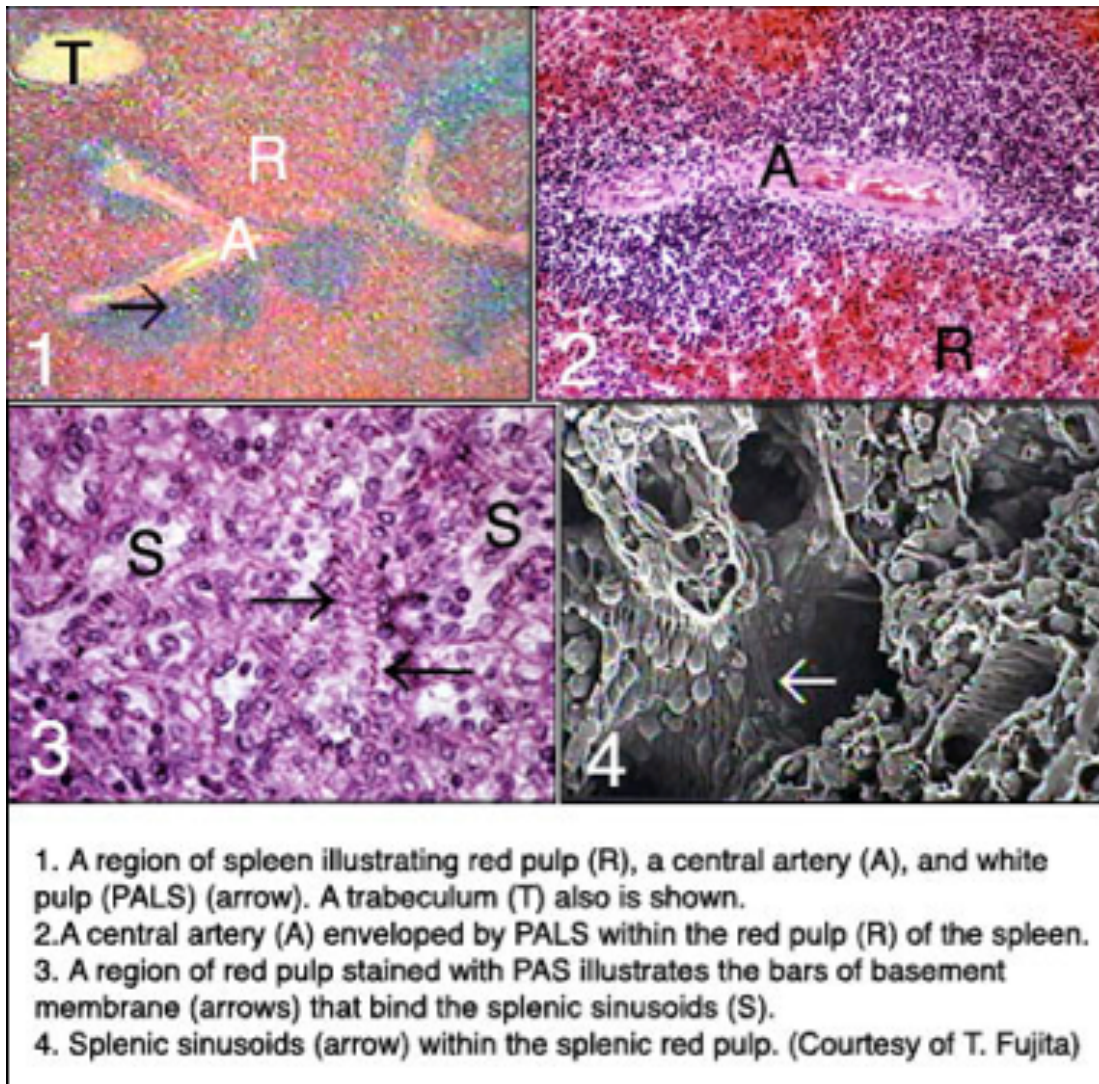


Spleen



The spleen embodies the basic structure of a lymph node and can be regarded as a modified, enlarged lymph node inserted into the blood flow. Unlike lymph nodes, the spleen has no afferent lymphatics and no lymphatic sinus system, and the lymphatic tissue of the spleen is not arranged into a cortex and medulla. It does have a distinctive pattern of blood circulation and specialized vascular channels that facilitate the filtering of blood.

