INDICATIONS AND RESULTS OF SPLENECTOMY*

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IN SPITE OF THE FACT that much progress has been made in the diagnosis and treatment of splenic disease during the past few decades, there is still considerable controversy in this subject, particularly concerning the indications for splenectomy. Thrombocytopenic purpura illustrates this point well, since in many instances, the disease is of the secondary (symptomatic) type in which splenectomy is rarely effectual.

FUNCTIONS OF THE SPLEEN

The functions of the spleen are but incompletely elucidated, but a knowledge of its function is essential in considering indications and contraindications of splenectomy. More is known of the adverse physiologic effects of a diseased spleen on the organism than of the functions of the normal spleen.

The removal of the normal spleen apparently does not have any detrimental consequences on the general well-being of the patient. Certain of its normal functions which it shares with other hemopoietic organs can be quickly taken over after extirpation of the spleen. On the other hand, the spleen in certain pathologic states may develop unusual importance and even become injurious to life.

Normal Functions of the Spleen. The spleen contains the largest collection of lymphoid tissue in the body and the bulk of the reticulo-endothelial cells. It is intimately concerned *with red blood cell destruction* (almost one trillion per day) and potentially with *blood formation,* although the physiologic mechanism involved in these splenic functions is not known. In *fetal life,* the spleen is active in the *formation of all types of blood cells* and can revert to this function upon demand at any period of life. In the adult this activity is limited to the *production of lymphocytes and monocytes.* The spleen actively participates in the *elimination of erythrocytes* and the products of their disintegration, together with bacteria and other foreign matter. It is interesting to note that this normal process of red blood cell destruction is greatly increased in certain pathologic conditions. In some unknown way the spleen renders *circulating erythrocytes more fragile.* By the reticulo-endothelium of the spleen the hemoglobin from worn-out erythrocytes is converted into bilirubin for passage to the liver.

Much of the iron in the body is stored in the spleen, where it is available for

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the elaboration of hemoglobin and the formation of new red blood cells. The spleen, by virtue of its spongy network of pulp elements, serves as a controllable blood reservoir, thus aiding the circulation when demand for blood is increased.

The spleen exerts an *inhibitory action on the hemopoietic function of the bone marrow,* as evidenced by the almost constant occurrence of thrombocytosis and leukocytosis following splenectomy. Other probable functions of the spleen are related to immunity, filtration of bacteria from the blood stream, digestion, metabolism and tumor formation.

Abnormal Functions of the Spleen. In reality, the abnormal functions are much more important to the clinician than the normal functions. Most of these abnormal functions are related to overactivity of one or more of the normal functions, thus giving rise to the term *hypersplenism.* The functions most often becoming abnormal or overactive are the inhibiting effect on the bone marrow and the increase in fragility of the red blood cells. If the inhibition on the bone marrow affects platelet formation (which probably is a failure of maturation of megakaryocytes to platelets, secondary to some chemical product formed abnormally by the spleen), thrombocytopenic purpura is produced. In hemolytic anemia the fragility of the erythrocytes, particularly the spherocyte, is increased, thus giving rise to sufficient erythrocytic destruction to produce anemia and jaundice, the latter from increased formation of bilirubin from the hemoglobin of destroyed red cells.

If the bone marrow inhibition is limited to formation of neutrophiles (*i.e.* granulocytic maturation), the disease is known as splenic neutropenia.

Various combinations of the above abnormalities are encountered. When all three are present the disease is designated as panhematocytopenia. In Banti's disease, and Felty's disease the inhibition of granulocytic maturation is also present, although in these diseases other abnormal features, as described later, are encountered.

The cellular elements of the blood may be formed in excess by the spleen. When the white cells are involved, one of the types of leukemia will result.

Effects of Removal of the Spleen. Removal of the spleen normally results in certain changes in the cellular elements of the blood or changes in the physiology. For example, leukocytosis and thrombocytosis regularly follow splenectomy. These changes reach a peak in 6 to 14 days and then slowly revert to normal. There is also a temporary slight increase in the erythrocyte count. The platelets may increase from a normal figure varying between 200,000 and 400,000 to 1,500,000. If the increase approaches the last figure named, it is desirable to give an anticoagulant such as heparin (Norcross[1]), particularly if the splenectomy has been performed for Banti's disease, because thrombosis (venous) and emboli (pulmonic) are so apt to develop. There is no greater tendency for an increase in the platelet count in Banti's disease than any other disease, but the stasis of blood in the portal vein and remnant of the splenic vein makes thrombosis at one of these sites more likely. The effects of splenectomy on bone marrow constituents have been described by Limarzi and associates.[2]

CO-OPERATION BETWEEN THE SURGEON AND THE HEMATOLOGIST

It is highly essential that close co-operation between the surgeon and the hematologist be maintained with every patient upon whom splenectomy is contemplated, particularly if indications are not definite. As a matter of fact, indications can rarely be classified as positive unless the results of a sternal puncture are known. The necessity of skill in the interpretation of bone marrow smears is the important factor demanding co-operation between the two clinicians mentioned. The technic of sternal puncture and interpretation of smears has been described elsewhere by Limarzi and associates.[3]

INDICATIONS FOR SPLENECTOMY

1. *Hemolytic Jaundice.* There are two types of hemolytic jaundice, namely congenital (familial) and acquired. Because results of splenectomy in the acquired type are so unsatisfactory, it is essential to differentiate between these two conditions. In the *congenital type* several members of a family may be affected, and the condition may be traced back through several generations. In the average case there is little interference with the well-being of the patient except for the marked yellow coloration of the skin and sclera and a slight anemia. Symptoms are occasionally not noted until adult life.

