spleen, either through an increased quantity of fluid within the pulp or through a contraction of the trabeculæ and capsule, will favor the flow of blood toward the vein and into it.

Preparations of the spleen made by maceration, cleansing, distention, and drying show the general arrangement of the trabeculæ to the veins. With the naked eye the veins can be followed to the interlobular spaces. Low powers show this relation of the veins to the lobule better (Fig. 4460), yet it is impossible by this method to follow with certainty the smaller veins between the lobules to the capsule. At the main junctions of the trabeculæ with the veins the tissues are more or less matted together, and an attempt to separate them without special methods always leads to some confusion. Ordinary injections of the spleen do not give better specimens, and for a long time I had to rely on sections of hardened spleen which had been injected by the ordinary method. Such specimens do not lead to good results, as the great quantity of colored veins in a thick specimen obscures the larger vessels, for at no time do any number of them lie in the same place. Finally, however, I obtained most definite specimens by macerating spleens after the veins had been injected with either colored celloidin or agar-agar. Both of these substances will not dissolve when the tissue is macerated or when it is digested in pancreatin. The agar can easily be forced throughout the whole venous system, and, if too much pressure is applied, into the tissues, while the celloidin flows with difficulty and under no condition will fill completely the venous plexus of the lobule.

FIG. 4464.—Double Injection of the Spleen with Prussian Blue into the Vein and Carmine Gelatin into the Artery. At many points the injection of the artery is more complete than is shown in the figure, the entire field being tinged red. Enlarged 40 diameters.

Fig 4463 is from a specimen injected with celloidin colored with Prussian blue digested with pancreatin, washed, and slightly tinged with acid fuchsin. It was next injected and dried, then cut into sections and mounted in Canada balsam. It shows most beautifully the interlobular veins and the intralobular venous plexus. Only at exceptional points is this plexus injected, and in numerous sections the larger veins, the interlobular veins, and the trabecular system alone are shown. In sections parallel with and immediately below the capsule the lobules form a beautiful honeycomb arrangement with the larger interlobular veins at the point of junction of several lobules. The veins now leave the trabeculæ and enter the lobule to form the intralobular venous plexus (Fig. 4464). The main venous branches upon entering the lobule give rise to numerous smaller branches, which anastomose with one another to form the intralobular venous plexus.

Specimens obtained by digesting with pancreatin a spleen in which the veins have been injected with colored celloidin outline most beautifully the spleen lobules. They are about as regular in shape and arrangement as those of the liver, and each is encircled by about three terminal interlobular veins, which are set equidistant from one another and lie within trabeculæ. The walls of the branches which arise from the interlobular veins to penetrate the lobule are formed by a delicate network of reticulum fibrils lined by a layer of peculiar spindle-shaped endothelium cells.

The spleen shows much more beautifully than any other organ the value of fibrils in the construction of a skeleton in which the various structures are suspended. This skeleton not only acts as framework for the larger veins, lobules, and muscles, but is also most delicately adjusted to the structures of the lobule. The arrangement of the whole skeleton is such that a contraction of the muscles (trabeculæ) will compress the lobule (pulp), at the same time pulling open the larger veins. When the contraction of the trabeculæ and capsule is at a maximum the larger veins are also compressed. This mechanism thus aids the circulation from the pulp to the smaller veins and from them to the larger ones. Within the lobule the elastic network of reticulum not only empties the intralobular plexus, but also aids to force the red blood corpuscles and plasma which have escaped into the interstitial spaces back into the veins.

If a portion of a spleen is made partly œdematous by injecting neutral gelatin into a few of its arteries, most instructive specimens are obtained by further injecting the whole venous system with a weak solution of nitrate of silver. A successful specimen made in this way shows the cells lining the veins, outlined and stained, throughout the whole organ. In the contracted portion of the spleen the veins are shown in a collapsed state, while in the œdematous portion they are shown distended. From specimens made in this way I find that the whole venous tree, up into the lobule, is lined by a complete layer of endothelium cells. From this portion of the venous tree no extravasation of blood can take place, as repeated injections have shown. When, however, the endothelial lining is followed into the lobule, it is soon seen that the walls of the veins are not by any means complete, but there are numerous stomata between endothelial cells which are greatly increased in size when the lobule is distended. A given vein followed from an interlobular vein into the lobule soon loses its sharp endothelial lining. At first, in the interlobular collecting veins, the outlines of the cells are sharp and line the whole vein, in either collapsed or distended condition, but as the vein breaks up into the venous plexus the cells no longer line the whole vein. The transition from the complete endothelial wall to an incomplete one takes

place in the collecting veins of the lobule, and no complete walls are found within the intralobular plexus.

