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The Effect of Splenectomy on the Leucocyte Count

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Summary. The effect of splenectomy on the peripheral blood leucocyte count has been studied in patients suffering from various types of hereditary haemolytic anaemias and in haematologically normal individuals. In each group of patients studied there was a marked increase in the total leucocyte count, and in the lymphocyte and monocyte counts, 3 months or more after splenectomy. The neutrophil count was also increased but to a lesser degree. The number of leucocytes of all categories in the peripheral blood did not seem to be influenced by the presence of anaemia persisting after splenectomy.

Removal of the spleen in man is frequently followed by thrombocytosis and leucocytosis. The increase in platelet count is usually transitory unless the patient continues to be anaemic (Hirsh and Dacie, 1966). The changes in the leucocyte count have been described by Ask-Upmark (1935), Singer, Miller and Dameshek (1941), Ek and Rayner (1950) and Lipson, Bayrd and Watkins (1959) and others. Most authors agree that there is an increase in the total leucocyte count: according to Crosby (1963) this is at first mainly due to an increase in the neutrophil count which takes place immediately after operation; within a few weeks, however, the neutrophil count subsides to about normal levels and the total lymphocyte and monocyte counts tend to rise. The present paper is concerned with the long-term effects of splenectomy on the leucocyte count in the peripheral blood, with particular reference to the effect, if any, of the persistence of anaemia after splenectomy.

PATIENTS AND CONTROL SUBJECTS

Patients

The subjects studied were haematologically normal people who had been subjected to splenectomy for rupture of the spleen or in the course of a gastrectomy, or patients suffering from various types of hereditary haemolytic anaemia. They were unselected, the only criteria for inclusion being that haemoglobin, leucocyte and platelet count data obtained from venous blood were available before splenectomy and/or 3 months or more after splenectomy. (Patients suffering from aplastic or hypoplastic anaemia or from a myeloproliferative disease were excluded from the study.) In most of the patients numerous total leucocyte and differential counts had been recorded. In all, 175 counts on 58 post-splenectomy patients were available for analysis. Of these 58 patients, 34 (119 counts available) had been subjected to splenectomy 10 or more years ago and 24 (56 counts available) had been splenectomized between 3 months and 10 years before this study. The mean values of the counts for each patient have been used in this study. The patients have been divided into four groups.

Group A: patients without a blood disease (ruptured spleen or splenectomy associated with gastrectomy).

Group B: patients with either hereditary spherocytosis or hereditary elliptocytosis. Data on 20 adult patients on whom information is available before and after splenectomy are tabulated separately. Children under the age of 10 years form a second small subgroup.

Group C: patients with hereditary non-spherocytic haemolytic anaemia, either of the pyruvate-kinase or glucose-6-phosphate dehydrogenase deficiency type.

Group D: patients suffering from miscellaneous haemolytic anaemias, not responding to splenectomy.

Normal Control Subjects

Total and differential leucocyte counts were carried out in 52 normal adults (26 male, 26 female) all of whom had normal haemoglobin levels (Control Group I). Venous blood

TABLE I

MEAN NORMAL LEUCOCYTE COUNTS AND MEAN LEUCOCYTE COUNTS FOLLOWING SPLENECTOMY IN HAEMATOLOGICALLY NORMAL SUBJECTS

	No.	*Total leucocyte count (per cu.mm.)*	*Neutrophils (per cu.mm.)*	*Lymphocytes (per cu.mm.)*	*Monocytes (per cu.mm.)*
		Mean± SD	*Mean± SD*	*Mean± SD*	*Mean± SD*
Control I	52	6500± 1412	3777± 920	2229± 640	348± 179
Control II	13	6250± 2220	3850± 1760	1810± 670	400± 190
Post-splenectomy					
Group A	7	9000± 2330	5080± 1960	3140± 1380	670± 510
Ek and Rayner (1950)	17	8235± 2270	4694± 1590	2660± 685	604± 370
Pedersen and Videbaek (1966)	30	7800	4080	2760	540

was used and the differential counts were based on the examination of 200 leucocytes. In addition, a number of blood counts were available in haematologically normal subjects who were later subjected to splenectomy. These data, together with leucocyte count data from unaffected individuals in whose family haemolytic anaemia had been found, served as a further small control group (Control Group II). The data from the two control groups are shown in Table I which also includes data on patients without haematological disease who had been subjected to splenectomy (Group A) together with some post-splenectomy data taken from the literature.

