SURGERY OF THE SPLEEN

Revised English Edition

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FOREWORD

Although the major textbooks of surgery all contain sections on diseases of the spleen and their surgical management, there are few modern texts entirely devoted to the subject. Dr. Rainer M. Seufert, who is a senior surgeon at the Goethe University in Frankfurt, West Germany, has written such a book, and the German edition was published in 1983. Following that publication, I was approached by the editorial staff of Thieme Inc., who asked my opinion on the desirability of translating the book into English. After reading Dr. Seufert's monograph, I agreed that it was a worthwhile project.

Surgery of the Spleen distils in less than 200 readable pages, much of what is known about splenic physiology and disease, as they relate to surgical patients. The author reviews voluminous and often conflicting literature, but has the ability to offer practical recommendations for patient management. Undoubtedly, this reflects his own vast clinical experience. The sections that deal with splenic salvage techniques and autotransplantation should be particularly interesting to an English speaking audience. Because of its extensive bibliography, it should continue to be a valuable reference source for years to come.

Howard A. Reber, M.D.

PREFACE

During the last decade the knowledge of the physiological functions and the importance of the spleen in the pathophysiology of certain hematologic disorders has increased rapidly. In surgery, a growing awareness about the longterm complications of splenic loss has produced a thorough discussion of the previously undisputed and uniform objective of splenic surgery—the splenectomy. Indications for exstirpation of the spleen, which had appeared harmless so long, has been reevaluated critically. This has led to attempts at preservation and repair in order to avoid the consequences of the asplenic state.

In this field, the advances have been made so fast since the publication of the German edition in 1983, that a partial revision has become necessary of the section on splenic autotransplantation. The lasting debate of pro's and con's of different techniques and their indications is not yet completed. However, it appears convenient to summarize the actual working hypotheses. The future will show which details of this summary have to be revised.

The current presentation is addressed to the surgeon in his daily practice. It should help him to weigh the expected therapeutic effect of an operation against the potential risk. Without a doubt this, in many cases, demands an ongoing dialogue between the surgeon and the hematologist. This book has fulfilled its aim, if it prompts considerations about the "organon plenum mysterii" (Galen), so that the spleen will be removed only for serious reasons.

R. M. Seufert
Autumn 1985

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1 The Healthy Spleen

The spleen lies deep in the left epigastrium, and is in close contact to a number of organs, to the bony thorax, and to the abdominal wall. The unusual latticework of the lymphatic channels, and the cells of the reticuloendothelial system, the variety of blood supply, the unusual intrasplenic vascular architecture, and the intimate relationship of the arterial and portal circulation all combine to create special pathogenetic features, diagnostic problems, and surgical requirements. To evaluate these, it is necessary to know the structure and function of the healthy organ. For that reason, attention will be turned first to the results of anatomic, histologic, and physiologic research and their clinical relevance.

Insight into the normal function of the spleen is difficult for a number of reasons. First, the results of animal studies must be applied to the human situation with caution because of the known differences among the species. Second, one must frequently deduce the physiology of the healthy organ from the abnormalities that occur in the diseased spleen. Third, information is gleaned as a result of the removal of the healthy spleen in situations in which a normal spleen is injured by blunt abdominal trauma or during operations on other abdominal organs. Such information is partly obscured by the consequences of hemorrhagic shock and its treatment or by the effects of other surgical procedures done simultaneously. So the paradoxical situation has developed that our current understanding of the pathologic processes of the spleen is greater than our knowledge of its normal physiologic functions. On the basis of today's knowledge of morphology and function, three tasks of the spleen are clear: its substantial role as an organ of immunologic defense, the far-reaching influence as an organ that partly regulates the turnover of blood elements, and finally an organ through which abnormal circulating blood elements are filtered.

1.1 Surgical Anatomy and Topography

The spleen is protected from external trauma deep in the left epigastrium by the ribs, and when it is of normal size it is not palpable. Its shape has been closely likened to a coffee bean. In the center of the concave medial side, the vessels and the nerves enter the hilus of the blue-gray or red-purple organ. Its anterior extremity is indented a variable number of times (margo anterius crenatus), and its posterior extremity is bluntly rounded (margo posterius obtusus). The convexity, laterally and dorsally, lies close to the ribs of the thoracic and abdominal wall. Therefore fragments of fractured ribs can easily puncture the spleen. Because of the close anatomic relationship with numerous organs, a large increase in the size of the spleen may impair the function of the left kidney, stomach, or colon. Often the tail of the pancreas lies well within the concavity of the spleen, and for this reason hasty attempts to control profuse splenic bleeding may result in injury to the tail of the pancreas (Fig. 1). When a distal pancreatectomy is done, the spleen must often be removed because of the close contact of the splenic vessels with the pancreas.

The position of the spleen in relation to the bony thorax depends on the amount of blood that the spleen contains as well as the shape of the thorax. Normally, the spleen lies with the upper pole tipped dorsally behind the 9th–11th ribs. In the long, narrow thoracic cavity it is situated even deeper than in a short, wider thorax. This should be considered in the selection of an incision.