With the change from a complete endothelial wall to an incomplete one the forms of the cells change also. When the wall is complete the endothelial cells have the usual and well-known form, but as the wall becomes broken the cells at first are irregular, flat protoplasmic masses, sometimes sharply outlined on the side toward the complete wall, but usually irregular in all directions. Soon, however, the cells change their form into a long spindle-shaped mass with rounded ends, with the nucleus protruding on one side of its body, as is well pictured in Henle's "Anatomy." These have been described as muscle cells, and when isolated look much more like them than those pictured by Henle. Yet their position and relation to the perfect endothelial walls lining the collecting veins show definitely that they are endothelium. These long spindle-shaped endothelial cells do not overlap at all in lining the veins of the intralobular plexus. Sometimes two nuclei are seen side by side, but in thin sections of organs made œdematous with gelatin, frozen, cut, and hardened in formalin, they are found to be fairly numerous. The spaces between them in distended organs are considerably larger than the diameter of their nuclei, large enough to allow cinnabar granules to pass into the tissue with ease when injected into the veins, but too small to allow many ultramarine blue granules to escape.

THE LOBULE OF THE SPLEEN.—It has been shown above in the study of the arteries, veins, and trabeculæ that each of these systems is ultimately related to a portion of spleen substance, always of about the same volume, which I have termed the anatomical unit or the lobule of the spleen. These units are outlined only by the larger trabeculæ with their enclosed veins, and not by a membranous layer of connective tissue, as is the case in the lobule of the pig's liver. So in sections it is almost impossible to detect the lobule because in the mass of splenic tissue there are seen only sections of the scattered trabeculæ, some of which are within the lobule.

With care and some imagination the lobule may be outlined in a thin section of spleen after the veins have been injected. Especially is this true if the section is immediately below and parallel with the capsule. In specimens so made the lobules are cut transversely and are outlined by the larger veins and trabeculæ. Yet a number of fairly large veins and smaller trabeculæ enter the lobule, and their section aids to obliterate it. When, however, the veins are injected with coarse granules which do not enter the smaller veins easily, thick sections show the lobules very clearly. Such a section is given in Fig. 4464. In this specimen the lobules, both peripheral and deep, are shown throughout the spleen. This method of preparation permits of the study of the lobules themselves more carefully than do the common specimens, the latter, however, giving more clearly the outlines of the lobules and their relation to one another.

The study of the artery also aids to define the lobule, as its main terminal branches always lie in the centre of it. The arterial injections always show the lobules best when the tissues have first been well distended with a fluid. In the specimen from which Fig. 4464 is taken this was done by means of the diffusion of the gelatin throughout the tissue after having been injected into the vein. The same result was accomplished in the second specimen by ligating the splenic vein in an animal half an hour before killing it. By so doing the lobules are all distended with blood and the main structures within them are spread apart. After this the artery was next injected and thick sections of the fresh spleen were placed in ten-per-cent. NaCl to extract the blood. Specimens made in this way show the distribution of the artery in the lobule most beautifully.

Not only does the artery mark the lobule by passing in through its centre, but it is especially well defined where the arterial sheath of lymphatic tissue becomes enlarged to a Malpighian follicle. These follicles usually lie at the point where the artery enters the lobule, but in rare instances they may extend well into the lobule or they may be so large that at the point of their location the whole lobule is not only filled but distended. This is especially the case in spleens which are empty and collapsed.

With thick sections of injected spleens the lobule is again well defined, confirming in every respect the results obtained from corrosion specimens. That this is so is of the utmost importance in outlining the lobules, because the tissues of neighboring lobules run together, and because the main trabeculæ, veins, and arteries undergo further branching over and into the lobules. A similar branching takes place among the interlobular veins, bile ducts, and arteries of the liver. At the middle of the lobule of the liver there are on an average three interlobular veins, while at the distal end or tip of the lobule there are six. Furthermore, the architecture of the liver lobule is by no means as simple as it is usually pictured; in fact, its very existence was not fully established until nearly two hundred years after it was described by Malpighi.