Methods

The haematological methods used were those described by Dacie and Lewis (1963).

RESULTS

Pre-splenectomy (Table II)

The mean leucocyte counts before splenectomy of patients in Group C and Group D were similar to those of the normal controls (Contol Group I). Patients with hereditary spherocytosis or elliptocytosis (Group B), however, had total leucocyte counts and total

TABLE II

MEAN PRE- AND POST-SPLENECTOMY LEUCOCYTE COUNTS AND PERCENTAGE INCREASES AFTER SPLENECTOMY

		No.	*Mean total leucocytes (per cu.mm.)*	*Per cent increase*	*P value*	*Neutrophils mean (per cu.mm.)*	*Per cent increase*	*P value*	*Lymphocytes mean (per cu.mm.)*	*Per cent increase*	*P value*	*Monocytes mean (per cu.mm.)*	*Per cent increase*	*P value*	*Hb (g./100 ml.)*	*P value*
Normal Control Group I		52	6500			3777			2229			348			13.1	
Group A: Post-splenectomy		7	9000	39	0.001	5080	35	0.01	3140	44	0.002	670	93	0.001	13.4	N.S.
Group B	Pre-splenectomy	39	7560			5460			1760			330			12.1	
	Post-splenectomy	28	11060	46	0.001	6570	20	0.1>P>0.05	3200	82	0.001	810	145	0.001	14.6	0.001
	Pre-splenectomy	20*	8350			5275			2070			340			11.3	
	Post-splenectomy	20*	11050	32	0.001	6000	13.5	N.S.	3700	79	0.05	770	126	0.001	14.7	0.001
Under	Pre-splenectomy	14	9860			4870			4200			380			10.1	
10 years	Post-splenectomy	7	12000	22	0.001	4990	2	N.S.	5900	40	0.001	940	148	0.001	13.1	0.001
Group C	Pre-splenectomy	9	6500			4060			1900			300			9.4	
	Post-splenectomy	6	11500	77	0.001	6380	57	0.01	3960	108	0.001	870	190	0.01	8.8	N.S.
Group D	Pre-splenectomy	6	6000			3570			1820			287			10.2	
	Post-splenectomy	9	10000	66	0.01	5454	53	N.S.	3200	76	0.01	961	230	0.001	10.2	N.S.

N.S. = not significant.

* Data were available before and after splenectomy on 20 of the patients in Group B. These data are recorded separately.

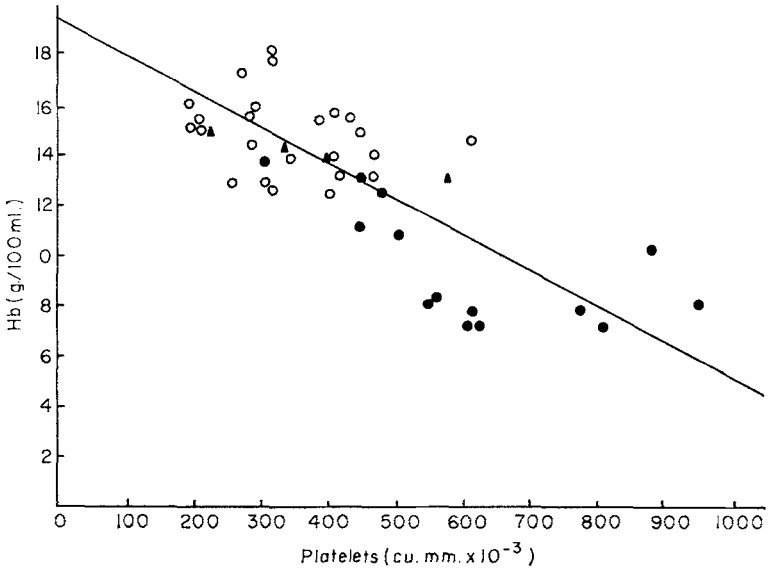

FIG. 1. The relationship between the platelet count and haemoglobin level in splenectomized patients. The regression line ($y = 18.66 - 0.013x$) is of high statistical significance ($P < 0.001$). For the sake of clarity some of the data have not been plotted. In every instance the excluded values fell within the area illustrated. (Data from Hirsh and Dacie, 1966.) ▲, Normal patients; ○, hereditary spherocytosis; ●, hereditary non-spherocytic haemolytic anaemias.

