RESULTS OF SPLENECTOMY IN SPLENIC ANÆMIA, HÆMOLYTIC JAUNDICE, AND HÆMORRHAGIC PURPURA*

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Splenectomy for certain types of anæmia and blood dyscrasia associated with disorders of the spleen is a modern surgical venture. Its development, in the absence of accurate knowledge of the function of the spleen in health and disease, has been attained entirely through empiric failures and successes. Although the beginning of an active interest in splenectomy may be said to date back only a quarter of a century, so far the operation has been employed many hundreds of times in a wide variety of diseases; therefore ample data, with regard to the operative results in certain of the more common diseases, have long been available to establish the procedure on a firm basis.

Notwithstanding the remarkable advances made in this branch of surgery, it is unfortunate that, today, many surgeons are unacquainted with these achievements. In consequence there are undoubtedly many cases of disease in which splenectomy is indicated, but which are not correctly diagnosed, nor the proper treatment undertaken. To substantiate this statement, it is only necessary to call to mind the prevailing view of the extremely hazardous nature of the operation, and the very common mistakes made both in diagnosis and in institution of treatment; often complications rather than diseases themselves are treated.

There are several reasons to account for the fact that knowledge of the results of splenectomy has not been more widely disseminated. As the diseases benefited by removal of the spleen occur comparatively rarely, relatively few surgeons have had sufficient personal experience on which to base definite convictions. In addition, published reports, the remaining source of information, have shown an exceedingly wide variation in results. For instance, the operative mortality has been reported as 10, 30, or 40 per cent., or even higher. Unless due consideration be given to the nature and details of these reports, their apparent contradictions would tend to create doubt and confusion. Reports of operative results based on data accumulated for many years, and collected from many hospitals, often do not reflect the true status of the operation, primarily because of the variable personal factors involved. This would seem to be especially true in surgery of the spleen, in which discrepancies in diagnosis and differences in care would necessarily affect adversely the record of operative results.

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It seems timely, therefore, to make a critical analysis of the results of splenectomy in the more common diseases, concerning which sufficient data are available to warrant drawing conclusions. For this purpose, a study was made of the records of all cases of splenic anæmia (including Banti's disease), hæmolytic jaundice, and purpura hæmorrhagica, in which splenectomy was performed at The Mayo Clinic between December 31, 1908, and January 1, 1931. The series comprised 326 cases in which splenectomy was performed, in 167 of which the reason for operation was splenic anæmia, in 118, hæmolytic jaundice, and in forty-one, purpura hæmorrhagica. The clinical diagnosis was made in each instance by Giffin and his associates.

Since this paper is restricted to presentation of the results of operation in these diseases, consideration of the physiology and pathologic changes relative to the spleen, the pathogenesis of the diseases, the details of operative technic, and the general indications for splenectomy in other disorders have been omitted. However, for purposes of clarity, the prominent clinical and hæmatologic features on which a diagnosis was based, are summarized briefly. Many of the data used in this study have been published in papers by W. J. Mayo, and by Giffin.

Splenic anæmia.—Osler defined splenic anæmia as: "Intoxication of unknown nature, characterized by great chronicity; primary progressive enlargement of the spleen which cannot be correlated with any known cause, anæmia of secondary type, with leucopenia, a marked tendency to hæmorrhage, particularly from the stomach (œsophagus), and in many cases a terminal state with cirrhosis of the liver and jaundice." It is the late stage of anæmia, that is, the stage in which there is secondary involvement of the liver, as manifested by evidences of portal obstruction and hepatic insufficiency, that today is commonly designated as Banti's disease. Strangely enough, in the presence of an enlarged spleen and associated anæmia, the diagnosis of this syndrome rests on the absence of any known etiology, and it is little wonder that many observers question whether splenic anæmia should be considered as a clinical entity, for if the cause of the splenomegaly is identified, the diagnosis of splenic anæmia is forthwith excluded.

