ESSENTIAL THROMBOCYTOPENIC PURPURA—PURPURA HEMORRHAGICA AND ITS TREATMENT BY SPLENECTOMY *

By Edwin Beer, M.D.
of New York, N. Y.

During the last ten years our knowledge of the purpuras and the proper treatment of one type of purpura by splenectomy has advanced very rapidly. This particular type which is benefited by splenectomy was described as a clinical entity by Werlhof in the eighteenth century. Advance in the differentiation of the different types of purpura has been so slow that only fifteen years ago as prominent a clinician as Litten totally misunderstood the condition, and in an article in Modern Clinical Medicine [1] made the statement, "I believe strongly and absolutely that the individual purpuric diseases are not essentially different, but are due to the same cause and only vary in degree; that is, the varieties depend upon the intensity of the affection." This startling statement was made even though a superficial knowledge of the literature might have indicated that careful blood examinations made years before had already indicated that there were distinct differences between the types of purpura that presented in the clinic.

A Belgian histologist, Denys, in 1887, had already called attention to the fact that there was a low platelet count in some of these hemorrhagic diseases and a few years later, in 1890, Georges Hayem was able to confirm this interesting observation and at the same time called attention to the fact that although the blood coagulated, the clot did not contract. In the latter's important work on Diseases of the Blood,[2] published in 1900, these various facts are brought together and their significance emphasized. Whether Denys was the first to call attention to this low platelet count or whether this observation had been made by Brohm in 1883 and published in the dissertation of E. Kraus, as noted by Minkowski,[3] I have been unable to confirm. Be that, nevertheless as it may, Hayem deserves the credit for his intensive study of these purpuras, both the essential and the secondary, and his careful work seems to be the foundation stone of our present conception of the disease and of its recognition. He emphasized the following five peculiarities in the type of disease known as Werlhof's disease or essential purpura hemorrhagica:

First.—That there was no anatomical change which was appreciable in the red blood cells.

Second.—That there was a considerable diminution of the number of blood platelets and that those that were present were often of a large size.

Third.—There was no constant modification in the leucocytes. In only

* Presented before the Surgical Section of the New York Academy of Medicine, February, 1926.

one case was there an increase in these elements, quite independent of any blood disease.

Fourth.—That the blood coagulates normally but that the fibrinous reticulum remained either invisible or developed as fibrils of unusual size.

Fifth.—That there was an absence of retraction of the clot and secondary expression of the serum.

The pathognomonic and constant characteristic of this disease he saw in the diminution of the number of blood platelets and the absence of contractility of the clot with the usual expression of serum. He also called attention to the fact that there were numerous cases of purpura not associated with these two striking characteristics. A very complete classification of the different types of purpura, those with low platelet count, and those without, has been published only recently in the article by Doctors Brill and Rosenthal,[4] which reclassification confirms many of the excellent observations made twenty-five years ago by G. Hayem.

In 1912 Duke[5] called attention to the fact that the bleeding time may be greatly prolonged while the clotting time is normal. This prolongation of bleeding time after a pin prick may in some cases exceed an hour, whereas normally, bleeding ceases within three minutes.

Following in the lines of Hayem's original work, E. Frank,[6] in Germany, in 1915, practically rediscovered the work of the earlier Belgian and French students and called attention to the various conditions associated with purpura, hæmophilia, scurvy, various blood diseases, etc., and again emphasized the importance of the type associated with low platelet count, to which he gave the name of essential "thrombopenie."

In 1916, Kaznelson[7] had an opportunity to study several of these cases in which the patients had an enlarged spleen, and under the impression that the low platelet count might be due to a destructive action of the spleen upon the blood, he advocated its removal. Experimental work had already shown that the corpuscular elements of the blood, the platelets and red blood cells following splenectomy, normally are increased, in fact Alfred Hess, in a paper on the Consideration of the Reduction of Blood Platelets in Purpura, published February, 1917, in the proceedings of the Society for Experimental Biology and Medicine, quite independent of the publication of Kaznelson in Vienna, apparently arrived at the same conclusion. He states that it has been established that the removal of the spleen, both in men and animals, brings about a definite increase in the number of blood platelets. It would, therefore, "seem worthy of trial to perform a splenectomy immediately preceded by blood transfusion in severe cases of purpura where extreme therapeutic measures and repeated transfusions have been resorted to in vain." I have been told by Dr. E. Peterson, of this city, that in this year, 1917, in one or two cases of this type of purpura, Doctor Hess had referred the patients to him for splenectomy on the basis of the above conclusions. Fortunately, it was known from the literature that in cases of purpura hemorrhagic Hungarian surgeons had operated for appendicular infection without encoun-

