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# An Historical Sketch of Splenic Function and Splenectomy

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**Summary**

Ideas about the spleen's functions as a blood filter, reservoir, scavenger of red cells and immunologic communication center are traced from the ancients to the present

In 1706, a fashionable London practitioner, Sir *Richard Blackmore,* published a "critical dissertation upon the nature and cure of colic and melancholy" raising the question – "whether the spleen is necessary or useful to the animal possessed of it? " (1). Although the text is largely a meandering litany of human frailities embellished with only an occasional biologic insight, the issue is now more than ever worthy of attention.

The ancients could not have guessed the functions of the spleen because the things the spleen accomplishes were not yet even imagined. *Erisistratus,* the great Alexandrian physician and founder of anatomy, charmed by symmetry, suggested that the spleen counterbalances the liver (2). The malaria-infested environs of the Middle East and therefore the endemic nature of splenomegaly made this concept especially attractive. Lack of an opening from the spleen added further to the confusion. The functions of other organs including kidney, stomach, liver, heart and lungs were historically viewed in terms of discharge of urine, chyme, bile, blood and air respectively. Even the brain, considered by ancients as the source of phlegm, drained through the nose. Yet the spleen seemed to be without an aperture – a blind organ. Then *Galen* "discovered" a small gastro-lienal communication, and the spleen became a "digestive" organ for over 1400 years. But after *Vesalius* established that Galen's duct was a mirage (3), the spleen once again receded into mystery.

*Marcello Malphighi,* the renowned 17th century Italian microanatomist, was also perplexed by the spleen. The white pulp, nowadays referred to as Malphighian corpuscles, seemed to him to resemble acinae of exocrine glands. But in the absence of a duct, Malphighi ingeniously conceived that secretions of the spleen were carried by the bloodstream to distant sites (4) (shades of hormones!). The red pulp, on the other hand, long regarded as an unfathomable morass of tissue fibers, was correctly perceived by *Theodor Billroth* in the mid 19th century to contain specialized cylindrical capillaries with slotted apertures (sinuses) draining blood from the red pulp (5, 6). Now called the cords of Billroth, the red pulp with its lattice architecture, is known to act as a sort of blood filter. Thus, working 200 years apart, these two great investigators, one an anatomist (*Malphighi*), the other later a preeminent surgeon (*Billroth*), uncovered the microstructure of the spleen.

After *Harvey's* epic description of the blood circulation, splenic physiology was perceived in a new light. Recognizing that blood was in perpetual motion and that spleen size in many animal species fluctuated widely, some workers compared this organ's function to the turgescence and detumescence of the penile corpora cavernosum (7–9) or the thrusting action of the heart (10, 11) and thus to waxing and

waning intrasplenic blood volume. The functional significance was, however, less clear. For example, the American physician, *Benjamin Rush,* suggested that during rage (venting one's spleen!) the spleen became engorged thereby reducing blood volume and preventing apoplexy (12). In fact, the opposite is true. In animals, such as the dog, where splenic reservoir function is prominent, the spleen enlarges during repose and discharges sequestered blood with excitement. Nonetheless, this reservoir function, though extremely limited in human beings, was the first non-imaginary function ascribed to the spleen.

A second splenic function was recognized more than 125 years ago by the Swiss-German anatomist, *von Kölliker,* who authored the first textbook of histology. Observing erythrophagocytosis in the spleen of healthy animals, he suggested that intrasplenic destruction of red cells by what are now called macrophages was a normal activity (13). Although sharply criticized by *Rudolf Virchow,* who viewed cell death exclusively as a sign of disease (14), *von Kölliker* was correct. Cells have finite life spans, and destruction of senescent red blood cells is now recognized as a chief function of the adult spleen. Splenic macrophages digest other particles as well, including bacteria and tumor cells, and hence the spleen is an important line filter strategically set into the arterial bloodstream. Splenic phagocytic activity extends not only to whole cells but also to particulates within cells. For example, as red blood cells pass through cracks in the lining of the splenic sinuses, inclusion bodies (e.g. intracytoplasmic nuclear fragments, degraded hemoglobin or Heinz bodies, malarial plasmodia, hemobartonella) are squeezed out of the cytoplasm and entrapped by perisinusal phagocytes.

