which demonstrates the improvement in reliability effected by adjustments with the several correction terms W^2, B, etc. Reducing the dosage range to 0-40γ decreases S to ±2.2γ, but since this corresponds to a coefficient of variation of 11.6% (compared with 11.3% for the longer range) it affords no actual improvement in reliability.

Concerning a unit of androgen activity for urine, we may define the *androsterone equivalent per liter* of any specimen as the number of tenths of a milligram (or hundreds of gammas) of crystalline androsterone which yield the same *adjusted* comb growth response as one liter of the specimen. Detailed statistical reports on this work are now in preparation.

11870

Leucocytosis Induced by Injection of Kaolin into Cisterna and Ventricles of Brain.

G. ROSENOW. (Introduced by B. Kramer.)

From the Department of Laboratories, The Jewish Hospital of Brooklyn, N. Y.

As has been shown in previous studies[1, 2] neutrophilic leucocytosis can be induced in rabbits by mechanical lesions in certain parts of the diencephalon, especially the hypothalamic region; the production of leucocytosis by bacterial proteins can be inhibited by the previous administration of narcotics such as luminal which incapacitates, functionally, the parts in question.[3] Thus, there seems to be no doubt that the diencephalon plays an important role in the regulation of the composition of the peripheral blood.

The nature of this regulation is not yet clear. It seems likely that the cerebrospinal fluid might be involved in the induction of cerebral leucocytosis.

Therefore, studies were now undertaken to determine whether a partial block in the flow of the cerebrospinal fluid would produce any characteristic changes in the number of leucocytes and the blood picture. I used the intracisternal or intraventricular injection of a suspension of kaolin in order to obtain stasis in the cerebrospinal fluid over a long period. This method was inaugurated for other

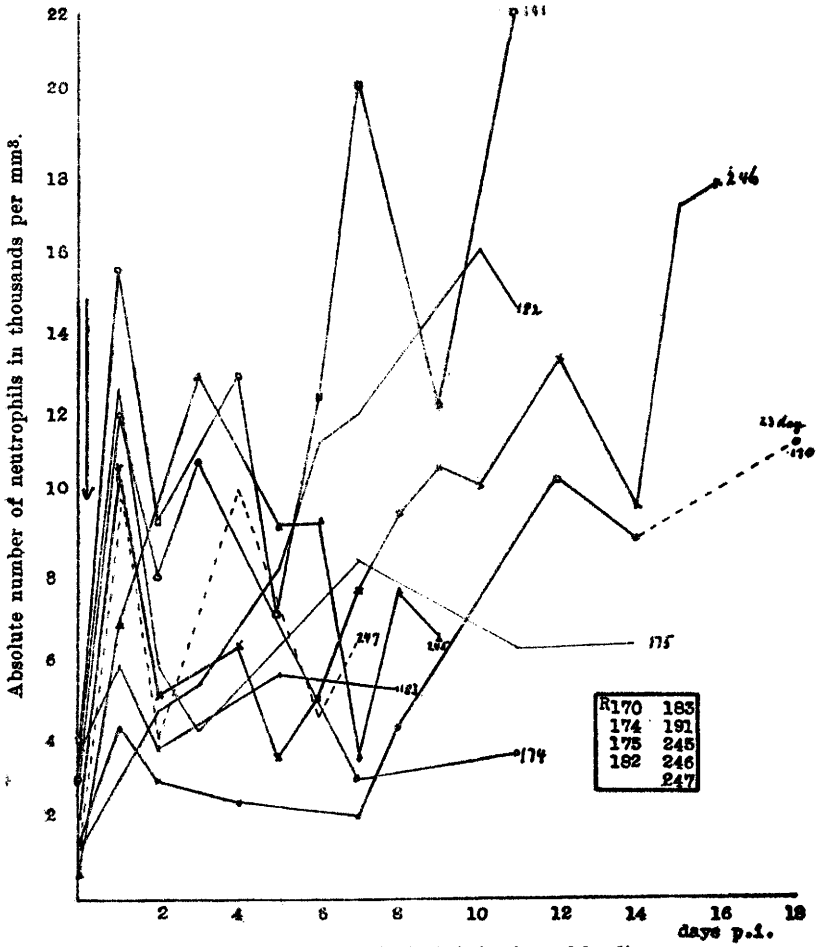
1 Rosenow, G., *Z. f. d. ges. exp. Med.*, 1929, **64**, 452.