Except for the hilus and the region near the pancreatic tail, the organ is covered by peritoneum. This results in three peritoneal folds, which are part of the bursa omentalis (Fig. 2). The phrenicolienal ligament forms to the left and lateral to the back wall of the bursa. It stretches from the undersurface of the diaphragm to the hilus of the spleen and here contains the tail of the pancreas, all of the splenic vessels as well as the root of the left gastroepiploic artery and,

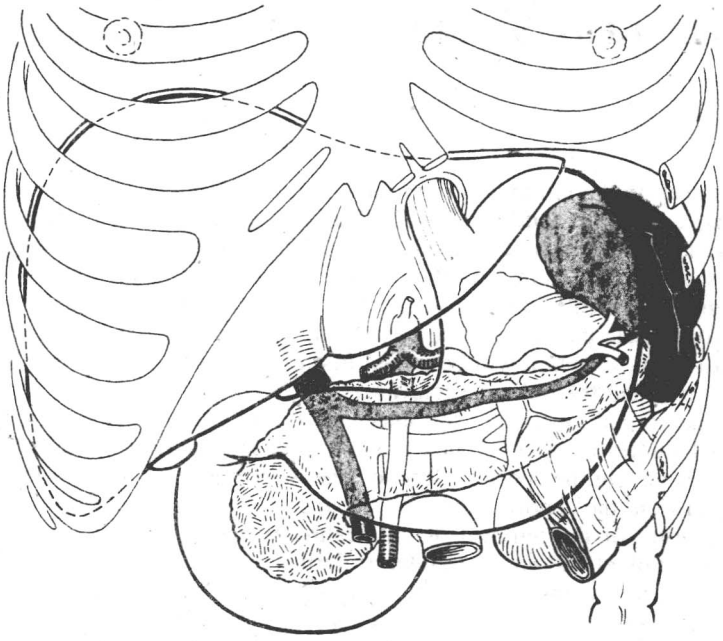

Fig. 1 Anatomic relationships of the spleen.

finally, joins caudally with the splenocolic ligament. This part of the phrenicolienal ligament, which involves the tail of the pancreas and the large vessels of the spleen, is also designated as the splenopancreatic ligament. During embryonic development, the vessels of the spleen and pancreas become fixed with the posterior wall of the retroperitoneal space (Töndury, 1981). Only the tail of the pancreas and the distal parts of the splenic vessels remain free. Therefore the tail of the pancreas moves together with the spleen. The thin serosal connection between the greater curvature of the stomach and the hilus of the spleen (gastrolienal ligament) closes the omental bursa ventrally. In its more proximal part are the short gastric arteries and veins and distally the left gastroepiploic artery. The splenic flexure of the colon is attached through the third ligament, the lienocolic ligament on the lower pole of the spleen. Next to these ligaments, numerous secondary attachments to neighboring organs develop during life. These other attachments are important, since the capsule is easily torn by traction on such secondary adhesions during surgery.

The spleen is fixed not only by these structures, but also by the pressure of many nearby viscera and through the phrenicocolic ligament, a secondary connection of the diaphragm with the splenic flexure of the large intestine. The lower pole of the spleen sits on this as if in a hammock. Besides the phrenicolienal ligament that contains the large vessels of the spleen and the connection between the spleen and the stomach containing the short gastric arteries and veins, only a few small vessels pass through the ligaments. The ligaments can therefore be easily separated, generally with little concern for bleeding. However, in some cases the vessels develop a dense collateral network and can almost totally compensate for a stenosis of the main splenic artery (Michels, 1955).

Normally, the spleen holds up to about 300 ml of blood. This amount of blood, and more with splenomegaly, is effectively removed from the circulation if splenectomy is performed when the venous outflow is interrupted before the splenic artery is ligated. Empty of blood, the organ weighs about 120–200 g. In adults it is 12 cm long, 6–7 cm wide, and 3–4 cm thick. After the 40th year of life, it loses some weight.

The spleen has a good and exceptionally variable arterial blood supply. Only in its source and distribution are some constant relationships of the splenic artery to be found (Michels,