Structure

The spleen is enclosed in a well-developed capsule of dense irregular connective tissue. Elastic fibers are present between bundles of collagen fibers and are most abundant in the deeper layers of the capsule. Smooth muscle fibers also may be present in small groups or cords, but the amount varies. On the medial surface of the spleen, the capsule is indented to form a cleft-like hilus through which blood vessels, nerves, and lymphatics enter or leave the spleen. Broad bands of connective tissue, the trabeculae, extend from the inner surface of the capsule and pass deeply into the substance of the spleen to form a rich, branching and anastomosing framework. As in lymph nodes, the trabeculae subdivide the organ into

communicating compartments. A reticular network of fibers and associated reticular cells fills the spaces between trabeculae. The meshes vary in size and tend to be smaller around blood vessels and aggregates of lymphatic tissue. The substance of the spleen is called the splenic pulp, and sections from a fresh spleen show a clear separation of the tissue into rounded or elongated grayish areas set in a greater mass of dark red tissue. Collectively, the scattered gray areas form the white pulp and consist of diffuse and nodular lymphatic tissue. The dark red tissue is the red pulp and consists of diffuse lymphatic tissue that is suffused with blood. The large number of red cells present imparts the color to the red pulp. The red pulp contains large, branching, thin-walled blood vessels called splenic sinusoids (sinuses), and such spleens are said to be sinusal.

White Pulp

The white pulp generally is associated with the arterial supply of the spleen and forms the periarterial lymphatic sheaths (PALS) that extend about the arteries, beginning as soon as the vessel leaves the trabeculae to enter the splenic pulp. The sheaths have the structure of diffuse lymphatic tissue and contain the usual cellular elements of lymphatic tissue. Small lymphocytes, mostly T-cells, make up the bulk of the cells. Here and there along the course of the sheath, the lymphatic tissue expands to incorporate lymphatic nodules that resemble the cortical nodules of lymph nodes. They represent sites of B-lymphocytes, and many contain germinal centers. The lymphatic nodules of the spleen are called splenic follicles. At the periphery of the lymphatic sheath, the reticular net is more closely meshed than elsewhere, and the reticular fibers and cells form concentric layers that tend to delimit the lymphatic tissue from the red pulp. This forms the marginal zone. Cells similar to the follicular dendritic cells of lymph nodes are present in the white pulp of the spleen. These dendritic-like cells are called interdigitating cells and also represent antigen-presenting cells.

Red Pulp

The red pulp is a diffuse lymphatic tissue associated with the venous system of the spleen. The reticular meshwork is continuous throughout the red pulp and is filled with large numbers of free cells, including all those usually found in the blood. Thus, in addition to the cells of lymphatic tissue, the red pulp is suffused with red cells, granular leukocytes, and platelets. Occasionally, macrophages can be seen that contain ingested red cells or granulocytes or that are laden with a yellowish brown pigment, hemosiderin, derived from the breakdown of hemoglobin. The red pulp is riddled with large, irregular blood vessels, the splenic sinusoids, between which the red pulp assumes a branching, cordlike arrangement to form the splenic cords. The sinusoids have wide lumina (20 to 40 μm diameter), and their walls have a unique structure. Almost the entire wall is made up of elongated, fusiform endothelial cells that lie parallel to the long axis of the vessel. The cells lie side by side around the lumen but are not in contact and are separated by slitlike spaces. Outside the endothelium, a basement membrane that is not continuous but forms widely spaced, thick bars that encircle the sinusoid support the wall. The bars of basement membrane are joined to each other by thinner strands of the same material and are continuous with the reticular network of the splenic cords.