Splenomegaly, jaundice, anemia, microspherocytosis and increased fragility of the red cells in hypotonic salt solution are the prominent manifestations of congenital familial jaundice; reticulocytosis and increased urobilinogenuria are usually noted. The spleen is usually greatly enlarged and may be ten times larger than normal. One-half to two-thirds of the patients have gallstones (Pemberton[4]). The tendency of the spleen to filter out and destroy the spherocytes (consistently present in the disease) is responsible for the jaundice and splenomegaly (Haden[5]). The bone marrow reveals hyperplasia of the myeloid, erythyroid and megakarocytic elements, although in this disease the marrow findings cannot be considered diagnostic. The increase in bone marrow activity results in an increase of nucleated red cells (especially reticulated red cells) up to 10 per cent in the blood.

The manifestations of *acquired hemolytic jaundice* are very similar to those of the congenital type as described above. Acquired hemolytic anemia may result from circulating hemolysins such as may follow the repeated transfusion of an Rh negative patient with Rh positive blood or the activation of a specific hemolysin in some syphilitic persons by exposure to cold, severe burns, bacterial infections (especially those due to anaerobic organisms) or snake venom. Lederer's anemia is an atypical (acquired) type of acute hemolytic anemia secondary to an infectious process. It has been found most commonly following respiratory infections among children. There may be a palpable spleen, spherical microcytosis and increased fragility. Lederer's anemia is corrected by transfusions of blood. Recovery is complete and the condition does not recur. Parasitic infections such as malaria, poisons such as lead or phenylhydrazine and sensitivity to drugs or plants are other etiologic factors which must be considered in the diagnosis. It must be remembered that hemo-

lytic anemia may be a complicating feature of many diseases in which splenomegaly may or may not be a characteristic finding, such as Hodgkin's disease, leukemia, myeloid metaplasia of the spleen (agnogenic myeloid metaplasia of the spleen), lymphosarcoma, carcinomatosis, severe liver damage, dermoid cyst of the ovary, *etc.* Some of these conditions may be associated with a spherocytic type of anemia and increased fragility. It is of importance that the hemolytic process sometimes disappears following treatment of the associated disease; for example, by the removal of a dermoid cyst. Not infrequently (but in less than 50 per cent of cases) splenectomy will effect a cure in acquired hemolytic anemia, but without affecting the underlying primary condition, such as the leukemia, Hodgkin's disease, *etc.*

In 35 cases of hemolytic jaundice studied by Watson,[6] 20 were of the microcytic type (familial or congenital) and 15 of the macrocytic (secondary or acquired). In only two of the latter group was there increased fragility of the red cells in hypertonic salt solution. In this group of 15 with secondary jaundice, eight were associated with liver disease, three with Hodgkin's disease, two with leukemia, one with hyperthyroidism and one with chronic bleeding into an ovarian cyst.

In hemolytic anemia, transfusions commonly produce severe reactions. This complication gives rise to a serious problem in the treatment of the disease, particularly when an acute hemolytic crisis develops. However, it is now fairly universally agreed to submit patients with the congenital type of hemolytic jaundice to immediate splenectomy if crisis is present; transfusions should be started only at the end of the operation, after the splenic pedicle has been ligated.

Since results are so consistently good and the operative mortality rate so low in the congenital type, this disease represents one in which indications for splenectomy are perhaps stronger than in any other disease. This is particularly true if symptoms, especially anemia, are manifested in childhood, since normal growth and development may be retarded.

2. *Thrombocytopenic Purpura.* In a consideration as to the indications for splenectomy in purpura it is essential to distinguish between primary (Werlhof's) and secondary or symptomatic purpura, since splenectomy is of little or no value in the latter condition which may be secondary to drugs, leukemia, aplastic anemia, radiation (roentgen and radium), tumors, infections, *etc.*

Classical manifestations are prolonged bleeding time, normal coagulation, no clot retraction, low platelet count, anemia, ecchymosis, petechiae and bleeding from mucous membranes or body orifices. The anemia is directly related to the loss of blood and gives rise to such symptoms as weakness, malaise and loss of weight. The tourniquet test (blood pressure cuff on arm at diastolic pressure for five minutes) is positive. Details of differential diagnosis and bone marrow studies have been discussed elsewhere (L. R. L.[7]). In essential (primary) thrombocytopenic purpura the spleen is only slightly enlarged. Marked enlargement of the spleen speaks against primary thrombocytopenic purpura.

Bone marrow examination is diagnostic, revealing a marked increase in the number of immature megakaryocytes without platelet production, due presum-

ably to an inhibiting effect of the spleen (hypersplenism) on their maturity and release from the bone marrow into the blood stream. In fact, the number of megakaryocytes in the bone marrow is such a reliable indication of true thrombocytopenic purpura that it may be used as an index of prognosis following splenectomy.

