished lightly anesthetized animals the blood is actively ejected by contraction of the sinusoid linings. The evidence is that the sinusoids may be completely empty and contracted so tightly that they have no lumen at the end of the ejection."

As far as is now known, blood does not pass from the portal vein bed into the liver without passing through the hepatic inlet sphincters. Note that during the autotransfusion reaction just described blood stored in the liver was forcibly ejected during a time that hepatic inlet sphincters prevented portal vein blood from entering the liver. Anatomically, the inlet sphincters of other species stand in a position which would permit controlled emptying of the liver without emptying of the portal vein bed and tributaries through the liver. Other than the foregoing, we have no clear-cut concepts of the functions of inlet sphincters, either for hepatic or for general circulatory physiology. Obviously, the functions of the inlets are now open for investigation.

Hepatic Outflow Control Mechanisms

When a segment of hepatic vein contracts tightly shut, it stops the outflow of blood from a relatively large volume of liver tissue. When a sublobular vein contracts, it can cause the storage of blood in one or more whole lobules. When a Deysach "small sluice channel" closes tightly, it can cause the retention of but a small amount of blood in the relatively few sinusoids which drain through it.

The individual sinusoid outlet sphincters of frogs can all open widely at once or take turns individually, opening and closing, relaxing and contracting; or various numbers of them may remain partially, tonically, contracted; or various numbers may all close at once. (These activities have been recorded in motion pictures taken through the microscope.) The outlet sphincters thus provide precise control of the flow of blood out of each and every sinusoid of the frog liver (for details, see Knisely, Bloch, and Warner, 7). Detailed knowledge of the behavior of sinusoid outlet sphincters in mammals is not yet available.

By and large, the four or five separate outflow control mechanisms have been discovered and studied during separate investigations, which usually employed quite different methods of study. Consequently, the knowledge that a given species has a certain type of outflow control mechanism does not indicate that the other mechanisms are absent in that species. Note that at least four of the mechanisms have now been found in dogs.

In various papers and reviews describing efforts to discover hepatic outflow control mechanisms, it is sometimes pointed out that "the mechanisms are absent" in one species or another. Careful reading of many of the original papers clearly shows that the investigators have not always determined whether they found the hepatic outflow mechanisms absent, or whether the methods they used failed to detect their presence.

As previously noted, Krogh and Lindhard (*15*) and Krogh (*16*) demonstrated that *human* liver and portal vein bed store and release blood and thereby limit and control the rate of filling of the heart, and thus the cardiac output.

As is well known, in many organs—human skin, for instance—there are direct vascular capacity changes as various numbers of arterioles, capillaries, or venules change caliber during different phases of functions of the organs. Further, every movement of fluid in or out of the vascular system acts toward changing the capacity of the system. If an animal's vascular system is to function as a competent hydraulic machine, it must have blood depots which can respond to the summations of all the direct and indirect changes in the capacities of the peripheral parts of the system.

Blood returns to the right heart by three major pathways: the superior vena cava, infrahepatic inferior vena cava,

and the hepatic veins which drain the liver, portal vein bed, and spleen. Various tributaries of the superior and inferior vena cava have flap valves which permit forward blood flow and stop back flow. The hepatic outlet control mechanisms stand as throttle valves controlling the outflow from the great hepatic and portal vein bed blood reservoir; they are the only known contractile structures which can dam back fairly large volumes of blood and restrict or stop the flow of that blood toward the right heart.

Portocaval Anastomoses

Currently, it is often assumed that no blood can pass from the liver and portal vein bed to the vena cava without passing through the hepatic veins. Were this true, the blood from the liver and portal vein would have to pass through one or more of the hepatic outflow control mechanisms. However, there are in human beings, and perhaps in other species, known collateral connections between the portal vein or its tributaries and the inferior vena cava. No single current textbook of human gross anatomy lists all of these. Comer and Knisely (*29*) present a list of known collaterals in man, collected from the original literature (see also *30*). The total numbers and total cross-sectional areas of the collateral connections between portal vein and vena cava are not known for any species, nor are their normal functions and vasomotor control mechanisms known.