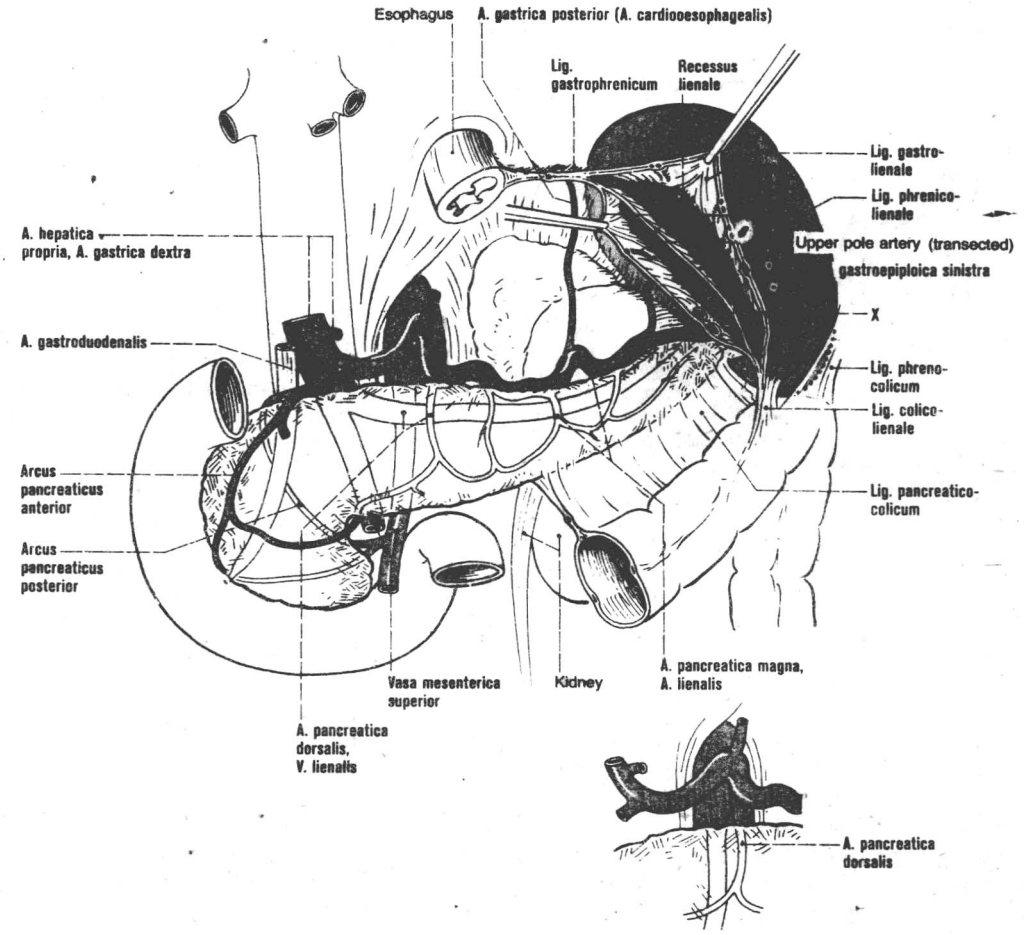

Fig. 2 Arteries and ligaments of the spleen. X: branches of the splenic artery, transected (in this view) as they enter the recesses of the spleen.

1955). The main artery of the spleen arises as the largest branch of the celiac trunk and moves typically in a large arc, and occasionally spirals on the cranial edge of the pancreas all the way toward the left side (Fig. 2). In approximately 80% of the cases, the splenic artery runs dorsal, under the upper edge of the pancreas, and comes into view several centimeters later above the pancreas and directly behind the serosa of the posterior wall of the omental bursa. In 8% of cases the vessel stays behind the pancreas, and sometimes it even courses through the pancreas for the whole distance. Then there is usually a second suprapancreatic artery for the upper pole of the spleen. One variation that occurs in approximately 3% of cases shows the vessel in its entire length ventral to the pancreas.

On its way to the spleen, the splenic artery gives off larger branches (the pancreatic magna and the pancreatica caudal arteries) and other vessels that supply a substantial part of the tail of the pancreas. It is important to note that tying off of the splenic artery near its origin from the celiac artery through the opened omental bursa can result in deterioration of the circulation of the blood through the pancreas, which may result in hyperamylasemia.

The splenic artery often divides after the exit of the left gastroepiploic artery approximately 2–6 cm from the hilus of the spleen into two branches to the upper and lower half of the spleen (Fig. 3). More than two branches occur less frequently. In the hilus of the spleen the terminal branches divide so that each pole of the spleen is supplied by two or three arteries.

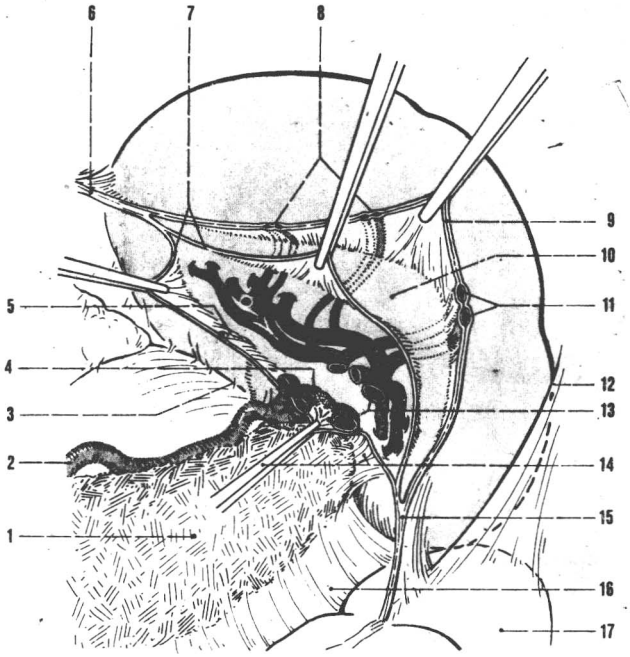

Fig. 3 Anatomy of the hilus. 1) Pancreas, 2) splenic artery, 3) phrenicosplenic ligament, 4) tail of the pancreas, 5) upper pole artery, 6) gastrophrenic ligament, 7) phrenicosplenic ligament (cut through), 8) short gastric vessels, 9) gastrosplenic ligament, 10) recesses of the spleen, 11) left gastroepiploic vesels, 12) phrenicocolic ligament, 13) splenic vein, 14) pancreaticosplenic ligament, 16) pancreaticocolic ligament, 17) colon.

From the upper terminal branch to the stomach, a variable number of short gastric arteries arise. Far to the periphery, arteries branch out to the greater omentum.

In 65% of the cases a particular vessel that arises directly from the splenic artery or earlier from the upper terminal branch supplies the upper pole of the spleen (Michels 1955). Sometimes the upper pole artery even comes from the celiac artery. Then the two splenic arteries are encountered from which the main branch, as described before, may proceed within the pancreas. Countless other varieties of blood supply exist, but have no particular surgical significance.

It has long been supposed that there are only rare intrasplenic connections between the terminal vascular branches, so that between two and four, and sometimes up to seven, distinct areas of blood supply result. It has been proved that discrete segments (diagonal to the longitudinal axis of the organ through avascular planes) are nearly totally separated (Fig. 4). Angiographic examination of the arterial network in surgically removed human spleens shows intersegmental anastomoses of the vascular system in only one of ten organs (Dixon, et al., 1980). With splenoportography, the contrast material is not distributed throughout the entire organ, but is drained by the veins from only the punctured segment (Dreyer and Budtz Olsen, 1952).

