SPLENECTOMY FOR PURPURA HEMORRHAGICA*

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In the past decade since splenectomy has been practiced for purpura hemorrhagica, there has been sufficient experience to make us feel that the results are more encouraging than in any other comparable group of blood diseases of uncertain origin, except perhaps in hæmolytic jaundice treated by splenectomy. The acceptance of splenectomy as a curative procedure has led to the reporting of brilliant results as observed immediately after operation, and one can easily understand the enthusiasm of the observers who have seen the almost hopeless situation change into a progressive improvement immediately following splenectomy. While a few of the cases have been reported in sufficient detail in their after course over a long period, one may think that perhaps our statistical reports are charged with a greater optimism than is justified until all these cases have been followed for several years.

As a clinical entity purpura hemorrhagica has been fairly defined for about 150 years (Morbus Maculosis Werlhofii), but our ignorance of the true nature of the disease leaves its place in the classification of purpuras in controversy. More recently, it has been suggested that primary purpuras be classified into (1) those in which there is a diminution or apparent absence of platelets; (2) those that have no change in the number of platelets, the latter probably resulting from changes in the capillaries or in other elements of the blood.

In the study of some cases with purpura and bleeding, we find difficulty in definitely placing them, but we can accept for our purpose a definition of purpura hemorrhagica as a disease usually beginning in early life, but which may come on at any age, showing petechia or purpuric spots, with serious hemorrhages from the gums or mucous membranes, with secondary anæmia (commensurate with the severity of the bleeding), the disease having remissions, or coming in cycles, and usually progressing with each attack. The small number of platelets or their absence, the prolonged bleeding time, the normal coagulation time, and the failure of the clot to retract, are the outstanding blood finding.

The spleen may or may not show an enlargement. There is an acute form which may prove rapidly fatal, and a chronic form which may continue over years.

To review at length the various opinions of this disease and the conflicting views expressed about the relation of the different blood factors is hardly necessary, as this has been so recently and ably done by several observers. (Brill, Krumbhaar, Cohn.)

The platelets, which are found in such small numbers or entirely lacking in

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all cases of purpura hemorrhagica, play an important rôle and Eppinger believes the disease should be called thrombocytopenic purpura hemorrhagica. Their absence in purpura was first noted by Denys in 1887. Wright's demonstration of the origin of platelets in the megacaryocytes of the blood-forming organs has been generally accepted, and this function is probably normally maintained in purpura. They are considered to supply a thromboplastic substance that hastens coagulation. If the platelets are formed in normal numbers, we must account for their disappearance. Kaznelson believes that the destruction of the platelets takes place in a diseased spleen, because he found a large number of platelets in the lymph-spaces of the spleen. Frank, on the other hand, thinks that there is a failure of the megacaryocytes of the bone-marrow to produce platelets, and that the bone-marrow is activated to increased platelet production by splenectomy.

