

with interposition of triquetrum between these displaced bones, is illustrated in Fig. 3. One mid-carpal dislocation was encountered and treated with satisfactory results.

Dislocation of the semi-lunar bone may occur in combination with other carpal injuries. Four patients were admitted with fractures of the scaphoid waist, and dislocation of the distal fragment and remainder of the carpus, in relation to the proximal fragment and lunate which remained in their normal positions. Two of these were pre-scapho-lunar, and two post-scapho-lunar fracture dislocations. One was not a true fracture dislocation in that the scaphoid was bi-partite, and the dislocation occurred at the congenital defect. Despite good anatomical reduction, the results in all four cases were disappointing. These men returned to duty in lower categories. One case of fracture dislocation, with congenital fusion of the triquetrum and lunate was reported elsewhere.¹

In three instances, severe fractures of the distal row of the carpus were associated with mid-carpal, and carpo-metacarpal subluxations. Imperfect reductions were obtained by manipulation, with subsequent ankylosis at the mid-carpal joint. The functional results, however, were good.

SUMMARY

1. The frequency of carpal injuries associated with fractures of the radius and ulna has been reported.
2. The efficacy of immediate and uninterrupted plaster immobilization of recent fractures, has been demonstrated.
3. Some features in the diagnosis of scaphoid fractures have been reviewed.
4. Sixteen, in a series of 145 fractures of the scaphoid, were treated by operative measures.
5. A few unusual fractures and dislocations have been recorded.
6. Eighteen cases with closed traumatic lesions of the carpus, under treatment at the present time, have not been reviewed.

We are indebted to Lloyd M. Hampson, M.D., for assistance in the preparation of this paper.

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SUBACUTE NEUTROPENIA TREATED BY SPLENECTOMY*

By Carlton Auger, M.D.,
J.-B. Jobin, M.D., F.R.C.P.[C.] and
L.-N. Larochelle, M.D.

Quebec

AMONG the physiological functions of the normal spleen, the phagocytic activity of its reticulo-endothelial cells for bacteria, foreign particulate matter, thrombocytes, red cells and leucocytes has long been recognized. There are also a few well defined splenic diseases already described, as for instance essential thrombocytopenic purpura and congenital hæmolytic icterus, in which this phagocytosis is abnormally enhanced.

In 1939, Wiseman and Doan reported three cases of neutropenia successfully treated by splenectomy. The presence of numerous elastomacrophages containing engulfed granulocytes in the splenic scrapings was held as convincing evidence of an abnormal splenic phagocytosis. In 1942,¹⁰ these authors extended their observations on the same cases to show that no relapse had occurred during the intervening period and reported two new cases. They suggested the term "essential or primary splenic neutropenia" for this newly recognized syndrome characterized by marked neutropenia and splenomegaly and, since varying degrees and combinations of hæmolytic anæmia and thrombocytopenia were present and coincidentally corrected by splenectomy in their five cases, they insisted upon the close relationship of their syndrome to hæmolytic icterus and essential thrombocytopenic purpura.

This granulocytopenic syndrome was confirmed by Moore and Bierbaum,⁶ who reported another case in 1939. Splenectomy was also followed by an immediate and permanent rise to a normal level of the leucocytes in the blood stream. A study of histological sections of the removed spleen showed numerous macrophages with ingested leucocytes.

Muether *et al.*⁷ gave a detailed report in 1941, of an additional case of granulocytopenia due to an excessive splenic lysis of neutrophils. In this case, however, phagocytosis of polymorphonuclear leucocytes in the spleen could not be demonstrated, but the splenic parenchyma con-

* From the Laboratories and the Department of Medicine of the Hôtel-Dieu Hospital, Quebec City.