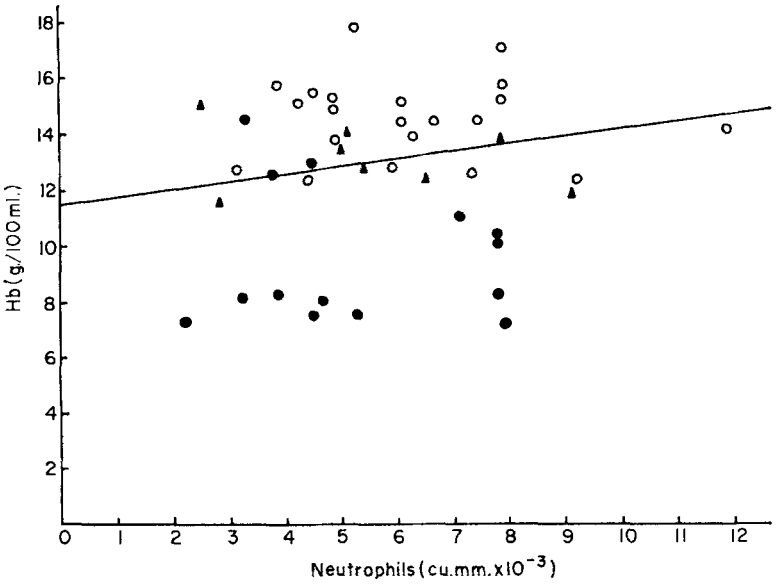

FIG. 2. The relationship between the neutrophil count and the haemoglobin level in splenectomized patients. The regression line ($y = 11.5 + 0.26x$) is not statistically significant ($0.1 > P > 0.05$). For the sake of clarity some of the data have not been plotted. In every instance the excluded values fell within the area illustrated. ▲, Normal patients; ○, hereditary spherocytosis; ●, hereditary non-spherocytic anaemias.

neutrophil counts somewhat greater than those found in either of the other two groups or in the control series. The mean total lymphocyte and monocyte counts in all groups studied were substantially the same before splenectomy.

Post-splenectomy (Table II)

Three months or more after splenectomy the total leucocyte count was increased in all four groups. The percentage increase was slightly greater in Group C and Group D than in Group A and Group B.

(a) *Neutrophil counts.* The number of neutrophils was increased (compared with the pre-splenectomy counts) and again the increases in Group C and Group D were slightly greater than in Group A. In hereditary spherocytosis (Group B), however, the results were slightly different. There was an increase in the total neutrophil count but the percentage increase was less than half of that found after splenectomy in patients suffering from non-spherocytic haemolytic anaemias (Groups C and D). The small nature of the increase is emphasized when the data from the 20 patients on whom counts were available before and after splenectomy are considered. The mean increase in the neutrophil count was only 750 cells per cu.mm. —an increase which is not statistically significant.

(b) *Lymphocyte and monocyte counts.* In children under 10 years the mean percentage increase in the total leucocyte count was only half of that found in adults and this was due almost entirely to increases in the monocyte and lymphocyte counts. The alterations in the leucocyte count following splenectomy in children suffering from hereditary spherocytosis are similar to those described by Wollstein and Kreidel (1936). In all four groups of adult patients studied there was a marked and statistically significant increase in both the lymphocyte and monocyte counts.

In contrast to the platelet count the total leucocyte count, and in particular the neutrophil count, does not seem to be in any way related to the post-splenectomy haemoglobin level (Figs. 1 and 2).

DISCUSSION

The changes that we have observed in the leucocyte counts of patients without haematological disease (Group A) after splenectomy are similar to those which have been described by Ek and Rayner (1950) and Pedersen and Videbaek (1966), who studied normal individuals whose spleen had been removed for traumatic rupture (see Table I). It is clear that the total leucocyte count rises following removal of the spleen for any cause. The increase is first confined mainly to the neutrophils. However, after several weeks to a few months, the neutrophil count falls to near normal levels and the number of circulating lymphocytes and monocytes rises and remains increased apparently permanently.