tering any difficulty, so that it was evident that though dealing with patients who were liable to bleeding, often uncontrollable bleeding, the operative interference of splenectomy would not be contra-indicated because of inability to control oozing from the incised wound. The first case of Kaznelson was published in the latter part of 1916, in the Wiener klinische Wochenschrift,[7] the operation being a splenectomy done by Professor Schloffer in Prague.

The patient presented the clinical picture of extreme thrombocytopenic purpura. She was a female of thirty-six and had been under observation for many years for chronic recurring hemorrhages. She had severe epistaxis petechiæ in the skin, ecchymoses, and had since youth the bleeding tendency. Ten years before the operation she had had severe bleeding from her genitalia, from her nose, from her gums, and general petechiæ. Her hæmoglobin had been as low as 10 per cent., and there was a sudden crisis with improvement, but the epistaxis and petechiæ frequently developed. In 1910, she had severe bleeding after parturition and thereafter had repeated attacks of severe menorrhagia. In 1913, the tendency to bleeding still persisted, and in 1916, the year of admission and operation, there was an uncontrollable epistaxis which dominated the picture. On physical examination her spleen was three fingers' breadth below the ribs, her blood pressure was practically normal, no lymphatic enlargement, no tenderness of the sternum or tibia. Her blood examination showed red blood cells 3,792,000, white blood cells 6710, and the platelets, which were almost exclusively giant forms, numbered 200. Coagulation began in three minutes but there was no clot reaction even at forty-eight hours. The patient's nose was packed for six weeks before the bleeding could be controlled. Petechiæ developed all the time under observation and there was bleeding from the gums. After removal of the spleen, which was a comparatively simple procedure, the change in the clinical picture was most astounding. The bleeding tendency stopped. The platelets rose to 500,000, the bleeding time was shortened, the patient prior to the splenectomy used to bleed from the slightest needle prick, whereas now there was difficulty in getting a specimen on pricking the finger. Moreover, the clot reacted normally. The patient was reported, four weeks after operation, as showing a marked improvement, if not a cure, by splenectomy, of essential purpura hemorrhagica or Werlhof's disease.

Since this startling report a great many cases, well over fifty, some perhaps of doubtful validity and not definitely proven cases of the disease under discussion, have been published in the literature of Austria, Germany and America, and a few isolated cases in England, the Dominions and France.

The disease under discussion seems to run at least two very different courses. The type that is usually encountered is the chronic recurrent or relapsing type, and it is in this type that splenectomy seems to be particularly useful, even though at the present time it is not absolutely certain that it is all that has been credited to it, namely that it leads regularly to a permanent cure. The other type, the acute type, is a much more rapidly progressing disease and judging from the published reports, splenectomy in these cases is of very questionable value. Even if its field be limited in this way, it may be a definitely life-saving measure in the chronic cases as the repeated hemorrhages and recurring attacks in the chronic cases may, if untreated by splenectomy, eventually lead to the death of the patient.

As far as the clinical picture of this disease is concerned, it differs altogether from hæmophilia in that it is not hereditary. It seems to occur more frequently in the young and hemorrhages may occur in almost any part of

the body, as small petechiæ or ecchymotic spots in and under the skin, as bleeding from the gums, stomach, intestines, from the genitalia, from the urinary organs, and from the nose and throat. The laboratory findings in the cases that have been studied all seem to show what Hayem originally called attention to, namely a low platelet count, an absence of retraction of the clot, a normal coagulation time usually associated with a prolonged bleeding time which may be instead of the average three to five minutes as long as one hour or more. In true hæmophilia the platelets are not diminished, the tourniquet produces no petechiæ, coagulation time is prolonged and bleeding time is usually normal.[8]