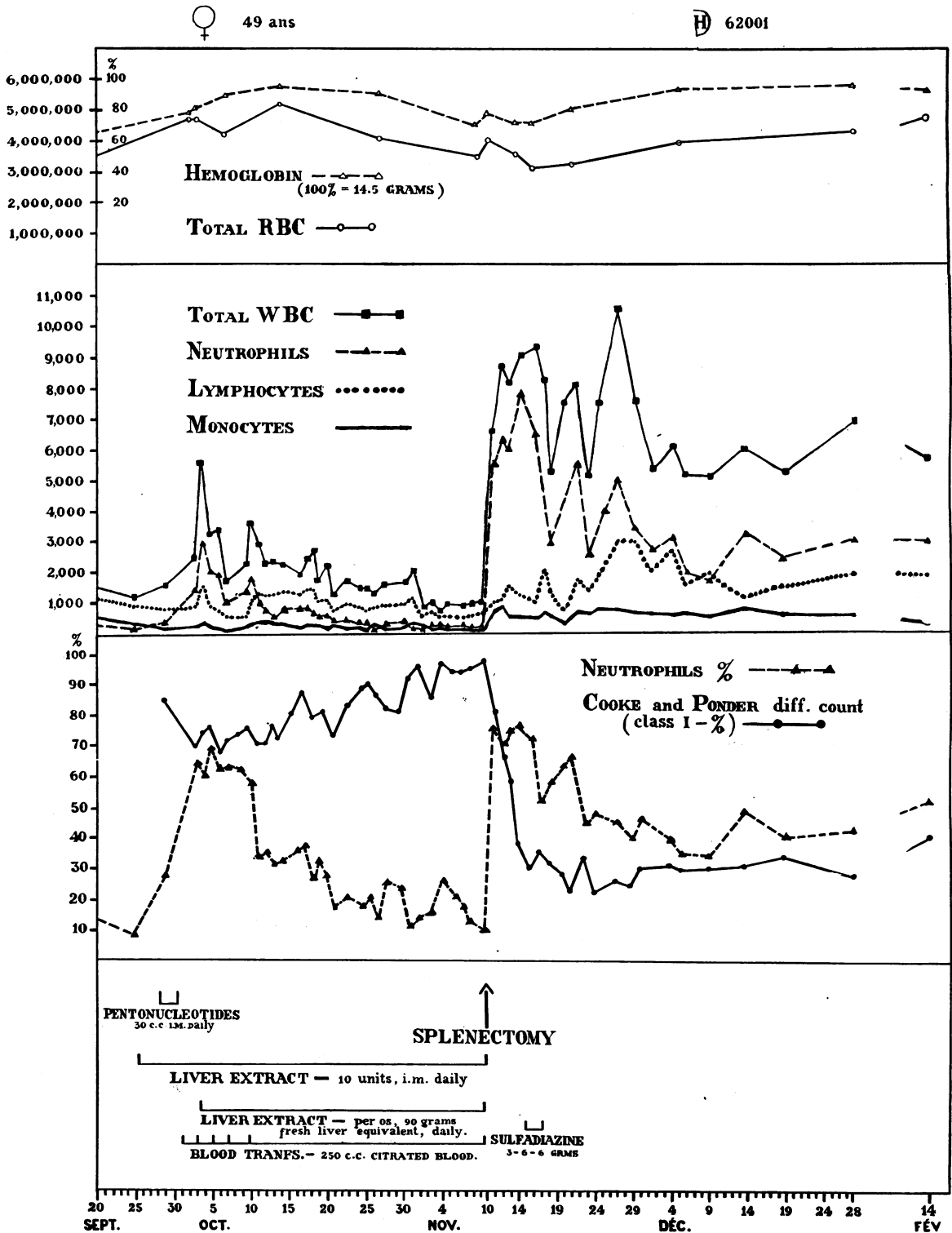


Chart 1

tained a great number of free granulocytes in different stages of degeneration. This different aspect may be explained by the fact that splenectomy was performed during a period when the neutropenia was not particularly pronounced.

This paper deals with an eighth case of neutropenia, which regressed after splenectomy.

CASE REPORT

J.B., white female, 49 years of age.

