Splenectomy:

Indications and Results in Hematologic Disorders *

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THIS is a report concerning the indications for and the results of splenectomy performed for hematologic disorders. During the period January 1, 1946 through December 31, 1962, 254 splenectomies were performed at the University of Virginia Medical Center. Of these 160 were carried out for non-hematologic conditions, and include splenectomy for trauma, as part of an *en bloc* resection, incident to the performance of splenorenal venous anastomosis, for the purpose of facilitating some other surgical procedure and, in isolated instances, for tumor, abscess, aneurysm of the splenic artery, or for diagnosis. There were 94 splenectomies for hematologic disorders. These form the basis for this report.

Indications for Splenectomy

As will be noted in the subsequent discussion, there are several hematologic conditions in which opinion concerning the indications for and the timing of splenectomy are in dispute. During the period under consideration the indications which were employed by us have, in many instances, remained essentially constant; in others significant changes in practice have been made to conform with new evidence concerning therapy, new concepts concerning disease mechanisms, as well as to take advantage of experience gained during the period. Within this framework our indications for splenectomy in hematologic conditions may be stated as follows:

An established diagnosis of *hereditary spherocytosis* was considered sufficient reason for splenectomy unless some contraindication to operation existed. Even if the hemolytic process was compensated, or nearly so, splenectomy was advised because of the tendency to cholelithiasis that exists in this disease, to avoid the later complications of gallstones, and to avoid the consequences of an aplastic crisis that sometimes follows an infection.

In those patients classified as having *hemolytic anemia other than hereditary spherocytosis,* splenectomy was performed when satisfactory improvement did not follow the use of corticosteroid preparations, or when transfusions were required or over a prolonged period, or when studies showed selective splenic sequestration of Cr^{51} tagged red blood cells.

Splenectomy was carried out on patients with *idiopathic thrombocytopenic purpura* who did not respond within six weeks to therapy with adrenocorticosteroids, and on those who have relapsed after the drug was discontinued.

Splenectomy was performed in those patients with *myeloproliferative disorders* who could not be managed with corticosteroids, testosterone, busulfan, or transfusions, when repeated hemorrhages, frequent infections, recurrent anemia or discomfort associated with the abdominal mass led to invalidism, or when there was selective sequestration of Cr^{51} tagged erythrocytes in the spleen.

In the group who were diagnosed as *aplastic anemia* splenectomy was done in the moderately ill patient who had developed splenomegaly associated with hyperhemolysis, when it was hoped that operation might mitigate this aspect of the illness; it was also performed in some seriously ill patients as a last resort measure when the need for transfusion was almost continuous.

All of the splenectomized patients considered in the group entitled *congestive splenomegaly with hypersplenism* had Laennec's cirrhosis and, in addition, one or more of the components of *hypersplenism,* namely, splenomegaly, anemia, leukopenia or thrombocytopenia.

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TABLE 1. *Hereditary Spherocytosis*

Case	Patient	Sex, Age*	Before Splenectomy Hematocrit %	Before Splenectomy Reticulocytes %	After Splenectomy** Hematocrit %	After Splenectomy** Reticulocytes %	Result	Follow up
1.	S. M.	F 8	29	8	40	2	Excellent	13 yr.
2.	D. L. S.	F 1 mo.	12	12	37	2.8	Excellent	13 yr.
3.	M. K.	F 15	26	--	—	—	Excellent	9 yr.
4.	J. E. W.	F 8	21	12	40	0.2	Excellent	4 yr.
5.	M. A. C.	M 54	25	4.7	38	—	Excellent	4 yr.
6.	E. A. C.	M 29	25	6.1	46	—	Excellent	3 yr.
7.	F. C.	F 28	32	1.7	32***	—	Excellent	2½ yr.
94.	M. B. T.	F 38	13	8	41	1.5	Excellent	2½ yr.
8.	G. E. D.	F 43	28	15	47	—	Excellent	2 yr.
9.	E. E. F.	M 54	6****	14	15****	—	Excellent	1 yr.
10.	I. K. A.	M 2	17	30	39	—	Excellent	7 mo.
11.	P. J. K.	F 4	6.2****	10	13.2****	—	Excellent	4 mo.
12.	L. P. R.	F 13	28	2.3	47	0.2	Excellent	2 mo.
13.	D. D.	F 8	8.6****	—	13****	—	Excellent	2 mo.
14.	K. E. N.	M 10 wk.	21	2.6	36	0.2	Excellent	2 mo.
15.	A. R. D.	F 25	30	7.6	41	—	—	Lost to follow up
16.	M. L. D.	M 6	33	—	—	—	—	Lost to follow up
17.	M. L. W.	M 9	15	18	—	—	—	Lost to follow up
18.	W. W. S.	M 65	30	6.8	—	—	Operative death	

* In this Table and in those to follow the term *Age* refers to the patient's age at time of splenectomy.
** In this Table and in those to follow the term *after splenectomy* refers to the most recent laboratory data available.
*** Hematocrit: 39% two months after splenectomy (see text).
**** Hemoglobin Gm. %

In the patients classified as having *granulomatous diseases,* splenectomy was performed because of the association of splenomegaly with evidence of *hypersplenism.* Often a definitive diagnosis was not disclosed by the preoperative diagnostic studies.