These independent vascular segments can often be recognized as notches on the outside of the organ. An extremely grooved spleen with uneven anterior borders and a wide hilus usually is associated with proximally branching arteries, more polar arteries, and a corresponding number of larger veins. An organ with a smooth anterior border and narrow compact hilus usually exhibits only one or two branches without additional pole arteries. This observation is of consequence in respect to operative tactics for splenectomy and segmental resection.

The intrasplenic branches of the vascular tree have surgical importance. Dixon and co-workers (1980) divided the spleen into those regions in which an injury requires a different technique of hemostasis (Fig. 4). With lesions of the peripheral zones, only small arterioles and sinuses are opened; the bleeding can be stopped with local hemostatic techniques. In the intermediary areas the bleeding can only be controlled by ligature, sutures, or infrared or laser coagulation. Lacerations or incisions in the region of the hilus involve not only the named arteries and veins, but also other large vessels that must be ligated or sutured. Local hemostatic agents,

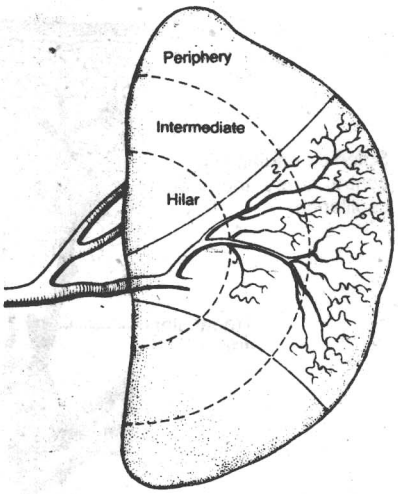

Fig. 4 Architecture of intrasplenic vessels. Each three-dimensional cone, going out from the entrance of the central artery, contains in the periphery arterioles and venous sinuses. The vessels become larger toward the center. In the intermediate area there are trabecular vessels and in the hilar zone there are segmental vessels. Between the supply areas of the segmental arteries (here, upper, middle, and lower pole), venous or arterial connections are rare. (Modified with permission after J.A. Dixon et al.: Anatomy and Techniques in Segmental Splenectomy. Surg Gynecol Obstet 150 [1980] 516.

adhesives, or coagulation techniques cannot be used because of the large size of the vessels.

The venous blood leaves the spleen through the splenic vein, which is formed by the union of the venous segments directly behind the hilus. The large vein moves distal to the splenic artery behind the pancreas and there picks up some short gastric veins, the left gastroepiploic vein as well as pancreatic and duodenal veins. After joining the inferior mesenteric vein, it combines with the superior mesenteric vein to form the root of the portal vein.

With the branches of the splenic artery, a great number of nerves reach the organ. These are sympathetic nerves almost entirely from the celiac plexus (Heusermann, 1979). Whether the human spleen also contains parasympathetic nerves is still unknown; their presence has been determined in some animals.

The regional lymph nodes lay in the hilus of the spleen. The lymph vessels run together with the lymphatic vessels of the pancreas on the upper edge of this organ and they join in the cisterna chyli somewhat to the right next to the aorta about the level of the first lumbar vertebra.

1.2 Histologic Structure

Histologically, the spleen is comprised of two structural elements: the stroma, a support framework made of capsule and trabeculae, in which a reticular network is embedded, composed of different cells. This is the pulp, which is instrumental in the functioning of the organ. One can easily differentiate the two parts of the pulp on a sectional plane: dark, large, blue-red regions (the red pulp) within which smaller, lighter regions (the white pulp) are scattered throughout.

The capsule is 1–2 mm thick and made of taut connective tissue and some elastic fibers and smooth muscle cells. From the capsule stream coarse, fibrous strands (the trabeculae) into the inner organ and the strands serve as a guide for the course of the arteries and the corresponding veins (Fig. 5). The arteries soon separate from their accompanying veins, but they still stay together in the connective tissue sheath (trabecular artery, Fig. 6). When a vessel reaches a width of approximately 0.2 mm, it leaves the support framework as the artery of the pulp. To this point the nerves follow its course. Some filaments branch off and supply the hilar parts of the capsule, the large trabeculae and veins down into the area of the pulp. The true parenchyma of the spleen, the red and white pulp, is free of nerve fibers (Heusermann, 1979).

Later on, the arteriole becomes surrounded by thick spindle- or oval-shaped collections of lymphatic tissue that contain primarily the thymus-dependent (T) lymphocytes. Finally, the