Medical history.—The patient had been in normal health until the middle of August, 1944, when she noticed the existence of a progressively enlarging tumour, in the left upper quadrant of the abdomen. Six days prior to her admission to the hospital, on September 19, the patient suffered violent abdominal pains. These pains awakened her during the night and persisted for four days, but varied in intensity. They were accompanied by a slight fever and on two occasions by the evacuation of a few diarrhoeic stools. She consulted her family physician, who prescribed sulfathiazole and opium, camphor and tannin tablets. She took about two grams of sulfathiazole; the diarrhoea and the abdominal pains ceased, but the temperature persisted.

On admission to the hospital the chief complaints were: the presence of a heavy tumour in the upper left abdomen, slight tenderness and dull, non-radiating pains in the same region, fever and a progressive general weakness and fatigue.

The systemic history was essentially negative and the hereditary and family histories were void. She had measles at an early age and from 1937 to 1940 presented recurrent painful swellings of most of the joints of both hands. This could be easily characterized as rheumatoid arthritis. In the preceding January, there had been an operation for traumatic fracture of the coccyx. The patient was the mother of thirteen children and had ceased menstruating three months ago.

Physical examination.—At the time of admission, the patient preferred to lie in bed. She was more or less co-operative and showed a certain degree of exhaustion. Her weight was 128 pounds, a few pounds under what she considered normal. The oral temperature was 103° F. and the pulse 96. There was a slight pallor of the skin and mucous membranes. The pharynx, on the other hand, was reddened and covered by a catarrhal exudate, but no ulcerative lesions were present.

At the base of the left lung, the murmur was noticeably decreased and the movements of the left diaphragm were slightly impaired.

The abdominal wall was soft and flabby. The liver and kidneys were not palpable. In the left upper quadrant there was a large mass with a sharp internal edge. This mass descended to the level of the umbilicus, presented a lumbar-contact and did not follow the diaphragmatic movements. Palpation occasioned some pain. The tentative diagnosis was that of an enlarged spleen of undetermined origin.

All the joints of the fingers were more or less hypertrophied and nodular. The fingers were slightly bent and crooked and complete extension could not be obtained.

Roentgenograms of the abdomen and the urinary tract confirmed the existence of a large spleen, which compressed the left kidney in the costo-vertebral corner. The left renal pelvis was distended and the proximal end of the ureter distinctly kinked.

Laboratory data.—The hematological findings are summarized in Chart 1. At the time of admission there was a low grade anaemia with 3,500,000 red cells and a profound leucopenia with 1,571 leucocytes, of which only 188 were granulocytes. An occasional neutrophil contained toxic granulations and the Cooke and Ponder

differential count showed a marked shift to the left. Lymphocytes and monocytes were qualitatively normal. In subsequent blood examinations, reticulocytes were found to be higher than normal: 2.5 and 4.8% (normal: 0.5 to 1.0%) and the thrombocytes lower: 152,070 and 132,830 (normal: 250,000 to 300,000 per c.mm.). Red cell fragility range: 56 to 36 gm. % salt equivalents (normal: 48 to 36 gm. %). Icterus index: 2.7 units (Fliessinger and Walter technique: normal 1.6 to 2 units). Blood coagulation time: 6 min. (capillary tube technique). Bleeding time: 2 min. 45 sec. Urinalysis: normal findings. Kline test: negative.

Widal tests for *Eberthella typhosa*, *Salmonella para. A*, *Salmonella para. B* and *Brucella abortus* were negative and no bacteria could be isolated from blood culture.

Bone marrow was obtained by sternal puncture on October 6. The differential count, tabulated in Table I, indicated a slightly hyperplastic bone marrow. No pathological cells were found.

TABLE I.

BONE-MARROW DIFFERENTIAL COUNT	
Myeloblasts	4.5%
Promyelocytes	8.8%
Myelocytes	
Neutrophil	11.7%
Eosinophil	3.4%
Basophil	0.0%
Metamyelocytes	
Neutrophil	11.0%
Eosinophil	1.1%
Basophil	0.5%
Non-segmented polymorphonuclears (stab)	
Neutrophil	18.0%
Eosinophil	0.5%
Segmented polymorphonuclears	
Neutrophil	2.0%
Eosinophil	0.8%
Erythroblasts	3.0%
Normoblasts	
Basophilic	2.8%
Polychrom	5.7%
Orthochrom	11.7%
Clasmatoocytes	4.0%
Megacaryocytes	0.2%
Lymphocytes	4.4%
Monocytes	0.8%
Plasmocytes	0.3%
W.B.C.: R.B.C. ratio	3.2:1.

