A REVIEW OF 500 SPLENECTOMIES WITH SPECIAL REFERENCE TO MORTALITY AND END RESULTS *

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It is my purpose in this paper to evaluate briefly our experience in the clinic in those dyscrasias which have led to the removal of the spleen, and to comment in general on what may be expected from splenectomy as borne out by the statistics.

I have grouped the cases under four headings, having in mind the clinical rather than the pathologic aspects; necessarily such grouping is only approximate: (1) diseases associated with abnormality of the white blood cells and related structures; (2) diseases associated with changes in the red blood cells, and blood platelets; (3) diseases due to infectious and toxic agents, and (4) miscellaneous diseases. Giffin and his associates have made a study of the blood changes in these cases and have correlated them with the clinical picture, and MacCarty and his associates have studied the pathology of the removed spleens and in due time will present their findings.

FUNCTIONS OF THE SPLEEN

The spleen is a part of the reticulo-endothelial system, as described by Landau and Aschoff, which includes the lymphoid tissues and certain endothelial and connective tissues. It is a hemolymph gland and is probably most closely associated in function with Kupffer cells of the liver. The arteries of the spleen as they separate into smaller vessels lose their middle and outer coats in the parenchyma of the spleen, so that the endothelium of the capillaries is continuous with the endothelium of the sinuses. The blood of the capillaries therefore passes directly into the sinuses themselves. The splenic vein joins with the portal vein and carries about 20 per cent. of the volume of the portal circulation.

The functionally active cell of the spleen, which corresponds to the Kupffer cell of the liver, is a large mononuclear endothelial leukocyte which has an exceedingly efficient phagocytic action and plays an important part in removing bacteria from the blood, as in typhoid and tuberculosis, and protozoa, as in syphilis and malaria. The strainer function of the spleen is well exemplified in those splenomegalias in which the spleen is unable to deliver bacteria, protozoa, and toxic material with sufficient speed to the liver for destruction and detoxication. The retention of this deleterious material in the spleen may lead not only to splenic enlargement but to systemic reinfections, as is known to be the case in syphilis and certain forms of sepsis.

It is worthy of note that the large supply of well oxygenated arterial

blood carried by the splenic artery is converted into venous blood without exerting an adequate known function. This oxygen is evidently not lost in combustion for the purposes of heat and energy. The fact that oxygen is utilized in the spleen in large quantities necessarily means that some other substance is oxidized. There is little evidence and no logical reason for believing that de-oxygenation of the blood in itself is a function of the spleen, for a sufficient quantity of de-oxygenated blood is already supplied to the liver through the portal vein. The question of whether or not the oxidation is for the purpose of destruction of undesirable substances (detoxication theory) or for the purpose of elaborating some complex substance, (for example, the highly complex hæmoglobin protein molecule), offers an interesting field for investigation. It might also be suggested that these oxidized substances are prepared in the spleen for the purpose of further treatment by the liver.

The removal of the normal spleen in cases of traumatism in man, and its removal in experimental animals, does not seem to cause permanent abnormal disturbance. On removing the spleen one is struck by the enormous amount of venous blood which it contains. It has been shown by Barcroft and Stevens that in the dog about 20 per cent. of the total blood volume may be stored temporarily in the spleen. The spleen contains a considerable amount of nonstriated muscle tissue and is known to possess a certain rhythmic contraction comparable to that of the gastro-intestinal tract and the uterus. It may be assumed that in times of stress stored blood is impelled through the portal circulation into the general circulation by splenic contractions, which possibly account for the pain in the left side so often experienced by long-distance runners. It may also account for the tradition that the ancients removed the spleen of runners in preparation for the Marathon races.

The spleen has some connection with the sympathetic nervous system through scanty fibres to the capsule, but it would appear to act largely through the influence of certain hormones which as yet have not been identified.

Normally the spleen probably does not produce white blood cells in the adult; this function or dysfunction of the spleen is apparent in splenomyelogenous leukemia.