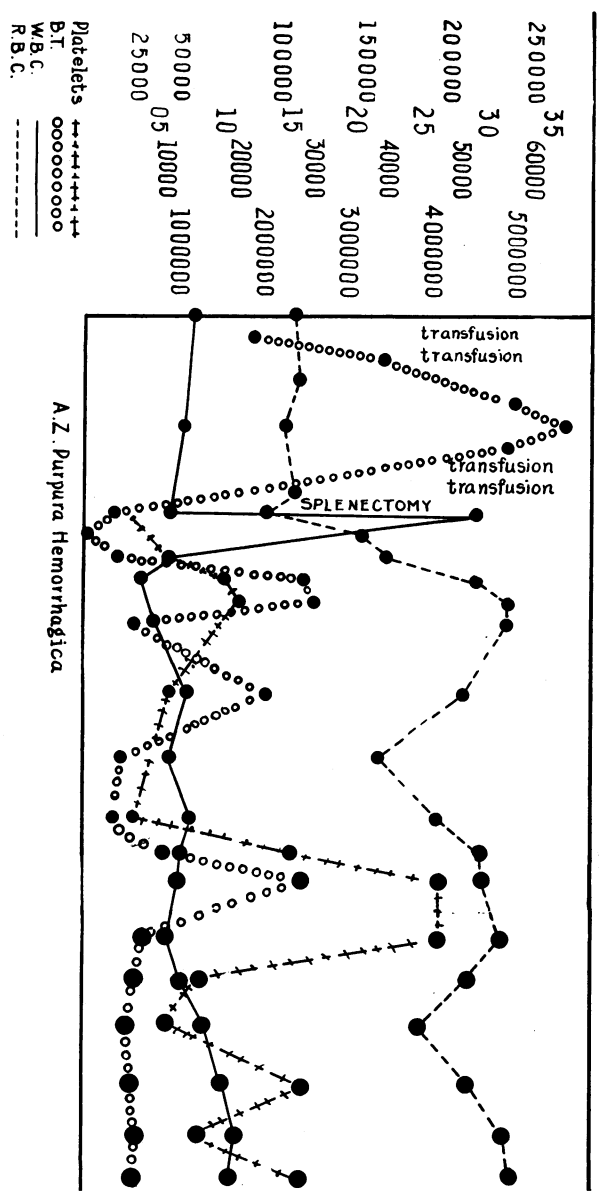

FIG. 1.—Chart showing influence of splenectomy upon the number of platelets in the blood.

The blood in purpura hemorrhagica clots normally, but the failure of the clot to retract, as normal blood does within an hour, is probably due to the lack of platelets. This at once differentiates this group of bleeders from hæmophiliacs, whose clotting time is markedly delayed and imperfectly executed, though after clot formation, clot retraction takes place, as the number of platelets in hæmophilia is normal.

The bleeding time in purpura is prolonged which is probably due in part to a vulnerability of the capillary vessels. This capillary weakness, combined with changes in the blood itself, accounts for the appearance of petechiæ, purpuras or ecchymoses of the skin and mucous membranes, and the hemorrhages that may occur from the gums, nose, stomach, kidneys and uterus or beneath the retina. Hemorrhages do not stop with the administration or application of any known remedy.

The anæmia that develops with the repeated hemorrhages varies with the amount of blood lost, and the capacity of the bone-marrow to form new cells. There may be no leucocytosis, but if it is present the increase is largely due to the increase in the mononuclear lymphocytes.

Kaznelson in 1916 suggested splenectomy in these cases and since then a number of reports of results following operation have been published.

Krumbhaar has collected 27 cases with two post-operative deaths (7.4 per cent. mortality) and no subsequent deaths. One of these cases was unimproved, 9 were improved, and 15 were apparently well. To these 27 cases I have been able to add 18 more, making a total of 45 cases with two operative deaths, 27 are regarded as well, 15 improved and one unimproved.

Two cases, from the St. Louis Children's Hospital, have been operated by me, both of them over fifteen months since, one with such marked improvement that it can reasonably be called a cure; the other with marked improvement, but with occasional hemorrhages that are easily controlled. A more recent case in the Barnes Hospital, a woman thirty-four years old, has had no reappearance of purpura or hemorrhages since her operation eight months ago.

The two cases in children had their first indication of the illness at the age of five years; one began as a mild, apparently simple purpura with only skin manifestations, but became severe after repeated nose bleeds, which started during a bad cold and otitis media. The other began with an influenza, the petechiæ and purpuric spots showing in successive crops before the bleeding started from the nose and gums. Both had been given numerous remedies by mouth and subcutaneously without effect. Transfusions had been repeated and not only had there been no influence on the bleeding, but on two occasions with the boy, fresh skin lesions and bleeding appeared almost immediately after the transfusions, an occurrence which was noted by Brill, who states that he thinks transfusion of blood has no curative effect, with which we agree. The anæmia was marked, the boy showing a red count of 3,600,000 and the girl showed a count of 2,500,000 red cells, after a transfusion that had been given to her immediately on admission because of extreme weakness. The boy came to operation almost exsanguinated from his bleeding, which repeated transfusions failed to combat. He was a bad risk for operation and it appeared for a time rather dubious whether he would survive the shock, despite the transfusion started during the operation. The girl was in better condition for operation, and responded well to the transfusion given at the time of operation. After removal

of the spleen from the boy, the oozing seemed to stop immediately from the surfaces left exposed by the tearing of adhesions. One hour later, the bleeding time was less than a minute, while it had been thirteen minutes before operation. The girl's bleeding time before operation had varied from thirty-seven minutes, seven days before operation to twelve minutes as she came to the operating room. Shortly after the operation the bleeding time was two minutes and bleeding from the nose was noted as stopping while the child was still on the operating table. The spleen in each instance was normal to microscopic examination. The one from the boy was rather large, the other normal in size. The short bleeding time persisted for a considerable period after splenectomy. In each case there was an immediate increase in the leucocyte count, with the boy, who had a count of 12,000 before operation, there was a jump to 59,000 in two days—with the girl, from 11,000 before operation to 53,000 the evening of the same day. The smears of the blood of the boy showed a remarkable pouring out of normoblasts and megaloblasts, in several fields as many as five or six nucleated reds. The girl showed only a few nucleated reds after operation.

