

are listed chymotrypsin values of treated patients with malignancies showing that the inhibitory power of serum decreased in patients that were responsive to X-ray treatment and surgical excision.

Summary. The antichymotrypsin content of serum, as found by this test, is not changed in early malignant disease. The presence of

hidden metastatic cancer, however, can be detected. Thus the test may assist in the diagnosis of advanced malignancies or in detecting such lesions when they appear in an obscure state. False positive values with this procedure fall in the same group as with the methods which measure proteolysis.

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Effect of Hypothalamic Lesions on the Peripheral Blood Picture of the Cat. (17949)

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This investigation was carried out in an attempt to verify reports in the literature to the effect that the peripheral blood picture may be influenced by the vegetative centers of the brain. The study was made using adult male and female cats which had undergone operations to produce bilateral lesions in the hypothalamus for induction of possible behavior changes. When the behavior study was completed, the animals were killed with ether, their brains fixed in formalin, embedded and sectioned for study of the areas damaged (1).

Method. The following data consist of a series of conventional blood counts and differential counts obtained from ear vein blood of 9 male and 19 female cats. The blood samples were collected for a period both before and after the production of the hypothalamic lesions. Blood counts were made with the standard pipettes and a Spencer haemocytometer. Differential counts were made after staining the smears with Wright's stain. The blood samples were taken at approximately the same time of day in each case in order to control the diurnal variations that are known to occur(2). Time of feeding was recorded in view of the possible

effect it might have on the blood picture(3,4). The animals were handled as gently and quietly as possible in order to avoid emotional disturbances which also are known to have a marked effect on the peripheral blood picture(5). The number of counts made on each animal varied somewhat, ranging from 6 to 9 in the preoperative period and from 6 to 8 counts in the post-operative period.

Findings. In the normal cats the blood picture before operation showed an average WBC count of 20,017 for the males, with a range from 10,361 to 28,950. After hypothalamic damage* the average WBC count was 25,224 with counts ranging from 10,333 to 35,117. Except for one male cat which showed a .3% decrease in the average post-operative count, the remaining males showed individual increases in WBC counts ranging from .5 to 49.1% (Table I). The average WBC count before operation for the females averaged 22,711 with a range from 13,525 to 32,786. After operation the average WBC count for this group was 22,962, an increase over the average count before operation.

3. Brinckerhoff, W. R., and Tyzzen, E. E., *J. Med. Research*, 1902, v7, 191.

4. Cheng, S. C., *Am. J. Hygiene*, 1930, v11, 440.

5. Izquierdo, J. J., and Cannon, W. B., *Am. J. Physiol.*, 1929, v84, 545.

* For extent and location of hypothalamic lesions see Wheatley(1).

1. Wheatley, M. D., *Arch. Neurol. & Psychiat.*, 1944, v52, 296.

2. Reifenstein, G. H., Ferguson, J. H., and Weiskotten, H. G., *Am. J. Path.*, 1941, v17, 219.

TABLE I.
Average White Blood Cell Counts Taken on Male and Female Cats Before and After Operation to Produce Hypothalamic Lesions.

Cat Male	Before operation Behavior normal WBC count	After operation		% increase or decrease
		Behavior change	WBC count	
P-26	10361	None (normal)	10333	— .3
19	24019	" "	24143	+ .5
13	16279	" "	28369	+12.8
44	21014	" "	25642	+22.0
15	27375	Slight-variable	30381	+11.0
28	28950	" "	35117	+21.3
37	21867	" "	28700	+31.2
43	17379	" "	25908	+49.1
18	12911	Decided	18421	+42.7
Avg	20017		25224	
Female				
P-33	32786	None (normal)	25217	—23.1
39	19350	" "	22529	+16.4
17	24239	" "	29309	+20.9
16	29281	" "	38157	+30.3
32	17129	" "	22808	+33.2
27	25093	Slight-variable	19967	—20.4
40	28850	" "	23975	—16.9
36	24317	" "	21142	—13.1
38	26033	" "	25683	— 1.4
25	21644	Decided	18229	—15.1
41	25607	" "	21800	—14.9
23	17889	" "	17264	— 3.5
35	20833	" "	21673	+ 4.0
24	18811	Savage	17964	— 4.5
30	17000	" "	17000	—
31	18874	" "	20050	+ 6.2
20	20378	" "	31650	+ 6.2
29	29864	" "	24258	+16.3
42	13525	" "	17586	+29.3
Avg	22711		22962	