Individuals with *lymphomatous diseases* who had splenectomy did not have the correct diagnosis established before operation. The indications for operation were the presence of an enlarged spleen associated with evidence of *hypersplenism* or gastro-intestinal bleeding, or the presence of a left upper quadrant mass that was causing considerable distress. Essentially the same considerations led to splenectomy in the group of *miscellaneous hematologic conditions.*

Results of splenectomy performed on 94 patients for hematologic conditions are presented in Tables 1 through 9, and in the text that follows.

Hereditary Spherocytosis. In this group of 19 patients, 15 have been observed long enough to justify classification as excellent results subsequent to splenectomy. Thirteen have maintained normal hematocrit or hemoglobin levels, despite the continued production of abnormal erythrocytes. One patient (Case 7) showed an increase in hematocrit from 32, prior to splenectomy, to 39, two months later. She subsequently has developed a blood loss anemia associated with menorrhagia. The only operative death occurred in the oldest patient (Case 18), a 65-year-old man, who was a very poor-risk patient, and who expired 24 hours after operation due to intra-abdominal bleeding. Three patients have been lost to follow-up.

Hemolytic Anemia Other than Hereditary Spherocytosis. The cases in this group are divided into autoimmune and non-autoimmune hemolytic anemias, predominately on the basis of the Coombs test. Both subdivisions include a variety of underlying disorders which were responsible for, or related to, the hemolytic anemia. The nature of the primary disease was an important factor in determining the post-operative result. Of the five patients with autoimmune hemolytic anemias, two (Case 19, 20) having been followed for three and eight years, respectively, are classified as greatly improved because of normal hematocrit findings, although they continue to

TABLE 2. *Hemolytic Anemia Other Than Hereditary Spherocytosis*

Case	Patient	Sex	Age	Preoperative Response to Steroids	Before Splenectomy			After Splenectomy			Result	Follow up
					Hematocrit %	Reticulocytes %	Bilirubin Mg.%	Hematocrit %	Reticulocytes %	Bilirubin Mg.%		
Auto-immune Hemolytic Anemias												
19.	J.A.B.	M	62	Slight improvement	20	37	6.0	40	5.9	—	Great improvement*	8 yr.
20.	N. E. H.	F	44	Slight improvement	15	12.4	4.6	45	0.9	0.3	Great improvement*	3 yr.
21.	F. W. (1)	M	76	Unimproved	21	3.1	2.8	—	—	—	Postoperative death	
22.	R. S. T. (2)	F	69	Unimproved	21	4.6	1.5	—	—	—	Died 1 mo. after operation	
23.	R. C.	M	55	Unimproved	12	12	3.4	—	—	—	Died 3 mo. after operation	
Other Hemolytic Anemias												
24.	L. J. E.	F	60	No therapy	30	19	3.0	44	—	—	Excellent	2 yr.
25.	M. D. W.	F	34	Unimproved	29	12	0.8	43	1.2	0.8	Excellent	8 mo.
26.	J. I. C.	M	55	No therapy	22	—	3.0	28	6	0.8	Moderate improvement	10 yr.
28.	R. C.	M	11	Unimproved	17	10	2.1	32	5.1	1.4	Moderate improvement	5 yr.
29.	H. M.	F	70	Unimproved	23	5.5	—	47	1.4	—	Moderate improvement*	2 yr.
30.	G. F. W. (3)	M	39	Unimproved	25	0.6	3.4	45	—	—	Moderate improvement*	3 mo.
31.	M. W. (4)	F	16	No therapy	31	9	3.0	29	12	6.4	Unimproved	18 yr.
32.	W. S. C.	M	39	No therapy	33	1.6	0.2	—	—	—	Unimproved	8 yr.
33.	L. L. (5)	M	23	Unimproved	30	5.4	1.0	35	0.8	—	Died 3 mo. after operation	

* On steroids.
(1) Primary disorder: Chronic lymphatic leukemia.
(2) Primary disorder: Reticulum cell sarcoma.
(3) Primary disorder: Rheumatoid arthritis.
(4) Primary disorder: Congenital nonspherocytic hemolytic anemia, type unknown.
(5) Primary disorder: Hodgkin's disease.

TABLE 3. *Thrombocytophenic Purpura*

Case	Patient	Sex	Age	Response to Steroids Preoperatively	Platelets per cu. mm. Before Splenectomy	Platelets per cu. mm. After Splenectomy	Result	Follow up
34.	H. F.	F	24	No therapy	30,000	200,000	Excellent	15 yr.
35.	M. F.	F	29	No therapy	5,000	475,000	Excellent	8 yr.
36.	L. H.	F	56	Unchanged	28,000	124,000	Excellent	8 yr.
37.	B. H.	M	17	No therapy	15,000	594,000	Excellent	5 yr.
38.	S. L. B.	M	8	Unchanged	6,000	350,000	Excellent	4 yr.
39.	A. S.	M	9	Unchanged	10,000	290,000	Excellent	1 yr. 4 mo.
40.	P. C.	F	34	Unchanged	15,000	230,000	Excellent	1 yr. 3 mo.
41.	E. H.	F	42	Slightly improved	23,000	500,000	Excellent	1 yr.
42.	L. A. H.	M	41	Slightly improved	12,000	251,000	Excellent	1 yr.
43.	N. L. A.	F	16	Unchanged	8,000	—	Excellent	10 yr.
44.	R. W. B.	M	8	Transient improvement	18,000	—	Excellent	8 yr.
45.	H. H.	M	43	No therapy	*	123,000	Greatly improved	3 yr.
46.	R. H.	M	35	Unchanged	20,000	40,000	Moderately improved	3½ yr.
47.	J. H.	F	10	Unchanged	20,000	48,000	Moderately improved	2½ yr.
48.	E. S. H.	F	62	No therapy	7,000	53,000	Moderately improved	2 yr. 4 mo.
49.	S. S.	M	44	Unchanged	48,000	55,000	Unchanged**	11 yr.
50.	G. T. E.	M	36	Moderately improved	20,000	84,000	Unchanged**	3½ yr.
51.	J. F. M.	F	33	Slightly improved	36,000	520,000	Lost to follow up	8 mo.