A variety of theories as to the origin of thrombocytopenia and its relation to the uncontrollable bleeding have been advanced. It has been suggested that the disease is primarily in the marrow and that there is a defective formation of platelets. Others have suggested that toxins in the circulation or otherwise destroy the platelets that are normally present in normal amounts in the blood. Kaznelson, in view of the fact that in his cases the spleen was enlarged, thought perhaps there was a lytic process which destroyed the platelets in the spleen. None of these theories has been entirely satisfactory, and Minkowski called attention to the fact that in his case the spleen was small and normal, pathologically. A platelet count of the blood aspirated from the splenic artery and from the splenic vein just prior to removal of the spleen in one of the patients operated upon by me, did not show any such change in the number of platelets as the theory of Kaznelson would suggest, Doctor Rosenthal having found practically the same number per cubic millimetre in both blood specimens. (Case III.) Further study along these lines is indicated. Apparently in only one other case has a note been made in the report of a comparative study of the two bloods, the splenic vein and the splenic artery blood, without any convincing difference in the number of platelets. Another interesting feature of this disease is that after the splenectomy, although there is a preliminary rise in the number of platelets in the blood, very frequently the platelet count drops again to very near the low number that had been present prior to operation and still the patient is rarely troubled with any severe bleeding. In one of the five cases reported in this paper it was noticed that whereas before the operation, adrenalin locally applied had but very little effect upon the capillary oozing, after splenectomy the oozing from the granulations of the drainage tract was quickly controlled by the application of adrenalin. This isolated observation might suggest that while the spleen is in, normal contractility of the capillaries is defective, and in view of the fact that the disturbance in the number and perhaps quality of the platelets has a distinct bearing upon blood coagulation, the combination of the disturbance in the capillaries plus the disturbance in the coagulability of the blood due to the thrombocytopenia may underly the pathogenesis of these varied bleeding phenomena. The peculiar swing in the platelet count to high figures after splenectomy and down again to low figures, Minkowski has suggested might be due to the influence of the remaining reticulo endothelial system or to

accessory spleens which possibly produce a lytic substance which destroys the platelets much as the original spleen had done, according to the viewpoint of Kaznelson.

Herewith I submit reports of five typical cases, four of chronic relapsing thrombocytopenic purpura in which the end results as seen months to years after the operation are most gratifying, the patients having been restored to complete health, as well as one acute case in which splenectomy was done but in which an early fatality ensued. The records of these cases I owe to the coöperation of Dr. N. Rosenthal.

Case I, reported by Brill and Rosenthal, *Archives of Internal Medicine*, 1923, p. 946:

CASE I.—A boy, aged fifteen, was admitted November 22, 1922, complaining of bleeding from the nose and vomiting of blood. The present illness began in April, 1919, when the patient had an attack of tonsillitis followed by hemorrhages into the skin, bleeding from the gums, painful joints, vomiting and pain in the upper part of the abdomen. He also had irritability of the eyes, weakness, fever, chills and sweats. He remained in the hospital for one month, after which he was apparently well except for an occasional ecchymosis following some slight trauma, until May, 1922, when he received a blow on the nose. This was followed by a severe epistaxis which continued for several hours. The bleeding was stopped by means of a tampon saturated with fresh normal blood. The skin hemorrhages had become more frequent since. In July, 1922, while drinking milk, blood began to issue from the anterior and posterior nares and soon the patient vomited blood and food. Some hemorrhagic areas again appeared on the skin. Röntgen-ray therapy was applied to the splenic region, with apparently good results. His condition improved. He lived a quiet life until November 22, 1922, when he was again struck on the nose, and he had been bleeding and vomiting blood ever since.

Physical Examination.—The patient was a well-developed and fairly well-nourished boy with marked pallor. There were a few petechiæ in the conjunctivæ of both lower lids. The teeth were in fair condition. The gums were spongy and bleeding, the tonsils large and covered with hemorrhagic spots. The heart was not enlarged. There was a systolic thrill and murmur at the apex. The spleen was not palpable, but it was large to percussion. There were numerous petechiæ over the back, chest, abdomen, thighs and legs.

On November 26, 1922, the blood count was: hæmoglobin, 45 per cent.; red cells, 2,584,000; white cells, 10,000; platelets, 10,000 (plasma); polymorphonuclear neutrophils, 71.6 per cent.; polymorphonuclear eosinophils, 1.6 per cent.; polymorphonuclear basophils, 0.3 per cent.; lymphocytes, 15.3 per cent.; and monocytes, 11 per cent. The coagulation time of the blood was ten minutes; the bleeding time four and one-half minutes. The tourniquet test was slightly positive. There was no clot retraction. The patient had secondary anæmia, thrombocytopenia and monocytosis. The blood picture was characteristic of essential thrombocytopenia.