Post-operatively, the average counts ranged from 17,000 to 38,157 (Table I). Here again, as in the male series, there is an apparent slight increase in the average white count after hypothalamic damage. Nine female cats showed individual increases in average WBC counts after the operation, ranging from 4.0 to 33.2% increases. After the production of lesions 9 females showed a decrease in average WBC counts ranging from 1.4 to 23.1%, while in one female the average count was exactly the same after operation as it was for the preoperative period (Table I). It may be concluded that there is probably no significant change in the number of white cells when the range of variation is taken into consideration.

Examination of the data for the RBC count showed the group count for the males

average 6,764,414 with a range from 5,661,111 to 7,898,571 in the preoperative period. After operation the average count was 7,116,580 with a range from 5,391,250 to 9,525,000. In the group of males, 2 animals showed a decrease in RBC count after operation ranging from 5.5 to 11.0% and 7 showed an increase ranging from 1.0 to 31.7% (Table II). In the female group the average RBC count before operation was 6,878,489 with a range from 4,300,000 to 8,497,143. After operation the average count dropped slightly to 6,747,970 with a range from 5,073,333 to 8,170,000. In this group 9 animals showed a decrease after operation ranging from 3.8 to 23.0% and 10 females showed an increased RBC count after hypothalamic damage that varied from .8 to 22.0% (Table II). In the RBC series, as well as in the WBC study, any

TABLE II.
Average Red Blood Cell Counts Taken on Male and Female Cats Before and After Operation to Produce Hypothalamic Lesions.

Cat Male	Before operation Behavior normal RBC count	After operation		% increase or decrease
		Behavior change	RBC count	
P-26	5661111	None (normal)	5720000	+ 1.0
19	7235000	" "	9525000	+31.7
13	6060000	" "	5391250	-11.0
44	7898571	" "	7903333	+ 1.3
15	7617500	Slight-variable	8308750	+ 9.1
28	6988571	" "	7403500	+ 5.8
37	6521667	" "	6778333	+ 3.9
43	6152858	" "	5813333	- 5.5
18	6744444	Decided	7205721	+ 6.8
Avg	6764414		7116580	
Female				
P-33	5951429	None (normal)	7258333	+22.0
39	7448333	" "	5770000	-22.5
17	6394444	" "	6233333	-10.1
16	7128750	" "	7617143	+ 6.9
32	4300000	" "	5073333	+18.0
27	7617143	Slight-variable	6886667	- 9.6
40	8497143	" "	6855000	-19.3
36	6793330	" "	5775000	-15.0
38	6756667	" "	7513333	+11.2
25	6528889	Decided	7142857	+ 9.4
41	6024286	" "	5795000	- 3.8
23	6617778	" "	5875714	-11.2
35	7285000	" "	8170000	+12.1
24	6550000	Savage	6984286	+ 6.6
30	7888571	" "	7068333	-10.3
31	8227143	" "	6233333	-23.0
20	6936667	" "	7141429	+ 3.0
29	6415714	" "	7431667	+15.8
42	7330000	" "	7386667	+ .8
Avg	6878489		6747970	

attempt to correlate these doubtful changes with the degree of behavior change in the post-operative animals or with the areas or degree of damage only gave negative results.

The data on the differential counts were likewise negative and show marked individual variability. Examination of the average differential counts for the individual animals, both male and female, showed considerable variation in the post-operative responses of these animals. These changes are not constant, however, even within the various groups and they cannot be correlated with the areas damaged or the degree of damage produced.