Approximately 20 per cent. of the volume of the arterial blood is oxygen. When the red blood cells are reduced in number, suboxidation results. The relief which is sometimes manifest in the anemias on increasing the respiratory oxygen intake artificially may be due in part to correction of the suboxidation.

The embryonic red blood cells have dimly visible nuclei which disappear when the oxygen-bearing function becomes established. Since the adult red cells do not have nuclei they do not reproduce themselves, and must be replaced. The work of Ashby of The Mayo Foundation showed that red blood cells continue their oxygen-bearing function for at least six or seven weeks and probably longer. It should be noted that there are one or more atoms of iron to each molecule of hæmoglobin, showing the foundation for

the improvement which sometimes follows the use of iron in the anemias.

The red blood cells and the blood platelets are formed in the bone marrow. The function of the spleen in destroying worn out red blood cells and blood platelets is an important one.

The experiments of Mann and his co-workers show that bile is not formed in large amounts in the liver, but that one of the functions of the liver is to filter bile from the blood. The destruction of the red blood-cells, which produce the pigments of the bile, is accomplished largely in the bone marrow (where also these cells and the blood platelets are formed), in the spleen, in the Kupffer cells, and, to a less extent, in the reticulo-endothelial tissues of the body generally.

In the removal by the spleen of worn out red blood cells and blood platelets from the blood-stream lies the explanation of increased function of the spleen in those specific splenic enlargements which accompany hæmolytic jaundice and hemorrhagic purpura, and one may surmise that although the splenomegaly in hæmolytic jaundice and hemorrhagic purpura may to some extent be a work hypertrophy, any enlargement of the spleen means distinct danger to the red blood cells, without regard to the nature of the enlargement, and probably will be accompanied by anemia.

In splenic anemia the red blood cells, and often the white blood cells, are reduced in number; the white cells not infrequently to 3,500 or below. In the late stages of this particular dyscrasia, the so-called Banti's syndrome of cirrhosis of the liver may occur, suggesting that diffuse irritating products are filtered from the blood-stream by the spleen or are formed in it. Failure of the liver to detoxicate these products leads to generalized hepatic fibrosis as the result of the attempt to encapsulate them. Just what these irritating substances may be is not known, but from our knowledge of the pepper and alcoholic cirrhoses originating in the gastro-intestinal tract we can surmise that they are chemical in nature. Giffin and Brown have shown recently that the blood volume is increased in cases of simple splenomegaly previous to the development of anemia; this indicates that there is an early factor in the disease which causes splenic enlargement with an increased circulatory bed.

I realize that this brief survey of the experimental and clinical fields is unsatisfactory and lacks greatly in detail, but at least it gives a perspective.

OPERATIVE EXPERIENCE

Between April 1, 1904 and March 1, 1928, splenectomy was performed in the clinic in 500 cases, with a mortality of 10 per cent. In speaking of the death rate, I refer to the deaths in the hospital. Many of the patients recovered from the operation, but for various reasons were not dismissed from the hospital and died there from causes other than the splenectomy. Eighty per cent. of the patients who recovered from the operation and are now living are in good condition, and the ultimate results are even more satisfactory than a cursory examination of the statistics might lead one to believe. As Bloodgood has pointed out in connection with a follow-up of patients operated

on for cancer: "Whereas bad news travels quickly, those patients who are difficult to trace, when heard from usually prove to be well." Further, we assume that all deaths in a series of cases occur from the disease, but it is only just to consider the natural death rate in a period of twenty-four years.

GROUP I.—*Diseases Associated with Abnormality of the White Blood Cells and Related Structures.*—Splenectomy was performed in fifty-four cases because of abnormal changes in the white blood cells and related structures, associated with enlargement of the spleen.

	Patients	Hospital mortality
Splenomyelogenous leukemia	45	3
Lymphocytic splenomegaly	8	
Hodgkin's disease	1	

Splenomyelogenous Leukemia.—In forty-five cases of splenectomy for splenomyelogenous leukemia there were three deaths in the hospital. Splenomyelogenous leukemia has been looked on as an incurable disease, and superficially it would appear that there was little excuse for removing the spleen. However, if we consider first that what we call splenomyelogenous leukemia may be a terminal stage of various types of blood dyscrasias which are recognized only when they have reached a fatal stage, perhaps to a certain extent we are naming a prognosis rather than the actual disease. Splenectomy is suggested in these cases by the fact that any treatment which reduces the size of the spleen improves the condition of the blood and thereby the condition of the patient.