Were it not that the section of the bile duct is so characteristic, we would have as much trouble in locating the liver lobule in most animals as we have in locating the spleen lobule.

Throughout the lobule there is a beautiful venous plexus which is suspended in a coarse network of trabeculæ penetrating the lobule. These trabeculæ are solid, having no veins within them, but toward the periphery of the lobule they usually accompany the collecting veins arising from the venous plexus. On an average there are nine of these intralobular collecting veins in each lobule. The distances between them are equal and they divide the lobule into nine pyramidal parts, within the centre of each of which parts there is a branch of the lobular artery. In a measure this arrangement is shown in Fig. 4464. If the subdivisions of the lobule marked by the intralobular veins were more definite, I would be inclined to consider them the lobules of the spleen, as they possess all the characteristics of lobules. But the extreme difficulty in demonstrating their presence by the different methods at our disposal, as well as the fact that the greater masses or lobules always exist and can be demonstrated with much greater ease, is the reason why I consider the larger the units, and the smaller ones the subdivisions of the units.

But if we did consider the subdivisions to be the lobular units, we should still not be at the end of our difficulty, for they are again cut up into compartments by branches of the intralobular collecting veins which finally arise from the venous plexus. The venous plexus, however, is definite and constant. This last surrounds small masses of spleen tissue, in the centre of which is the final arteriole. This mass, with the end of the artery in its centre and the venous plexus around it, I shall term the histological unit. Within it lies the whole mystery of the spleen.

The spleen is composed of many histological units which are arranged in great clusters within the anatomical units or lobules. The lobules are repeated a sufficient number of times to form the whole spleen.

The Histological Unit or Pulp Cords.—The histological units occupy all the space of the spleen with the exception of that occupied by the Malpighian corpuscles and their extension into the lymphatic tissue which accompanies the arteries. The boundaries of the units being outlined by the veins of the intralobular plexus, which pass in all planes, are not separated from one another any more than are the holes in a sponge, although these are outlined by the sponge substance. The units together, as well as the veins, form a ramifying network, the two together filling all the available space.

Fig. 4463 is a low-power drawing of the network of veins within the lobule, *L*, the meshes of which are filled with the histological units or pulp cords. In Fig. 4462 the veins and units are shown with a higher power. As the veins are emphasized in this drawing, the units appear as islands, but it is easy to imagine them communi-

cating with one another between the meshes of the vein plexus lying in a deeper plane. Fig. 4464, which is still more highly magnified, shows the units as a plexus of the spleen pulp marked by the sections of the intralobular veins. When the boundary lines of the units are emphasized by examining with low powers thick sections which have been stained intensely, the veins are seen to outline the histological units as distinct islands. Thinner sections with higher powers, however, show that the units communicate with one another very freely and are also outlined by the sections of the veins of the intralobular vein plexus, as shown in Fig. 4465. The separation of the histological units and their relation to one another is a repetition on a smaller scale of the relation of the anatomical units or of the lobules.

Fig. 4462 is from a specimen in which the veins had been filled by an interstitial injection of aqueous solution of Prussian blue. In all specimens made in this way the blue fluid passes directly into the intralobular vein plexus and outlines the histological units. Interstitial injections of other organs usually fill the lymphatic channels, in case they exist, and in the spleen the anatomical arrangement of the venous plexus is similar to that of the lymphatics in other organs. This fact is remarkable, and although it may suggest ideas regarding the circulation through the spleen, it does not help us much regarding its anatomy, because we do not know the anatomy of the lymph radicals. When the veins of the spleen are filled either by means of interstitial injection or by injection into the main veins, the fluid never passes over into the arteries. This has been observed repeatedly by many investigators and appears to show conclusively that there is no direct connection between the arterics and veins.

The specimen from which Fig. 4465 was drawn was made by injecting chrome yellow suspended in gelatin into the vein until the spleen was distended to its maximum, and then an aqueous solution of Prussian blue was injected into the artery. In specimens made in this way the spleen is distended to its maximum with gelatin, with yellow granules in the veins and a blue precipitate in the artery. In the portion of the section drawn the arterial injection did not pass beyond the terminal arteries, but in many other portions of the specimen it did.

