large majority of *Rana sylvatica* larvae raised in such a solution from hatching to metamorphosis. The relationship of these results to similar work on other vertebrates is discussed.

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Concerning the Relation Between Pituitary Adrenocorticotrophin and the Circulating Blood Platelets.

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Although it has been known for some time that infection, trauma, hemorrhage, asphyxia, etc. result in rather marked alterations in the number of circulating blood platelets, the exact mechanism controlling the number of platelets is as yet unknown. With the discovery by Dougherty and White[1] that pituitary adrenocorticotrophin caused a dissolution of lymphoid tissue and a peripheral lymphopenia a new line of investigation was opened up. Since the conditions under which changes in the platelets have been reported are those which would stimulate a release of pituitary ACTH, and since this hormone has been shown to affect other blood elements through the adrenal, it did not seem too unreasonable to believe that the platelets might also be at least to some extent under the control of corticotrophin.

Consequently experiments were undertaken in both rats and humans to determine whether any effect of ACTH upon the blood platelets could be demonstrated. As far as could be determined by these experiments, there is no effect upon the platelets of either species by this hormone.

Experimental. Sixteen 100-150 g, hooded, male rats were injected subcutaneously with 80 mg of a suspension of acetone-dried hog pituitary after two control counts had been made, and determinations of the platelets* and RBC were made from the capillary tail blood every hour for 8 hours. No significant change was seen to occur in either blood element.

Six rats were injected in a similar manner with 40 mg of hog pituitary powder every morning for 3 days. Again there was no significant change in the number of platelets.

Four rats were injected with 10 mg of a purified pituitary corticotrophin preparation and counts made every hour for 8 hours with similarly negative results.

Following these experiments a preparation of pituitary ACTH† which was quite pure was made available to us, and it was decided

[1] Dougherty, T. F., and White, A., *Endocrinology*, 1944, **35**, 1.

* Three methods were used to count the platelets: (1) that of Rees and Ecker[2]; (2) a direct chamber count using 3.8% sodium citrate as the diluting fluid; (3) an indirect count of a wet preparation containing platelets stained with brilliant cresyl blue. The direct counts were used chiefly on the rats and the indirect on the human subjects.

[2] Rees, H. M., and Ecker, E. E., *J.A.M.A.*, 1923, **80**, 621.

† Kindly supplied by Dr. John R. Mote of the Armour Laboratories, Chicago, Ill. It was believed that each vial in the lot supplied (Lot G-59703-H) contained the equivalent of 12 mg of the Armour ACTH standard. After the completion of these experiments Dr. Mote informed us that on re-assay each vial contained only the equivalent of 5.2 mg of their standard. The doses given in this paper conform to the final assay.

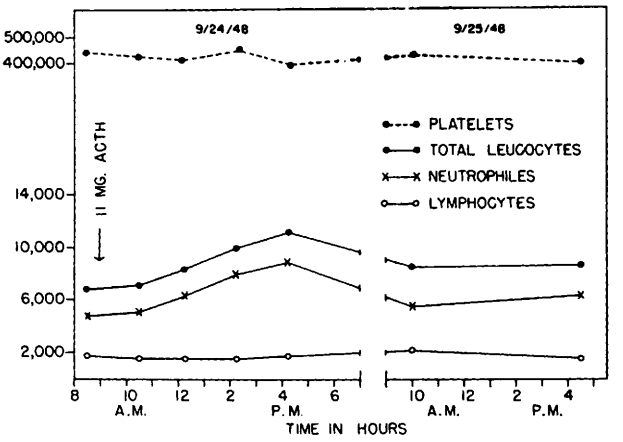

FIG. 1.

The effect of a single, intramuscular injection of 11 mg of ACTH

to test this in human subjects. Following a control determination of all blood elements, 11 mg of this preparation were injected intramuscularly into a normal male subject every 4 hours for 24 hours. A white count, differential, and platelet counts were performed every 2 hours for the first day and in the morning and afternoon of the second day.

The same procedure was followed in a young woman with idiopathic thrombocytopenic purpura who had not had a favorable response to splenectomy.‡ (It was reasoned that an increase in the platelets might show up much more readily in a patient in whom they were quite low originally.)

Two normal young women were given 11 mg of ACTH intramuscularly and the above counting procedure followed.

One young woman with hypopituitarism, which had presumably resulted from postpartum pituitary necrosis 3 years previously, was given 11 mg of ACTH in the morning and 7 mg in the afternoon and counts made as above.

In no instance could any significant change in the number of circulating platelets be observed, although there was a definite and usually quite striking rise in the total white count and the polymorphonuclear leukocytes.

‡ Patient of Dr. William Dameshek.

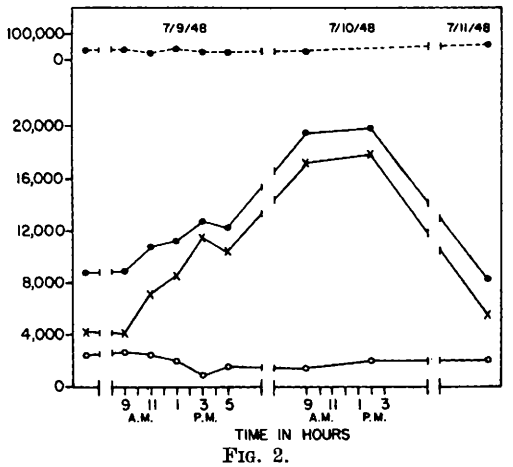

FIG. 2.

The effect of 66 mg of ACTH on a patient with idiopathic thrombocytopenic purpura. 11 mg were given intramuscularly every 4 hours for 24 hours beginning at 8 A.M. July 9. The legend corresponds to Fig. 1.

It is interesting that the number of circulating lymphocytes remained relatively constant, no true lymphopenia being observed in any instance. In the patient with hypopituitarism the increase in the polymorphonuclear leukocytes was much less marked than in the other subjects.

Summary. Under the above experimental conditions, no effect of pituitary adrenocorticotrophin upon the number of circulating blood platelets could be detected.