One of us (M. H. K.) recently was present at the autopsy of a 20-year old previously healthy man who had been killed 10 hours before by a single stab wound in the upper right thorax. From rather cursory examination of the vessels of the portal vein bed and collaterals to the inferior vena cava, he is of the opinion that the whole topic of portocaval anastomoses in the healthy normal human being now needs rigorous reinvestigation. One problem is to be sure to distinguish an anastomosis which is a part of healthy normal anatomy from one which developed as a consequence of, or as a part of, circulatory pathology of the abdominal territory. For this, resort to histologic sections may be necessary. The information currently in elementary textbooks of human anatomy is not useful for this purpose; it was not collected for the specific purpose of making it possible to understand the structure and function of normal human beings. As noted, when attempting to understand normal and pathologic physiology, the presence of portocaval anastomoses in *normal healthy* men is frequently unknown, ignored, or forgotten.

Those who are interested in the control of cardiac output should read the detailed and comprehensive analysis of the literature dealing with the blood-cell reservoir functions of the spleen, and the blood reservoir function of the hepatic veins and the liver, in Knisely, Bloch, and Warner (*7*).

Reservoir Retention Shock

The "pooling of blood" in the liver and portal vein bed has been thought to be a major factor in some, not all (see Knisely *et al., 31*) types of circulatory shock. The forcible closing of adequate numbers of one or more types of hepatic and portal outflow control mechanisms can be one factor which initiates the pooling (*13*). The plugging of enormous numbers of small hepatic blood vessels, sinusoids, intrahepatic radicles of the portal vein and hepatic artery, and so forth, with masses of agglutinated blood cells is another mechanism which can initiate the "pooling of blood" in the liver and portal vein bed.

Conclusion

We now need to know the following:

1) A great deal more about the numbers, total cross-sectional areas, histologic construction, vasomotor control, and normal functions of the portocaval anastomoses in each of a series of species.

2) The cytological characteristics of various contractile sphincter mechanisms of the liver [Warner (*32*) reported structures (in guinea pigs) similar to smooth muscle cells surrounding the sinusoids efferent ends; these cells contained fibrils similar to myofibrils (see also Arey *et al., 12*)].

3) The physiological reactions in which the hepatic sphincter mechanisms continually participate (for the currently available information, see Knisely, Bloch, and Warner, *7*).

4) The neurological and hormonal mechanisms which normally control the hepatic sphincters.

5) How the various types of outflow control mechanisms take turns operating and otherwise coordinate their activities.

6) Pharmacological and therapeutic agents which will cause each type of sphincter in each species to contract or to relax (for a beginning of this, see *11, 19, 22, 33*).

7) The responses of each type of sphincter mechanism to noxious stimuli applied to the whole animal, such as hemorrhages, both rapid and short, and long and slow; and also the responses to severe burns, crushing injuries, experimentally induced infections, or perhaps even to just a severe fright.