The course of the disease in cases in which operation has not been done is progressive, without any tendency toward abatement or spontaneous recovery, and the patient ultimately succumbs, usually within a few years, as a result of recurrent excessive hæmorrhages or hepatic insufficiency. The first manifestation of this syndrome is often discovered by the patient, or in a routine examination, as enlargement of the spleen, and in some instances the organ attains considerable dimensions without other recognizable evidence of the disease. Commonly, however, there are alterations in the blood when the patient presents himself for examination. These consist of secondary anæmia of varying degrees, and extreme poikilocytosis; leucopenia with lymphocytosis is not uncommonly present, but the leucocytes may be normal in number or even slightly increased.

One or more episodes of copious hæmorrhage from the gastro-intestinal

tract, usually from œsophageal varices, occurred before operation in ninety-eight cases (59 per cent.) of this series. These are more common in the late than in the early stages of the disease, but, not uncommonly, sudden severe hæmorrhage from the gastro-intestinal tract is the patient's first warning that he is sick. Thirteen patients in this group with hæmorrhagic splenic anæmia had been treated for peptic ulcer. About a year ago during the course of a röntgenologic examination of the stomach of a patient suffering from splenic anæmia, unusual shadows were seen that suggested hugely dilated œsophageal varices; later this impression was confirmed by means of the œsophagoscope. Since then, röntgenologic examination of the œsophagus has been adopted as a routine procedure in all cases of splenic anæmia. Subsequently, similar evidence of œsophageal varices has been discovered on röntgenologic examination in other cases of splenic anæmia, in one of which clinical evidence of a hepatic condition was lacking. Likewise, a test of hepatic function, based on retention of bromsulphthalein, often indicates definite injury to the liver that otherwise would not have been suspected from clinical examination.

Of the 167 patients with splenic anæmia and Banti's syndrome who were subjected to splenectomy, sixteen died in the hospital, an operative mortality of 9.6 per cent. The sixteen deaths included one by suicide. The causes of death of the remaining fifteen patients cannot be accurately classified, for in some instances the pathologist was unable definitely to distinguish from several possible contributory conditions the immediate cause. Broadly, however, it may be said that pulmonary infections, including pneumonia, pleurisy with septicemia and hæmorrhagic œdema of the lungs accounted for four deaths, pulmonary embolism for two, portal thrombosis for three, hepatic insufficiency for four, and subdiaphragmatic abscess and peritonitis each for one death.

Of the 151 patients who survived the immediate effects of the operation, eighty are known to be living, three of them eighteen years after operation. Two are still living, fifteen and seventeen years after operation, and fifteen have lived from ten to fifteen years. Ten of the sixty-eight patients who recovered from the operation but who died later lived for more than nine years, one for eighteen, one for thirteen, and three for twelve years. Although the causes of many of the subsequent deaths were not attributable to the disease itself, it is of interest that more than a third were directly attributable to hæmorrhage.

The number of patients in the series is too small to permit accurate statistics regarding the influence of sex on the operative results, but records of the deaths in hospital suggest that the operation is more hazardous if the patients are females. Seven of the ninety-seven male patients, and nine of the seventy female patients died in the hospital. However, there were no appreciable differences in the end-results as regards the sexes. Age (Table 1) played a more definite part in the immediate as well as in the late results. If the patients are divided into two groups, it will be seen that the operative

mortality of those aged less than forty years was only half that of patients aged more than forty years; about 53 per cent. of patients aged less than forty years are still living, whereas only 40 per cent. of those who are older are alive.

Owing to the difficulty of accurately estimating the functional efficiency of the liver, it is not possible to determine with exactness the influence which secondary hepatic injury has had on the operative results. Except in the more advanced cases, in which evidences of cirrhosis and portal obstruction are obvious, it is not always possible from clinical data to judge accurately the degree of hepatic injury. Likewise, in some cases in which gross changes characteristic of advanced cirrhosis are lacking, the surgeon is often unable, from observation of the size, color, and consistence of the organ, to estimate