* Studies done but records of laboratory data lost.
** On steroids.

receive steroids. The remaining three patients died between six weeks and three months, respectively, following operation. Case 22 had an underlying reticulum cell sarcoma which probably contributed to the gram-negative septicemia, resulting in his death one month after operation. Case 23 had an associated thrombocytopenia with a platelet count of 37,000, and had been suspected of having thrombotic thrombocytopenic purpura; he died three months after operation, but autopsy findings did not confirm this diagnosis. Case 21, whose underlying disorder was chronic lymphatic leukemia, died six weeks following operation of an intra-abdominal staphylococcal abscess and pneumonia. This was the only surgical complication in these groups.

The remainder of the patients with hemolytic anemias (the non-autoimmune group) showed somewhat better results. Two (Case 24, 25) are classified as excellent results, having showed no clinical or laboratory evidence of hemolysis during the eight months and two years of post splenectomy observation. Four are classified as moderately improved, inasmuch as the rate of hemolysis has decreased; two patients are unchanged, and one patient (Case 33) died three months postoperatively of the primary condition, Hodgkin's disease. Case 26 had associated ulcerations of the legs and osteomyelitis. Case 29 had associated thrombocytopenia. Case 30 has associated rheumatoid arthritis and requires steroids to control the hemolytic anemia. A young girl (Case 31), diagnosed as having congenital non-spherocytic anemia, underwent a splenectomy in another hospital; she failed to improve and was subsequently operated upon by us at which time an accessory spleen, $1.5 \times 1.5 \times 0.8$ cm. in size, and a calculus gallbladder were removed. Although her strength is sustained, she remains anemic and icteric and is classified as unimproved. Case 32 has an undiagnosed disorder with cyclic episodes of hemolysis, and Case 33 had underlying Hodgkin's disease.

Idiopathic Thrombocytopenic Purpura. Nine of the 18 patients with idiopathic thrombocytopenic purpura have shown no clinical or laboratory evidence of disease following splenectomy and are classified as excellent results. Of these, five have been followed for four years or more, and four

have been followed for at least one year. Two patients (Case 43, 44) are classified similarly, since they have been free of any bleeding tendency and without therapy for at least eight years, although platelet counts are not available. Four patients, having been followed for two to three years, are classified improved on the basis of decreased bleeding tendency and a higher platelet count. Two patients are unchanged and require steroids for control. One patient was lost to follow up after eight months, at which time his platelet count was normal. In two patients classified as excellent result (Case 35) and improved (Case 45), respectively, there is uncertainty concerning the part splenectomy played in the improvement, because remission did not occur in these cases until six months and two years, respectively, after operation. The only complications encountered in this group were two instances of postoperative thrombophlebitis (Case 36, 45).

Myeloproliferative Disorders. Of the seven patients with myeloproliferative disorders, there were but two which showed even moderate improvement after splenectomy. Two died within two weeks of operation, two died approximately two years after splenectomy of their primary disorder, and one has been lost to follow up. In four cases, the definitive diagnosis was not established prior to the time of splenectomy.

Case 52, with known polycythemia vera, developed persistent gastro-intestinal bleeding; cavernous transformation of the splenic vein was demonstarted by splenoportography; therefore splenectomy was performed. There has been no further bleeding. Case 53, with known polycythemia vera and myelofibrosis, required splenectomy because of a hemolytic process. Three days following operation she developed pyelonephritis, complicated by *E. coli* septicemia; she responded favorably to antibiotic therapy. Splenectomy has altered favorably the hemolysis. Case 54 presented with hepatosplenomegaly and mild pancytopenia. He was unimproved by splenectomy, and bone marrow examination nine months postoperatively revealed changes of myelofibrosis. Case 55 presented with gastro-intestinal bleeding and was found to have carcinoma of the stomach, splenomegaly, and the hematological changes of chronic myelogenous leukemia. Case 56 presented with splenomegaly and pancytopenia and had 11 per cent myelocytes in the peripheral blood. Following operation 30 per cent blast forms appeared in the peripheral blood and he expired two weeks postoperatively with pneumonia. Case 57 was an undiagnosed problem of splenomegaly and pancytopenia; she died 16 days postoperatively, having developed a staphylococcal wound abscess and pneumonia. Autopsy findings revealed changes compatable with myeloid metaplasia. Case 58 had previously known polycythemia vera and myelofibrosis, and developed anemia and persistent left upper quadrant pain requiring splenectomy. She has been lost to follow up.