2 Rosenow, G., *Z. f. d. ges. exp. Med.*, 1929, **65**, 557.

3 Rosenow, G., *Verhandl. d. deutsch. Gesellsch. f. inn. Med.*, 1931, **43**, 75.

purposes by Dixon and Heller in dogs,[4] and by Griffiths, Jeffers and Lindauer[5, 6] in rats and cats.

Eighteen rabbits (2.5-4 kg) were used. After the normal level of the leucocytes (under the usual precautionary measures) was determined, 0.25-1.0 cc of a sterile 25 vol. % suspension of kaolin in saline was slowly injected intracisternally (in some experiments in



↓ Intracisternal (R191 intraventricular) injection of kaolin.

FIG. 1.

Absolute number of neutrophils, immature cells included, in thousands per mm³ in 9 rabbits.

[4] Dixon, W., and Heller, H., *Arch. f. exp. Path. u. Pharm.*, 1934, **166**, 265.

[5] Griffiths, I. Q., Jr., Jeffers, W. A., and Lindauer, M. A., *Am. J. Physiol.*, 1935, **113**, 285.

[6] Lindauer, M. A., and Griffiths, I. Q., Jr., PROC. SOC. EXP. BIOL. AND MED., 1938, **39**, 547.

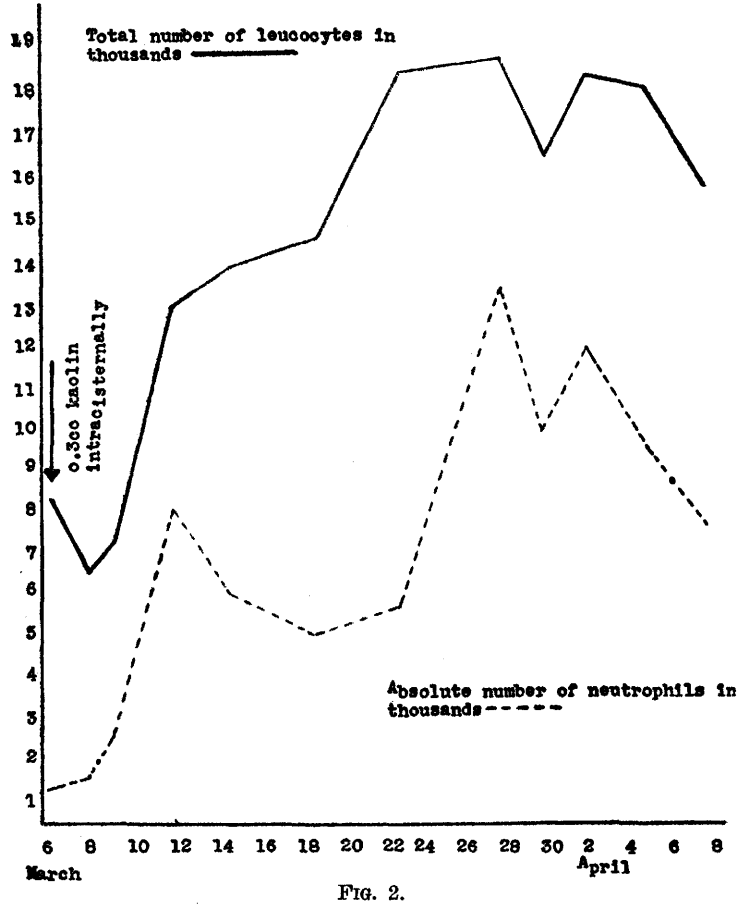


FIG. 2.
Rabbit No. 171 0.3 cc suspension of kaolin injected intracisternally.

one of the lateral ventricles). No narcotics were used. Blood was taken from the vein of the ear and leucocytes and differential counts (Wright and Giemsa) were made almost every day. Some of the animals died spontaneously, the others were killed after various periods of observation (6-30 days). Brain and medulla were examined macro- and microscopically after formalin fixation. In no case signs of infection or meningeal irritation were found. The results of 8 rabbits used are not included as the autopsy showed either coccidiosis or the rabbit did not survive for at least one week.

Results. In most of the experiments there appeared a marked neutrophilic leucocytosis on the 1st-3rd day after the kaolin injection. (Fig. 1). Usually this primary leucocytic response subsided after 2 to 5 days partly or completely, following which the number of

neutrophilic leucocytes increased progressively during the next 10-20 days. Only 2 rabbits which survived more than 7 days had no leucocytosis; all the others showed a lasting and marked secondary leucocytosis which amounted to more than 100% of the initial value with a marked shift to the left. Fig. 2 gives an example of this type. In some experiments a few metamyelocytes and normoblasts were found in the peripheral smears at the peak of the leucocytosis.