In the present study the mean neutrophil count 3 months or more after splenectomy was increased in each group studied compared to the pre-splenectomy values. In Group A and Group C the increases were statistically significant. When the data from Group C and Group D were pooled (i.e. taking together all patients whose haemoglobin level had not risen after splenectomy), the mean increase in the neutrophil count became statistically significant. In every group there was a marked and statistically significant increase in both the lymphocytes and monocytes.

The mean differential leucocyte counts of the normal individuals and of the splenectomized patients are given in Table III. After splenectomy there is a reduction in the percentage of circulating neutrophils although the absolute neutrophil count is increased.

The striking feature of post-splenectomy thrombocytosis is the inverse relationship which exists between the haemoglobin concentration and the height of the platelet count (see Fig. 1) (Hirsh and Dacie, 1966). A fall in haemoglobin concentration seems to stimulate both red cell and platelet production, and Linman (1962) has shown that injections of extracts

TABLE III

MEAN DIFFERENTIAL LEUCOCYTE COUNTS BEFORE AND AFTER SPLENECTOMY

		No. of patients	*Neutrophils (per cent)*	*Lymphocytes (per cent)*	*Monocytes (per cent)*
Control I		52	58	34	5
II		13	62	29	6
Group A	Post-splenectomy	7	56	35	7
Group B	Pre-splenectomy	39	72	24	4
	Post-splenectomy	28	59	29	7
	Pre-splenectomy	20*	63	25	4
	Post-splenectomy	20*	54	33	7
Under 10 years	Pre-splenectomy	14	49	43	4
	Post-splenectomy	7	42	49	8
Group C	Pre-splenectomy	9	62	29	5
	Post-splenectomy	6	55	34	8
Group D	Pre-splenectomy	6	60	30	5
	Post-splenectomy	9	54	32	10

* Data were available before and after splenectomy on 20 of the patients in Group B. These data are recorded separately.

of human plasma which stimulate platelet production in the experimental animal also stimulate leucopoiesis. In man, however, the increase in neutrophil count is not correlated with persistence of anaemia after splenectomy (Fig. 2).

The mechanisms by which anaemia persisting after splenectomy stimulates platelet production are not well understood. But in view of the fact that red cells, platelets and neutrophils appear to be derived from a common precursor and that red-cell and platelet production seems to be stimulated simultaneously by chronic anaemia (although this is only obvious after splenectomy) a comparable rise in neutrophils could have been anticipated. Our data, however, do not provide evidence of this. There is, however, one important difference between red cells and platelets and neutrophils which has to be borne in mind: this is that although red cells and platelets live out their life-span in the circulating blood stream, neutrophils do not—many if not all are cells in passage to extravascular tissues where they can exert their physiological function. Hence, a change in the rate of leucocyte production is not likely to be reflected in a change in peripheral leucocyte count to anything like the extent that are changes in the rates of erythropoiesis and thrombopoiesis.

A further point is that in man about half of the blood neutrophils, though remaining within the vascular system, do not circulate freely. Neutrophil numbers in the peripheral blood can, therefore, change easily and independently of alterations in the rate of production. Indeed, the redistribution resulting from the movement of temporarily sequestered cells into the circulating blood stream causing an increase in the number of circulating neutrophils does not even reflect a change in the total number of neutrophils in the peripheral blood.

The increases in the lymphocyte and monocyte count after splenectomy are difficult to explain. Crosby (1963) suggested that after removal of the spleen its functions are to some extent at least taken over by other organs. It is certainly obvious from the present data that the spleen plays some part in the regulation of the lymphocyte and monocyte counts. At first sight, removal of a spleen which is rich in lymphoid tissue might be expected to lead to lymphopenia rather than the reverse. The present evidence suggests that the spleen normally may also act as a storehouse for lymphocytes produced elsewhere. However, the long life-span of the lymphocytes and their repeated recirculations make it difficult to infer anything about alterations in the production rate of lymphocytes from changes in the lymphocyte count of venous blood.

The spleen is also thought to be one of the major sites of monocyte production. But again, and paradoxically, splenectomy seems to be associated with an increase in the number of monocytes in the peripheral blood. Knowledge of the kinetics of monocyte production is unfortunately sparse and the significance of the increased numbers of monocytes in the peripheral blood after splenectomy can at present only be a matter for speculation.

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