The disease has numerous recurring cycles and is rarely seen under the age of 10 or after the age of 40. Hemorrhage (from the uterus, gums, nasal septum, *etc.*) may be severe and in fact is not uncommonly fatal. The authors are convinced that severe hemorrhage is a strong indication for immediate operation and not a contraindication. Without question the high operative mortality rate noted in such cases in previous years was related to the failure to have enough blood available at the time of operation or the failure to give it. As many as four to six pints of blood may be necessary before the operation is started and as many more during and shortly after operation. Rapid transfusion (of the intra-arterial type) may be indicated when bleeding has progressed to the shock level.

The disease responds so well to splenectomy, and the danger of severe hemorrhage is so great and unpredictable, that some authorities[8] advise splenectomy in practically all cases, once a definite diagnosis of thrombocytopenic purpura is made.

3. *Banti's Disease.* Symptoms vary considerably in this disease, which frequently is difficult to differentiate from cirrhosis of the liver and other diseases of the liver and spleen. The disease has been designated as congestive splenomegaly by Rousselot[9] because of the portal hypertension produced by obstruction of portal blood in the liver or vein itself.

Important manifestations are splenomegaly, anemia and leukopenia; jaundice and ascites developed relatively late. Fibrosis is present in the spleen and liver, but hepatic cirrhosis is not as pronounced as in the classical atrophic cirrhosis. Adhesions between the spleen and adjacent structures are more dense than in any other disease with splenomegaly. These adhesions are usually vascular; the vessels are venous channels shunting blood from the portal to the systemic circulation. In 43 cases studied by Borg and Dulin,[10] 39 per cent had a history of hematemesis.

Bone marrow findings are variable, depending largely upon the stage of the disease. In the earliest stage the bone marrow shows a myeloid hyperplasia (maturation arrest) and there is a moderate anemia and leukopenia in the peripheral blood. In the last stage of the disease, in which cirrhosis of the liver has developed, the marrow reveals a marked erythroid immaturity as well as a maturation arrest of the myeloid tissue and an increase in the number of megakaryocytes. In a study of 21 cases Limarzi and associates[3] noted that the anemia was normocytic in 16, microcytic in three and macrocytic in two. The platelet count was low in six of the 21 cases. The icterus index was elevated in about half.

Opinions vary considerably as to whether or not splenectomy is indicated in this disease. The present authors agree with many authors that splenectomy

may have curative but more often only remedial effects on the disease in early cases. Since hepatic insufficiency exists, as will usually be revealed by hepatic function tests, extensive preparative treatment consisting of transfusions as indicated, high carbohydrate and high protein diet and vitamin supplementation should be instituted before operation is performed.

In the advanced cases we are convinced that the operative mortality rate is so high (5 of 13 in our series) that it overweighs by a large margin any benefit produced by splenectomy. As a matter of fact, it is reasonable to expect that splenectomy would actually be deleterious when vascular adhesions between the spleen and abdominal wall exist, since removal of the spleen would destroy venous channels which carry blood from the engorged portal system to the systemic. We are of the opinion that ligation of the splenic artery, with preservation of the vascular adhesions, would diminish the pressure in the portal system, and portal blood would thus have a better opportunity of gaining access to the systemic circulation. Ligation of the splenic artery is not designed to take the place of splenorenal or portacaval shunt when either of these operations is indicated.

4. *Thrombosis or Anomalous Obstruction of the Splenic Vein.* There is controversy as to whether or not this condition should be classified as a separate entity since many observers believe that a large percentage of patients with Banti's disease have some type of obstruction of the portal or perhaps the splenic vein as the etiologic factor. They remark that in the early stages of Banti's disease, as in this condition, the liver shows no change. We have no final opinion as to whether this condition should or should not be included in Banti's disease, but have been unable to produce an hepatic cirrhosis of the Banti's type experimentally[12] by various types of obstruction of the portal and splenic veins; we are therefore inclined to classify this lesion separate from Banti's disease. We have identified five cases in our series as thrombosis or obstruction of the splenic vein, none of which revealed any fibrosis of the liver. However, our impressions are confused by the fact that an additional patient with a liver of normal appearance, and a large spleen at the time of operation, died 18 months after splenectomy with a large liver (without confirmation of autopsy). We classified this patient in the Banti's group, primarily because of the fatal outcome and the unconfirmed report of an enlarged and diseased liver obtained from the attending physician. We are strongly of the opinion that splenectomy in the early stages of splenic vein obstruction should be curative, but equally convinced that splenectomy in early Banti's disease will by no means be curative in all cases.

The manifestations of chronic obstruction of the splenic vein are similar to the manifestations of early Banti's disease, namely splenomegaly with slight and varying degrees of anemia, leukopenia and thrombopenia. Hemorrhage from esophageal varices is common; it was present in all five cases of our series. In these cases with bleeding and many others, roentgen-ray examination of the esophagus with barium will reveal varices. Jaundice was not present in any of our cases. Bone marrow findings are similar to those of early Banti's disease.