Table 1

Splenectomy for splenic anemia

Age by decades	Cases	Hospital mortality	Subsequent deaths	Living	Well	Fair	Poor	Not traced
0 - 9	11		5	5	4	1		1
10 - 19	19	2	7	10	8	2		
20 - 29	42	2	15	24	21	2	1	1
30 - 39	40	4	16	20	13	4	3	
40 - 49	30	3	14	12	10	1	1	1
50 - 59	20	4	8	8	7		1	
60 - 69	5	1	3	1		1		
Total	167	16	68	80	63	11	6	3

the degree of injury. In livers adjudged on gross examination to be only slightly enlarged or congested, microscopic examination of specimens removed for diagnostic purposes has demonstrated repeatedly the presence of marked hepatitis or degeneration of the parenchyma. Accordingly, in the appraisal of hepatic injury the surgeon is more likely to underestimate than to overestimate the seriousness of the condition, and unless biopsy is obtained, this potential error should be taken into consideration in the evaluation of the influence of hepatic disease on operative result. Pre-operative estimations of hepatic function, based on retention of bromsulphthalein, have been carried out in only thirty-two cases of splenic anæmia. It may be significant that the patient in this small series who died, belonged to a group of fifteen whose hepatic functional activity was believed to be impaired. As these tests have been employed only in recent years, sufficient time has not elapsed to permit a determination of their value in prognosis with regard to later results.

In Table 2 (see chart) the results of the operation have been tabulated according to the gross condition of the liver as observed by the surgeon at operation. If the cases in which the condition of the liver was not mentioned are grouped with those in which the hepatic condition was classified as normal, and all others are considered as cases in which there was more or less hepatic injury, and the results of the two groups compared, it will be seen that the secondary affection of the liver had an appreciable effect on the early results, and apparently only a slight influence on later results. The

Table 2

Splenectomy for splenic anemia

Condition of liver as noted by surgeon at operation

Condition	Cases	Hospital mortality	Subsequent deaths	Living	Well	Fair	Poor	Not traced
Hepatitis	4		2	2		2		
Cirrhotic	62	6	26	28	21	4	3	2
Enlarged	15	3	7	5	3	1	1	
Congested	2	1	1					
Enlarged and congested	1	1						
Thick, not large	1			1	1			
Adherent	6		3	3	2		1	
Atrophic	6		1	5	4	1		
Hard	2		2					
Normal	42	3	14	24	23	1		1
Not mentioned	26	2	12	12	9	2	1	
Total	167	16	68	80	63	11	6	3

operative mortality was 7 per cent. in the former group, as compared with 11 per cent. in the latter, whereas the proportion of patients who are now living is 57 per cent. in the former, and 50 per cent. in the latter.

The sixty-two cases in which cirrhosis of the liver was present at operation form an interesting group. Of the forty-six patients who survived the operation, twenty-eight (50 per cent.) are alive. This not only furnishes proof of the wisdom of accepting for operation patients with advanced Banti's disease, but indicates the remarkable power of the liver to regenerate following removal of the diseased spleen. As pointed out by W. J. Mayo,

removal of the spleen in this disease greatly lightens the load which has been thrown on the liver by reducing, by at least 20 per cent. the volume of blood entering the portal circulation, by removing possible toxic substances originating in the spleen, and by producing adhesions for the establishment of collateral circulation.

In spite of the most gratifying benefit derived from the operation, even in many of the advanced cases, as evidenced by the improvement of the blood and of general health, and by prolongation of life, the recurrence of gastro-intestinal hæmorrhages in a large group of these cases presents a discouraging problem. In approximately 50 per cent. of the ninety-eight cases in which there was gastro-intestinal hæmorrhage before operation, there has been one hæmorrhage or more subsequent to splenectomy. Since the hæmorrhage commonly results from rupture of greatly dilated varices situated beneath the mucous membrane of the lower end of the œsophagus, it has been suggested that this complication might possibly be minimized by tying the coronary vein, with the view of reducing the enormous turgescence by breaking communication with the portal circulation. In the hope of promoting additional collateral circulation, which is, in fact, nature's means of combating portal obstruction, it would seem that some form of omentopexy is indicated in selected cases as a measure supplementary to splenectomy. Because inclusion of a segment of the omentum in closure of the wound jeopardizes healing, I prefer to incorporate it in the abdominal wall, lateral to the incision for laparotomy. After separation of the several layers of the abdominal wall for 3 centimetres from the edge of the wound, a small incision is made through the peritoneum and posterior sheath of the rectus abdominis muscle, and a segment of omentum 14 to 20 centimetres is then drawn up through this opening and sutured. Similar incisions are made in the muscle and anterior sheath of the rectus abdominis, at successive levels, each lower than the preceding one, 2.5 centimetres or more apart, and the omentum is drawn through these; the distal 5 to 8 centimetres is then buried beneath the skin.