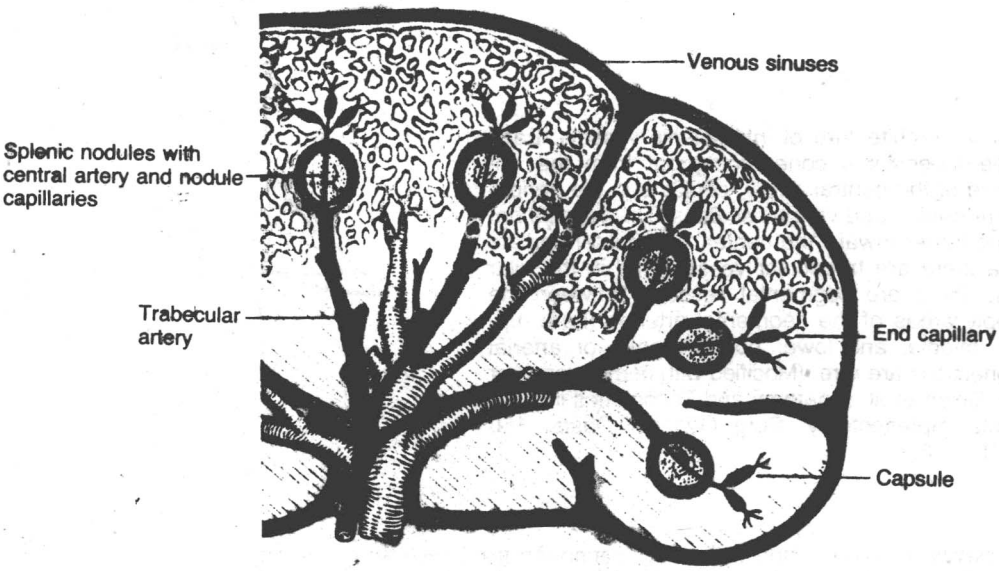

Figure 5 Schematic representation of the human spleen. Arteries black, veins crosshatched (From W. Bargmann: Histologie und mikroskopische Anatomie des Menschen, 6th ed., Thieme Stuttgart, 1967.)

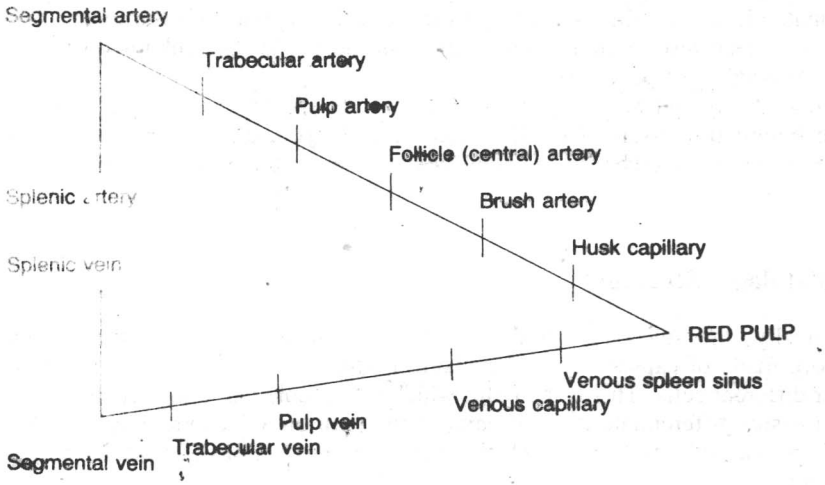

Fig. 6 Arrangement of the intrasplenic vessels.

lymphatic sheath develops round, small splenic nodules (Malpighian bodies, spleen follicles) with a preponderance of thymus-independent B lymphocytes, passed through by the central or follicular artery. Para-arteriole lymphatic accompanying sheaths and splenic follicles make up the white pulp. They represent, with approximately 15% of the volume of the spleen, one quarter of the lymphatic system of the whole body. Spleen follicles are responsible for the production of specific antibodies. Accordingly, their number and size increase with antigenic stimulation.

The artery finally separates from its lymphatic sheath and enters the red pulp together with other precapillary arterioles forming a structure like thin hairs or fibers of a brush (brush arteries).

The capillary at a diameter of approximately 5μ and now without a tunica muscularis is ensheathed by an especially compact reticular tissue. The purpose of this structure is not known. The arteries from this area end free in the reticulum of the red pulp (open blood vessel system) or communicate directly with the venous sinus (closed blood vessel system).

In the periphery of the spleen, the white pulp tissue merges indistinctly with that of the red pulp (marginal zone). This makes up the largest section of the splenic tissue, approximately 80–85%. Its spaces are lined with pulp or reticulum cells and are filled with blood. In the marginal zone the vascular bed suddenly widens, in order to slow the flow of the blood. With slower vascular streaming, the phagocytizing reticulum cells and macrophages come into close contact with the cellular components and particulate antigens of the blood. The sinuses are wide, thin-walled anastomosing spaces within the red pulp that are lined by a specialized endothelium. These cells, capable of phagocytosis, form a lattice and are held together through ring filaments, like tires. From the red pulp the blood can reach the venous side, that is, the lumen of the sinus only through pores in the wall. In this manner the defective cells stay hanging, as if in an oyster basket; others are freed by being milked out from the detritus. Theodor Billroth first adequately described the red pulp in 1854 and identified the spleen's sinus. This perisinus network is now called the Billroth sinus and Billroth cords.

From the sinus, the blood is collected in venous capillaries and along with the arterial branching of the pulp in the trabecular veins, it is again delivered to the hilus (Fig. 6). Lymphatic vessels have their source in the white pulp and move with the vessels in close contact with the hilus of the spleen where they empty into the regional lymph nodes. There is hardly any superficial lymph network around the capsule of the spleen (Heusermann, 1979).

1.3 Physiologic Function

The physiologic functions of the spleen are made possible by the close intrasplenic relationships of the cells of the reticuloendothelial system with the lymphatics, on the one hand, and with the blood, on the other. The activity of the organ is seen as the sum of the functions of all of these systems. Figure 7 gives an overview of the locations and functions of these various cellular populations.