Aplastic Anemia. All eight patients in this group presented with pancytopenia. Three patients (Cases 27, 59 and 62) had associated hemolytic components, which constituted the indication for splenectomy. In this group of eight there was one excellent result (Case 59), a patient who has maintained normal blood counts for four years and whose marrow has reverted from hypocellular to normocellular. One patient was unchanged, one died two weeks following operation from the primary disease; two went on to develop the changes of acute myelogenous leukemia. One (Case 27) presented with associated pancytopenia and, following splenectomy, the leukocyte and platelet counts returned to normal and the rate of hemolysis decreased. This improvement was maintained for six years only to be followed by worsening of anemia and death. The primary disease remains obscure. One case was lost to follow up. Case 89 developed hemolytic anemia dur-

TABLE 4.

Case	Patient	Sex	Age	Indication for Operation	Final Diagnosis	Before Splenectomy				
						Hematocrit %	WBC per cu. mm.	Platelets per cu. mm.	Marrow	Myelocytes %
52.	S. D.	M	46	GI bleeding	Polycythemia vera	27	11,000	28,000	Normoblastic hyperplasia	0
53.	V. H.	F	59	Hemolytic process	Polycythemia vera with myelofibrosis	28	7,400	500,000	Hypocellular, nondiagnostic	4
54.	D. R. F.	M	56	Splenomegaly	Myelofibrosis	35	3,900	92,000	Hypocellular, nondiagnostic	0
55.	E. R. D.	M	68	Splenomegaly, gastric mass	Chronic myelogenous leukemia, & gastric carcinoma	30	22,000	—	*	6
56.	J. W. K.	M	40	Anemia, splenomegaly	Chronic myelogenous leukemia &/or myeloid metaplasia	27	12,000	86,000	Hypocellular, nondiagnostic	11
57.	R. S.	F	63	Pancytopenia	Chronic myelogenous leukemia &/or myeloid metaplasia	32	3,100	33,000	Normoblastic, nondiagnostic	0
58.	W. M.	F	69	Symptomatic splenomegaly	Polycythemia vera with myelofibrosis	28	11,000	293,000	Normoblastic, myeloid hyperplasia	1

* Probable chronic myelogenous leukemia or leukemoid reaction.

ing the course of his congenital hypoplastic anemia; he died five months postoperatively of hepatic hemosiderosis. Cases 27, 59 and 62 have been reported in detail by Mohler and Leavell.[12]

Congestive Splenomegaly with Hypersplenism. Six patients with Laennec's cirrhosis of the liver and congestive splenomegaly also exhibited some degree of hypersplenism and underwent splenectomy for this reason. Two of these six patients were followed and are classified as excellent results, in that their blood counts have returned toward normal; two have been lost to follow up; and two died following operation. One of these (Case 67) had Laennec's cirrhosis of the liver, portal hypertension, esophageal varices and hypersplenism. A portacaval shunt was considered to be the procedure of choice, but because of a clotting defect splenectomy was performed initially. Following this there was a significant rise in platelets, but there was delayed clotting and poor clot retraction. Three weeks later a side-to-side portacaval shunt was done, but unfortunately the patient died on the eighth postoperative day when a retroperitoneal hematoma ruptured into the left thorax. The other patient (Case 68) died in the postoperative period of uncontrolled bleeding. He was a 55-year-old man with Laennec's cirrhosis of the liver, ascites, anemia, leukopenia, thrombocytopenia and splenomegaly. He was not considered a good candidate for portacaval shunt, but it was thought that splenectomy would be beneficial in correcting the hypersplenism and in reducing the portal blood flow. This was performed, but in the postoperative period he developed uncontrollable hemorrhage and, in spite of re-operation (at which time no

Myeloproliferative Disorders

After Splenectomy					Weight of Spleen Gm.	Result	Follow up
Hematocrit %	WBC per cu. mm.	Platelets per cu. mm.	Marrow	Myelocytes %			
53	13,000	1,000,000	—	0	1170	Improved, no GI bleeding	3 yr.
31	18,000	500,000	Normoblastic hyperplasia, myeloid hyperplasia	4	1975	Moderate improvement	Death 2 yr. after operation
18	21,000	—	Myelofibrosis	8	1020		Death 2 yr. after operation
—	—	—	—	12	637		Death 18 mo. after operation
—	—	—	—	—	2157		Died 2 wk. postoperatively blastic crisis & pneumonia
—	—	—	—	—	1782		Postoperative death; wound abscess & pneumonia
—	—	—	—	—	870		Lost to follow up

specific bleeding point was determined) and transfusion with massive quantities of blood, he died.

Granulomatous Diseases. Of the five patients with granulomatous disease, three are classified as moderately improved on the basis of relief of symptoms or improved blood counts, or both. One patient was unchanged, and one patient (Case 74) died five days after operation of disseminated histoplasmosis. Three patients were found to have nonspecific granuloma in their spleens resembling sarcoidosis, but have not developed further evidence of the disease; one patient does have sarcoidosis.

Lymphomatous Diseases. In this group of seven patients, there were four with Hodgkin's disease, two with lymphosarcoma and one with chronic lymphocytic leukemia. In all but two cases the correct diagnosis was not established until after operation. The results in this group are uniformly poor, except for one patient (Case 76) with lymphosarcoma, who has been followed for one and a half years since splenectomy, and who has shown improved blood counts. Another (Case 77), with chronic lymphocytic leukemia, has been followed for three years without change in blood counts. The remaining patients died of the primary disease within one month to two years following operation.

