

LEUKOCYTIC STUDIES ON SOLDIERS WITH IRRITABLE HEARTS *

LESLIE N. GAY

First Lieutenant, M. C., U. S. Army

LAKEWOOD, N. J.

INTRODUCTION

This study of the morphology of the blood with reference to the leukocyte in cases of "irritable heart of soldiers" was suggested by the report of the Medical Research Committee, under the direction of Dr. Thomas Lewis.¹ In comparing this work to that which has been published in England, it must be borne in mind that the cases studied in the Hampstead Military Hospital may have differed from the type observed in U. S. Army General Hospital 9, at Lakewood, N. J. However, the basis of this work was a large series of selected cases in which no organic lesion of the heart and no foci of active infection were found by careful and repeated examination. The following are the more common symptoms given by these patients:

1. Breathlessness, produced by slight exertion.
2. Precordial pain, coming on suddenly after exertion, spreading over the left chest.
3. Fatigue, with or without exertion.
4. Vertigo, and occasionally fainting spells.

The studies here reported were undertaken in the following order:

1. A series of cases with "irritable hearts" was studied with no attempt at subdivision into special groups. The leukocytes were studied with reference to the number of cells; in addition a differentiation of the cells in the blood smear of each case was made by counting 200 cells.

2. A series of normal individuals, and a series of patients with organic heart lesions were used as controls. These were studied in a manner similar to the men with "irritable hearts."

3. The series of functional patients was then analyzed and each type was compared, one with the other. The classification used was based on a study of these patients made by Dr. C. Macfie Campbell.²

* From the Cardiovascular Service, U. S. General Hospital 9.

1. Lewis: Medical Research Committee, Special Report Series 8.

2. Campbell: J. A. M. A. **71**:1621, 1918.

4. Special observations on the morphology of the blood following the injection of epinephrin were also carried on in conjunction with the special studies in the reactions to epinephrin, the preliminary report of which has already been published.³ Patients from the Surgical Service, ready for full duty, were used as controls.

5. The type of patient considered "constitutionally inferior" was selected for study to determine his reaction to exercise. Patients with organic heart lesions and those convalescent from rheumatic fever were chosen as controls.

For the differential studies the leukocytes were divided into the following groups:

1. Polymorphonuclear neutrophilic leukocytes (P. M. N.).
2. Polymorphonuclear eosinophilic leukocytes (P. M. E.).
3. Polymorphonuclear basophilic leukocytes (P. M. B.).
4. Lymphocytes, large and small (L. L., S. L.).
5. Mononuclears, large and small (M.).
6. Transitionals (T.).

1 and 2. *Study of General Group of "Irritable Heart" Cases and Controls.*—Two hundred and sixty counts were made on sixty-five patients to determine the number of leukocytes per cubic millimeter of blood. The procedure followed in each case was to have the patient rest for one hour before the blood was taken, and the puncture was made at least two hours after the ingestion of food. The possibility of a variation in the morning and afternoon counts was considered, and each patient was studied with this in mind. Two morning and two afternoon counts were made on each patient on different but not necessarily successive days. With one of the morning counts a blood smear was made by the coverslip method. The pipets were of the Leitz make and each had been checked for error. A Thoma-Levy hemocytometer was used.

Leukocytic Counts:

Average of two a. m. counts on 61 patients.....	8,162
Average of two p. m. counts on 64 patients.....	8,450

Total average day count on 65 patients.....	8,290
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Differential Counts:

Average P. M. N. percentage of 74 patients.....	56.0
Average P. M. E. percentage of 74 patients.....	4.0
Average L. percentage of 74 patients.....	32.6
Small.....	31.0
Large.....	1.7
Average M. and T. percentage of 74 patients.....	7.4

100.0

3. Peabody, et al.: J. A. M. A. **71**:1912, 1918.

The results with the controls were as follows:

Leukocytic Counts:

Average of two a. m. counts on 12 organic cases.....	8,460
Average of two p. m. counts on 12 organic cases.....	8,740
Total average day count on 13 organic cases.....	8,400
Average of eight counts on eight normals.....	7,060
Total average count on 21 controls.....	7,900

Differential Counts:

	Thirteen Organics	Eight Normals
Average P. M. N. percentage.....	61.0	60.0
Average P. M. E. per centage.....	1.9	2.6
Average L. percentage:		
S.	26.0	25.0
L.	2.4	2.0
	28.1	27.0
Average M. and T. percentage.....	9.0	11.4
	100.0	100.0