By bringing the omentum out in a steplike manner, conditions are established for the formation of new blood channels in each layer of the abdominal wall, and on account of the oblique course of the openings, the chances of troublesome herniation are minimized. (Fig. 1.)

One or both of these procedures, ligation of the coronary vein and omentopexy, have been employed in conjunction with splenectomy in thirteen of the cases seen more recently, but there has not yet been sufficient time to permit estimation of their value in the prevention of recurrent hæmorrhages.

Hæmolytic jaundice.—This condition may be defined as hæmolytic disease affecting primarily the spleen and secondarily the liver, characterized by varying degrees of anæmia, by acholuric jaundice, that is, jaundice with unaltered stools and urine, splenomegaly, microcytosis, and increased fragility with active regeneration of the erythrocytes. Two types of the disease have been described, the congenital and the acquired, distinguished chiefly

by differences in the age of onset and the severity of the course of the disease. However, Giffin seriously questions whether many of the cases of the acquired type reported in the literature, should, in the absence of characteristic changes in the blood, be rightfully included as cases of hæmolytic jaundice. Regardless of the age at which the prominent features of the disease become manifest, he believes that all the cases of the series reported herewith were probably fundamentally congenital in origin.

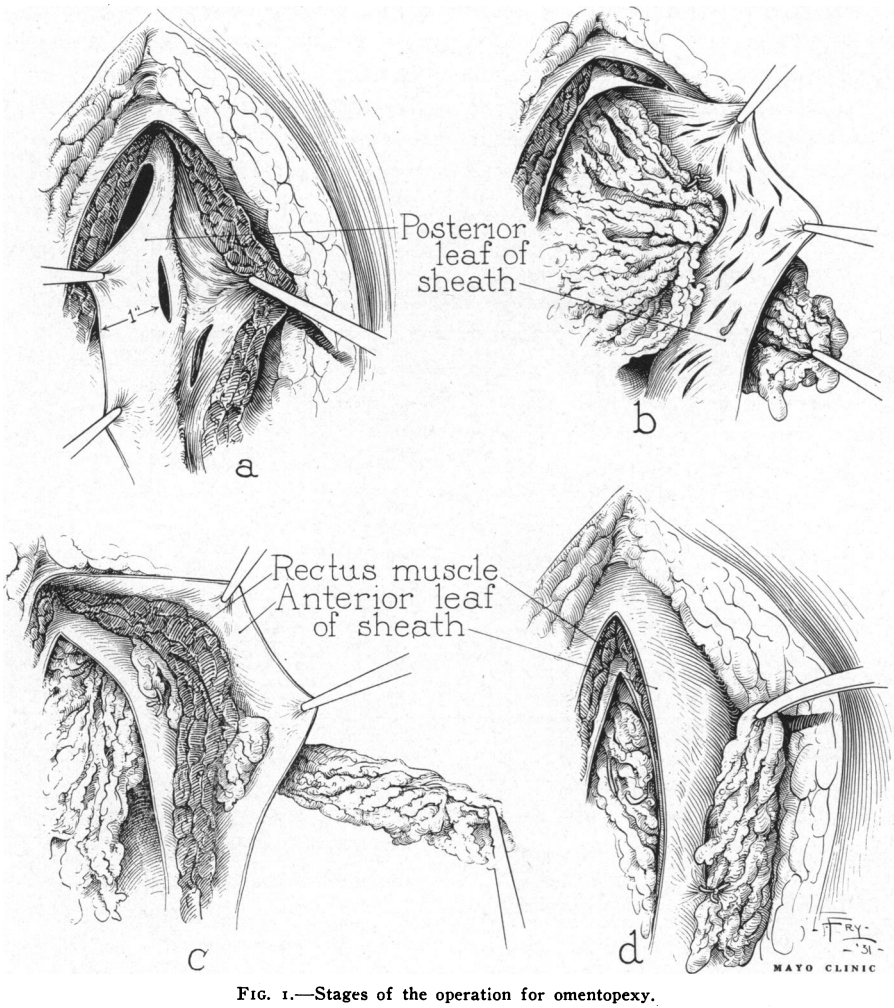

FIG. 1.—Stages of the operation for omentopexy.

Between June 30, 1911, and January 1, 1931, 118 patients with hæmolytic jaundice were subjected to splenectomy at The Mayo Clinic (Table 3). Four of the patients died in the hospital (3.4 per cent.). There was considerable variation in the course of the disease. Among children, and adolescent patients, it was for the most part continuously mild and chronic; the health of the patient apparently was little affected. In other cases the chronic course

was interrupted by one or more attacks of "crisis," characterized by malaise, abdominal pain, fever, increase in size of the spleen, deepening of the jaundice, and increase in anæmia. Not uncommonly, the crisis is mistaken for biliary colic, and operation is advised. Conclusive evidence of disease of the gall-bladder, with and without stones, occurred as a secondary complication in eighty-one cases (68.6 per cent. of the series) and in twenty-three of these, operations on the biliary tract had been performed elsewhere, presumably without knowledge of the presence of the primary disease. In none of these cases were gall-stones found in the common bile-duct, although in several cases a direct van den Bergh reaction was obtained.