By this method of procedure there can be no doubt whatever in determining arteries from veins. In case the whole injection is made with a colored fluid into the artery, it is usually very difficult to determine whether or not a certain vessel is an artery or a vein, and in case it is a vein whether or not it had been injected through an artery in the immediate neighborhood. To illustrate: If an ordinary spleen, hyperæmic at points, is injected with Prussian blue through the artery, it is found that when the injection is complete there is usually much extravasation of fluid. Arising from these extravasations there are many injected veins, from which neighboring veins, including the intralobular plexuses, are injected. Of course, the arteries in portions of the spleen with secondary venous injections are also filled with fluid of the same color, and thus false conclusions are often drawn. Such specimens must be viewed as double injections with fluid of the same color, and are of little value in studying the relations of the blood-vessels of an organ, especially of the spleen.

To mark definitely the veins of the intralobular plexus, it is desirable to employ substances which will fill these veins and go no further. Ultramarine blue is an excellent substance for this purpose, as few of its granules will pass over into the tissues. Yet for purposes of double injection the color is wrong, for in all instances aqueous Prussian blue is the best for the artery. On this account I used most frequently chrome yellow granules in gelatin for the veins and Prussian blue for the arteries. After the spleen has had its veins all filled with the yellow granules suspended in gelatin, the gelatin passes over into the tissue, leaving the granules in the vein, for its walls act like a sieve. If the arteries of a specimen prepared in the above-described manner are injected with a solution of Prussian blue, but little of it enters the veins; nor can secondary injections of the spleen take place through the veins, as all of them have been plugged by the chrome-yellow.

A spleen having been made œdematous by the extravasation of the gelatin, by injecting it as described above, is easily cut into thin sections on the freezing microtome, either fresh or after it has been hardened in formalin. Such sections may be treated in various ways and are most instructive. They always have their veins decidedly marked with the yellow granules, which is of greatest importance in studying sections of the spleen. Repeated tests have shown that veins are very characteristic and need not be confounded with the *capillaries* or *ampullæ*, as I shall show presently.

Sections of the intralobular venous plexus are shown in Figs. 4461 and 4465, which are from specimens prepared in various ways. The figures show sufficiently the nature of the walls, the intralobular veins, venous sinuses, or spleen sinuses, as they have been termed. By injecting dilute solutions of nitrate of silver into the veins, endothelium cells are sharply outlined throughout the interlobular veins and fairly well in the intralobular collecting veins. From now on throughout the intralobular venous plexus the cells lining the veins no longer make a continuous layer. They become spindle-shaped with rounded ends, their nuclei protruding at their sides, as described by Henle. When the veins are collapsed these cells come in contact with one another, and in sections look much like non-striated muscle fibres. With the veins distended, however, the cells separate, leaving wide openings between them, which are large enough to allow cinnabar granules to pass through them with ease, but not large enough to allow ultramarine-blue granules to pass through freely. Although the blue granules are smaller than red blood corpuscles, they have sharp edges which certainly do not favor their passage through the openings in the walls of the veins, which are considerably larger than the diameter of the granules. The openings between the endothelial cells in the veins may be also shown by ligating the splenic vein in the living animal (Thoma). At first the spleen becomes hyperæmic, and sections at this stage show that all the blood is lodged in the veins and but very little in the tissues. After a greater length of time the veins become enormously distended, and then the blood begins to pass from the veins over into the tissues of the spleen pulp or the histological units. This experiment in itself is a strong argument in favor of a closed circulation through the spleen, for were it otherwise the blood would begin to accumulate in the tissues long before the veins are distended to their maximum. The pictures obtained after tying the veins all speak most strongly in favor of the idea that the blood in the spleen pulp extravasated from the veins and not from the arteries.

At any rate, both experiments and specimens show that the endothelial lining of the venous plexus is very incomplete, having openings between them large enough to allow the passage of red blood corpuscles with ease, and of course blood plasma with the greatest freedom. These openings are the largest when the spleen is distended to its maximum, and smallest when it is completely contracted. The two pictures obtained by examining distended and contracted spleens are so different that it is difficult to recognize that both are from the same organ. We are all familiar with sections of contracted spleens, but the sections obtained from a distended spleen are certainly a great surprise to one who has not seen them before. The most instructive specimens are made by injecting the veins of a portion of the spleen with ultramarine-blue gelatin, leaving the remaining portion uninjected. In the injected portion the tissues of the histological units are distended with the gelatin, while the blue granules remain in the veins. At the junction of the injected portion with the uninjected all gradations may be seen, which when put together give the idea that the cells have been washed out of the part distended. This interpretation is out of the question in this case, as the spleen substance has simply been distended with gelatin and all of its tissues have been held fast and fixed by the hardened gelatin.