In three of our five cases we were fairly certain that the splenic vein was absent or completely obstructed, since no sizable vein could be found even at the hilus. However, as has been emphasized by Whipple,[13] the presence of obstruction, or its location, can not be accurately demonstrated at operation in more than half the cases unless injection of diodrast into portal tributaries is carried out with the roentgenogram. As stated previously, we believe that splenectomy will be curative in all cases when performed reasonably early in the disease. We are likewise of the opinion that most of the patients with so-called early Banti's disease cured by splenectomy are patients with obstruction of the splenic vein.

5. *Felty's Disease.* There is likewise controversy as to whether or not this syndrome as described by Felty[14] nearly 25 years ago is a separate entity. After studying the five cases we have classified as such, we are convinced they cannot be classified in any other group, although in reality they do represent cases of secondary splenic panhematocytopenia. Four of the five cases originally described by Felty had an anemia, whereas all had a neutropenia; there was no record of a platelet count.

The spleen shows reticular hyperplasia and erythrophagocytosis. The bone marrow is usually hypercellular, predominantly involving the granulocytic elements. The usual manifestations are chronic deforming (rheumatoid) arthritis, painful joints, anemia, splenomegaly, leukopenia, cutaneous pigmentation and lymphadenopathy. All of our five cases had an anemia as well as neutropenia; two of them also had a thrombocytopenic purpura. For this reason it appears that our cases, at least, could be classified as splenic panhematocytopenia, but of the secondary type, since the rheumatoid arthritis was an important feature of the disease. Although splenectomy, originally performed by Hanrahan and Miller[15] for the disease in 1932, may not be curative in this disease, there was such definite improvement (at least of temporary nature) in three of our five cases that we recommend it if the physical condition of the patient permits.

6. *Splenic Neutropenia.* This is a relatively rare condition, described in 1939 by Wiseman and Doan,[16] consisting of splenomegaly and peripheral granulopenia. The disease probably represents a selective form of hypersplenism in which the splenic hormones have a deleterious effect on the maturation and delivery of granulocytes from the bone marrow to the blood. The bone marrow, in most cases, reveals a myeloid hyperplasia, which must be demonstrated before splenectomy is advised. According to Wiseman and Doan, the spleen shows clasmatocytosis with excessive phagocytosis of granulocytes. Results of splenectomy will be very good if the bone marrow shows a normal or increased number of normally developing granulocytes in the bone marrow.

7. *Primary Splenic Panhematocytopenia.* This is likewise a rare disease[17] which responds very well to splenectomy. It may be congenital, acute or even secondary to such conditions as Hodgkin's disease, drug sensitization, Gaucher's disease, *etc.* The disease also represents a type of hypersplenism in which the splenic hormonal functions become exaggerated and result in an inhibitory

effect on the maturation and delivery of granulocytes, erythrocytes and platelets from the bone marrow to the blood. In some cases the spleen at the same time destroys red blood cells excessively; thus, a hemolytic component may be added to the three factors just mentioned. Examination of the peripheral blood reveals a neutropenia, anemia and thrombopenia, or in others words a pancytopenia results. Figuratively speaking, the disease is therefore a combination of hemolytic anemia, purpura and neutropenia. Bone marrow smears show a hyperplasia of all marrow elements with normoblasts predominating. These marrow findings must be demonstrable before a splenectomy is advised.

8. *Rupture of the Spleen.* This injury is, of course, an indication for splenectomy but since it involves no controversial points in the physiologic mechanism of the spleen, it will not be discussed, and our cases will not be reviewed herein.

9. *Cysts, Primary Tumors and Abscesses.* These lesions constitute a fairly definite indication for splenectomy, although a definite diagnosis can usually be made only by exclusion, and then not with a high degree of accuracy. In a review of this subject, Fowler[18] has noted that some cysts are true cysts of the dermoid or lymphangiomatous type whereas the majority (about 80 per cent) are false cysts of the hemorrhagic type caused by trauma, inflammation or parasites. *Abscess* of the spleen is extremely rare and difficult to diagnose. If the spleen is not densely adherent, it should be removed; otherwise drainage may be the procedure of choice, particularly if it is not necessary to drain across the free peritoneal cavity.

MISCELLANEOUS CONDITIONS FOR WHICH SPLENECTOMY MAY BE INDICATED

Of this group of lesions, *Gaucher's disease* is probably the most important. The primary pathologic feature of this disease is deposition of a large amount of lipoid material in the spleen, bone and lymph nodes. Important manifestations are splenomegaly, anemia, and pigmentation of the skin, especially over the face and neck; the disease is usually observed in young girls. Late in the disease a large liver develops. Reticular cells and foam cells in the bone marrow are fairly diagnostic. The bone marrow appears to be just as important in the etiology as is the spleen, which explains why splenectomy is only palliative. Occasionally panhematopenia develops, on which occasion splenectomy is definitely indicated. In the absence of this complication, splenectomy is rarely indicated in late cases.

Not infrequently in massive operations for malignant tumors such as carcinoma of the cardiac end of the stomach, the operation is made much easier if the *spleen is removed with the stomach* and omentum.

Ptosis of the spleen is occasionally an indication for its removal, but usually only when it is enlarged by some secondary process as it was in one of our patients with early Banti's disease.

Occasionally *malaria* constitutes an indication for splenectomy but only when the disease is completely eradicated and the residual enlargement of the spleen is so marked as to give rise to symptoms because of its size. When recurring

attacks of malaria develop in spite of adequate therapy, and a large spleen is present, it may be justifiable to remove the organ, hoping to eliminate the site where the malarial organisms remain and give rise to recurrent attacks.