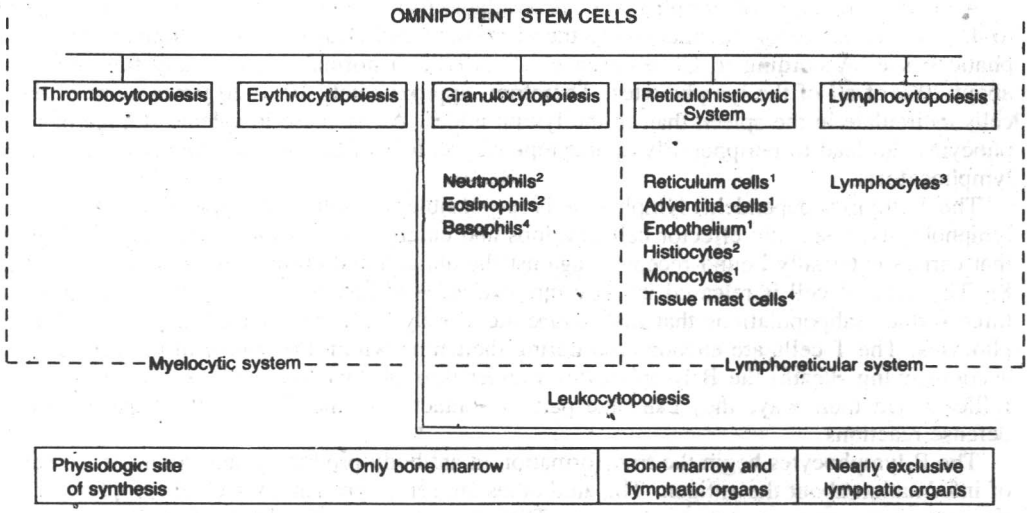

Fig. 7 Topical and functional division of the blood cells. [1]Phagocytosis (stationary, fixed), [2]Amoeboid motility and phagocytosis, [3]Synthesis of immunoglobulins, [4]Release of heparin, histamine. (Reproduced with permission from R. Gross, H.E. Bock: Erkrankungen der Leukopoese und des retikulo-histiozytären Systems. Klin. Gegenw. 10 [1962] 567.)

1.3.1 Participation in the Immune Reaction

The present knowledge about the role of the spleen in the highly complicated immunologic response is still incomplete. However, a specific function of the spleen has been proved in all four aspects of the immune reaction, in specific and nonspecific, as well as in humoral and cellular immunologic responses (Table 1). The active role of the spleen is emphasized through the sizeable number of immune competent cells that exist either transiently or permanently in the organ. The spleen contains an extraordinarily high number of phagocytizing cells (macrophages, reticulum cells). Such stationary splenic macrophages occupy a very key position if an antigen enters the bloodstream for the first time (primary response) or has left behind only a low titer of a specific antibody from an earlier contact. In this situation the phagocytes have the function of removing the bacteria. They must transform the information and pass it on to the lymphocytes of the splenic follicles and the T lymphocytes through means of messenger

Table 1 Overview of the Body's Defense Mechanisms

	Humoral	*Cellular*
Specific	B lymphocytes Immunoglobulins (IgA, IgG, IgM, etc.).	T lymphocytes: T helper cells T memory cells T suppressor cells T killer cells
Nonspec	Complement system Kinin system Lysozyme Clotting system Interferon Tuftsin	Macrophages (monocytes and granulocytes) K (killer) cells Thrombocytes

RNA and humoral factors, so that they are able to mobilize a defense against the specific determinants of the antigen. Without this interaction with the macrophages, the lymphocyte response to an initial hematologic confrontation with a pathogen would be inadequate.

A plentiful quantity of lymphocytes are available to the spleen. They remain for about 30 to 45 minutes in the blood, then leave the circulation and return for some hours to the lymphatic tissue. According to Christensen et al. (1978), a normal organ at any time contains about 20% of all of the lymphocytes. Therefore, approximately 10 to 20 times more of these cells recirculate in the spleen than in the lymph nodes. An increase in splenic storage of lymphocytes can lead to peripheral lymphocytopenia and loss of this storage capacity can lead to lymphocytosis.

The T (thymus dependent) lymphocyte is responsible for cellular defense. Originating from lymphoblasts, a specific effector cell develops and enlarges as a result of an antigen stimulus that carries externally bound receptors against the antigen and eliminates the target cell (Fig. 8). This type of cell is released into the circulation. Additionally, the T cells differentiate to three further subpopulations that may cooperate closely with the "bursa" dependent B lymphocytes. The T cells are encountered during their time within the spleen in the para-arterial accompanying sheath; the B lymphocytes wander through this zone and are bound up in the follicles. On their way, they can take part in contact with the T cells, the basis for many defense reactions.

The B lymphocytes begin the transformation in antibody-producing cells after the exchange of information about the antigen. The antibodies are serum proteins, which electrophoretically are part of the gamma globulin fraction. They are carriers of the humoral immune reaction and because of this quality are named immunoglobulin (Ig). Antibodies are mainly in the large immunoglobulin classes of A, G, and M. Early in the immune reaction antigens of type IgM