Henle washed out the spleen by a long-continued artificial circulation of a solution of sulphate of soda through the artery. If the circulation is continued for half an hour or longer, the spleen loses its red color, becomes pale, distended, and very œdematous. The first fluid which comes from the veins has in it many red corpuscles, but as the spleen becomes paler and paler they gradually diminish in number. This experiment appears to prove that the blood-vessel system of the spleen is open and that the circulation passes through the spaces in the pulp. For a long time this argument seemed incontestable to me, and it, with another and apparently contradictory experiment, showed that the mystery had not been fully solved. Ten years ago I found that when cinnabar gelatin is injected into the artery with a pulsating pressure for a long-continued time, most of the cinnabar passed over into the intralobular venous plexus and not into the tissues of the pulp, as it should were the circulation through the spleen open. While Henle's experiment speaks for an open circulation, this experiment calls for a closed one.

I have repeated Henle's experiment many times, and am now fully convinced that he never washed out the pulp cells at all, but only washed out the cells and red discs which were lodged in the veins. In addition to this, he made the spleen œdematous, which in all cases appears "washed out." After the artificial circulation has been carried on through the spleen for hours, the pulp spaces of the histological units have within them just as many cells as are present when the œdema is produced by a simple injection of gelatin into the veins. In the latter instance the cells certainly were not washed out, as the gelatin simply passed into the tissues and after hardening held everything in place. Furthermore, in numerous tests I have never succeeded in removing the cells from the pulp by means of artificial circulation. Fig. 4461 is from a frozen section of a spleen made œdematous by injecting gelatin into the vein. The section was then placed in warm water to dissolve the gelatin, and then shaken a short time. Most of the cells have been removed. Further shaking would destroy the section entirely.

Reticulum of the Histological Unit.—That the framework of the pulp is made up of anastomosing fibrils which must be viewed as a variety of reticulum has been shown sufficiently above. At present I shall consider the arrangement of this reticulum within the lobule. In the description of the delicate reticulum fibrils of the lobule the terms reticulum of the lobule or of the pulp are used, while the tougher and more resistant reticulum of the capsule and trabeculæ is referred to as the reticulum of the trabeculæ.

The reticulum of the lobule forms a delicate network throughout the lobule, which in turn is suspended within the meshes of the network formed by the trabeculæ. The main strands of the fibrils accompany the vein plexus as pictured by Oppel. When sections of a fresh œdematous spleen are washed in water to remove most of the cells and then tinged with picric acid, the same picture is seen as that gotten by Oppel by using Golgi's method. The main strands of the reticulum accompany the interlobular venous plexus, while a more delicate network with more open meshes extends throughout the histological unit. In the centre of the unit the network becomes more dense again, which marks the position of the terminal artery with its accompanying ellipsoid lymphatic tissue.

Within the meshes of the reticulum are located all the cells known as pulp cells, *i.e.*, free cells including all the elements of the blood, giant cells, pigmented cells, and the fixed cells, which are more or less spindle-shaped. Many of the multipolar cells are only such in appearance, as their prolongations are the reticulum fibrils upon which they lie. Fig. 4461 is from a spleen partly washed out; it shows only the cells which are more firmly attached to the reticulum.

The reticulum fibrils are very extensible as well as elastic. The fibres may be stretched at least to twice their former length and when liberated will immediately rebound to the position they occupied before stretching. If a spleen is distended to its maximum by injecting it full of gelatin, it is found that all of the dimensions of the spleen have been doubled, as the spleen has increased its volume eight times. After the gelatin has hardened the spleen can be cut into sections on the freezing microtome and further experiments made upon them. When the section is placed in warm water to dissolve the gelatin, it is found that all its dimensions shrink to one-half. In other words, removing the gelatin allows the section to take the form it possessed before the spleen was injected. The reticulum is under no tension when the spleen is contracted to its maximum. When the spleen is distended the least its reticulum is stretched.