It should be emphasized that it has been largely through trial and error for many years past that indications and contraindications have been clarified. However, it is true that during the past few years the range of indications has increased slightly to include lesions in which splenectomy can be considered only as palliative. This has been brought about through improvements in surgical skill and anesthetic technic, better preoperative and postoperative care and the use of massive transfusions, sulfonamides and penicillin.

CONTRAINDICATIONS FOR SPLENECTOMY

Pernicious anemia, Hodgkin's disease, leukemia and *polycythemia* are diseases for which splenectomy is contraindicated. The same may be said for *agnogenic myeloid metaplasia* (myeloid metaplasia of the spleen) although we have one patient in our series of splenectomies classified as such. The reports on the value of splenectomy in cases of sickle cell anemia have been contradictory. In the hypertrophic stage, splenectomy has been recommended. We have observed no clinical or hematologic benefit from splenectomy in a case reported herein and in another case observed before the date when this series was started. Splenic enlargement of the *acute splenic tumor* type, so commonly seen in certain acute infections, is a definite contraindication for splenectomy. Splenomegaly due to such parasites as those encountered in *trichinosis, filariasis, kala-azar* and *distomiasis* constitute contraindications, although splenectomy in echinococcus disease may occasionally be justified. Obviously, there is no justification for splenectomy for *metastases* of malignant tumors.

IMPORTANT POINTS IN THE TECHNIC OF SPLENECTOMY

It is not our intention to discuss technic in this presentation, although we do wish to emphasize a few of the important features of the operation. The details of splenectomy have been presented elsewhere by one of us (W. H. C.[19]). The authors appreciate that any operation may be performed through a variety of incisions, but have given up the paramedian incision because exposure is so poor, particularly on the lateral side. We have adopted an incision which starts at the ensiform cartilage as a left paramedian incision, proceeds downward and across the rectus muscle, thence laterally, parallel to the costal margin. The Singleton incision,[20] which may be classified as an oblique transverse incision, starts in the midepigastric line half way between the ensiform and umbilicus, retracting the rectus to the right without cutting it. Our objection to this incision is that exposure is very poor just under the diaphragm, where large vessels are constant in the upper portion of the gastrosplenic ligament, and in the diaphragmatic attachment when portal hypertension exists. Any of the oblique transverse incisions, including the one preferred by us, will sacrifice the eleventh spinal nerve, but no paralysis will result from section of just one spinal nerve. The twelfth can readily be retracted laterally and preserved. When the spleen is large we have found it to be of great advantage,

and frequently a relief to the surgeon's blood pressure, to ligate the splenic artery as practiced by Singleton and many others. The artery can be secured through an opening in the gastrohepatic omentum, but we have found it more desirable to ligate it at the superior border of the pancreas, where it is found readily after incision through the thin posterior peritoneum. When the artery is large, as will be the case when the spleen is large, exposure of the vessel will be most readily obtained. A great advantage of preliminary ligation lies in the fact that the spleen is emptied of its blood during manipulation incident to its mobilization, thus supplying an autogenous transfusion. The fascia in any incision for splenectomy should be closed with silk or cotton. We have had no wound separations or hernias following use of the incision as described herein. A thoraco-abdominal incision makes splenectomy easier and in difficult cases will often be justifiable.

RESULTS OF SPLENECTOMY

The operative mortality following splenectomy will vary moderately, depending to a great extent upon the number of patients in the series having Banti's disease. It has been noted by practically all authors, as indicated below, that the mortality is much greater in Banti's disease than in any lesion for which splenectomy is performed. In our total series of 87 splenectomies during the past ten years, we had seven deaths, constituting a mortality of 8.0 per cent. Haden reports an operative mortality of 14 per cent in 56 splenectomies, closely resembling a rate of 16.6 per cent in 30 patients reported by Singleton. Lahey and Norcross report a remarkably low death rate of 2.2 per cent in 83 patients. All the above figures are related to splenic disease and do not include patients operated upon for rupture of the spleen, nor patients in whom splenectomy was performed for malignant disease of some adjacent organ.

Hemolytic Anemia. In our series of 28 patients having splenectomy for hemolytic anemia, 23 were classified as congenital or familial; the results in all of this group can be classified as good to excellent. In congenital hemolytic jaundice the spherocytes function normally after splenectomy, thus explaining why removal of the spleen relieves the jaundice (Haden[5]).

In our series of hemolytic anemias there were five cases of atypical ("acquired") hemolytic anemia of unknown cause; results in this group are very poor. In the *first case,* splenectomy was performed in a six-months-old infant with acute hemolytic anemia with an erythroblastosis that failed to respond to blood transfusions prior to removal of the spleen. The boy is now approximately eight years old and presents the blood findings of a chronic hemolytic anemia. Spherocytosis and increased fragility of the red blood cells have not been observed. The clinical and hematologic findings are not those of Cooley's or Mediterranean anemia. The result is classified as poor.