During the following month there were a succession of hemorrhages from nares and gums, producing an anæmia so marked that transfusion was done December 17, 500 c.c. being injected. There were no hemorrhages after this transfusion, but successive crops of petechiæ formed. December 23, the hæmoglobin content was 28 per cent.; red cells, 2,010,000; platelets, 24,000. December 29, a second transfusion was done, 450 c.c. being injected. The following day, December 30, 1922, splenectomy was performed by Dr. E. Beer through a subcostal incision. Tube drainage of subphrenic space. There was profuse oozing of the wound. Continuous oozing from the nose occurred during the anæsthesia.

A soft slightly enlarged spleen with omental adhesions between the stomach and

hilus was found. The adhesions were doubly divided and cut. The spleen was delivered with some difficulty. The hilus was ligated and cut, taking special care not to include the adherent stomach.

Summary of pathologic report by Dr. F. S. Mandlebaum: The macroscopic specimen consisted of a moderately enlarged spleen weighing 300 gm. and measuring 14 x 7.5 x 3 cm. It was elastic and cut easily. Malpighian bodies were visible. Microscopic examination showed only hypertrophy. No blood platelets were found.

Immediately after the removal of the spleen, all oozing of blood stopped. The bleeding before splenectomy was profuse at the end of six minutes when it was stopped. The bleeding time during manipulation at the hilus was six minutes; immediately after splenectomy, three minutes; two hours after splenectomy, three minutes; eight hours after splenectomy, three minutes; and fifteen hours after splenectomy, two and one-half minutes.

January 9: Some oozing from granulations about drainage tract which stopped at once with application of adrenalin.

January 19, 1923: The patient was out of bed. Many petechiæ appeared on the legs and a few on the right lower conjunctivæ.

February 3, 1923: A few petechiæ on the face and lower legs appeared from time to time. The gums had improved; there was no sponginess and no bleeding.

February 8, 1923: There were hypostatic petechiæ on the legs only. The general condition was excellent. The hæmoglobin content was 76 per cent.

February 14, 1923: For the first time clot retraction was present. There was a thrombocytopenia and slight positive capillary resistance test. The petechiæ were disappearing from the legs. There had been no hemorrhages since February 9, 1923.

February 17, 1923: The patient was discharged well.

Blood changes following splenectomy:

(1) Hæmoglobin and red blood cells: The transfusion of 500 c.c. before splenectomy raised the hæmoglobin to 48 per cent. and the transfusion given immediately after the operation produced a further rise to 60 per cent. and a rise to 3,232,000 red blood cells. This gradually dropped during the first four days to 38 per cent. hæmoglobin and 2,832,000 red blood cells. Improvement then began and at the last examination (April 6, 1923) the hæmoglobin was 81 per cent. and the red blood cells were 4,840,000. Normoblasts and Howell-Jolly red cells were occasionally present.

(2) White blood cells: Just before the operation there was a leucocytosis of 22,000; six hours after the operation the leucocytes were 36,000, and on the following day they rose to 55,000. The differential blood picture after the post-operative polynucleosis showed a persistent monocytosis (increase of the large mononuclear and transitionals).

(3) Blood platelets: The day following the operation there was a slight rise to 31,200; then a gradual fall to 1000 on the third day after the operation. After this there was a gradual increase to 10,000 and then to about 20,000. The morphology remained about the same. The day following the operation a few giant blood platelets appeared in the smears.

(4) Bleeding time: For a month and a half this was prolonged, usually over two minutes, and even as long as twelve minutes. This became normal (two to three minutes).

(5) Tourniquet test (capillary resistance): This was constantly positive until the third month after the operation. It then became constantly negative.

(6) Clot retraction: There was no clot retraction for six weeks after the operation. This appeared on February 14, 1923, and slight clot retraction remained present, although the blood platelets remained low. It is interesting to note that the blood of this patient never showed clot retraction on previous examinations.

Summary.—This was a case of chronic thrombocytopenia of four years' duration. The patient's condition became worse as time went on; the bleeding was more frequent and more severe. Splenectomy brought about a turn for the better and the patient has steadily improved since.