That the shortening of the section, when treated with warm water as described above, is due to the elasticity of the reticulum of the pulp and not to that of the structures of the trabeculæ, is proved by the fact that all the trabeculæ have been cut into small blocks in the sections. The small blocks of trabeculæ can no longer influence the dimensions of the section, for all of their main attachments have been broken. The trabecular network and capsule of the spleen are, however, very elastic, but the experiments with the œdematous section exclude these factors.

Fig. 4461 is from a section of œdematous spleen, the gelatin having been removed with warm water. The bundles of fibrils have taken on their natural shape, leaving a considerable lumen to the vein. Any further reduction of the meshes of the reticulum could be brought about only by external force, such as contraction of the trabeculæ in the living spleen. At any rate, it appears as if any marked distention of the spleen lobule can be brought about only by stretching the reticulum fibrils, and that these in turn are constantly pressing upon the fluids and elements within the meshes. In so doing the only outlet for them is through the vein, and this is favored by the openings in the vein walls. If the lobule is further distended the reticulum is stretched still more, and the veins, as well as the openings within their walls, are made larger. Everything, then, seems to favor the flow of fluid and cells from the spleen pulp into the veins when the pulp has become distended.

Henle has described spiral fibrils around the smaller veins in the spleen. In searching for them I have used his method over and over again, and occasionally I have obtained specimens which confirm his observations. It appears to me that the spiral fibrils which he describes are the reticulum fibrils around the larger veins, for only at these points have I been able to find them in specimens treated with KOH. I have already stated on a previous occasion that dilute HCl and KOH solutions do not cause white fibrous nor reticulated tissues to become transparent and swell when they are under tension. At the point where the larger veins (intralobular collecting veins) leave the lobule, the opportunity to stretch the reticulum surrounding them is extremely good while the specimen is being treated with KOH, because a pressure upon the cover slip will cause the trabeculæ to separate. These collecting veins are then stretched, as they are frequently located at the junction of two trabeculæ. Although, according to Hoehl, some elastic fibres leave the trabeculæ to enter the pulp, I do not think that Henle's spirals are anything but reticulum. If it were not difficult to obtain pictures like Henle's, the question could be easily settled.

The reticulum of the histological unit not only encircles the vein but extends to the artery, and in so doing passes through the lymphatic tissue surrounding it. If the reticulum is followed into the lymph follicle, it is found that the fibrils of the pulp are directly continuous with those of the follicle. Whether or not the reticulum of the follicle of the spleen gives the same reactions as that of the pulp cord, I have not been able to determine.

The Arteries Within the Lobule.—After the artery of the spleen has divided and subdivided a number of

times, a final branch enters the base of each lobule, passes through its centre, and gives off numerous branches which radiate toward the periphery of the lobule (Figs. 4464 and 4466). In all there are eighty thousand lob-

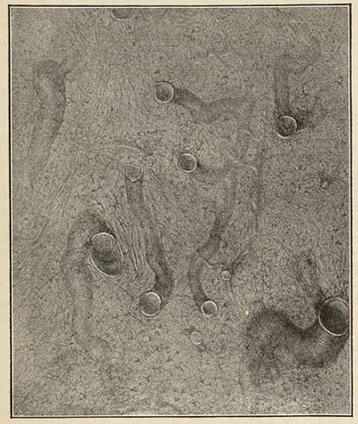

FIG. 4465.—Section of a Spleen the Veins of which had First been Injected with Chrome Yellow Suspended in Gelatin. The gelatin formed an œdema and the yellow granules remained in the vein. The artery was next injected with an aqueous solution of Prussian blue. Enlarged 80 diameters. At the point from which the drawing was taken the injection in the artery did not reach the vein.