The *second case* is that of a 56-year-old white female with splenomegaly, jaundice and chronic hemolytic anemia, who was subjected to splenectomy in 1939. She gave a history of frequent upper respiratory infections and temperature elevations. Following the removal of the spleen the hemolytic process subsided but the anemia was only moderately improved. This case probably

represents an acquired hemolytic anemia on an infectious basis. Although splenectomy apparently corrected the hemolytic component, the infection which was still present suppressed the bone marrow erythropoiesis. Chemotherapy had little effect on her phases of temperature elevation which was never absolutely explained. She died in 1948.

The *third case* was a four-year-old white girl with acute hemolytic anemia (red blood count as low as 990,000 and a reticulocytosis of 90 per cent) in whom the erythrocytes and hemoglobin failed to show any appreciable rise with repeated transfusions. She was splenectomized with no immediate postoperative difficulty. There was a temporary but definite improvement in the hemolytic process. Two weeks following the operation she suddenly became worse and died 24 hours later with what appeared to be a recurrence of the acute hemolytic process.

The *fourth case* of acquired hemolytic anemia was a white girl, 15 years of age, in whom autohemolysins were demonstrated (Doctor Davidsohn) during a hemolytic crisis. During the subsiding crisis, which was not associated with an increase in the hemolysin titre, splenectomy was performed. There was an increased fragility of the red blood cells but no microspherocytosis. The hemolytic process showed little improvement following the removal of the spleen. At the present time the hemolytic condition is unchanged, jaundice has become more intense and the liver is now palpable.

The *fifth case* of acquired hemolytic anemia is that of a white female, 19 years of age, who suddenly became ill with an upper respiratory infection and developed extreme weakness and jaundice. An anemia was discovered, for which she received 21 transfusions over a period of two weeks, before she was admitted to the Research and Educational Hospitals. There was no history of taking any medication prior to the onset of the jaundice. Although the reticulocyte count was 17 per cent, microspherocytosis and increased fragility of the erythrocytes were absent. It was thought that the numerous transfusions may have obscured a true spherocytic anemia. The spleen, which was two to three times normal size (300 Gm.) along with several small accessory spleens, was removed shortly after the patient was admitted to the hospital. Repeated transfusions postoperatively helped to elevate the hemoglobin and red blood count. However, shortly after the postoperative transfusions had lost their effect, the hemolytic process became as marked as prior to removal of the spleen. Over a period of three and one-half months following splenectomy, the patient received approximately 15 transfusions of 500 cc. each, as well as a course of streptomycin for an undetermined fever that was associated with pain and tenderness over a palpable liver. The patient was type A, Rh positive, but this was not held to be entirely accurate because of the number of transfusions she had received and it was decided to give her type O, Rh negative blood. It is interesting to note that it was finally necessary to give the patient type A, Rh negative blood, because type O, Rh negative blood that was available was incompatible. She finally made an uneventful recovery and has remained well up to the present time.

Thus, of the five cases of atypical or acquired hemolytic anemia having splenectomy, two have died; of the remaining three, only one has finally had a complete recovery from the unknown hemolytic process. These cases serve to emphasize an important point, namely, that in patients with acute and chronic *acquired* hemolytic anemias, the prognosis is poor and the mortality high. This corresponds almost entirely with the experience of Lahey and Norcross, who report splenectomy in six patients with hemolytic anemia, but excellent results in only one. However, good results do follow splenectomy in such cases in a few instances, perhaps in a greater percentage than indicated by our results.

At operation the surgeon must search carefully for accessory spleens, as has been emphasized by Curtis and associates.[21] Persistence or recurrence of symptoms may be ascribed to the presence of accessory spleens.

2. *Thrombocytopenic Purpura.* In our series of 26 patients having splenectomy for thrombocytopenic purpura, we had no operative mortality. Results were classified as good to excellent in 23 of the 26. In the remaining three, results were classified as fair to good. One of these had relief from purpura, but died a couple of years later with pulmonary tuberculosis. The other two had good symptomatic but poor hematologic results.

Lahey and Norcross report a recurrence in three of 17 patients having splenectomy for purpura. In two, the response of platelet rise was slow at first but later was fast. Wintrobe reports 16 splenectomies for purpura, three of whom died in the hospital, constituting operative deaths. All but one of the remainder improved sharply. In these 13 patients followed after operation, the platelets rose rapidly in nine, but rose slowly in four.

As indicated in hemolytic anemia, the operator must search the field around the hilus of the spleen and adjacent areas for accessory spleens. If there is recurrence, thought must always be given to the possibility of a remaining accessory spleen, as has been emphasized by Curtis and associates.

3. *Banti's Disease.* In our series of 13 patients classified as Banti's disease, we had five operative deaths. Practically all authors reporting mortality rates have had the same experience, namely that nearly all operative deaths occur in this group.

Our operative mortality for this group is probably higher than others, largely because we have split it into two groups, one of which is listed below as obstruction, or anomalies of the splenic vein; in these patients the mortality will be very low. Four of the five patients listed as operative fatalities died of postoperative hemorrhage. One died of pneumonia and liver insufficiency.

One patient is listed as having only a fair result because of symptoms of cirrhosis; another is still having hemorrhages from esophageal varices. One patient died two years after splenectomy, and another 18 months after splenectomy. We were unable to follow two others. The results in the remaining two patients can be classified as good to excellent. In other words, only two of the 11 patients followed with Banti's disease can be classified as having had good to excellent results from splenectomy.