The patient was again seen in April, 1923. He had no hemorrhages since he left the hospital. He had gained weight and strength steadily. Static purpura of the legs did not occur. Examination of the blood still showed a thrombocytopenia (blood platelets, 22,000), but all other evidence of the previous condition was absent. The capillary resistance test was negative and clot retraction was present. February, 1925, presented at the New York Surgical Society, the patient is entirely well. February, 1926 patient in excellent condition three years after splenectomy.

CASE II.—E. G.: A young girl, aged seventeen years, was admitted on October 9, 1924, to the First Medical Service, complaining of uterine bleeding for nine months, black and blue spots of skin and bleeding from mouth two weeks, and bloody urine two days. About nine months before admission to the hospital, she noticed that her menses occurred three days before the usual date and that the period lasted several days longer with profuse bleeding. At that time she began to find black and blue spots on her skin, especially after the slightest bruise. About March, 1924, she began to bleed from the gums. October 7 she felt some pain in her left loin and since then she noticed that her urine was bloody. The blood in the urine has become less.

She appeared a well-nourished and well-developed girl, not acutely ill. Petechial hemorrhages were present on the mucous membranes of the mouth (gums, lips and fauces) and petechiæ and ecchymoses were present on all parts of the skin. The heart and lungs showed no abnormalities. The liver was not felt, but the spleen was easily felt, and extended two fingers below the costal margin.

Laboratory Examinations. (1) Urine—bloody at first, but later clear. (2) Blood, Wassermann—negative.

Blood

Hæmoglobin	94%	Bleeding time	42 min.
Red blood-cells	5,120,000	Coagulation time	8 min.
White blood-cells	12,600	Tourniquet test	Positive
Platelets	10,000	Clot retraction	None
Polys. neut.	64.6%	Temperature	98° to 99°
Lymphocytes	31.3%	Pulse	88/120
Monocytes	4.0%	Respiration	20–24

Platelets very large.

The condition of the patient did not improve on the usual medical treatment and after a week in the hospital she began to menstruate profusely. She complained of feeling weak and this was reflected in the blood examinations. The hæmoglobin and red blood cells began to drop rapidly. October 18, 1924, the hæmoglobin was 69 per cent. and the red blood cells were 3,890,000. Pallor was becoming marked and the hemorrhages in the skin and mucous membranes increased. Splenectomy was done October 24, 1924, by Dr. Edwin Beer before the members of the Clinical Congress of Surgeons. Ether was used as an anæsthetic. A long left subcostal incision was made. The spleen was found high up under the diaphragm, adherent posteriorly and anteriorly. The spleen was not much enlarged and did not extend below the ribs. At the hilum of the spleen an accessory spleen, the size of a cherry, was found. No intraperitoneal bleeding was noticed. The patient stood the operation well. The pathologist reported no abnormal changes in the spleen except a relative increase in the number of Malpighian bodies.

The post-operative course was very stormy. The hæmoglobin kept steadily going down and November 1 reached 33 per cent. A blood transfusion of 500 c.c. was again given, but with little effect. The progressive fall in the hæmoglobin was due to the menorrhagia which was not checked by the splenectomy. The bleeding into the skin and mucous membranes, however, stopped. November 8, radiotherapy, to the hypophysial region to check the hemorrhage from the uterus was done. After this her bleeding became less and a week later the uterine bleeding stopped. She was then transferred to

the medical side November 16, with the wound almost healed. From then on she improved steadily and was discharged well December 3, 1924. Her hæmoglobin on discharge was 62 per cent.

A few of the blood examinations done since the splenectomy show the following:

	Oct. 29, 1924	Nov. 5, 1924	Dec. 11, 1924
Hæmoglobin	35%	29%	62%
Red cells	2,464,000	1,960,000	4,320,000
White cells	30,400	50,800	18,000
Platelets	12,000	10,000	80,000
Polys. neut.	85.3%	90%	78.5%
Lymphocytes	12.6%	8%	11.0%
Monocytes	2.0%	2%	8.0%
Coagulation time	8 min.		9 min.
Bleeding time	6 min.	7 min.	2 min.
Tourniquet test	Neg.	Neg.	Neg.
Clot retraction	None (24 hrs.)		Normal

The blood platelets do not show any great increase at first, compared to their number before operation. The leucocytosis has persisted. The blood picture is gradually assuming a normal aspect. Presented at the New York Surgical Society, ANNALS OF SURGERY, June, 1925.

The platelet count went up after operation and then dropped to pre-operative figures, but never returned to normal.

Patient continues in excellent health—no more bleeding.

