

cytes decolorize the oxidation-reduction indicator, 2,6 dichlorophenol indophenol. This reduction was inhibited by the cytotoxic agents, lipo-adrenal cortex, cortisone, nitrogen mustard and x-rays but was not affected by desoxycorticosterone. The method was used

to titrate lipo-adrenal cortex, the titer being .00,08 rat unit. This color test seemed to be a convenient method for demonstrating and measuring the toxicity of the adrenal cortex hormones to lymphocytes.

Received January 19, 1951. P.S.E.B.M., 1951, v76.

Action of Various Hormones on the Spread of Subcutaneously Injected Hemoglobin.* (18556)

PIERRE DUCOMMUN,[†] PAOLA S. TIMIRAS,[‡] AND FRANCO DORDONI.[§]
(Introduced by Hans Selye)

From the Institut de Médecine et de Chirurgie Expérimentales, Université de Montréal, Montréal, Canada.

The spread of a subcutaneously injected dye is dependent on numerous factors, the most important being Duran-Reynals' spreading factors(1). The hyaluronidase acting on hyaluronic acid in the mesenchymal ground substance is the best known but it is beyond doubt that apart from hyaluronidase, numerous enzymatic and non-enzymatic factors are involved in the spread mechanism. Hechter(2) has shown recently that spread is dependent upon various factors such as edema, trypsin, peptones and so forth. The mechanism of their action is not yet clarified. It seems to be either correlated with an increase of the local hyaluronidase secretion by the non-enzymatic injected spreading factor, or explained by alterations of non-hyaluronic components of the dermal barrier such as chondroitin sulfuric acid(3,4). Hormonal

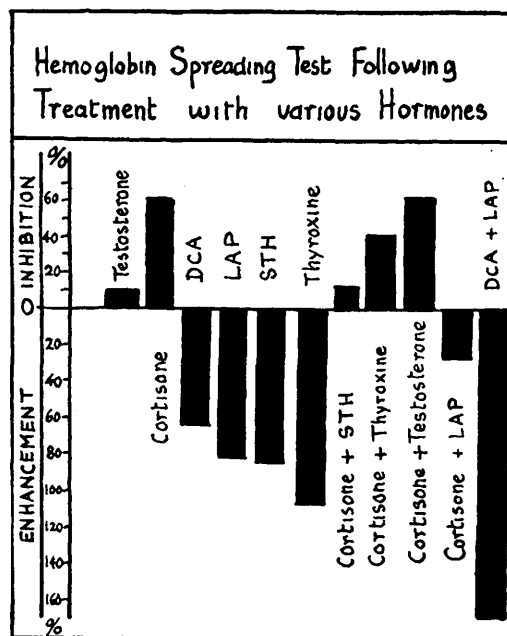


FIG. 1.

* This work was subsidized by a grant from the National Cancer Institute of Canada.

[†] Fellow of the Swiss Academy of Medicine and Biology.

[‡] Fellow of the Canadian Life Insurance Officers Assn.

[§] UNESCO Fellow (Canada).

1. Duran-Reynals, F., *Comp. rend. Soc. Biol.*, 1928, v99, 6.

2. Hechter, O., *Ann. N. Y. Acad. Sci.*, 1950, v52, 1028.

3. Hobby, G. L., Dawson, M. H., Meyer, K., and Chaffee, E., *J. Exp. Med.*, 1941, v73, 109.

4. Duran-Reynals, F., *Bact. Rev.*, 1942, v6, 197.

control of the spread was shown by Menkin (5) and Opsahl(6,7). They stated that adrenal secretions were related to the spread regulatory mechanism.

The purpose of this work was to control

5. Menkin, G., *Am. J. Physiol.*, 1940, v129, 691.

6. Opsahl, J., *Yale J. Biol. and Med.*, 1949, v21, 255.

7. Opsahl, J., White, A., and Duran-Reynals, F., *Ann. N. Y. Acad. Sci.*, 1950, v52, 1061.

the spread of an hemoglobin spot in the skin of the rat, under standard conditions of treatment with various hormones or hormone combinations.

Material and methods. Seventy-five piebald, female rats of an average initial body weight of 150 g were divided into 11 groups. The animals of the first group were used as controls. The rats of the other groups received separate daily injections of 5 mg of desoxycorticosterone acetate (DCA), 10 mg of methyl testosterone, 0.5 mg of thyroxine, 5 mg of cortisone, 3 mg of somatotrophic hormone (growth hormone or STH), 40 mg of lyophilized anterior pituitary (LAP) and the following combinations at the same dosage level: LAP and DCA, STH and cortisone, methyl testosterone and cortisone, thyroxine and cortisone. After 10 days of treatment 0.1 cc of a 15% solution of hemoglobin was injected into the posterior region of the back, which area had been depilated the previous day. The spot was measured two and one half hours later. The area was calculated by the following formula:

$$S = \pi \frac{\text{larger diameter} \times \text{smaller diameter}}{4}$$

Results. As seen in Fig. 1, cortisone significantly inhibits the spread while DCA, STH, LAP and thyroxine enhance it. Testosterone has no notable action. In the association of cortisone with STH and thyroxine, the spread inhibiting effect of cortisone prevails over the enhancing action of these compounds. This property is less pronounced when cortisone is combined with LAP. The enhancement observed following concurrent treatment with DCA and LAP represents the sum of their separate actions.

Summary and conclusions. The spread of an hemoglobin spot was studied under various hormonal conditions. At the dose level utilized, cortisone antagonizes the enhancement of the spread normally occasioned by STH, thyroxine and LAP. Our results confirm the antagonism between DCA and cortisone first suggested by Selye(8) concerning their action on vessels and inflammation. LAP, STH and thyroxine in this respect have a DCA-like action opposite to the effect of cortisone.

8. Selye, H., Stress, Acta Inc. Publ., Montreal, 1950.

Received February 14, 1951. P.S.E.B.M., 1951, v76.

Failure of ACTH to Protect Against Acutely Lethal Toxins of Influenza Virus and Rickettsiae.* (18557)

EDWARD H. KASS,[†] FRANKLIN A. NEVA,[‡] AND MAXWELL FINLAND.

From the Thorndike Memorial Laboratory, Boston City Hospital, Department of Medicine, Harvard Medical School and Department of Microbiology, Harvard School of Public Health.

The capacity of adrenocorticotrophic hormone (ACTH) to alter the clinical course of certain infectious diseases(1-3) suggests the need for investigation of the mechanisms in-

involved in these changes. One of the possible explanations of the effect of ACTH in clinical infections is that the adrenal cortical hormones aid in the detoxification of the noxious products of the infectious agent. In order to test this hypothesis, the effect of ACTH

* Aided by grants from the U. S. Public Health Service.

[†] Senior Fellow in Virus Diseases, National Research Council.

[‡] Fellow in Poliomyelitis, National Research Council.

1. Kass, E. H., Ingbar, S. H., and Finland, M., *Ann. Int. Med.*, 1950, v33, 1081.

2. Freeman, S., Fershing, J., Wang, C. C., and Smith, L. C., Proc. First Clinical ACTH Conference, Blakiston Co., 1950, p. 509.

3. Tompsett, R., LeMaistre, C., Muschenheim, C., and McDermott, W., *J. Clin. Invest.*, (Abst.), 1950, v29, 849.