Borg and Dulin report six operative deaths in 22 cases. Three of these died

of postoperative hemorrhage. Lahey and Norcross report splenectomy in 25 patients with Banti's disease with an operative mortality of only eight per cent. In their series of 12 patients having bleeding from esophageal varices before operation only three had recurrences.

4. *Thrombosis or Anomalous Obstruction of the Splenic Vein.* There were five patients in our series which we described as having obstruction of the splenic vein of one type or another. As stated previously, many authors include this group of patients in with their patients with Banti's disease. We have separated them largely because there is such marked difference in the results of this group from the Banti's group described above. All five of our patients in this group had hemorrhage before operation. Four of the five patients had an excellent result with no history of hemorrhage since operation. One listed as having a fair to good result had two attacks of hemorrhage shortly after splenectomy, but has not had any hemorrhage for the past two or three years. Very significant is the fact that even though splenectomy has relieved the patients of hemorrhage in at least four of the five cases, roentgen-ray examination with barium still shows varices present in all.

5. *Felty's Disease.* We had no operative mortality in the five patients diagnosed as Felty's disease. However, one patient died about two years after splenectomy; autopsy revealed a malignant tumor of the thymus. The remaining four patients had excellent results although one has had splenectomy so recently (six months) that final results are not definite. It should be added that, although the symptomatic and hematologic results are good in these patients, there has been very little improvement in their arthritis.

6. *Splenic Neutropenia.* We have had no patients which we have identified in this group. However, the hematologic data suggest that results should be excellent in the vast majority of patients. Preliminary reports from Doan and associates reveal good results after splenectomy in this condition.

7. *Primary Splenic Panhematocytopenia.* We have likewise had no patients in our series classified in this group. However, it is very possible that our five patients classified as Felty's disease could or should be classified as panhematocytopenia, but of the secondary type. For example, Lahey and Norcross classify patients with anemia, neutropenia and thrombocytopenic purpura with rheumatoid arthritis as patients with secondary panhematocytopenia. Likewise, in this condition results should be excellent in the great majority of patients.

8. *Results in Miscellaneous Types of Splenomegaly.* Table 1 reveals the fact that we have performed splenectomy in ten miscellaneous conditions, some of which had contraindications or doubtful indications. One patient had splenectomy for a cyst of the spleen and one for aneurysm of the splenic artery, with excellent results. The results in one patient with Gaucher's disease and one patient with Hodgkin's disease are classified as fair, but only 12 and 18 months, respectively, have elapsed since splenectomy. One patient with sickle cell anemia and another with atypical hemolytic anemia have had no improvement since splenectomy. One patient operated on for anemia and

hyperplastic bone marrow of uncertain etiology later showed a myeloid leukemia (aleukemic). The patient is feeling better since splenectomy, but only one year has elapsed since operation and a fatal outcome is expected soon. The patient with atypical aplastic anemia died on the eleventh postoperative

TABLE I.—*Types of Patients for Whom Splenectomy Was Performed (Illinois Research and Educational Hospitals, 1936-1948)*

Disease	No. of Cases	Results: Good	Fair	Poor	Died after left Hospital	Oper. Death	Remarks
Hemolytic jaundice	28	24	1	2	2	1	5 of this group were acquired hem. anemia. 1 died 9 yrs. after op., 1 op. death 2 poor result.
Purpura	26	23	3	..	..	..	1 died of tuberculosis after splenectomy but relieved of purpura. 2 had good clinical, but poor hematologic result.
Banti's disease	13	2	1	1	2	5	4 op. deaths due to postop. hem. 1 fair result with symps. of cirrhosis. 1 died 2 yrs. p. o. with hem., 1 poor result still bleeding, 1 died 18 mo. large liver. 2 not followed.
Obstruction of splenic vein	5	1	1	.	..	..	All 5 cases had preop. hem., but only 1 has had postop. hem. X-ray still shows varices.
Felty's disease (Sec. panhematocytopenia)	5	4	..	..	1	..	1 patient died 1 yr. later with malig. thymoma. 3 patients had little or no improvement in arthritis.
Congenital cyst	1	1		..	..	..	
Aneurysm splenic artery	1	1		..	..	..	
Gaucher's disease	1	..	1	..	..	..	Only 1 year since splenectomy.
Hodgkin's disease	1	..	1	..	..	..	Alive and well 18 mos. after operation.
Sickle cell anemia	1	..	1	..	..	..	
Atypical hemolytic anemia	1	..	1	..	..	..	
Myeloid leukemia	1	..	1	..	..	..	At time of op. patient had anemia and hyperplastic bone marrow—now shows leukemia.
Atypical aplastic anemia	1	..	..	..	..	1	Died on 11th postop. day of cerebral hemorrhage
Agnogenic myeloid metaplasia	1	.	.	..	1	..	Patient had hemolytic process with cellular bone marrow, but preop. diag. not possible.
Splenomegaly and anemia of unknown cause	1	..	1	..	.	..	

day of a cerebral hemorrhage. In this case there was no evidence of regeneration of platelets following splenectomy. We operated on one patient with agnogenic myeloid metaplasia, which in reality is a contraindication to splenectomy. It is well known that it is extremely difficult to make this diagnosis

until a section of the spleen is obtainable. Operation was performed in this case without a positive diagnosis, but because she had a hemolytic process with a cellular bone marrow showing a normoblastic reaction in keeping with a hemolytic process. She died three months after operation with a pericarditis. One patient with splenomegaly, anemia and gastric hemorrhage of unknown etiology had a splenectomy with no improvement in symptoms.