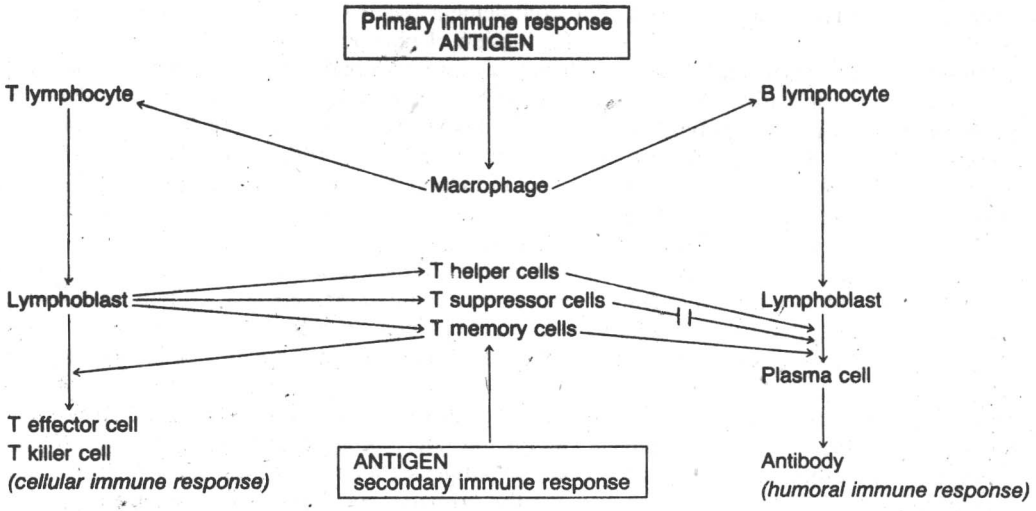

Fig. 8 Differentiation of the lymphocytes in an immune reaction. (Modified with permission from P.G. Scheuerlen. In H.E. Bock (Ed): Pathophysiology. Abridged textbook in two volumes, vol. 1. Thieme, Stuttgart, 1972, p 375.)

are formed. The gamma globulin M can be found very early in the blood, at first contact with an antigen; it therefore seems to play an important role, together with the phagocytes of the spleen, as the first line of defense in bacteremias. It is particularly effective against bacteria with a carbohydrate capsule, for example, pneumococci. The quantitatively heaviest IgG fraction is made up of plasma cells that transform themselves as end cells from B lymphocytes (Fig. 8). This transformation of the B cell is supported by the helper T cells, whereas the T suppressor lymphocyte suppresses the B cell transformation, so that a regulation exists. IgG contains antibodies against bacteria and viruses and is predominantly produced in the late phase of the immune reaction or during a secondary response by renewed contact with the same antigens to which the organism has been previously exposed.

The immune globulins fulfill many tasks: they neutralize bacterial toxins, importantly IgM globulins occupy the surface area of the target cell and recognize it as a foreign particle (opsonization), and they serve the complement system as marks of recognition and as an attack point. IgA has another function: through the building of complexes with other proteins, it prevents the entrance of various antigens through mucous membranes.

The T memory cell does not take part in the various aspects of the primary response just mentioned, but has the function of storing the information about the antigen and making it available for the secondary response. Thus, it induces a quick transformation of the blast form of the lymphocyte so that in case of a later immune reaction with the same germinal form, phagocytosis, information deciphering, etc., by the macrophages is not needed. This retention of information acquired on a single occasion is important, since in the event of a secondary response a high concentration of antibodies is quickly achieved (booster reaction).

The previously described nonspecific complement system completes the opsonizing activity of immune globulin (classic pathway). As in the clotting system a cascade of numerous components is induced. Finally, there stands an active membrane complex that is able to penetrate the cell wall of the antigen. Through the influx of sodium ions and water that follows, the antigen is destroyed. In many cases it is only through the completion of the attached immunoglobulin with complement that the destruction of the antigen is possible.

The activation cascade of the complement system can also come about without the presence of immunoglobulins, especially with higher concentrations of antigen. This mechanism is called

alternative, or properdin, activation. The complement factor C3B is in that respect also independently capable of opsonization, i.e., facilitation of phagocytosis.

Besides these nonspecific defense mechanisms, the tetrapeptide tuftsin (named after its place of discovery, Tufts University, Boston) should be mentioned. This separately stimulates the phagocytic activity of the polymorphonuclear leukocytes and the macrophages (Constantopoulos et al., 1972). Its significance is stressed by the observation that the risk of an infection after splenectomy is inversely related to the reduction of tuftsin (Spirer et al., 1977). The immune response ends in an optimal synergistic reaction of the phagocytic system, the lymphocytes, and specific and nonspecific defense mechanisms.

The particular role of the spleen is immediately obvious from the first step of the immune defense from which a majority of the subsequent antigen action depends. Only a healthy population of splenic phagocytes is able to incorporate pathogens without the existence of opsonizing antibodies. This achievement is required especially in the primary hematologic contact and whenever there exists only a scanty antibody titer despite earlier contacts with the antigens. The long contact time with the blood makes this special achievement of the spleen macrophages possible, whereas the phagocytes of the liver, because of the higher rate of blood flow, can only eliminate previously opsonized antigens (Schulkindt et al., 1967). An experimental animal without a spleen can survive the primary inoculation with bacteria only when opsonins are given simultaneously in very high concentrations (Schwartz et al., 1977). This is especially true for bacteria with polysaccharide capsules, which are especially difficult to phagocytose. Since opsonin production depends, however, on primary contact with the phagocyte, this mechanism cannot come fully into play in animals without a spleen. An insufficient immune response follows.

The wealth of lymphocytes and plasma cells strongly suggest a splenic production of antibodies. The spleen is recognized as the primary site of synthesis of gamma globulin M (Ellis and Smith, 1966; Spivack, 1977).