CASE III.—A man, M. S., eighteen years of age, was admitted June 6, 1925, with the history summarized as follows:

Summary.—1. Measles in childhood. 2. Eczema in infancy—duration one year. 3. Influenza eight years ago. 4. Frequent sore throats up to three years ago. 5. Tonsillectomy three years ago. 6. Papular eruption associated with pruritis and bleeding one year ago. Duration two months. Bled easily and freely. Spontaneous disappearance. 7. Onset of present illness two and one-half months ago. 8. Onset with small hemorrhagic spots on feet, legs, forearms and chest. No pain or other sensations. 9. Eruption shows regression under treatment but recurred. 10. Two months ago began to spit blood. Unassociated with pain in chest, fever, chills or cough or sweat. Lasted one day. 11. Epistaxis two weeks ago. 12. Hæmaturia thirteen days ago. 13. Bleeding from gums at present. 14. Pain in left knee since yesterday. 15. Splenectomy advised at Bellevue.

Present Illness.—Two and a half months ago, found small hemorrhagic pin point to pin head sized flat spots on the feet. No pain, tingling or other sensations. Came out on the legs at the same time. Later in the day noted same condition on the forearms. The next day it came out on the chest. Felt perfectly well during this time. At the end of a week went to M.D. who gave patient a tonic and advised rest. Took tonic and rested for one week. Improvement noted during that week. Whole skin had previously appeared red and hemorrhagic at the site of the eruption but at end of week the skin showed a very great improvement so that comparatively few hemorrhagic spots were left. Returned to work. (Feeder on a printing machine; comes in contact with the metal of the linotype machine and the printed sheets.) Second day after returning to work, noticed he was spitting blood. No cough. No pain in chest. Thought blood came from throat. Blood was bright red. Eruption on body returned. Returned to M.D. Not relieved. Went to Bellevue three weeks ago. Was there fifteen days. Was given capsules. Eruption disappeared under medication but returned three days later. Two weeks ago nose began to bleed. Next day urine became bloody. Lasted two days. Never had blood in stool. Left Bellevue six days ago. Returned for observation few days ago. Told he needed a splenectomy. Bleeding from nose has ceased. Bleeding from mouth (gums) continues.

Hemorrhagic eruption persists. Since yesterday has pain in left knee. Lost six and one-half pounds in three weeks.

The patient is poorly nourished. General examination negative. The skin presents generalized multiple petechiæ, most numerous over chest. Hæmoglobin index, 65 per cent.

Bleeding time, eighteen and one-half minutes. Clotting time, six and one-half minutes. Tourniquet test, negative. Clot retraction, none after twenty-two hours, none after three days.

Red cells, 3,200,000; white cells, 9,875; polymorphonuclears, 65 per cent.; lymphocytes, 23 per cent.; eosinophiles, 2 per cent.; large monocytes, 10 per cent.

Blood-pressure, 110/60; hæmoglobin, 70 per cent.; platelets, 96,000. First sound at third interspace left of sternum reduplicated.

June 9, 1925

Hæmoglobin	76%	Polys. neut.	71%	Myelocytes	8%
Red cells	3,840,000	Polys. eos.	6%	Coagulation time ..	7 min.
White cells	20,600	Polys. bas.	2%	Bleeding time	14 min.
Platelets	5,000	Lymphocytes	13%	Tourniquet test ..	Sl. Pos.
				Clot retraction	None

The blood picture is typical for thrombocytopenic purpura hemorrhagica. The leucocytosis is probably the result of hemorrhage. Splenectomy is indicated provided that tuberculosis or any cause for symptomatic purpura are ruled out. Vide post. X-ray report on lungs which were negative.

The operation was done July 16, 1925, through a curved incision from close to ensiform process down to rectus sheath; across flat muscles of abdominal wall laterally between tip of twelfth rib and anterior superior spine.

The spleen with four accessory spleens at hilum was removed without any particular difficulty, vasa brevia were first doubly tied and splenic vein and artery exposed. After freeing tail of pancreas, on surface of which a small vein was tied, pedicle of spleen was ligated and dropped back. There was no oozing and abdominal wall was closed with modified "figure of 8."