Clinical course before splenectomy.—During the first two weeks of hospitalization, the patient's oral temperature varied between 102 and 103° F. In the first few days of October, this hyperthermia gradually decreased. On the 6th, the temperature was normal and the patient remained afebrile up to the day of splenectomy. During this period of pyrexia there were frequent chills followed by profuse sweating, severe anorexia, some loss of weight and a progressively alarming state of exhaustion. On one occasion the patient became delirious.

Pentnucleotides, liver extracts and blood transfusions were administered as summarized in Chart 1.

In the middle of October, following five transfusions of citrated blood, the patient's condition had improved. The spleen, after having gradually decreased in volume, finally disappeared behind the costal wall. The red cell count reached 5,260,000 cells, but the total number of leucocytes remained low: 2,071, with only 30% neutrophils (October 14).

An adrenalin test was performed on October 31. After the subcutaneous injection of 1 c.c. of 1:1,000 adrenalin, the red cells rose from 4,260,000 to 5,600,000 and the leucocytes from 2,642 to 8,285. The detailed hematological variations obtained during this test are indicated in Charts 2, 3, 4.

At the beginning of November, the spleen became once more palpable and descended approximately 4 cm. below the costal margin. The total number of leucocytes fell to 678 on November 2 and 785 on November 4. The patient's general condition became very serious. She had continued to lose weight and had now lost approximately 25 pounds since her admission.

Splenectomy was suggested and the patient immediately consented.

Operation.—Splenectomy was performed on November 10, by Dr. François Roy and Dr. E. Samson. A few minutes before placing ligatures on the splenic pedicle, ½ c.c. of 1:1,000 adrenalin was injected intramuscularly. After liberating a few fibrous adhesions at the upper part of the anterior aspect of the spleen, the organ was easily removed. The liver appeared normal and there were no signs of portal hypertension.

PATHOLOGY OF THE SPLEEN

Gross.—The spleen weighed 966 grams. All diameters were equally augmented (19.5 x 12.5 x 7.0 cm.) and the normal shape of the organ was conserved. The capsule was moderately thickened and presented evidence of mild chronic perisplenitis in the upper part of the anterior aspect; elsewhere it was normal. Upon section,

the parenchyma was firm and of a deep cherry-red colour. Malpighian corpuscles, not exceptionally numerous, could be easily recognized.

Microscopic.—The examination of paraffin sections revealed no great abnormality in the white pulp. The lymphatic nodules were of normal size and only very moderately increased in number. Clear (lymphocytopoietic) centres were not exceedingly numerous and presented only here and there a few mitotic figures. No "reaction centres" were seen.

The Billroth cords and venous sinuses, on the other hand, were more abundant than normal. The former contained many reticulo-endothelial elements of two types: cells of moderate size with relatively little protoplasm and dark staining nuclei and large pale irregular cells with abundant, but indistinctly outlined, protoplasm and poor staining nuclei. A relatively high number of these cells were in mitotic division. Scattered through the red pulp were some red cells, lymphocytes, plasmocytes and eosinophils, occasionally myelocytes.

Many venous sinuses were distended. They were lined with large irregularly shaped pale staining elements, very alike in aspect to the large reticulo-endothelial cells of the red pulp. Some of these cells rested with a broad base on the wall of the sinus. Others were held only by a narrow protoplasmic process and projected far into the lumen. Neighbouring cells were often united with each other through cytoplasmic bridges and thus formed foci of a cellular meshwork replacing the greater part of the lumen. A considerable number of these cells were detached and free, becoming round or oval in shape. The sinuses contained also some red cells, a few lymphocytes and eosinophils and an occasional neutrophil.

The reticulum was found to be normal after silver staining by the Laidlaw technique.