Appreciation of the third and perhaps most important function of the spleen – immune activity – is of more recent vintage. After the bacterial and parasitic basis of many infectious diseases was established, it soon became apparent that an animal without a spleen was especially prone to fatal intravenous inoculum of a variety of microorganisms. These included paratyphoid, anthrax, trypanosome, and bartonella, injected systemically at concentrations much lower than in an animal with an intact spleen (15–17). Later, it was further recognized that if a sublethal intravenous dose was administered, the production of antibacterial antibody titers was greater if the spleen was left in situ (17, 18). In other words, the spleen's scavenger function seemed to cooperate and participate with immune reactivity.

In the last few years, infusions of radioactive particulate antigens have further elucidated the mechanism of interaction. Following bloodstream injection, radioactivity is promptly captured by macrophages in the red pulp but within a few hours migrates to white pulp and becomes visible in cells of the germinal follicles. Thus, antigenicity has been transferred from intrasplenic macrophages to cells of the lymphocyte-plasmacyte series. These latter cells proliferate and gradually differentiate into vacuolated plasma cells from which synthesized antibody is ultimately discharged into the blood (19, 20).

Until anesthesia and asepsis made laparotomy a practical procedure, splenectomy was limited to amputating spleens already nearly totally avulsed following traumatic wounds to the abdomen. But after *Micheli* (1910) in Italy (21) "cured" a patient with severe hemolytic anemia and *Kaznelson* (1961) in Czechoslovakia reported (22) prompt regression of severe thrombocytopenia after splenectomy, peripheral cytopenias became a prime indication for splenic extirpation.

Careful observation during the past 80 years, however, has provided a better understanding of subtle morphologic red cell changes as well as the serious physiologic drawbacks of the asplenic state. In otherwise healthy individuals, red blood cells while of full volume are thinner because the erythrocyte membrane retains a greater surface area. Small dark staining spherical remnants of destroyed red cell nuclei which are ordinarily removed by an intact spleen (Howell-Jolly bodies) persist in blood, and their presence denotes lack of splenic activity. Other morphologic red cell abnormalities in asplenia such as cratered cells

and spur cells reflect less culling, an activity by which the intact spleen removes substandard circulating blood elements. In some instances titers of splenic immunoglobulin or complement components are also lower following splenectomy.

Writing in the British Medical Journal, *O'Donnell* (1929) first reported (23) lethal postsplenectomy sepsis in a child from whom the spleen was removed several years earlier for hemolytic anemia. Tragically but ironically, the child's father had previously died from the same sequence – splenectomy for hemolytic anemia followed by fulminant sepsis. In 1952 (24), the condition "reemerged" but this time appropriately attracted widespread attention. Since then, it has been increasingly recognized that spleenless hosts are susceptible to abrupt, deadly bloodstream infections especially from encapsulated bacteria such as Streptococcus pneumoniae (pneumococcus) and H. influenzae. This risk while greater in young children and those with underlying immune deficiencies and blood dyscrasia exists for all individuals at all ages (25).

Of less clear significance is the increased mortality recorded from pneumonia and ischemic heart disease in soldiers who underwent splenectomy during World War II for abdominal injury (26). Whether these phenomena are real and in some way related to the known hematologic and immunologic functions of the spleen is unknown.

While much remains to be learned, it is fair to conclude that the spleen is indeed "useful to the organism possessed of it." Perhaps this answer to Blackmore's question was already anticipated by Sir Richard's compatriot and fellow essayist, *Joseph Addison*, who in 1711 (27) freely translated the following verse:

*In all thy humours whether grave of mellow*
*Thou'rt such a touchy, testy, pleasant fellow*
*Hath so much wit, and mirth and spleen about thee*
*There is no living with thee, nor without thee.*

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