August 4, 1925, Blood Examination

Hæmoglobin	55%	Baso.	4%
Red cells	3,610,000	Myelocytes	4%
White cells	13,000	Myeloblasts	2%
Polys.	71%	Bleeding time	2½ min.
Lymphocytes	12%	Coagulation time	2½ min.
Monos.	3%	Tourniquet time	Neg.
Eosino.	4%	Platelets	130,000

Wound healing slightly disturbed by serous accumulation at lower angle requiring period of drainage. Rapid recovery, sutures removed on the tenth day, examination of the spleen after removal showed normal structure. Pulp shows myeloid metaplasia. February, 1926 the man is in perfect health.

CASE IV.—M. A., a boy thirteen years of age was admitted September 11, 1925, suffering from epistaxis. Bleeding from gums, ecchymoses and purpuric spots on skin, four weeks.

No history of bleeding tendencies in family so far as patient knows. No history of other chronic familial disease. Father and mother living and well, one sister living and well.

Had mumps at age of eight. Had slight epistaxis previously only on rare occasions—perhaps once in two to three years and then of very short duration. No previous bleeding from the gums, no previous purpuric manifestations. No injuries or operations. Systems entirely negative. Head, eyes, ears, nose and throat negative. Cardiorespiratory—no

dyspnœa or palpitations, no cough. G. I.—appetite always good. Bowels regular. No digestive disorder. No melena or hæmatemesis. No dysuria—no hæmaturia.

Four weeks ago, the boy began to bleed from the nose. For a full week the bleeding persisted as a steady ooze and then stopped. Three weeks ago, for the first time he began to notice large and small ecchymotic blotches appearing over his body, chiefly in the lower extremities and hip regions. As these disappeared in the course of several days, new ones appeared. At the same time, crops of small pinhead sized purpuric spots began to make their appearance, most profusely over the extremities especially the lower but also over the rest of his skin. During these three weeks, he has also had bleeding from the gums. Has had no hæmoptysis, or hæmatemesis, has noted no blood in his stool or urine, has had no pains in the abdomen nor elsewhere. Since the onset of his illness, he has complained of slight dizziness at times when suddenly changing position. No visual disturbances. Thinks he has lost weight but does not feel particularly weaker than formerly. For two days, he has noted dryness and roughness of skin of hands and toes with vesiculation and desquamation of the superficial layers of the skin. No itching. Appetite is good, bowels are regular. Has had no digestive disorders. No urinary symptoms. No fever or chills. General examination negative.

He is a well-developed and well-nourished boy of thirteen, with no marked pallor, cyanosis or jaundice. Distributed over the body, posteriorly on legs, shoulders and back innumerable small cutaneous hemorrhages, most about 1 to 1½ mm. wide. In about ten places on the body, back, legs and arms are fading ecchymotic areas in stages of resorption, most about 2 to 3 cm. wide.

August 12, 1925, Blood Examination

Hæmoglobin ..	67%	Polys. neut.	64%	Coagulation time—5 min.	
Red cells	3,472,000	Polys. bas.	2%	Bleeding time—greater than 10 min.	
White cells ...	10,500	Lymphocytes ...	31%	(stopped)	
Platelets	20,000	Monocytes	3%	Tourniquet test—positive (2 min.)	
				Retraction of clot very slow at end of 18 hours	

Impression.—Typical blood picture of purpura hemorrhagica.

Pre-operative diagnosis.—Thrombocytopenic purpura.

Operation.—Splenectomy by Doctor Beer. Sub-costal incision. Stomach pulled mesially exposing the vasæ breviæ which were carefully tied and the vessels of the pedicle were in turn tied with chromic, pushing the tail of the pancreas from the hilus. The opening in the peritoneum, over the tail of the pancreas, was drawn together after the removal of the spleen. There was no particular bleeding from anywhere except the parietes which was controlled by ligatures before opening the peritoneum and by two layers of chromic sutures in closing the parietes. The deeper layer through muscle and peritoneum being continuous interlocking and the second layer being interrupted fascio-muscular. The skin was closed with silk.

Primary wound—healing.

August 21, 1925, Blood Examination

Hæmoglobin	75%	Polymorphonuclears	74%
Red cells	3,850,000	Lymphocytes	12%
White cells	26,550	Monocytes	14%
Platelets	550,000		

September 6, 1925—Final Note: Typical case of thrombocytopenic purpura hemorrhagica treated by splenectomy. Discharged to P. P. Well.

Urine examinations (7) negative.

February, 1926, patient is in excellent health.