The most outstanding microscopic finding was definite evidence of an exaggerated phagocytic activity of the splenic macrophages (Fig. 1): the large, pale, poorly delimited reticulo-endothelial cells lining the sinuses and those found in large number in the Billroth cords. At medium magnification, five to six of these cells containing still easily recognizable whole polymorphonuclear neutrophils could be seen. In others the ingested granulocytes showed signs of more or less advanced degeneration: the nuclei were either pycnotic or swollen or were broken into two or three very dark minute fragments. The cytoplasmic granulations of the engulfed leucocyte had generally more or less disappeared and in many the cytoplasm was transformed into an amorphous substance, which often showed a great

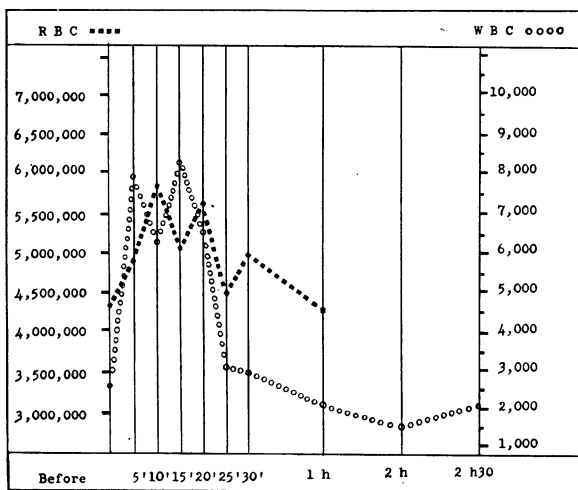


Chart 2.—Adrenalin test: total red blood cell and white blood cell values.

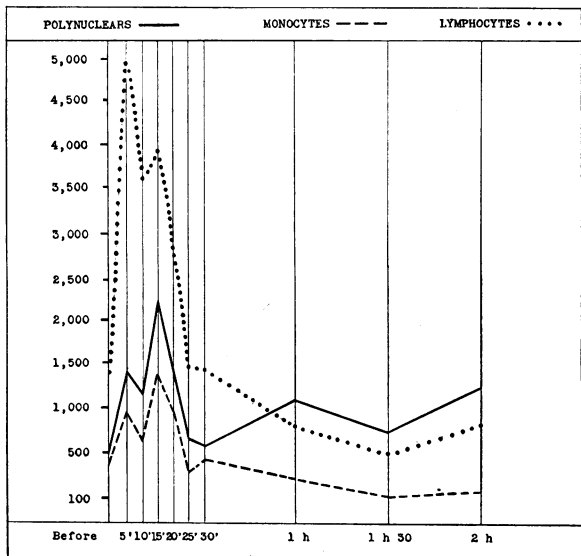


Chart 3.—Adrenalin test: absolute polymorphonuclear, lymphocyte and monocyte values.

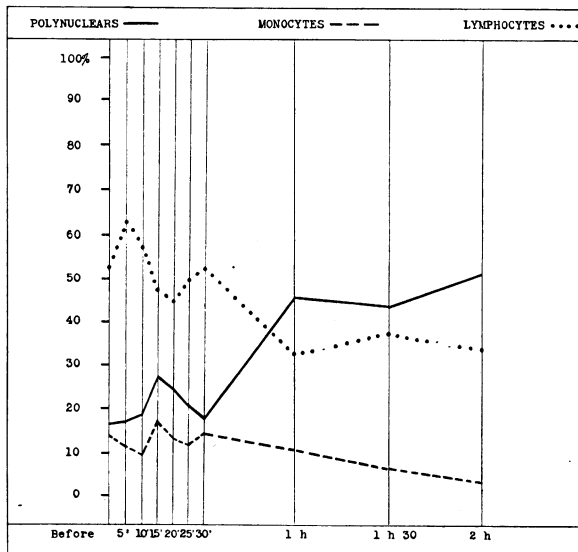


Chart 4.—Adrenalin test: polymorphonuclear, lymphocyte and monocyte percentages.

affinity for eosin. In many macrophages, dark staining particles with clear centres and small eosinophilic globules could be demonstrated. These formations were interpreted as nucleic and cytoplasmic remnants of phagocytized leucocytes.