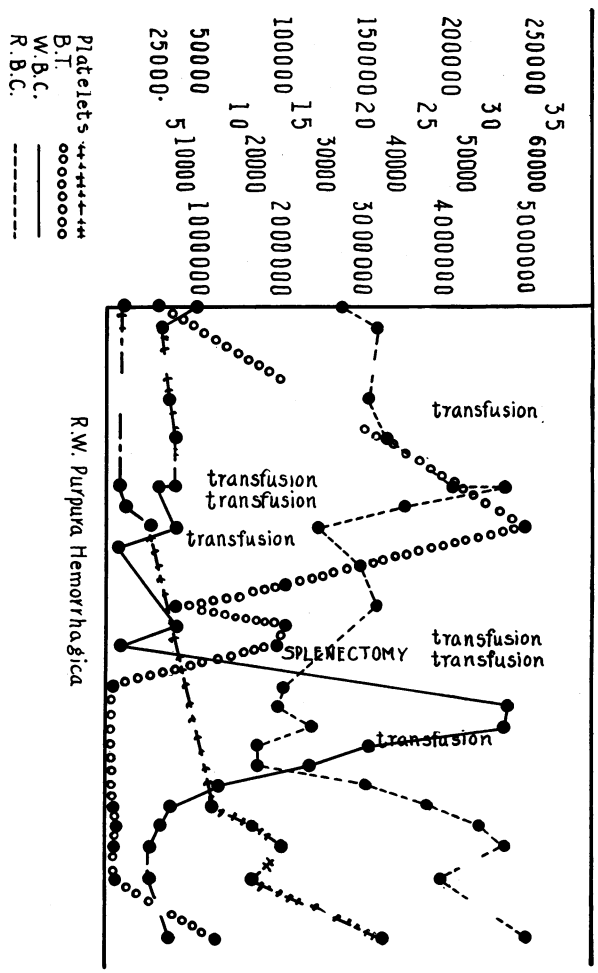

FIG. 2.—Chart showing the influence of splenectomy on the number of platelets in the blood.

The platelets, which had been hard to find before operation, showed on smears of the boy's blood a few hours after operation, but it was two weeks before they could be counted as much increased, when they numbered 60,000. They rose to 95,000 six weeks after operation, and during the first few months never got any higher, in fact, they appeared to gradually reduce in number, but the amount nine months after operation showed they were 150,000. The other child showed a few platelets on the smears six hours after operation, but it wasn't until ten days after operation that they were noted at 50,000, slowly rising to 90,000 one month after operation, and ten months after operation the count was 200,000, which is her highest count. There have been some variations in the count which I will discuss later.

The bleeding time remained at the low level in both cases for some time, and during this period there was no bleeding except an occasional slight oozing from points in the nose where previous to operation there had been brisk hemorrhages. This later oozing stopped either spontaneously or after pressure on the outside of the nostril and did not require packing.

While the boy's bleeding time remained about two minutes, he had several small hemorrhages from the nose at long intervals, from an ulcer on the septum. A virulent culture of diphtheria bacilli was grown from the nose, but whether the ulcer was due to this infection, or a result of the old weakness, one cannot say. The ulcer was very sluggish, and on last reporting the boy was still carrying the virulent organisms, but there has been no bleeding, only an occasional purpura, and the youngster is in robust health.