Operative data were suggestive of secondary affections of the liver in fifty-five cases. Cirrhosis of the liver was noted by the surgeon in seven cases, and in six cases ascites was found, but the condition of the liver was

Table 3

Splenectomy for hemolytic jaundice

Age by decades	Cases	Hospital mortality	Subsequent deaths	Living	Well	Fair	Poor
0 – 9	21		2	19	16	3	
10 – 19	20		2	17	13	4	
20 – 29	38	2	2	32	28	2	2
30 – 39	24	1	4	18	15	1	2
40 – 49	11		1	9	8	1	
50 – 59	4	1		3	2	1	
Total	118	4	11	98	82	12	4

not mentioned. In the remaining thirty-two cases, the liver was described as enlarged, congested, hard, or adherent.

On comparing the results of the operation in these cases with the results in cases in which the liver was normal or was presumed to be normal, it would seem that the secondary affection of the liver exerted a decisive influence. The operative mortality was 5.4 per cent. in the former group, as compared to 1.6 per cent. in the latter, whereas the proportion of patients who survived the operation and who are living, is 80 per cent. in the former group, and 90 per cent. in the latter.

Evidence of the benefits of splenectomy usually becomes apparent within five or eight days after the operation; the jaundice then begins to fade and it disappears completely within two or three weeks. In many instances the patient is now free of jaundice for the first time in his life. Rapid and progressive improvement of the anæmia is also commonly noted before the patient is dismissed from the hospital. However, certain of the most char-

acteristic changes in the blood, such as microcytosis and increased fragility of erythrocytes, usually do not disappear after removal of the spleen.

The late results are equally gratifying. Approximately 86 per cent. of the patients who recovered from the operation are living, and 83 per cent. of these are in good health. Of the eleven patients who died subsequent to recovery from splenectomy, the cause of death of six was not attributable to the effect of the operation or the disease. The remaining four died of conditions probably secondary to the hæmolytic jaundice, such as cirrhosis of the liver, gastro-intestinal hæmorrhage, and severe anæmia.