SUMMARY

The results in four or five of the diseases for which splenectomy is performed are very good, but are markedly dependent upon the choice of patients. The best results are obtained in hemolytic jaundice and thrombocytopenic purpura, but even in these diseases extreme care must be exercised in selecting the patient. So important are the indications for splenectomy that close co-operation between the surgeon and hematologist is essential. The data herein presented were obtained from our study of 87 patients having had splenectomy during the past 12 years.

TABLE II.—*Mortality Rate in Splenectomy*

Disease	No. of Cases	Oper. Deaths
Hemolytic jaundice	28	1
Thrombocytopenic purpura	26	0
Banti's disease	13	5
Obstruction splenic vein	5	0
Felty's disease (Sec. panhematocytopenia)	5	0
Miscellaneous diseases (Cyst, Gaucher's disease, atypical aplastic anemia, etc.)	10	1
Total	87	7

Operative mortality rate 8.0 per cent.

It is frequently very difficult to differentiate congenital hemolytic jaundice, in which splenectomy is so universally successful, from acquired hemolytic jaundice in which poor results are so common. The anemia in the former condition is microcytic and in the latter macrocytic. In many of the patients with acquired anemia there is no increase in fragility of the red cells. In 28 patients with hemolytic anemia, results were good to excellent in 23 having the congenital type, but were good in only one of five having acquired hemolytic anemia.

Although results will be good in fully 90 per cent of patients having splenectomy for thrombocytopenic purpura, they will rarely be good in secondary or symptomatic purpura. The best means of differentiation between these two conditions is by bone marrow studies. A marked increase in megakaryocytes is indicative of thrombocytopenic purpura; this feature is of great prognostic value. In 23 of 26 patients have splenectomy for thrombocytopenic purpura,

results were good to excellent in 23, and fair to good in three. There were no operative deaths in this group.

We encountered 13 patients which we classified as Banti's disease and five in whom we considered obstruction (anomalous or thrombotic) of the splenic vein to be the primary cause of the splenomegaly and portal hypertension. Some authors classify these two groups as one, namely portal hypertension, but we prefer to separate them into the two groups mentioned, since the results are so different. Of 13 patients having Banti's disease we lost five following splenectomy. In only two were results good. In contrast, four of five cases with obstruction of the splenic vein had good results following splenectomy. The fifth case is still having occasional hemorrhages from esophageal varices; a portacaval shunt is contemplated in this patient. We are now convinced that splenectomy should be performed in Banti's disease only in its early stages.

Good results were obtained in four out of five patients having Felty's disease, which may also be classified as secondary panhematocytopenia, although there was very little improvement in the arthritis. The fifth case died of a malignant thymoma one year after splenectomy.

We have had no patients with primary splenic neutropenia or primary splenic panhematocytopenia, but Doan and associates report good results in their cases.

In our entire series of 87 patients upon whom we performed splenectomy we had seven operative deaths (8 per cent mortality). Five of these seven deaths occurred in Banti's disease, indicating that careful study must be made in this disease and splenectomy not be performed if hepatic insufficiency or other significant complications are present.

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DISCUSSION.—DR. LON GROVE, Atlanta: I have before me a summary of a personal experience in 52 consecutive splenectomies, covering a period of 20 years from 1927 to 1948. Four of these were done for trauma and will not be discussed.

Our results in the remaining 48 cases parallel very closely the experience related by Doctor Cole. I might say here that we are thoroughly in accord with what Doctor Cole said about the absolute necessity of having a hematologist of experience associated with you on these cases. I do not see how anyone could approach this type of surgery without the help of a really experienced hematologist. All these cases have been studied by a hematologist of experience, most of them by Dr. Roy Kracke.

Twenty of this series were diagnosed as familial jaundice but now, in the light of subsequent follow-up, we should change the diagnosis in one patient to acquired jaundice, because she has not done well.

In the purpuras, 13 were diagnosed as idiopathic or primary purpura and one as secondary, and we would like to give in some detail the history of this latter patient. This case of secondary purpura was under observation for a long time. Even though she showed all the clinical and laboratory findings that would fit a primary purpura, including repeated bone marrow studies; with a history of two sisters and one brother having died with the disease, we were very hesitant to classify her as a primary purpura. She responded to no form of conservative treatment and finally was splenectomized. She did well for a time, but returned in nine months with all the symptoms she had shown primarily, and died from a subdural hemorrhage.

There have been nine patients with Banti's syndrome, two of whom we have lost track of. Of the remaining seven, we know five have had subsequent hemorrhages and, of that five, three have died. It is interesting that one of these patients went nine years before he had his first hemorrhage; this occurred approximately a year and a half ago and he has not hemorrhaged since. This is a poor showing in Banti's syndrome. As you see from the age incidence most of these patients were children; the oldest was aged 28 years and the youngest 7 weeks. We believe that most of them were diagnosed early but, notwithstanding, they have not done well.