The girl's bleeding time remained low for several months, and there were no hemorrhages, but on one visit to the hospital three months after splenectomy, when she came to have her tonsils removed, the platelets were 50,000, the bleeding time was noted at fourteen minutes and she had a purpuric eruption, therefore, the tonsils were not touched. Eight months after splenectomy the bleeding time had returned to two minutes, but there were petechia and ecchymosis over the body, however no new petechiæ were brought out on the arms when the tourniquet was applied (capillary resistance test of Hess). There were only 20,000 platelets, which made us hesitate to subject her to tonsillectomy, which was indicated because of their large size and the fact that whenever she had an attack of tonsillitis she broke out with many petechiæ and purpuric spots. Under proper care in the country she showed the first marked improvement in general condition since her splenectomy. In the first seven months there had been a gain of only three pounds, but she felt well and seemed strong, while in the next six weeks in the country, she gained four and one-half pounds, and her red count jumped from 3,400,000 to 4,650,000, and the platelets rose to 106,000, with a bleeding time of five and one-half minutes. A month later she had gained in weight to what was normal for her age and height, she seemed robust, and had no anæmia, with a platelet count of 200,000, but a bleeding time of sixteen to twenty-five minutes, which would seem to indicate that there is some other factor than the diminution of platelets which helps determine the long bleeding time. In another month during which she continued to gain, and had not bled, the bleeding time returned to three and one-half minutes. A tonsillectomy was performed under gas oxygen with no more bleeding than is customary after this operation. It is interesting to note that thirty minutes after the operation the child broke out with petechiæ over the face, neck and forearm. These had disappeared in ten days, when the second tonsil was removed and another crop of petechiæ made their appearance within forty-five minutes. The platelet count at this time was 90,000, bleeding time three minutes, and while there was no unusual post-tonsillectomy bleeding, on the succeeding day the child began to bleed profusely from the nose, which had to be packed to control it. It is three months since the tonsils were removed and the child is in excellent health, strength and weight, with 5,000,000 red cells, a platelet count of 120,000 and bleeding time of two minutes, a clotting time of four and one-half minutes, but her clot does not retract. During these last few months she has had three hemorrhages from her nose, one quite profuse, and each time we have found the platelets count reduced to 45,000 or 50,000, but the bleeding time, usually determined by the same observer, has been around two minutes. In each instance we believe we could connect the bleeding with an upper respiratory infection.

Another interesting phase of this child's case was that she was practically blind on admission and Dr. Lawrence Post found an optic atrophy, which he thought was due to the extreme anæmia following an earlier severe hemorrhage. He regarded the eye condition as stationary, but as her general condition improves, she uses her eyes better and has been able to do some work in the hospital school. She will have to complete her education in a school for the blind.

The third case, a woman thirty-four years of age, was admitted to the Medical Service of Barnes Hospital on September 22, 1924. One month before she bruised herself and developed a large black and blue area which was slow in disappearing, then other smaller areas and spots on arms and legs were noticed which began as red, turned blue, then brown, and disappeared.

Four months before admission, after a severe cold, she developed a sinusitis and the left maxillary sinus was operated at the City Hospital. When the packing was removed from the nose there was a severe hemorrhage and subsequently up to September 7, there were several unaccountable hemorrhages from the nose.

On admission to the hospital there were scattered purpuric spots over the legs. The

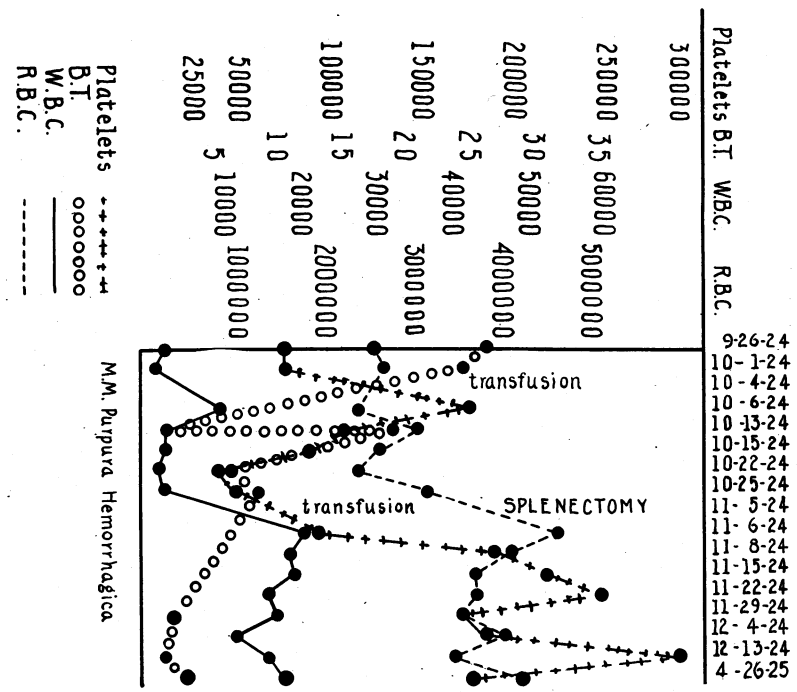

FIG. 3.—Chart showing the influence of splenectomy on the number of platelets in the blood.