Miscellaneous Hematological Conditions. The majority of the patients in this group were undiagnosed at the time of splenectomy and the operation was performed because of hypersplenism. Unfortunately, the two patients with hepatosplenomegaly and pancytopenia (Case 90, 91) classified unsatisfactorily as *idiopathic hypersplenism* were lost to follow up. Had they been observed for a longer period, it is

TABLE 5. *Aplastic Anemia*

Case	Patient	Sex	Age	Final Diagnosis	Before Splenectomy				After Splenectomy				Result	Follow up
					Hematocrit %	WBC /mm.³	Platelets/mm.³	Marrow	Hematocrit %	WBC /mm.³	Platelets/mm.³	Marrow		
59.	M. L. H.*	F	68	Idiopathic aplastic anemia	11	2,500	200,000	Hypocellular	50	7,400	200,000	Normocellular	Excellent	4 yr.
27.	S. W. A.**	F	37	Idiopathic aplastic anemia	28	3,900	75,000	Hypocellular	25	8,500	266,000	Hypocellular	Moderate improvement****	6 yr.
60.	J. W.	M	48	Idiopathic aplastic anemia	20	3,800	6,900	Slight myeloid hypoplasia	12	6,900	10,000	Hypocellular	Unchanged	3 yr.
61.	R. E. L.	M	48	Acute myelogenous leukemia (terminal)	20	600	8,000	Hypocellular, many blasts	—	—	—	—	Died 1½ yr. postoperatively	
62.	T. L. J.***	M	67	Acute myelogenous leukemia (terminal)	23	3,500	175,000	Hypocellular	23	2,000	3,000	—	Died 1½ yr. postoperatively	
89.	R. B. R.	M	39	Congenital hypoplastic anemia	—	—	—	—	—	—	—	—	Died 5 mo. after operation	
63.	E. A. M.	M	74	Idiopathic aplastic anemia & tuberculosis	22	5,100	65,000	Hypocellular	—	—	—	—	Died 2 wk. postoperatively	
64.	D. M.	F	24	Idiopathic aplastic anemia with toxic exposure	16	2,400	15,000	Normoblastic hyperplasia	40	6,400	5,000	—		Lost to follow up after 2 mo.

* Case No. 4 of Mohler and Leavell.[12]
** Case No. 1 of Mohler and Leavell.[12]
*** Case No. 25 of Mohler and Leavell.[12]
**** See text for details.

possible that the underlying primary disease might have been discovered. An additional patient (Case 83) might be similarly classified, although his bone marrow was suggestive of reticulum cell sarcoma. Case 84 had splenectomy for anemia and thrombocytopenia and was later shown to have Hemoglobin C disease; he died six years later of cardiac failure unrelated to his hematologic disorder. Case 85 had proven Letterer-Siwe's disease and underwent splenectomy because of a massive spleen which interfered with normal movement; there was associated anemia and thrombocytopenia. Case 86 developed a hemolytic component in the course of an unusual anemia which, since splenectomy, has been shown to be a familial iron loading disorder; he has subsequently died of a cause unrelated to this disorder. Case 87, with massive splenomegaly and thrombocytopenia, was shown to have Gaucher's disease on examination of the spleen. Case 88 underwent splenectomy in hope of improving his idiopathic erythrocytic hypoplasia. Case 92 had migratory polyarthralgias for seven years and skin ulcerations for six months prior to splenectomy. The spleen revealed pathological changes of periarteritis nodosa. She has been on steroids since splenectomy and has maintained normal blood counts. Case 93, an eight-year-old Negro girl with sickle cell anemia, splenomegaly, hemolysis and pancytopenia, has been reported in detail by Shotton, Crockett and Leavell.[13] Following splenectomy there was marked objective and subjective improvement as determined by a careful observation over a ten-year period.

Mortality Following Splenectomy. Each death occurring within the first six weeks after splenectomy has been discussed under the appropriate grouping. Among the 37 patients with hereditary spherocytosis and idiopathic thrombocytopenic purpura there was one death, giving an operative mortality rate of 2.7 per cent. Among the remaining 57 patients, four died within six

TABLE 6. *Congestive Splenomegaly with Hypersplenism*

Case	Patient	Sex	Age	Indication for Operation	Operative Procedure	Final Diagnosis	Before Splenectomy			After Splenectomy			Result	Follow up
							Hematocrit %	WBC /mm.³	Platelets/mm.³	Hematocrit %	WBC /mm.³	Platelets/mm.³		
65.	D. J. S.	F	36	Pancytopenia	Splenorenal shunt	Laennec's cirrhosis	34	3,400	27,000	39	12,000	94,000	Excellent	3 yr.
66.	C. J. M.	M	79	Pancytopenia	Splenectomy	Laennec's cirrhosis	24	4,300	40,000	37	9,600	—	Excellent	3 yr.
67.	C. G. B.	F	64	Leukopenia, thrombocytopenia	Splenectomy portacaval shunt	Laennec's cirrhosis	34	4,100	70,000	—	—	—	Postoperative death	
68.	M. T. P.	M	55	Pancytopenia penia	Splenectomy	Laennec's cirrhosis	30	1,200	26,000	—	—	—	Postoperative death due to hemorrhage	
69.	B. H.	M	55	Leukopenia, thrombocytopenia	Splenectomy	Laennec's cirrhosis	36	3,100	35,000	—	—	—		Lost to follow up
70.	J. P.	F	30	Pancytopenia	Splenectomy	Laennec's cirrhosis	28	3,200	74,000	—	—	—		Lost to follow up