Discussion. From study of the data of this investigation, the inconsistency and variability of the individual responses of both male and female cats to hypothalamic damage raises a question concerning the interpreta-

tion of comparable studies by previous investigators. Many investigators have reported changes in the peripheral blood picture following various experimental procedures on the central nervous system. Rosenow(6) has reported neutrophilic leucocytosis after intraventricular injection of a suspension of kaolin. Schulhof and Matthies(7) observed a polyglobulia of long duration after the injection of siliceous earth into the proximal part of the vegetative centers of the brain in rabbits. Hecht and Weil(8) found a polycythemia after cerebral trauma. Following bacterial

6. Rosenow, G., *PROC. SOC. EXP. BIOL. AND MED.*, 1941, v46, 5.

7. Schulhof, K., and Matthies, M. M., *J.A.M.A.*, 1927, v89, 2093.

8. Hecht and Weil, *Deutsche Med. Woch.*, 1929, v55, 380.

protein injection, Hoff and von Linhardt(9) reported that in man and animals there was a fever combined with a marked leucocytosis. However, after sectioning the cord, no change was observed following the bacterial protein injection, but leucocytosis could still be produced by experimental acidosis and it was concluded that peripheral changes as well as central nervous activity influence the blood composition.

Other similar results have been reported, but all are deficient in a precise delimitation of nuclei and structures of the brain involved by the lesions. Furthermore, many of the results were complicated by the presence of a foreign substance in the brain. A very comprehensive review and evaluation of the pertinent papers concerning the role of the central nervous system in affecting hematopoiesis was published in 1944 by Lucia and Marasse(10). In a summary these authors state "that the experimental evidence offered to establish the existence of an erythropoietic or a leukopoietic center in the diencephalon is insufficient." From our data it is evident that the types of hypothalamic destruction in the cats studied could not be responsible primarily for any consistent changes occurring in the peripheral blood picture in this particular group of animals. If the male and female group averages only had been considered, our findings would have been comparable to the results published by Rosenow, *et al.*(6), who reported rises in peripheral blood counts after hypothalamic damage. However, if the responses of the individual animals are considered no such consistent rises are found. One is aware only of the variability in the response of the individual animals to lesions placed in similar areas of the brain.

As noted previously, Izquierdo and Cannon (5) found that emotional disturbances have a marked effect on the peripheral blood picture. No doubt hormonal and humeral factors are the immediate effectors of the changes produced. By way of attempting to explain the extreme range and variability of the blood counts in these animals, and particularly in the animals made savage, attention should be called to the fact that these animals undoubtedly were subjected to various emotional situations beyond our control. Even with great care in handling, certain of the cats displayed signs varying from uneasiness to fright and rage. Irritated cats and those showing post-operative savagery and rage all evidenced signs of increased autonomic activity and the associated release of chemical effector substances might have affected the blood picture. Although there were outward manifestations of emotional change in our animals, we had no means of measuring the activity of the central nervous system to ascertain a possible correlation.

Conclusions. Blood counts and differential counts were taken on a series of 28 cats before and after production of hypothalamic lesions for study of behavior changes. The average blood counts for individual cats (male and female) post-operatively is marked by the variability of response. Attempts to correlate the post-operative changes with areas damaged, degree of damage, or with behavior changes gave negative results. It seems apparent that the peripheral blood picture of these animals is not primarily under the control of the hypothalamic areas damaged by these lesions, since it does not show consistent permanent changes. Nor is the blood picture affected apparently by neighboring areas whose fiber tracts traverse this region and would be interrupted by the lesions.

9. Hoff, F., and von Linhardt, S. E., *Z. f. d. gesam. Exp. Med.*, 1929, v63, 277.

10. Lucia, S. P., and Marasse, H. F., *J. Nerv. & Ment. Dis.*, 1944, v99, 734.