References and Notes

1. T. Sjöstrand, *Physiol. Revs.* **33**, 202 (1953); E. Asmussen and M. Nielsen, *ibid.* **35**, 778 (1955); O. H. Gauer, *ibid.* **35**, 143 (1955); D. E. Gregg, D. C. Sabiston, E. O. Theilen, *ibid.* **35**, 130 (1955); A. C. Guyton, *ibid.* **35**, 123 (1955); W. F. Hamilton, *ibid.* **35**, 161 (1955); L. N. Katz, *ibid.* **35**, 91 (1955); R. F. Rushmer, *ibid.* **35**, 138 (1955); S. J. Sarnoff, *ibid.* **35**, 107 (1955).
2. This work was aided by U.S. Public Health Service grants H-1638 and H-2057.
3. C. S. Yang, *Chinese J. Physiol.* **2**, 163 (1928).
4. ——— and H. C. Chang, *ibid.* **4**, 21 (1930).
5. R. M. Berne, *Spleen Changes in Size* (16-mm. motion picture; available through the Medical Audio-Visual Institute of the Association of American Medical Colleges, 185 N. Wabash Ave., Chicago 1, Ill.).
6. J. Barcroft *et al., J. Physiol.* (*London*) **60**, 79 (1925); J. Barcroft, *Lancet* **1926I**, 544 (1926); J. Barcroft and J. G. Stephens, *J. Physiol.* (*London*) **64**, 1 (1927); J. Barcroft and L. T. Poole, *J. Physiol.* (*London*) **64**, 23 (1927); L. Binet, *La rate organe reservoir* (Masson, Paris, 1930); S. E. Björkman, *Acta Med. Scand. Suppl. No. 191* (1947); G. Gelin, *La rate et ses maladies* (Masson, Paris, 1954); M. H. Knisely, *Angiology* **6**, 363 (1955); J. Barcroft, *Naturwissenschaften* **14**, 797 (1926).
7. M. H. Knisely, E. H. Bloch, L. Warner, *Kgl. Danske Videnskab. Selskab Biol. Skrifter* **4**, No. 7 (1948).
8. Stolnikow, *Pflügers Arch. ges. Physiol.* **28**, 255 (1882); S. E. Bradley *et al., J. Clin. Invest.* **24**, 890 (1945).
9. A. Benninghoff, *Handb. Mikroskop. Anat. des Menschens* **6**, 153 (1930).
10. K. J. Franklin, *A Monograph on Veins* (Thomas, Springfield, Ill., 1937).
11. L. N. Katz *et al., J. Pharmacol. Exptl. Therap.* **62**, 1 (1938); L. N. Katz and S. Rodbard, *ibid.* **67**, 407 (1939).
12. L. B. Arey, R. Sohlberg, Jr., R. B. Rutherford, *Anat. Record* **81**, 21 (1941).
13. W. D. Thomas and H. E. Essex, *Am. J. Physiol.* **158**, 303 (1949).
14. J. E. Johansson and R. *Tigerstedt, Erste Abhandl. Skand. Arch. Physiol.* **1**, 331 (1889).
15. A. Krogh and J. Lindhard, *Skand. Arch. Physiol.* **27**, 100 (1912).
16. A. Krogh, *ibid.* **27**, 126, 227 (1912).
17. A. Jarisch and W. Ludwig, *Naunyn-Schmiedeberg's Arch. Exptl. Pathol. u. Pharmakol.* **124**, 102 (1927).
18. W. Grab, S. Janssen, H. Rein, *Klin. Wochschr.* **8**, 1539 (1929).
19. W. Bauer *et al., J. Physiol.* (*London*) **74**, 343 (1932).
20. L. B. Arey and J. P. Simonds, *Anat. Record* **18**, 219 (1920).
21. L. Testut and A. Latarjet, *Traité d'anatomie humaine* (Doin, Paris, ed. 9, 1949), vol. 4, p. 638.
22. L. J. Deysach, *Am. J. Physiol.* **132**, 713 (1941).
23. F. Harding, *Anat. Record* **121**, 305 (1955).
24. R. Spanner, *Atlas of Human Anatomy* (Little, Brown, Boston, ed. 15, 1954), part 2, Fig. 673a.
25. R. D. Seneviratne, *Quart. J. Exptl. Physiol.* **35**, 76 (1949–50).
26. J. W. Irwin and J. Macdonald, *Anat. Record* **117**, 1 (1953).
27. E. H. Bloch, *Angiology* **6**, 340 (1955).
28. A. M. Rappaport, personal communication.
29. R. Comer and M. H. Knisely, in *Transactions of the Fifth Conference on Shock and Circulatory Homeostasis* (Josiah Macy, Jr. Foundation, New York), in press.
30. E. A. Edwards, *Arch. Internal Med.* **88**, 137 (1951); C. G. Child, III, and R. D. McClure, Jr., in *Surgical Forum* (Saunders, Philadelphia, 1952), pp. 140–146; J. L. Madden and J. M. Loré, Jr., in Surgical Forum (Saunders, Philadelphia, 1952), pp. 133–140; L. Schiff, *Diseases of the Liver* (Lippincott, Philadelphia, 1956); A. Gräsbeck, *Duodecim* (1927), pp. 904–916 [reprinted in *Anat. Ber.* **13**, 365 (1928)]; P. Cordier, L. Devos, J. Wattel, in *Compt. rend. assoc. anatomistes* 33ème réunion, Bâle, 10–14 Apr. 1938 (1938).
31. M. H. Knisely *et al., Anat. Record* **106**, 43 (1950); *Transactions of the Third Conference on Shock and Circulatory Homeostasis* (Josiah Macy, Jr. Foundation, New York, 1953, p. 30.
32. L. Warner, *Anat. Record* **76**, 57 (1940).
33. E. H. Bloch, *ibid.* **76**, 7 (1940).