The phagocytic cells contained also an abnormally high number of red blood corpuscles. In many fields, macrophages with two or three ingested red cells were found. A few contained even side by side red blood corpuscles and granulocytes (Fig. 2). Some of the phagocytized red cells stained very poorly and were in different stages of degeneration. Coarse granules or fine particles of yellow intracellular and extracellular pigment, doubtlessly derived from hæmoglobin, was present in very moderate quantities.

Postoperative course. — A blood count taken 30 minutes after ligation of the splenic pedicle showed that the leucocytes had risen to 4,142. Four hours later they had reached the level of 5,642. As indicated in Chart 1, during the 48 subsequent days of hospitalization, the leucocytes never fell below 5,000 and the Cooke and Ponder PN differential count showed a progressive turn towards normal. There was also a marked rise in the blood platelets with figures as high as 896,400 (November 23) and the percentage of reticulocytes gradually returned to normal, finally reaching 0.3%.

During the first four days following splenectomy the patient's temperature varied between 101.6 and 103° F.; after that it became normal. Fifteen grams of sulfadiazine were given during this period in treatment of a localized pulmonary congestion at the base of the left lung.

The patient improved steadily thereafter. She gained strength and recovered most of her lost weight. The only complaint was intermittent and dull pain in the upper mid-abdomen. This pain disappeared in the fourth postoperative week.

The patient was discharged to her home on December 28. She returned for a check-up 96 days after splenectomy and was found in good health with a leucocyte count of 5,785 and 53% polymorphonuclears.

DISCUSSION

When the patient was admitted to the hospital, a tentative diagnosis of agranulocytosis was made. No signs of infection were present, however, and a thorough inquiry did not reveal that any drugs, amidopyrine in particular, had been taken prior to the onset of the present illness. The patient had taken a few grams of sulfathiazole four or five days before her admission, but at that date she had been complaining of an enlarged spleen for at least a month, her oral temperature was above normal since two days and she had already lost some weight.

Study of the sternal bone marrow did not fit into this preliminary diagnosis either. There was no "maturation arrest" of the myeloid elements as commonly found in malignant agranulocytosis.^{3,4} The differential count, compared with normal values,⁸ indicated an hyperplastic bone marrow with mature cells present in suffi-

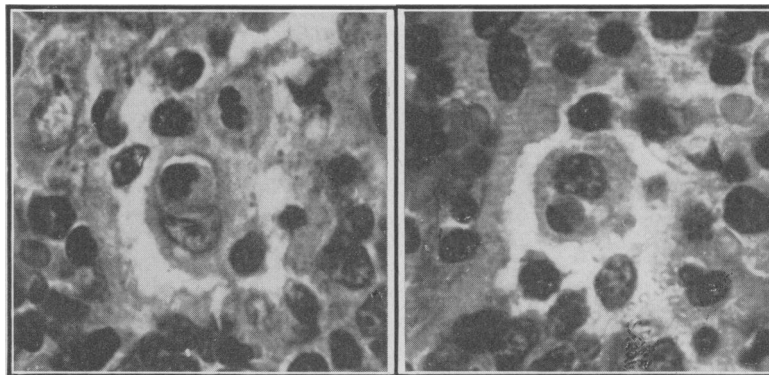


Fig. 1

Fig. 2

Fig. 1.—Distended splenic sinus containing two phagocytized neutrophils. Fig. 2.—Distended splenic sinus; in the centre there is a free macrophage containing a polymorphonuclear and two erythrocytes.

cient quantities. The percentage of segmented neutrophils in comparison to stab forms, however, was low and approached the ratio of these cells in the peripheral blood.