patient was fat and flabby, with marked pallor. The spleen was enlarged, the liver edge could be felt. Red blood-cells 2,700,000; white blood cells 3500; differential count normal. Hæmoglobin 40 per cent.; platelets 70,000; bleeding time four minutes, and two days later eight minutes. Clotting time three minutes. Clot did not retract after two hours. There was occult blood in the stool, but on admission no other evidence of bleeding.

Patient was transfused and had a severe reaction followed by an herpetic eruption about the lips, and subsequently there were hemorrhages from these cold sores and from the gums and nose. The patient was worse after the transfusion. The bleeding time rose from seven minutes before, to nineteen minutes when taken ten days after the transfusion. She developed a transient jaundice.

Through a left rectus incision the enlarged spleen was removed. The liver was cirrhotic. There was no trouble with bleeding from the few adhesions torn during the operation, as oozing stopped as soon as the spleen was out. Patient had a stormy time after operation, developed a pneumonia of the left base and had a severe cough, which

broke some of the silkworm gut sutures, and the abdominal wound gave way, requiring a secondary suture ten days later.

Despite these serious complications and the very poor condition of the patient before operation, for the first few months she has made a steady improvement. The platelets rose to 250,000 two days after operation and have stayed between 175,000 and 250,000 ever since. The bleeding time dropped to three and one-half minutes and has stayed there since. The leucocytes rose to 20,000 after operation and have not gone below 12,000. The red cells stayed between 4,500,000 after operation and 3,500,000 a month later. The hæmoglobin has increased from 35 per cent. to 45 per cent. No purpuric spots have appeared and there has been no bleeding.

The menstruation, which had been prolonged to over a week the two periods before operation and had been most profuse, was recorded as three days and normal since operation.

About four months after the spleen was removed, when the patient had gained enough strength to return to her work in a shoe factory, she had a severe injury in an automobile accident, in which she received a fracture of the pelvis and several other bones. No unusual ecchymoses appeared, and there was no unusual bleeding from her wounds. She has recovered in a satisfactory way from these injuries and is up and about. A blood count made almost six months after the splenectomy records red blood-cells 4,060,000, white blood cells 19,600, hæmoglobin 49 per cent., differential count: polymorphonuclears 64 per cent., small mononuclears 35 per cent., large mononuclears 1 per cent. Bleeding time two minutes. Clotting time five minutes. Clot retracted in one hour. Platelets 180,000.

With these findings one can feel warranted in expecting a cure of the purpura.

TABLE I.

Cases of Splenectomy for Purpura Hemorrhagica.

	Cases operated	Well	Improved	Unimproved	Dead
Krumbhaar ...	27	15	9	1	2
Mayo Clinic...	8	4	4		
Vincent.....	3	3			
Ricardo.....	2	1	1		
Cohn	1	1			
Blumer	1	1			
Clopton.....	3	2	1		
	45	27	15	1	2

It would seem that the platelets are the most important factor so far discovered in this disease, and their decrease as is found in purpura hemorrhagica is not explained. The decrease may possibly be due to infection of the upper respiratory tract.

Taking out the spleen has been followed by an increase in the platelet count, not only in purpura hemorrhagica, but in Banti's disease. The platelet count may be slow in rising after splenectomy and it may recede after it has reached a normal number.

The hemorrhages of purpura seem to come when the platelet count is the lowest. The platelet count usually is low with a long bleeding time. The bleeding time is not necessarily short because of a high platelet count, as we have seen a long bleeding time with a high platelet count.

We agree with Brill, who feels justified in saying that splenectomy in this

disease is a life-saving measure, and should as such be employed in all cases of chronic thrombocytopenic purpura.

There is evidence that it is also curative. Kaznelson's first case had no recurrence in a period of over five years.

The risk of operation is obviously greater as the patient is weakened from repeated hemorrhages, and should therefore be performed as early as a positive diagnosis is made. The mortality is surprisingly low in the reported cases.

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