TABLE 1.—COMPARISON OF THE LEUKOCYTIC COUNTS IN PATIENTS AND CONTROLS

	Leuko- cytes, Average	Differential Formulas					
		P. M. N.		P. M. E.		Lymphocytes	
		Per Cent.	No.	Per Cent.	No.	Per Cent.	No.
"Irritable hearts".....	8,290	56.0	4,642	4.0	332	32.6	2,702
Organic hearts.....	8,400	61.0	5,124	1.9	160	28.1	2,360
Normal controls.....	7,060	60.0	4,236	2.6	184	27.0	1,906
Miller's normal average.....	7,705	63.5	4,895	2.7	218	21.9	1,734

DISCUSSION

The variation in these cases is seen by a comparison of the accompanying tables and charts. There is no appreciable difference in the leukocyte counts of the Organics and the Functionals; in fact, the former show averages slightly above the latter. The normal controls show averages 1,000 cells below either of the series of patients. The averages of Miller⁴ for normals show a less marked difference. It may be concluded that the leukocytes of "irritable heart" patients are slightly increased above the normal, but only to a small degree. In both controls and patients the morning counts average lower than the afternoon, which finding is a normal reaction. The high leukocytosis which Lewis mentioned in his report has not been present in the average of the patients studied in this hospital. The highest count in the "irritable heart" patients was 16,350; the lowest count was 4,700. In the controls the counts varied between 12,300 and 4,500.

From the percentages obtained from counting 200 cells in each smear preparation, the absolute values of the various leukocytes per

4. Miller: Johns Hopkins Bull. **25**: 1914.

cubic millimeter of blood were calculated, using as a basis the total day average count. A comparison of the differential results shows that there is a relative lymphocytosis and a decrease in the polymorphonuclear neutrophilic cells in the functional cases. In the controls the figures for the organic cases and the normal individuals are practically the same. The formulas of the controls correspond to the figures determined by Miller.* His figures are tabulated for comparison in Table 1. An eosinophilia was present in all but sixteen patients of this series. The exceptions had a normal percentage. The limits of the eosinophilia ranged from 13 per cent. to 1.5 per cent.

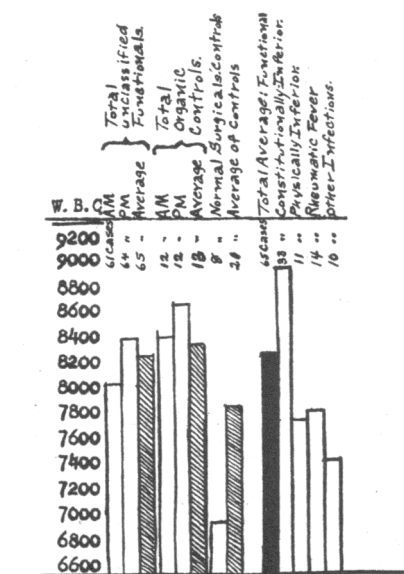


Chart 1.—General comparison of leukocyte counts.

3. *Analysis of the "Irritable Heart" Group.*—The classification used is based on the general suggestions given by Dr. C. Macfie Campbell. Four clinical types have been considered:

1. Constitutional Inferiority. This term is used in a very broad sense to cover a very heterogeneous group.

2. Physical Inferiority. Separated from the general group of Constitutional Inferiors because of its prominence by numbers among the other types.

3. Post-rheumatic Type. Soldiers with a definite history of at least one attack of rheumatic fever without discoverable organic findings.

4. Postinfection Type. Soldiers convalescing from some infection other than rheumatic fever without organic findings.

The average total counts and the differential formulas of these types are shown in the tables and charts. (Table 2 and Charts 1 and 3.)