The "primary" leucocytosis appeared sometimes very promptly after the injection. Table I shows the onset of the leucocytic response within 2 hr after the injection of kaolin into one of the lateral ventricles. The leucocytosis in this experiment was very marked. The number of segmented neutrophils increased from 3800 to 15500

TABLE I.

Rabbit No. 191. 11:25 injection of 0.65 cc of a 25% suspension of kaolin into the left lateral ventricle.

Date	Total Leuk.	Segm. neutrophils		Stab cells	
		%	Abs.	%	Abs.
5/9/40					
11:20 A.M.	9900	38.5	3812	1	99
11:25	Injection of 0.65 cc of kaolin into left ventricle.				
11:30	11450	38	4351	0.5	57
11:50	6300	38	2394	3	189
1:10	20950	74	15503	9	1885
2:10	15900	72	11448	7.5	1192
4:15	17600	75.5	13288	5.5	968
5/10	19050	75.5	14383	6	1143
5/11	17150	53.5	9175	2.5	429
5/13	19850	65	12903	1	198
5/14	12100	56.5	6837	3.5	423
5/15	18000	65	11700	4	720
5/16	27250	68.5	18666	5.5	1499
5/18	19550	58	11339	5	978
5/20	27750	67.5	18731	11	3053

Date	Lymphocytes		Monocytes		Basophiles		Plasma cells	
	%	Abs.	%	Abs.	%	Abs.	%	Abs.
11:20 A.M.	58.5	5792	1	99	0.5	49	0.5	49
11:30	55.5	6355	4	458	2	229	0	0
11:50	56.5	3560	0	0	2.0	126	0.5	31
1:10	15	3143	1.5	314	0.5	105	0	0
2:10	17	2703	1.5	239	1.5	238	0.5	80
4:15	17.5	3080	1	176	0.5	88	0	0
5/10	13	2476	2.5	476	3.0	572	0	0
5/11	35.5	6088	4	686	4.5	772	0	0
5/13	27.5	5459	2.5	496	4.0	794	0	0
5/14	32.5	3933	4.5	544	3.0	363	0	0
5/15	23.5	4230	4	720	3.5	630	0	0
5/16	18.5	5041	5	1363	2.5	681	0	0
5/18	30.5	5963	5	978	1.0	195	0.5	97
5/20	20	5550	0	0	1.5	416	0	0

in 1 mm^3 and the juvenile neutrophils (stabcells) from 99 to 1885 within 2 hr. Table I shows, furthermore, that there was first a short leucopenic stage as in most of the hitherto known forms of induced leucocytosis.[7]

In some instances (No. 170, 182) there was no primary leucocytic response after the injection of the kaolin and marked changes in the number of leucocytes and the blood picture did not appear before the 5th or 6th day.

Whether the mechanism of the primary and secondary leucocytosis is different remains questionable. Lindauer and Griffiths (*l.c.*) have found a pleocytosis of short duration in the cerebrospinal fluid in rats after injection of kaolin; however, it seems unlikely that the primary peripheral leucocytosis of the first days is due to an aseptic inflammatory irritation of the meninges as there were no signs of any meningeal irritation. For our problem the leucocytosis after the first days is more significant.

Summary. Intracisternal or intraventricular injection of a suspension of kaolin produces in rabbits a marked peripheral neutrophilic leucocytosis. These findings add another form of cerebrally induced leucocytosis to the other previously described; they furnish further support to the view of a central vegetative regulation of the cellular composition of the blood.

11871

Sulfanilamide, Sulfapyridine, Sulfathiazole and Sulfamethylthiazol in Experimental Gas Gangrene in Guinea Pigs.*

ALFRED B. LONGACRE AND EDITH HONOLD.
(Introduced by E. W. A. Ochsner.)

From the Department of Surgery, School of Medicine, Tulane University, New Orleans, La.

Since the publication of Domagk,[1] presenting the results of his experiments with Prontosil-S in streptococcal infections, numerous

[7] Doan, C. A., Zerfas, L. G., Warren, S., and Ames, O., *J. Exp. Med.*, 1928, **47**, 403.

* Aided by a grant from the David Trautman Schwartz Research Fund.

[1] Domagk, G., *Deut. med. Wchnschr.*, 1935, **61**, 250.