CASE V.—A woman, twenty-two years of age, was admitted November 27, 1924 complaining of bleeding from nose on and off for four months and also increasing weakness. Past history—Negative. Six months ago, she started feeling weak, lost her appetite and began to have severe pains in front part of head with buzzing in the ears. She became gradually worse until four months ago when she had a severe nose bleed after blowing her nose; this lasted for two hours. She bled again one month later and again three weeks ago. She became weaker after each attack of nose bleeding. For past three weeks has been vomiting and noted the presence of blood in the vomitus one day before admission. Two weeks, the stools were tarry. No red spots were noticed in the skin. There was no bleeding from any other region except the nose. Her menstruation which stopped a week ago began again on day of admission.

She was a well-developed, pale woman with hemorrhagic blebs on lips. Conjunctivæ very pale. Fundi show multiple hemorrhages. The gums were swollen and bleeding actively. Numerous hemorrhages of mucous membrane of mouth and tongue. The tonsils were covered with numerous small hemorrhagic spots. The neck showed no glandular enlargements. Lungs were negative. The heart was normal in size; systolic murmurs at apex and base were not transmitted. Liver was soft, felt three fingers below costal margin. Spleen was firm, rounded edge felt three fingers below costal margin. Skin showed numerous petechial hemorrhages over neck, back, chest, abdomen and extremities. Symmetrical vitiliginous lesions over the back, chest, neck, breasts and lower extremities.

The admission diagnosis rested between acute purpura hemorrhagica and acute leucopenic myeloid leukemia.

Clinical Course.—Temperature varied between 99 and 103 before splenectomy. Pulse—80–140. Respiration—24–28.

November 27, 1924—Blood Examination on Admission (Doctor Rosenthal)

Hæmoglobin	22%	Lymphocytes	23%
Red cells	1,168,000	Monocytes	11%
White cells	7,400	Normoblasts—3 per 100 white cells	
Platelets	2,500	Coagulation time—4 min.	
Polys. neut.	62%	Bleeding time—10 min. (stopped on account	
Polys. bas.	11%	of profuse bleeding)	
Myelocytes n.	2%	Capillary resistance test—Positive	
Myeloblasts	1%	Clot retraction—None (48 hours)	

The blood picture is suggestive of leucopenic myeloid leukemia and symptomatic purpura hemorrhagica.

November 28, 1924—A direct transfusion of 800 c.c. was given. The hæmoglobin rose to 33 per cent. The general condition remained poor. No fresh petechiæ but gums were still swollen and bleeding.

December 1, as her condition remained the same and as the outlook was not encouraging, a splenectomy was decided upon to stop the hemorrhagic tendency although the blood picture suggested the presence of leukemia on account of the rapidly progressive anemia and the presence of a few premature myeloid granulocytes, the opinion was held that the condition may also be an essential thrombocytopenic purpura hemorrhagica. As no other form of therapy was available, splenectomy was considered as a last resort. A preliminary transfusion of 800 c.c. was given prior to the operation to put patient in condition to permit the operative procedure. The splenectomy was done by Dr. E. Beer, December 2, 1924, through a subcostal incision, ten inches long.

Procedure.—The enlarged spleen gradually delivered as vessels were tied. The gastro-splenic ligament was very short and had to be ligated to the greater curvature of the stomach. The splenic artery and vein were easily ligated. The capsule of the tail of the pancreas was intimately adherent to the hilum and had to be stripped away

leaving an oozing area—this was buried with a few sutures. This oozing could not be completely controlled. Drainage—Gauze covered with rubber dam.

A blood transfusion of 700 c.c. was given just before the operation and another transfusion of 750 c.c. was given immediately after the operation as the patient was in shock.

Three hours after the operation the patient died. Permission for autopsy could not be obtained.

REFERENCES

[1] Modern Clinical Medicine. D. Appleton and Company, 1911.
[2] Hayem, G.: Maladies du Sang, 1900.
[3] Minkowski, O.: Mediz. Klinik, December 7, 1919.
[4] Brill, N. E., and Rosenthal, N.: American Journal of the Medical Sciences. Oct., 1923.
[5] Duke: Archiv. Int. Medicine, 1912.
[6] Frank, E.: Berl. Klin. Wochenschrift, 1915.
[7] Kaznelson, P.: Wiener Klin. Wochenschrift, 1916, No. 46.
[8] Hess, A. F.: Archives Int. Medicine, 1916–1917, p. 203.