In view of the low operative hazard, and the exceedingly satisfactory results of surgical procedures, and considering the high incidence of hepatic and biliary complications in the untreated cases, I believe that splenectomy should be advised as the safest method of treatment in all cases of hæmolytic

Table 4

Splenectomy for hemorrhagic purpura

Age by decades	Cases	Hospital mortality	Living	Well	Fair	Poor
0 - 9	7		7	6		1
10 - 19	12		12	11	1	
20 - 29	14		14	13	1	
30 - 39	5	1	4	4		
40 - 49	2		2	2		
50 - 59	1	1				
Total	41	2	39	36	2	1

jaundice; certainly in the severe cases and in those in which there is a history of recurrent crisis.

Hæmorrhagic purpura.—From March 7, 1923, to January 1, 1931, splenectomy was performed for hæmorrhagic purpura in forty-one cases, with two deaths (Table 4).

Hæmorrhagic purpura is an idiopathic hæmorrhagic disease, characterized by hæmorrhage from the mucous membranes, petechiæ, varying degrees of secondary anæmia, diminution in the number of blood platelets, and usually slight enlargement of the spleen. It occurs in two forms, the acute and the chronic relapsing. It is essentially a disease of early life, although occasionally patients past middle life are affected. In this series only three patients were aged forty years or more. The incidence was twice as great in females as in males. Crops of petechiæ and hæmorrhages from the mucous membranes were often the only prominent clinical features of the disease. The bleeding varied in severity from slight oozing usually from the gums,

nose and uterus, to intractable hæmorrhages. One patient died as a result of cerebral bleeding.

The typical changes in the blood in these cases were: (1) Reduction in the number of platelets; (2) prolonged bleeding time; (3) delayed retractility of the clot; (4) normal coagulation time, and (5) secondary anæmia with evidence of the normal regeneration of the erythrocytes. The capillary resistance test, indicating abnormal permeability of the capillaries, was positive in all cases in which it was employed.

Since the principal indication for splenectomy in hæmorrhagic purpura is a definite diagnosis, it is extremely important to distinguish this disease from others in which hæmorrhagic tendencies are common, notably, aplastic anæmia, hæmophilia, and acute leucemia. This usually can be readily accomplished by correlating the results of detailed examination of the blood with the clinical history. However, the diagnosis may at times be extremely difficult, and failure of an accurate diagnosis undoubtedly accounts for many of the poor results reported in the literature.

In but few diseases in which symptoms are so alarming are the beneficial results of operation so dramatic as in hæmorrhagic purpura treated by splenectomy. It occasionally happens that the patient is bleeding at the time of operation, and sometimes the hæmorrhage ceases before the patient is returned to his room.

An appreciable rise in the number of the blood platelets has been noted within twenty-four hours after removal of the spleen, and often by the third day the platelet count is within normal range. The thirty-nine patients who survived the operation are alive, and all but three are in good health. Giffin observed, in some cases, mild recurrence of hæmorrhage, which ceased following elimination of infected tonsils or teeth.

CONCLUSIONS

From these data it is evident that, contrary to the prevalent view of the hazardous nature of splenectomy, the operative results (6.7 per cent.) compare favorably with those of other major abdominal operations, and in spite of the relatively common mistakes made in diagnosis, the conditions associated with disorders of the spleen and amenable to splenectomy can readily be identified, provided complete data concerning the blood are correlated with the clinical history.

Since the operative results in cases of splenic anæmia are largely contingent on the presence of secondary affections of the liver and portal obstruction, the need for early diagnosis and operation is apparent. Enlarged spleens, in the absence of definite etiology, should be considered as instances of the splenomegaly of potential splenic anæmia, and operation should be advised. However, clinical evidence of the presence of hepatic injury should not in itself be considered a contra-indication to splenectomy, since many patients in this group lived active lives for many years after removal of the

spleen. The relative frequency of recurrent hæmorrhages in these cases indicates the need for additional effort toward their prevention, such as ligation of the coronary vein and omentopexy.

In view of the high percentage of secondary affection of the liver, the small operative hazard, and the extremely favorable late results, splenectomy would seem to be the safest procedure in all cases of hæmolytic jaundice.

Splenectomy for hæmorrhagic purpura is a comparatively safe procedure, and the benefits are lasting. In the severe cases, delay of operation is fraught with danger.

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