Splenic contraction obtained by the subcutaneous injection of 1 c.c. of 1:1,000 adrenalin furnished significant findings. As seen in Chart 2, the injection of adrenalin was followed by a rapid and transitory rise in the total red and white blood counts: after 10 minutes, the red blood corpuscles had passed from 4,200,000 to 5,800,000 and after 15 minutes, the leucocytes from 2,500 to 8,250. A blood count made 1 hour after the injection showed that the counts had returned to their initial levels. The curves obtained are twice as high for the red cells and six times higher for the white cells than those recorded in normal individuals.¹

Even in splenectomized patients adrenalin causes normally, after the initial level has been reached, a second and more permanent rise of the circulating leucocytes.¹ One hour, 30 minutes, 2 hours and 3 hours after an injection, counts of 8,000, 10,000 and 12,000 are regularly obtained. This leucocytosis is generally due to a polynucleosis, following the contraction of other granulocytopoietic tissues: *i.e.*, the bone marrow. A study of the subsequent total leucocyte counts made 1 hour 30 minutes and 2 hours after the adrenalin injection in the present case does not show this second rise of leucocytes (Chart 2). But graphs of the neutrophil, lymphocyte and monocyte absolute values (Chart 3) and especially of their percentages (Chart 4) clearly indicate that this polynucleosis did occur. That it was not evident in the total white cell counts may be explained by the

fact that the momentarily higher output of the bone marrow must have been continually balanced by an exaggerated depletion of neutrophils from the blood stream. The logical hypothesis, made at the time of the test, was that this depletion might be due to an abnormal activity of the patient's enlarged spleen. This organ did contain an abnormally high number of leucocytes, as the height of the first rise of leucocytes due to splenic contraction (Chart 2) clearly indicates.

Splenectomy was followed by a quick and decisive change in the hæmograms. Within four hours the number of white cells per c.mm.³ was above 5,000 and during the seven postoperative weeks of hospitalization they never fell below this figure. Seven weeks later their number was still 5,785, of which 53% were polymorphonuclears.

A study of the Cooke and Ponder PN differential counts made before and after splenectomy is of considerable interest (Chart 1). Up to the day of operation this count showed a striking shift to the left with from 75 to 97% of the polymorphonuclears in class 1. Following splenectomy the intensity of this shift gradually diminished; for the first time polymorphonuclears with 3 and 4 distinctly lobulated nuclei appeared in the peripheral blood. These findings are in support of the fact that the return of the white cells to a normal level is not to be confounded with the leucocytosis not infrequently found following the removal of even a normally functioning spleen, but is the direct consequence of the disappearance of the depleting factor. The Cooke and Ponder differential count, however, did not return completely to normal and 14 weeks after splenectomy it still read 41-41-14-3-0.

Histological study brought conclusive evidence of an abnormal phagocytic activity of the spleen. An increase in number, in size and in activity of the splenic macrophages was easily demonstrated. There were no fundamentally pathological cells present and no tumoral or inflammatory process could be detected. No nuclear or protoplasmic inclusions were seen.

There is little doubt that our case is a perfect example of the syndrome first described by Wiseman and Doan under the term "Primary or Essential Splenic Neutropenia"¹⁰ and cannot be confused with other neutropenic syndromes such as Banti's disease or Felty's syndrome.²⁻⁵

The etiology of Wiseman and Doan's syndrome is still unknown. These authors suggest that their syndrome is closely akin to congenital hæmolytic icterus and essential thrombocytopenic purpura and possesses in all probability a comparable mechanism.¹⁰ The accentuation of the physiological function of the spleen in congenital hæmolytic icterus, as stressed by Haden, is a direct response to microspherocytosis, an inherent constitutional defect of the red cells. The primary lesion in thrombocytopenic purpura, where the spleen shows also an exaggerated activity, is still unknown, but may also lie in a basic defect of the platelets. It is impossible to ascertain with which cause the neutropenia in our case may be correlated. The overactive phagocytosis of the spleen may be due to some hereditary or environmental factor or again the spleen simply have removed from the peripheral blood in great numbers effete and fundamentally altered granulocytes. There was no morphological evidence of any alteration in the circulating polymorphonuclears in our case, except the fact that, even after splenectomy up to 14 weeks later, polymorphonuclears with one lobe and two-lobed nuclei were still predominant. The Cooke and Ponder differential counts obtained can be compared to those seen in Pelger-Huët's leucocytic anomaly, where due to an hereditary defect the maturation of neutrophils is arrested in the one or two-lobe stage.⁹