TABLE 2.—COMPARATIVE FINDINGS IN THE TYPES OF "IRRITABLE HEART"

Type	Cases No.	Leukoocytes No.	P. M. N.		P. M. E.		Lymphocytes	
			Per Cent.	No.	Per Cent.	No.	Per Cent.	No.
Constitutional inferiors..	32	9,000	55.0	4,950	3.8	342	32.0	2,890
Physical inferiors.....	11	7,800	58.0	4,524	4.0	312	31.6	3,485
Postrheumatic.....	13	7,900	52.0	4,108	4.0	316	36.5	2,884
After other infections.....	8	7,500	60.0	4,500	3.7	276	29.0	2,175

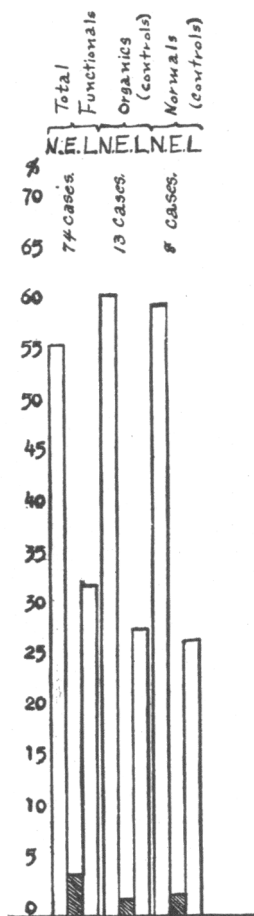


Chart 2.—Comparison of differential counts in "Irritable Hearts," Organic Heart Disease and Normal Controls. N, polymorphonuclear neutrophils; E, polymorphonuclear eosinophils; L, large and small lymphocytes.

In the general Constitutional Inferior Group, the highest leukocytic count was 13,350, and the lowest was 6,000. With the exception of three cases out of a total of thirty-two of this type the white cell count

was above 8,000 cells. The other groups have normal counts. No evidence is found of any direct proportion in leukocyte increase to the severity of the symptoms. In the differential counts the absolute number of cells closely corresponds in all types of the cases.

4. *Studies on the Blood Morphology after Epinephrin Injection.*—The controls used in the blood studies in these observations were

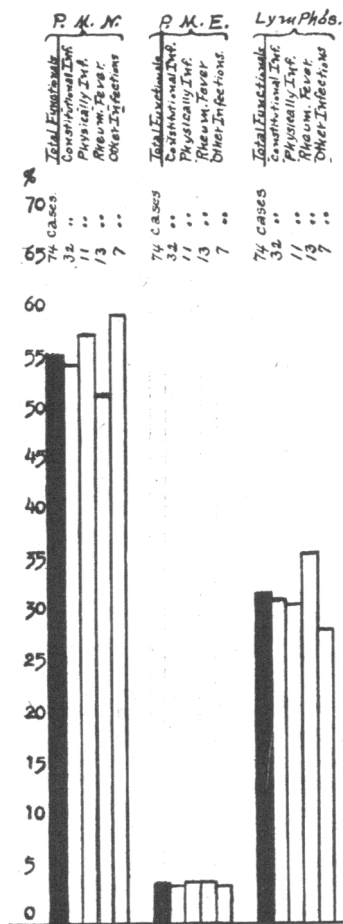


Chart 3.—Comparison of differential counts in four types of "Irritable Hearts."

patients on the Surgical Service, who gave no "effort syndrome" symptoms and gave no reaction after the injection of epinephrin. In each case, with controls and subjects, the patient was placed at rest in bed for one hour previous to the epinephrin injection. At the end of this hour the first specimen of blood was taken. Then 0.5 c.c. of a 1:1,000 solution of epinephrin chlorid was injected intramuscularly. At the height of the reaction in the "epinephrin positive" cases,

and at the end of thirty-five minutes in the negative cases, a second specimen of blood was taken. At the end of an hour, when all the reaction symptoms had subsided, a third specimen was taken. From each of these three specimens leukocytic and differential counts were made. The same pipet was used for each of the three specimens of each individual case in order to avoid any possible error that could be made constant.

TABLE 3.—LEUKOCYTIC COUNTS AFTER EPINEPHRIN INJECTION

	Number Cases	Reaction	After First Hour of Reaction	At Height of Reaction	After Quiescence
Controls.....	12	Neg.	8,671	11,100	8,425
"Irritable heart".....	16	Pos.	7,812	11,525	8,181

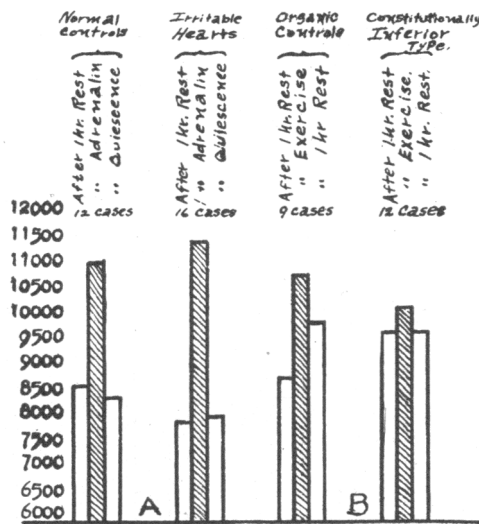


Chart 4.—A. Comparison of leukocytic increase from injection of epinephrin.
B. Comparison of leukocytic increase from physical exercise.