TABLE 7. *Granulomatous Diseases*

Case	Patient	Sex	Age	Indication for Operation	Final Diagnosis	Before Splenectomy			After Splenectomy			Result	Follow up
						Hemato-crit %	WBC /mm.³	Plate-lets/mm.³	Hemato-crit %	WBC /mm.³	Plate-lets/mm.³		
71.	V. K.	F	58	Pancytopenia	Nonspecific granuloma	27	3,000	66,000	18	5,000	130,000	Moderate improvement	3 yr.
72.	D. H. C.	F	44	Splenomegaly	Sarcoid	37	4,000	178,000	43	11,000	200,000	Moderate improvement	2 yr.
73.	B. A. H.	F	20	Pancytopenia	Nonspecific granuloma	28	2,200	33,000	37	9,300	—	Moderate improvement	8 mo.
74.	J. H. B.	M	59	Pancytopenia	Histoplas-mosis	29	2,400	13,000	—	—	—	Death 5 days after operation	
75.	R. M. M.	F	3½	Thrombo-cytopenia	Fibrocaseous granuloma	—	—	10,000	—	—	30,000	Unchanged	2 yr.

TABLE 8. *Lymphomatous Diseases*

Case	Patient	Sex	Age	Indication for Operation	Final Diagnosis	Before Splenectomy			After Splenectomy			Result	Follow up
						Hemato-crit %	WBC /mm.³	Plate-lets/mm.³	Hemato-crit %	WBCs /mm.³	Plate-lets/mm.³		
76.	W. H. M.	M	51	Pancytopenia, splenomegaly	Lympho-sarcoma	29	5,900	58,000	43	9,400	136,000	Moderate improvement	1½ yr.
77.	S. G.	F	43	Thrombocyto-penia, anemia	Chronic lymphocytic leukemia	27	8,500	50,000	31	34,000	100,000	Unchanged	3 yr.
78.	A. J. P.	M	60	Thrombocyto-penia, anemia	Hodgkin's disease	30	4,300	55,000	25	9,100	70,000	Died 2 yr. after operation	
79.	N. C.	F	20	Hepatosplen-omegaly	Hodgkin's disease	11.4*	3,800	—	13.6*	16,000	—	Died 15 mo. after operation	
80.	J. L. F.	M	64	For diagnosis of left upper quadrant mass	Lympho-sarcoma	13.5*	4,900	—	—	—	—	Died 8 mo. after operation	
81.	J. S. T.	M	77	Thrombocyto-penia, anemia	Hodgkin's disease	22	—	5,000	34	—	50,000	Died 4 mo. after operation	
82.	J. H. M.	M	67	Pancytopenia	Hodgkin's Disease	31	1,400	57,000	—	—	—	Died 1 mo. after operation	

* Hemoglobin Gm. %.

TABLE 9. *Miscellaneous Hematological Conditions*

Case	Patient	Sex	Age	Indication for Operation	Final Diagnosis	Before Splenectomy			After Splenectomy			Result	Follow up
						Hemato-crit %	WBC /mm.³	Platelets/mm.³	Hemato-crit %	WBC /mm.³	Platelets/mm.³		
83.	C. H.	M	56	Pancytopenia	?	33	2,500	63,000	41	3,700	176,000	Great improvement	6 yr.
84.	F. B.	M	57	Thrombocytopenia, anemia	Hemoglobin C disease	30	—	48,000	36	—	235,000	Moderate improvement	Died 6 yr. after operation of an Unrelated disease
85.	S. W. S.	M	20 mo.	Hypersplenism massive spleen	Letterer-Siwe disease	31	—	40,000	43	—	100,000	Moderate improvement	1 yr.
86.	H. J. B.	M	19	Hemolytic component to anemia	Familial iron loading disorder	26	—	—	24	—	—	Unchanged	Died 6 yr. after operation of an Unrelated disease
87.	T. L. M.	M	16 mo.	Thrombocytopenia, diagnostic problem	Gaucher's disease	32	5,300	43,000	28	16,000	—	Unchanged	4 yr.
88.	D. C. M.	M	56	Diagnostic problem	Erythrocytic hypoplasia	23	6,000	450,000	20	10,000 2,900	570,000	Unchanged	1 yr.
90.	V. H. C.	F	51	Pancytopenia	Idiopathic hypersplenism	34	2,100	55,000	34	5,400	139,000	Unchanged	4 yr.
91.	F. C. C.	M	10	Pancytopenia	Idiopathic hypersplenism	19	2,000	27,000	—	—	—		Lost to follow up
92.	L. M. F.	F	48	Leukopenia, anemia	Periarteritis nodosa	27	2,700	—	42	8,200	—	Improved*	4 yr.
93.	H. C.**	F	8	Splenomegaly thrombocytopenia, anemia	Sickle cell anemia	3.2***	9,800	50,000	9***	—	—	Great improvement	10 yr.

* On Steroids.
** Previously reported by Shotten, Crockett and Leavell.[14]
*** Hemoglobin Gm. %.

weeks after splenectomy of causes judged due to the primary disorder; while there were five who died in the postoperative period as the result of splenectomy; thus, in this group the surgical mortality is 8.7 per cent.