ules, which are piled upon one another in such a manner that their bases point toward the nearest main trunk of the artery. The term base is arbitrary, not being the largest side of the lobule; in the case of the deep lobules the "base" is as large as any other side; while in the subcapsular lobules it is, in fact, the smallest side. In spite of this, however, it is well to consider the base the side of the lobule, the side that is most firmly attached in case they are separated from one another. In other words, as in the liver, in the lung, or in the intestine, the base is the proximal side of the anatomical unit. Within the lobule the long slender artery gives rise to about ten main branches, which are located in the centres of each of the subdivisions of the lobule outlined by the intralobular collecting veins. Finally, the smaller branches run in the centre of the pulp cords and each artery terminates in the centre of the histological unit, as shown in Fig. 4466. As the subdivisions of the central artery of the lobule pass to their destination, they are seen to curl under and over the veins of the intralobular venous plexus, remaining as far as possible from the veins. Their course in the pulp cords is the same as that of arteries of the lymph cord of a lymphatic gland.[9] The relation of the final artery to the intralobular veins surrounding the pulp cords is again identical with the relation of the artery to the vein in the lymphatic gland, as described recently by Calvert.[10]

The artery of the spleen and all of its branches are long and slender throughout their course, and they are surrounded by a sheath of lymphatic tissue, which accumulates into the Malpighian follicles at the origin of the central artery of the lobule and continues to the ends of the arteries as the ellipsoid sheath. The central artery of the lobule gives rise to ten main branches, each of which in turn gives rise to about six hundred terminal branches. The final branches lie in the centre of the histological unit, and in a distended spleen the distance between them and the vein plexus is about 20 μ.

When the artery of the spleen is injected with fluids, *e.g.*, gelatin, an extravasation takes place as soon as the injection enters the lobule; it is most intense around the periphery of the lymph follicle, around the arteries toward their termination, and throughout the histological units or pulp; it never takes place within the lymph follicle. When the injection of the spleen is incomplete it is found that the veins are injected only at the points of extravasation. The various authors who advocate an open circulation through the spleen base their conclusions upon the above tests, while those who advocate a closed circulation have occasionally observed a direct communication between the artery and vein. It matters little which opinion is correct, for in any case an extravasation invariably takes place when the artery is injected with a fluid, showing that a similar thing may take place in the living spleen. And since this takes place in part at least, we must admit that there is constantly a stream of blood plasma passing out of the artery into the pulp, which again must flow into the vein and not into the lymphatic channels, for they are not present. When, however, the spleen is distended to its maximum by tying the splenic vein, as well as its anastomoses with the gastric, half an hour before killing the animal, a subsequent injection of the artery with an aqueous solution of Prussian blue gives specimens which are most instructive. The spleen pulp is so distended with blood that there is no further space for the Prussian blue in it and it must take the course of the least resistance. This naturally is over toward the vein for before injecting the artery of the spleen the veins were opened to relieve the tension in them. If then there is any direct connection between the artery and vein it must be injected by this method. Fig. 4467 is from a specimen made by this method. It is seen that the terminal artery suddenly widens, passes toward the vein, and then communicates with it. In every respect this confirms Thoma's description of the termination of the artery within the spleen.[11] For a long time I have been obtaining specimens from time to time, which show that there is a communication between the artery and vein, but until recently I was unable to obtain complete injections in every specimen until I invented this method; for with ordinary methods the injections may be complete in one specimen while the next specimen treated in the identical way has a diffuse injection, barely showing the terminal arteries. I finally found that these ampullæ are very marked if an œdematous or a hemorrhagic spleen is injected with aqueous Prussian blue, a fluid which precipitates very easily. I have never been able to demonstrate them with carmine gelatin as it diffuses with the greatest ease.

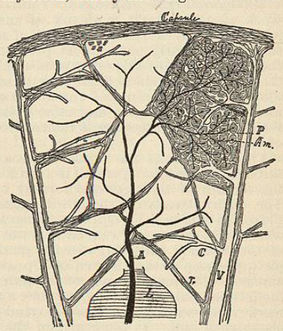

FIG. 4466.—Diagram of the Lobule of the Spleen. *A*, Artery in the centre of the lobule; *V*, interlobular vein within the interlobular trabeculæ; *Tr*, intralobular trabeculæ; *L*, Malpighian follicle; *C*, intralobular collecting vein; *P*, intralobular vein plexus which surrounds the pulp cords or histological units; *Am*, ampulla of Thoma.

There are then marked channels, or the ampullæ of Thoma, connecting the arteries with the veins, which can be demonstrated by certain methods. From time to time it appeared to me that the ampullæ marked artificial channels, but their constancy, their direction and their arrangement being always so characteristic, as well as the fact that they are present in uninjected specimens, are sufficient evidence against this view. The fact that

they are easily injected only when the rest of the spleen is filled with fluid appears to indicate that they may be reserve channels through which the circulation can pass only when the spleen is hyperæmic, as it is during digestion.