TABLE 4.—DIFFERENTIAL STUDIES AFTER EPINEPHRIN

	After Rest				After Epinephrin				After Quiescence			
	P. M. N.		Lymphos.		P. M. N.		Lymphos.		P. M. N.		Lymphos.	
	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.
Controls.....	59	5,116	26	2,254	53	5,883	31	3,441	58	4,886	29	2,443
Subjects.....	60	4,687	30	2,344	58	6,684	29	3,342	62	5,072	27	2,209

In both patients having a positive reaction to epinephrin, and in the controls with a negative reaction there was a marked leukocytosis after a period of thirty minutes following the injection of the drug. The percentage of increase in the patients was 47.5, while the percentage in the controls was 28.1. Whether this more marked increase in the patients would also be found in cases of "irritable heart" that do not show a positive reaction to epinephrin has not been determined.

The eosinophil cells were not charted because no variation was found, there being a normal eosinophil count in the controls and a high eosinophilia in the patients before and after the injection of epinephrin.

5. *Blood Morphology in the Type Constitutional Inferior After Exercise.*—A group of patients with organic heart disease was chosen as controls in this study. The subjects were cases of definite "constitutional inferiority." Both controls and subjects were given the same exercises for a period of twenty minutes.

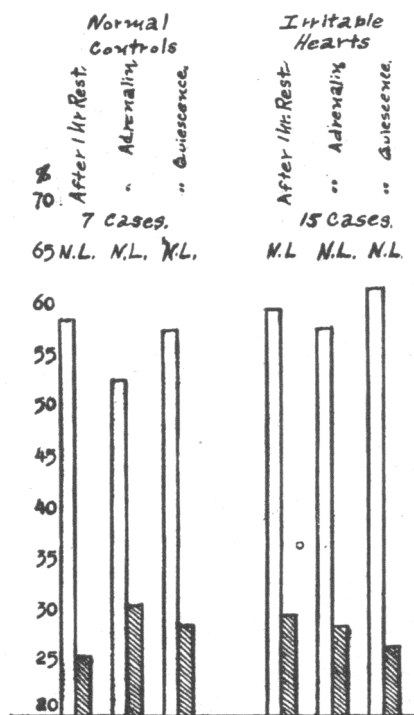


Chart 5.—Comparison of differential counts. Normal Controls, epinephrin negative; Irritable Heart cases, epinephrin positive. Specimens taken at the same time intervals as in Chart 4.

TABLE 5.—LEUKOCYTIC COUNTS BEFORE AND AFTER EXERCISE

	Case Number	After 1 Hour of Rest	After Exercise	After 1 Hour of Rest
Controls.....	9	8,870	10,890	9,960
Subjects.....	12	9,730	10,240	9,740

The subjects show a leukocyte increase of 5.2 per cent. after the exercise, compared with 22.7 per cent. shown by the controls. This difference is explained by the lack of "push" in the inferior type.

They do not make enough effort to cause a normal reaction. Further observations were interrupted by the transfer of the writer to another station.

SUMMARY

1. There is a slight leukocytosis in the unclassified group of patients with "irritable heart." The figures in this correspond, however, to those found in the patients with organic heart disease.

2. The type of patient classed as "Constitutional Inferior" has a high leukocytic count. The other types studied have a normal count.

3. There is a relative lymphocytosis present in the blood of patients with "irritable heart," the limits being between 15 and 51 per cent. An eosinophilia is likewise present, but too much importance cannot be given to this finding, since the presence of parasites was not ruled out.

4. A marked leukocytosis occurs in both patients and controls after the injection of epinephrin. This increase is much greater in the patients with positive reaction than in the controls, who did not respond to the drug.

5. There is no greater variation in the differential formulas after the injection of epinephrin than was to be found before. The eosinophilia persisted in about the same proportion as before.

6. The morphologic studies of the blood in cases of "irritable heart" show nothing of significance that might assist in the diagnosis.