Discussion

It is generally agreed that splenectomy is the treatment of choice in **hereditary spherocytosis.** Although spherocytes and increased fragility remain, anemia and jaundice almost invariably are relieved. Unless there is a contra-indication to operation, an established diagnosis of hereditary spherocytosis is sufficient reason for splenectomy. There are, however, those who would avoid, if possible, performing splenectomy during infancy, on the basis of a presumed increase in susceptibility of the splenectomized infant to infection.[9]

In those **hemolytic anemias other than hereditary spherocytosis** the response to splenectomy is unpredictable and the chance of a lasting remission is no better than fifty per cent. For this reason, it is a general practice to employ splenectomy in this group of hemolytic anemias only when there has been failure of response to treatment with the adrenocorticosteroids [10] or when there is selective splenic sequestration of Cr^{51} tagged erythrocytes.

Idiopathic Thormocytopenic Purpura. Subsequent to 1916, when the medical student, Kaznelson, persuaded his professor of surgery to perform the first splenectomy for thrombocytopenia purpura,[1] this operation has occupied a significant place in the management of this disorder. Modern methods of platelet transfusion and the introduction of the adrenocorticosteroids have all but eliminated the requirement for emergency splenectomy. Moreover, the employment of the latter agents has altered the selection of cases for splenectomy.

Although the unpredictable course of the disorder makes it difficult to evaluate various forms of treatment, it is interesting to note the effectiveness of splenectomy alone as reported by Doan, Bouroncle and Wiseman.[4] In 1960 these authors were able to report a good response without recurrence in 85 per cent of 167 patients with idiopathic thrombocytopenic purpura treated by splenectomy alone. On the basis of an extensive experience over a 28-year period, these authors conclude that splenectomy remains the treatment of choice for thrombocytopenic purpura, both primary and secondary, except in selected patients. Corticosteroids are reserved for children and young adults with thrombocytopenic purpura secondary to transitory infections, for those in whom operation is contraindicated, and for splenectomy failures.

At the University of Virginia we have approached the management of idiopathic thrombocytopenic purpura somewhat differently. When first seen these patients are started on Prednisone, 40 to 60 mg. daily*; those that do not respond to this therapy within six weeks, and those who have relapsed after the drug is discontinued, are treated by splenectomy. It is to be noted that on this program 60 per cent of those followed have had complete remission. Had splenectomy been resorted to initially, to the exclusion of other forms of therapy, undoubtedly it would have been used in some patients in whom either spontaneous or drug-induced remission might have occurred. Moreover, by employing corticosteroid therapy initially, it is possible that the more refractory cases remain and the results from splenectomy may appear poorer. In this connectin, it is of interest that when Leavell and Thorup [11] reviewed the experience at the University of Virginia, it was apparent that failure of hormonal therapy did not prejudice the results of splenectomy, nor did the failure to respond to splenectomy affect the future response to ACTH or adrenocorticosteroids.

* In the series there are a few exceptions in which Prednisone therapy varied from this schedule in some detail.

Myeloproliferative Disorders. Until recently the presence of myeloproliferative disease of the spleen was considered almost universally a contraindication to splenectomy. It was reasoned that in this disorder extramedullary blood formation occurred in the spleen and liver as a compensatory reaction, and that removal of the spleen eliminated an important site of blood formation. It was believed that splenectomy under these circumstances would be followed by harmful or even fatal consequences. Nonetheless, occasionally splenectomy had been done in myeloproliferative disease, and by 1953 Green, Conley, Ashburn and Peters[6] were able to collect 29 reported cases, five of which were their own. They use the term *agnogenic myeloid metaplasia* for this condition, and conclude that in no case did splenectomy have a deleterious effect; one patient showed hematologic improvement. Moreover, their review of the literature failed to confirm the belief that splenectomy leads to disastrous effects because of removal of a large blood-forming area; most of the reported cases showed no improvement, but there were occasionally patients, particularly those with severe thrombocytopenic or hemolytic anemia, who did derive benefit from splenectomy. It has not been our practice to employ splenectomy in those patients who could be managed adequately by other forms of treatment, such as corticosteroids, testosterone, busulfan or transfusions. However, when repeated hemorrhages, frequent infections, recurrent anemia, or the discomfort of splenomegaly led to invalidism, or when there is selective splenic sequestration of Cr^{51} tagged red blood cells, splenectomy has been employed.

Aplastic Anemia. There is considerable diversity of opinion relative to the employment and usefulness of splenectomy in aplastic or hypoplastic anemias. The ratonale for its use lies in the hope of stopping the production of auto-antibodies, improving bone marrow function and prolonging the survival of red cells when a hemolytic element is present.[12] Moore[8] believes it should be performed only if there is evidence of a hemolytic component to the anemia, or a response to corticosteroid therapy. Others would employ splenectomy when other forms of therapy have failed and still others believe it is of no value.

Our indications for splenectomy in aplastic anemia, in the moderately ill patient, has been splenomegaly with associated hyperhemolysis, and in the seriously ill patient, as a means of last resort when the need for transfusion has been almost continuous, or in either group when survival studies indicate increased destruction in the spleen.

During the period 1930 to 1956, Heaton, Crosby and Cohen[7] found 35 documented case histories of splenectomy for hypoplastic or aplastic anemia. Of these, 20 appeared to have been improved by splenectomy. To the reported cases these authors add 12 of their own; six were apparently benefited by operation; three were not; and three died.