Patients in this group have lived and have been able to work for a number of years after splenectomy. At no time has the blood become normal, but great, and, in some instances, prolonged palliation has resulted. The results are better than they appear, because in cases of possible splenomyelogenous leukemia, when the condition of the blood approaches normal after splenectomy, it is assumed that the disease was not true splenomyelogenous leukemia, and the case is classified with the splenic anemias or is left unclassified. These cases will be explained later in the light of future knowledge.

It has been found that by reducing the size of the leukemic spleen either with X-ray or radium preliminary to operation, the spleen can be removed with not to exceed 5 per cent. mortality. In younger and middle-aged patients in the early stages of this apparently hopeless condition, the merits of splenectomy should be considered.

Lymphocytic Splenomegaly.—Splenectomy was performed in eight cases of lymphocytic splenomegaly with no deaths. These cases are closely related to the cases of generalized lymphosarcoma, and possibly also to lymphatic leukemia on the one hand and to Hodgkin's disease on the other. They vary greatly in the degree of malignancy. Half of them apparently have been of a benign type and the patients are living from one to six years after operation.

Hodgkin's Disease.—The spleen was removed in one case for a curious

condition which was classified temporarily as localized Hodgkin's disease. The classification of this case awaits further knowledge.

GROUP 2.—*Diseases Associated with Abnormality of the Red Blood Cells (and Blood Platelets).*—Splenectomy was performed in 330 cases for enlarged spleen associated with abnormality of the red blood cells.

	Patients	Hospital mortality
Splenic anemia	140	15
Hæmolytic jaundice	88	4
Hemorrhagic purpura	27	1
Pernicious anemia	62	4
Polycythemia vera	3	1
Indeterminate hemorrhagic disease	4	
Acute aplastic anemia	2	
Chronic aplastic anemia	2	
Chronic hæmolytic anemia	1	
Indeterminate congenital jaundice	1	

Splenic Anemia.—Splenectomy for splenic anemia was performed in 140 cases. There were fifteen deaths in the hospital. More than half the patients are living, and all but six are in satisfactory condition. The hospital death rate in this group is high, but when it is considered that a goodly proportion of patients operated on were in the terminal stages with advanced cirrhosis of the liver, ascites, and œdema, and that many of these recovered and remained well for a term of years, the results are satisfactory, and demonstrate the remarkable power of the liver to regenerate. This encouraging showing, however, led to operation in many cases in which conditions were such that the risks, although justified, were great. Ten per cent. of the patients who died during the ten year period after splenectomy for splenic anemia died from gastric hemorrhage. It is assumed that bleeding was due to varices in the lower part of the œsophagus and around the cardia of the stomach.

Hœmolytic Jaundice.—Splenectomy was performed in eighty-eight cases of hæmolytic jaundice, with four deaths in the hospital. Eighty-one of the patients have been traced. Seventy-three are known to be living, of whom seventy-two are in good condition. Splenectomy in hæmolytic jaundice stands out as a life-saving operation. It was first used in the clinic in 1911, and our interest in the procedure was given further impetus by the publication in 1915 by Elliott and Kanavel of their splendid contribution on the value of the operation in hæmolytic jaundice.

Hemorrhagic Purpura.—Splenectomy was performed in twenty-seven cases of hemorrhagic purpura, with one death in the hospital. Twenty-six patients are living and in good condition. Here again is a triumph for splenectomy. It is most important to make a correct diagnosis before coming to a decision concerning surgical treatment. Acute aplastic anemia especially simulates hemorrhagic purpura, and differentiation of the two may at times be very difficult.