As in Moore and Bierbaum's⁶ case, eosinophilia was a constant finding in our patient during her hospitalization. This eosinophilia was always high and was never completely explained. On admission, however, there were no eosinophils present in the routine blood count. They only appeared following liver extract therapy. After splenectomy this eosinophilia persisted for some time, but, when the patient returned for a check-up 14 weeks after operation, their number had considerably decreased. Postoperative eosinophilia is not infrequent after the removal of even a normal functioning spleen.¹

SUMMARY

An eighth case of "essential or primary splenic neutropenia", a syndrome first described by Wiseman and Doan, is presented.

A pronounced neutropenia and splenomegaly with a low-grade anæmia of the hæmolytic type and a moderate thrombocytopenia, in a woman, 49 years of age, did not regress under standard

therapeutic management. Study of the bone marrow and of the hæmatological variations during splenic contraction obtained by adrenalin indicated that the spleen could be the incriminating factor in this hæmolytopoietic disequilibrium.

Splenectomy was curative. Histological examination demonstrated an increase in the number and in the phagocytic activity of the splenic macrophages. The opinion is expressed that this macrophagic hyperplasia may only constitute a response to some still undetermined alteration of the circulating granulocytes.

We wish to express our thanks to Dr. Louis Berger for his helpful criticism of this paper and to Sister St-Maurice for invaluable technical assistance.

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**A STUDY OF ASCORBIC ACID
 NUTRITION**

By H. Jean Leeson, M.D.,
 Jean F. Webb, M.D., D.P.H.,
 Helen P. Ferguson, M.A.,
 Evelyn M. Semmons, M.A.,

and

E. W. McHenry, Ph.D.

*School of Hygiene, University of Toronto,
 Toronto*

THERE has been considerable discussion regarding human requirements for ascorbic acid and also about the incidence of mild deficiencies of this vitamin. In the course of an examination of hospital diets an opportunity was available to study the effects of supplementing a customary "low" intake of ascorbic acid.

All of the subjects in this study were adult patients in a mental hospital, who had been in the institution for at least several years. It had been noted that the institutional diet provided rather small amounts of ascorbic acid, and the study was designed to demonstrate whether any

beneficial effect could be observed in the physical condition of the patients when their ascorbic acid intake was increased. Many of the subjects were suffering from degenerative heart disease or from hypertension; otherwise, none were known to have any disease, other than mental illness. No member of the group was suffering from an acute infection or hyperthyroidism, so far as could be detected by physical examination.

The institutional diet supplied ascorbic acid only in the form of (a) canned tomatoes, which were served about once a week alone, and two or three times a week in mixed dishes such as rice and tomatoes; (b) other vegetables; and (c) cooked fruit. Cabbage salad appeared on the menu about once a week. No raw fruit was served. Since the vegetables were cooked in a central kitchen and transported to the wards for consumption, it is extremely doubtful whether any considerable amounts of ascorbic acid were retained. Although individual records of food intake could not be obtained from each patient separately, it was estimated that the average supply of ascorbic acid could not exceed 20 to 25 mgm. daily. The intake was about one-third of the allowance recommended by the U.S. Food and Nutrition Board but not much below the League of Nations' standard.

Approximately equal numbers of males and females were studied, with an age distribution of 20 to 70 in both sexes. All the subjects were given the same institutional diet. Each of the two main groups, male and female, was divided into three parts; one group, the control, was given no supplementation of the diet; in the second group, each subject was given 100 mgm. of synthetic ascorbic acid daily in two tablets; in the third, each subject was given 8 ounces of canned grapefruit juice daily, which was found by assay to provide 58 mgm. of ascorbic acid in 8 ounces. Sufficient supervision was given to ensure that these supplements were actually taken by the patients. Supplementation was continued for a three-month period in the spring of 1944. The subjects were examined at the beginning and end of the period of observation.

The examination consisted of an appraisal of the individuals' apparent nutritional status, with detailed examination of gums, skin and joints. The gums were examined macroscopically, by daylight, and with the biomicroscope for evi-