Mohler and Leavell[12] in an analysis of 50 cases of aplastic anemia seen at the University of Virginia Medical Center between 1933 and 1956, reported the use of splenectomy in five; there was one remission, two improvements and two failures. These five cases are not in those collected from the literature by Heaton, Crosby and Cohen. Scott, Cartwright and Wintrobe[13] have employed splenectomy in 15 patients with aplastic anemia, five of whom showed substantial reduction in transfusion requirement following operation. More recently Duckett[5] has reported the results of splenectomy in 19 cases of aplastic and hypoplastic anemia. There were two excellent and four good results.

Hypersplenism is the term used to denote a syndrome characterized by: 1) splenomegaly; 2) anemia, leukopenia, throm-

bocytopenia, singly or in combination; 3) a marrow that has normal or increased cellularity; and 4) correction of the blood picture by splenectomy.

This syndrome occurs in a variety of disorders that are associated with splenomegaly. The most common of these may be grouped as follows:

1. Congestive splenomegaly
2. Chronic infection (especially tuberculosis, brucellosis, fungus, syphilis, malaria, bacterial endocarditis)
3. Diseases of the lymphoma group (especially lymphosarcoma, giant follicle lymphoma, Hodgkin's disease)
4. Other diseases of uncertain etiology (rheumatoid arthritis, collagen diseases, sarcoidosis)
5. Splenomegaly of undetermined cause (? idiopathic)

In nearly every case the diagnosis can be established before splenectomy, or at least at the time of the operation. However, in the occasional patient the cause of the splenomegaly remains obscure, even after careful histologic study of the spleen and other biopsy material. It is these patients who are classified, somewhat unsatisfactorily, as *idiopathic* or *primary.*

At present the mechanism responsible for the reduction of the circulating cellular elements in many patients with splenomegaly is not understood. The actual sequestration and destruction of the cells or platelets in the spleen have been considered the important factors by some authors.[3] The presence of a marrow inhibiting factor, elaborated in the spleen and transported in the plasma, also has been suggested.[2] The role of antibodies, particularly leukocyte antibodies, has not been clarified despite considerable study; autoimmune hemolytic anemia and iodiopathic thrombocytopenic purpura, syndromes in which the role of antibodies has been more firmly established, usually are not included in *hypersplenism.*

The decision regarding the advisability of splenectomy in this syndrome can be made only after careful consideration of the individual patient. The first objective is the recognition of the disease responsible for the splenomegaly by means of appropriate diagnostic procedures. In addition to a study of the peripheral blood and bone marrow, these may include radiographic study of the chest, esophagus and stomach, blood cultures, skin tests, agglutination tests, liver function tests, serum electrophoresis, and biopsy of the liver or available lymph nodes. Recognition of the primary disease is important because splenectomy relieves only one aspect of the underlying disorder and rarely effects a cure. If the underlying disease is one that is amenable to more definitive treatment, splenectomy may not be necessary because the hypersplenism syndrome may disappear after such therapy. When the nature and course of the underlying disease are such that an early fatal outcome can be predicted, splenectomy is rarely a justifiable procedure. If the nature of the underlying process cannot be diagnosed, or if it is identified as one for which no satisfactory therapy is available, splenectomy is indicated if the presence of anemia, neutropenia, or thrombocytopenia is disabling or hazardous to the patient. In such circumstances gratifying results occur often, but not invariably.

Susceptibility to Infection after Splenectomy. Recently there have appeared a number of reports concerning increased susceptibility of the splenectomized individual to subsequent infection; there are equally as many reports which refute this. Our observations in this regard have not been as complete as they would have been had we followed each patient from the time of splenectomy with this point in mind, however, from a retrospective standpoint, the only serious post splenectomy infections occurred in those individuals whose primary disorder was one predisposing to infection.

Summary

We have presented the experience of a university medical center with splenectomy for hematologic disorders. In some patients splenectomy was performed for well-established indications, namely, hereditary spherocytosis and idiopathic thrombocytopenic purpura, with the expectation and the achievement of excellent hematologic results and a 2.7 per cent mortality. In other patients, those with hemolytic anemia, aplastic anemia, myeloproliferative disorders and secondary hypersplenism, it was recognized that, at best, the outcome was problematical. While the over-all results in the latter groups are far from excellent, and this includes surgical mortality of 8.7 per cent, individual instances of significant improvement have been most rewarding.

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Discussion

Dr. S. W. Moore (New York): There are several points that I would like to mention. One, we have heard about finding the ruptured spleen when doing a thoracotomy. I woud like to call to your attention that sometimes it is very safe to do a thoracotomy and take out the spleen. One patient had two previous attempts at splenectomy, both unsuccessful; we opened the chest, spent four hours, and finally were able to remove his spleen; so it is very useful to have an additional approach.

Another patient with collagen disease had been on cortisone, developed fluid in the chest, and came in with all the symptoms and signs of blood and hemorrhage in the abdomen. We finally decided to explore this patient and to the chagrin of everyone, found a ruptured spleen as the result of aspiration of the chest.

Spontaneous rupture of the spleen, I think, is very doubtful, and if we look further, we will usually find that there is a history of trauma.

Abdominal exploration is very necessary. At times it does cause trouble. We have had a recent death following abdominal exploration in which the spleen was ruptured and not recognized, and I must admit that I have taken out the spleen twice fairly recently, because of a small tear while doing an exploration and trying to mobilize viscera.