The arterial end of the ampulla is much more easily injected than the venous end, and apparently for this reason Thoma divides the communication between the artery and the vein into two parts, the ampulla or the arterial end, and the *Zwischenstück* or the venous end. There is no sharp line of demarcation between the ampulla and the Zwischenstück, for the one passes directly over into the other. This division I find very artificial, and in describing the different portions of the ampulla I shall divide it into thirds, numbering them from the artery to the vein.

The first third of the ampulla is a marked space lined with spindle-shaped cells, which are a continuation of the endothelial cells of the artery.

In the second third the ampulla has a tendency to divide the subdivisions in such a way that some of them communicate with the divisions from neighboring ampullæ. The anastomoses of ampullæ pass along the middle of the pulp cord, and if care is not taken it may be mistaken for the vein. However, double injections with granules in the veins excludes this source of error. The last third is much more difficult to demonstrate than the first two thirds. Thoma has already emphasized this point in stating that the ampulla appears to communicate with the vein when viewed with a low power of the microscope; that with the high power, however, it is shown that the ampulla passes over and under the vein, but not into it. This description applies to what I have called the first two thirds of the ampulla. Successful injections leave no doubt whatever about the ampullæ communicating directly with the vein, as shown in Fig. 4467. To be sure, it may be asserted that the spleen pulp in this specimen was so gorged with blood that the Prussian blue injected was forced to take the direct course through the tissues into the vein. To settle this question further I made rapid injections with Prussian blue into the artery of a spleen which had been distended, but not to its maximum, by injecting chrome yellow suspended in gelatin into the vein. The gelatin passed over into the tissues and the yellow remained in the vein. The smaller quantity of blue injected into the artery extravasated as usual at numerous points and flowed into the veins in the immediate neighborhood. Where the injection was not so intense spots were found in which the blue from the artery passed directly over into the vein. In such specimens the extravasation of the blue takes place along the artery as much as it does in any portion of the ampulla, and it appears from this that the walls of the last third of the ampulla are fairly complete, otherwise the injection would have passed into the pulp spaces immediately surrounding it.

By studying numerous successful injections of the last third of the ampulla I find that its communication with the vein is not wide, but is cut up by bridges of tissue passing across its lumen before it connects with the vein. This is so extensive that in uninjected specimens it has been impossible for me to show that the ampulla communicates with the vein. That the ampulla can never be injected from the vein is an additional argument for the idea that there is an obstruction near its connection with the vein.

If the artery of the spleen is injected with gelatin in which cinnabar granules are suspended it is found that the granules are forced over into the veins only under special conditions. Ordinarily the granules pass to the origin of the ampullæ and then can be forced no farther, nor can they be forced through the walls of any of the arteries. When, however, the cinnabar is driven into the artery with a high pulsating force for a long-continued

FIG. 4467.—Section of a Spleen Distended to its Maximum by Tying the Vein One Hour before Killing the Animal. The artery was then injected with aqueous Prussian blue. Enlarged 60 diameters. The ampullæ communicate with one another and also directly with the intralobular venous plexus.

time, it is found that the granules pass beyond the ends of the arteries and the gelatin diffuses, thus causing an artificial œdema. Many of the granules enter the pulp spaces, but by all odds the greater number of them pass over into the veins. Often so many of the granules pass over into the veins that it appears as if the veins had been injected by them. The extravasation of granules into the pulp spaces is most intense around the lymph follicles, which is also true in the case of other injections. It appears as if in the neighborhood of the lymph follicles the walls of the ampullæ are most porous.

In all of the specimens in which the artery had been injected with cinnabar the ampullæ are not sharply outlined. All granules which enter them are carried over into the veins at once. This result corresponds fully with natural injections made by ligating the veins. In any case there must be some mechanism which empties the ampullæ, as they are never found distended with cinnabar granules or with red blood discs.

Whether the course of the granules is from the ampullæ directly to the veins, or indirectly through the pulp is another question. Were it through the pulp we would expect to find the tissue first filled with granules or blood, as the case might be, before they entered the veins. Instead of this we find that in the natural injections the blood first fills the veins and then the pulp spaces, and