The cellular reaction is possibly controlled by the spleen by influencing the opportunity for cooperation between B and T lymphocytes in the periarterial sheath. Antilymphocyte serum, which eliminates the T helper cells, lowers the apparent response of the antibodies. However, this does not occur in splenectomized animals, so the spleen must be recognized as the source of these cells (Amsbaugh et al., 1978). The T memory cells, at the very least, partially depend on the functions of the spleen also. When a splenectomized animal is given a dose of polysaccharide antigen, memory cells are only formed when very high doses of antigen are used (Benner and van Oudenaren, 1975). Therefore the T memory cells in response to carbohydrate antigen must come mostly from the spleen. Whether the spleen in addition influences the T cell immunity in other ways is still unclear.

The nonspecific humoral defense is also only capable of functioning with an intact spleen. Endocarboxypeptidase, an enzyme produced only in the spleen, is responsible for the separation of phagocytosis stimulator tuftsin from neutrophil gamma globulin. Tuftsin activity decreases after splenectomy. Some of the 11 plasma proteins of the complement system are formed in the splenic follicles. However, after loss of the spleen, only a temporary reduction occurs. This part of the nonspecific humoral defense is evidently compensated for by other components of the lymphocytic system.

In summary, the spleen itself has all of the known important immune response functions, and they can only be taken over partially by other organs after its loss. The function of the spleen is thus constantly required whenever bacteria that must be phagocytosed and opsonized bypass the lymphatic pathways and reach the bloodstream directly. Then, only the spleen can build the primary lines of defense and set the necessary immune response processes in motion. Despite countless experimental findings, the cellular defense pathways have still not been completely defined. At the very least, it is clear that splenic control of T and B lymphocytes is very important. The spleen has been proved to be an important source of lymphocytes, plasma cells, macrophages, opsonizing specific antibodies and the site of synthesis of complement and of tuftsin. The most conspicuous feature, for which no other system can assume the responsibility, is the ability to phagocytize unprepared antigen, especially those with a polysaccharide capsule.

An additional immunologic function, the splenic reaction that mediates against tumors, is completely unexplained. To be sure, extensive experimental work has determined that the spleen influences the growth of malignant tumors. Examination of the contradictory results produces confusing and incomplete information that even today cannot be integrated coherently. Inhibition or stimulation of malignant growth depends obviously on the timing of the removal of the spleen, the type of tumor, and the tumor burden. Loss of the spleen reduces the rate of tumor growth and the incidence of metastases (Ferrer, 1968; Wallenberg et al., 1979). The existing body of experimental data is only sparsely supplemented by clinical information that attempts to measure the function of the spleen by the growth of tumors. At least for carcinomas of the stomach, studies from Japan are becoming well known; (see 4.3), but even so, no definitive statements may be made from their experimental results.

1.3.2 Circulation and Blood Purification

The spleen fulfills a threefold filter function: it sequesters erythrocytes that have reached the end of their life span (gerontocytes), it separates pathologic cells from the bloodstream (clearance function), and it is able to rid red blood cells of intracellular inclusion bodies, degenerated mitochondria, or iron granules, and also of infectious agents, such as malaria (pitting function). A good blood supply is necessary for the fulfillment of these roles. The small organ makes up about 0.1% of the body weight, but it receives 300 ml/minute of blood, approximately 6% of the cardiac output per minute. (This assumes a normal cardiac output of 5 L/minute in the resting state). This corresponds with approximately 3 ml/min/g of splenic tissue. With increasing spleen size, the specific blood supply decreases per unit of weight (Wolf and Fischer, 1970).

The blood that perfuses the spleen passes through it in two ways. Only a small part passes through the arteriovenous short circuit from the end of an arteriole directly into the end of a sinus. Under normal conditions, the great part of the blood enters the meshes of the red pulp, as if in a cul-de-sac, and must, in order to reach the lumen on the sinus around the venous side, flow through the narrow pores of the sinus wall. There exists therefore, side by side, an open and a closed circuit. Because the direct flow takes less time than that through the red pulp, one may also refer to a slow and a quick compartment of the microcirculation.

The spleen is able to differentiate between normal and abnormal cells and to remove defective particles. The release of these particles is controversial. Imperfectly formed cells such as spherocytes appear to be held back from their passage through the sinus wall, as if with a net. Membrane changes of pathologic cells or old cells cause an increase of their permeability for cations. With a longer stay in the relatively glucose-poor splenic environment, the sodium pump is quickly depleted, the intracellular sodium concentration increases, and the cell dies. Lennert and Stutte (1968) were able to prove that a defective membrane of the blood cells promotes the phagocytic activity of the reticulum cells and the large macrophages and, to a lesser extent, the sinus wall cells. Then, an active elimination rather than a passive death is likely, especially since in normal blood circulation no free hemoglobin appears in the blood.

In experiments in which the body is saturated with unlabeled iron preceding all of the steps of erythropoiesis, recognizable red blood cells with labeled iron in their hemoglobin molecules are found only in the spleen. This substantiates the notion that old erythrocytes are eliminated almost entirely in the spleen (Finch, quoted by Walker and Löhr, 1972). On the other hand, the observation that after splenectomy the life span of erythrocytes does not increase, speaks against the significance of the spleen in normal circulation. Actually, the decomposition of the cells is undertaken in its entirety by the liver, lungs, and bone marrow.

Normally, approximately 20 g of erythrocytes are removed by the spleen daily. The waste products of the erythrocytes are used again. The protein part of the hemoglobin molecule is decomposed into its composite amino acids and goes back into the amino acid pool. More than 20 mg of iron comes from the decomposition of the hemoglobin molecule, and this immediately enters the bone marrow. Up to 90% of this is used in the synthesis of new hemoglobin. Therefore the spleen plays an important role in iron-metabolism. The breakdown of