Pernicious Anemia.—The modern treatment of pernicious anemia by a diet containing liver and high in vitamines has at least temporarily replaced splenectomy. Splenectomy was performed in sixty-two cases of pernicious anemia, with four deaths in the hospital. Three of these deaths occurred in the first nineteen cases, in which the operation seemed justified only in the late stages of the disease. Splenectomy should be performed, if at all, only when the patient is on the upgrade following transfusions and other methods of rehabilitation. The temporary improvement which followed removal of the spleen was marked in practically every case, and the prolongation of life in 25 per cent. of the cases was about two and a half times the life expectancy if splenectomy had not been performed. None of the patients was considered cured, for if apparent cure resulted, the case was placed in a different classification since probably it was not true pernicious anemia. I think every case should be carefully considered on its merits in order to detect the occasional doubtful case in which splenectomy may be advisable. There is a group of cases in which there is achlorhydria and what seems at the time to be secondary anemia in which the other features of pernicious anemia have not developed; in these splenectomy might logically be considered if the spleen is enlarged.

Polycythemia Vera.—Splenectomy was performed in three cases of polycythemia vera, with one death. The results in the two cases were extraordinarily good. While the patients are not well, they have been able to work for several years.

GROUP 3.—*Diseases Due to Infectious and Toxic Agents.*—In the group of splenomegalies in which the spleen acts as a filter and removes microorganisms and toxic agents, splenectomy has a field of usefulness. The enlarged spleen was removed in eighty-six cases in this group.

	Patients	Hospital mortality
Tuberculosis of spleen	9	1
Syphilitic splenomegaly	10	1
Acute, subacute and chronic septic splenomegaly	30	7
Portal cirrhosis	37	7

Tuberculosis of the Spleen.—In nine cases in which the tuberculosis appeared to be confined to the spleen, seven patients have remained well over a long period of years since splenectomy. One patient died of generalized miliary tuberculosis which came on immediately after operation, possibly due to direct venous contamination in the course of the operation.

Syphilitic Splenomegaly.—There were ten cases of splenectomy for syphilitic splenomegaly, with one death in the hospital. These patients all had advanced anemia, large spleens, secondary gummata in the liver, and were unable to maintain a negative phase under antisyphilitc treatment carried on for months. The removal of the spleens, which in some instances were found to contain spirochetes and small gummata, was followed by rapid recovery.

The improvement in these resistant cases following splenectomy and subsequent treatment amounted to cure.

Septic Splenomegalies.—The septic splenomegalies are unsatisfactory cases for operation. In the thirty acute, subacute, and chronic cases in which splenectomy was performed, there were seven deaths. In the more acute cases in which bacteria were cultivated from the blood, the results were poor, and it probably would have been wise to delay the operation until a greater degree of natural immunity had been established. In the cases in which septic endocarditis was present at the time of the splenectomy, there were no cures. In the chronic cases the results were much better; where natural immunity had been established the results were good, and the risk small.

Portal Cirrhosis.—The results of splenectomy in the Banti stage of splenic anemia for the relief of cirrhosis of the liver were so extraordinarily good as to lead to the removal of the spleen in thirty-seven cases of cirrhosis of the liver in which the spleen was only moderately enlarged. The operation was performed late in the history of the disease which was evidently of gastro-intestinal origin. There were seven deaths in the hospital in this series. Although there were brilliant exceptions, the results in these cases on the whole were only fair, not better than in a comparable group of cases in which some type of Talma-Morison operation had been performed with less risk.

GROUP 4.—*Miscellaneous Conditions.*—Splenectomy was performed in thirty-one cases for miscellaneous conditions.

	Patients	Hospital mortality
Gaucher's disease	7	2
Ruptured spleen	4	1
Wandering spleen	2	
Hemorrhagic cyst	2	
Multiple serositis (Pick's disease)	1	1
Eosinophilia with splenomegaly	1	
Neutrophilia with splenomegaly	1	1
Hemangioma	1	
Condition necessitating secondary splenectomy	9	
Unclassified	3	1

Gaucher's Disease.—Splenectomy was performed seven times for Gaucher's disease. The five patients who lived were greatly improved and, although they were not cured, were able to work and earn a living.

Time does not permit me to discuss further this interesting group of cases, which I have tabulated merely for general information.