Blood Supply

The architecture of the spleen is best understood in relation to the blood circulation, which shows some special features. Branches of the splenic artery enter the spleen at the hilus, divide, and pass within trabeculae into the interior of the organ. These branches have an overlapping, segmental arrangement, with each main branch serving a defined area of the spleen. The trabecular arteries, as they now are called, branch repeatedly, finally leaving the trabeculae as central arteries that immediately become surrounded by the lymphatic tissue of the periarterial lymphatic sheath. Where the sheath expands to form nodules, the central artery (more appropriately called the follicular arteriole) is displaced to one side and assumes an eccentric position in the nodule. Only rarely does the vessel retain a central position in the nodular tissue. Throughout its course in the white pulp, the central artery provides numerous capillaries that supply the sheath and then pass into the marginal zone surrounding the white pulp. How these capillaries end is not certain. Many arterial branches appear to open directly into the marginal zone, often ending in a funnel-shaped terminal part. There is no direct venous return, and the white pulp is associated only with the arterial supply. Although the term artery commonly is used for the different levels of the splenic vasculature, once the vessel has reached lymphatic tissue, it is actually an arteriole. The central artery continues to branch, and its attenuated stem passes into a splenic cord in the red pulp, where it divides into several short, straight penicillar arteries, some of which show a thickening of their wall and now form sheathed capillaries. The sheath consists of compact masses of concentrically arranged cells and fibers that become continuous with the reticular network of the red pulp. Close to the capillary the cells of the sheath are rounded, while at the periphery of the sheath the cells become stellate. The cells of the sheath are avidly phagocytic. Not all the capillaries are sheathed, and occasionally, a single sheath may enclose more than one capillary. Sheathed capillaries may continue as simple capillaries or may divide to produce two to four non-sheathed, terminal capillaries. How these end still is a matter of some debate and has led to the "open" and "closed" theories of circulation. According to the open circulation theory, the capillaries empty into the meshwork of the red pulp in the splenic cords. The blood then slowly seeps through the red pulp and finds its way into the venous system through the walls of the splenic sinusoids. The closed circulation theory holds that the capillaries open directly into the lumina of the venous sinusoids; blood enters the sinusoid at the capillary end and leaves at the venous end because of a decreasing pressure gradient between the two ends of the sinusoid. A compromise between the two views suggests that a closed circulation in a contracted spleen becomes open when the spleen is distended. Splenic sinusoids drain into pulp veins, which are supported by a thin muscle coat and, more externally, are surrounded by reticular and elastic fibers. A sphincter-like activity of the smooth muscle has been described at the junction of the pulp veins and sinusoids. Pulp veins enter trabeculae, where, as trabecular veins, they pass in company with the artery. Trabecular veins unite and leave at the hilus as the splenic vein. The spleen has no afferent lymphatics, but efferents arise deep in the white pulp and converge on the central arteries. The lymphatics enter trabeculae and form large vessels that leave at the hilus. Areas of the spleen supplied by sinusoids (i.e., the red pulp) lack lymphatics. Thus, the spleen serves as a filter for blood, removing particulate matter that is taken up by macrophages in the marginal zone, splenic cords, and sheathed capillaries. The sinusoidal endothelium and the reticular cells of the reticular net have no special phagocytic powers and contribute little to the clearing of foreign materials from the blood. The spleen also functions as the graveyard for worn out red cells and platelets and possibly for granular leukocytes as well. As the blood filters through the splenic cords, it comes under constant scrutiny and monitoring

by macrophages. Viable cells are allowed to pass through the spleen, but damaged, aged, or infected cells are retained and phagocytosed. Several factors are probably involved in the recognition of old cells. As the cell ages, changes in the surface may permit antigenic reaction with opsonizing antibodies that enhance phagocytosis. The sinusoidal wall is a barrier to the re-entrance of cells into the circulation, since the cells must insinuate themselves through the narrow slits between sinusoidal endothelial cells. Normal cells are pliant and able to squeeze through the interendothelial clefts, but cells such as spherocytes or sickled red cells are unable to pass through the sinusoidal barrier. As red cells age, their membranes become more permeable to water, and the relatively slow passage through the red pulp may allow the cells to imbibe fluid, swell, and become too rigid to pass into the sinusoids. Red cells that have been excluded are phagocytosed, and the cells appear to be taken up intact without prior lysis or break down. Components of the red cells that can be reused in production of new blood cells are recovered by the spleen; it is especially efficient in conserving iron freed from hemoglobin and returning it to accessible stores. A "pitting function" has been described for the spleen. Red cells that contain rigid inclusions (malarial parasites or the iron-containing granules of siderocytes, for example) but that are otherwise normal are not destroyed, but the inclusions are removed at the wall of the sinusoid. The flexible part of the erythrocyte passes through the sinusoidal wall, but the rigid inclusion is held back by the narrow intercellular clefts and is stripped from the cell. The rigid portion remains in the splenic pulp and is phagocytosed; the rest of the cell enters the lumen of the sinusoid. The spleen has great importance in the immune system, mounting a large-scale production of antibody against blood-borne antigens. However, antigen introduced by other routes also evokes a response in the spleen, since an antigen soon finds its way into the bloodstream. The reactions in the spleen are the same as those occurring in lymph nodes and include primary and secondary responses. In the primary response, clusters of antibody-forming cells first appear in the periarterial lymphatic sheaths, then increase in number and concentrate at the edge of the sheath. Immature and mature plasma cells appear, and germinal centers develop in the splenic nodules. Ultimately, plasma cells become numerous in the marginal zone between white and red pulp and in the red pulp cords, either by direct emigration from the white pulp or indirectly via the circulation. During a secondary response, germinal center activity dominates, occurs almost immediately, and is of large scale.

The spleen produces red cells, platelets, and granulocytes only during embryonic life, but production of lymphoid cells continues throughout life. In some conditions (leukemia and some anemias) the red pulp contains islets of hemopoietic tissue, even in the adult. This probably results from sequestration of circulating stem cells from the blood rather than from activation of an indigenous population of potential stem cells in the spleen. Removal of the spleen (splenectomy) emphasizes its primary functions. The peripheral blood shows an increase in the number of platelets and abnormal erythrocytes. Older erythrocytes often contain Howell-Jolly bodies that normally would have been removed by the splenic cord-sinus system. Following splenectomy, individuals are at risk of developing bacterial septicemia. Under normal circumstances, blood-borne vectors would stimulate the immune component of the spleen and prevent infection via the blood.