

Effect of Reduced Oxygen Tension Upon Formed Elements of Blood of Hypophysectomized Animals.*

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It has been suggested^{1, 2} that the hypophysis, in addition to its many other functions, may play a part in erythropoiesis.

It has long been known that in man and animal, under the conditions of reduced oxygen tension, there occurs an increase in hemoglobin, erythrocytes and reticulocytes in the blood, and hyperplasia of the bone marrow. It was thought that if the hypophysis furnished a hormone which affected the erythrogenetic tissues, the response to a diminution in oxygen tension in the tissues of hypophysectomized animals might be deficient in one or more respects. To test this hypothesis, 8 male white rats weighing 150 to 220 gm. were hypophysectomized after complete blood counts were done by the usual methods. Erythrocyte counts were done in duplicate; reticulocyte counts of 1,000 cells on a cover slip smear stained with cresyl blue, hemoglobin determinations with the Haden-Hauser hemoglobinometer. Eight days later, 4 of the experimental animals with 4 normal controls of similar weight were placed in the respiratory chamber devised by Dallwig, Kolls and Loevenhart.³ The remaining 4 animals were placed in the chamber 25 days after hypophysectomy, and a second group of 8 hypophysectomized animals was similarly divided and exposed to the same experimental procedures 9 and 32 days after operation. In all instances complete blood counts were done on the day the animals were placed in the chamber. The pressure was reduced in all experiments to 422 mm. Hg.; equivalent oxygen tension, 12% of an atmosphere, which corresponds to an altitude of approximately 16,000 feet. This level was maintained constantly with but 2 to 3 mm. Hg. variation. Blood counts were made at intervals between 3 and 6 days. Some of the animals died in the first week under the experimental conditions, so that adequate data were obtained on but 14 hypophysectomized and 14 normal animals. The results were remarkably constant and they appear to be significant.

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¹ Evans, H. M., *J. A. M. A.*, 1935, **104**, 464.

² Moehlig, R. C., and Bates, G. S., *Arch. Int. Med.*, 1933, **51**, 207.

³ Dallwig, H. C., Kolls, A. C., and Loevenhart, A. S., *Am. J. Phys.*, 1915, **39**, 67.

The 14 control rats, in the chamber for periods of 3 to 12 days, showed an average increase of hemoglobin from 14.6 to 16.7 gm. Simultaneously, the erythrocytes increased 700,000 and the reticulocytes from a control level of 2% to a peak of 7%. There was no significant change in the weight of these animals during the experiment.

The 7 rats that were exposed to the reduced pressure 8 and 9 days after hypophysectomy, exhibited a similar rise in the hemoglobin and erythrocytes. The hemoglobin rose from a level of 14.6 to 16.8 gm. and there was an average increase of 1,300,000 erythrocytes. The reticulocytes, however, which fell from a preoperative level of 2.9% to 0.1% after hypophysectomy, showed no response to the stimulus of oxygen want, and the highest level was 0.2%. The average weight loss of these animals, while in the chamber was 23 gm.

The 7 rats that had had hypophysectomy 25 and 32 days before being placed in the chamber, however, showed no significant rise in the hemoglobin or erythrocyte count. The control level was 13.2 gm., at the end of the experiment the hemoglobin was 13.5 gm. The control erythrocyte count was 8,410,000, the final count 8,545,000. The reticulocytes, which averaged 3.3% before operation, fell to 0.3% the day the experiments started. At the conclusion of the experiments they numbered 0.1%. The average weight loss of these animals while under the influence of the reduced pressure was 13 gm.

Most striking of these results is the sharp fall in the number of reticulocytes after hypophysectomy and the failure of increase under the stimulus of oxygen want. In the experiments done 8 and 9 days after hypophysectomy there was a regular increase in hemoglobin and erythrocytes simulating in degree that of the controls, whereas in the experiments done 25 and 32 days after hypophysectomy there was just as regularly no significant increase in these components of the blood. If a specific hypophyseal hormone exists, it might be argued that some residue persisted in the tissues for a short time after hypophysectomy but was absent after a longer postoperative period. These results may not be due to a specific hormone; the action may be an indirect one upon some other organ, or may be due to the general derangement in metabolism that follows hypophysectomy.

Examination of the bone marrow of several of these hypophysectomized animals has been made. This shows a lack of the pronounced hyperplasia noted in the marrow of the controls; thus the marrow resembles that of normal animals at atmospheric pressure.

A conclusion as to the significance of these results is not as yet

possible but they seem to offer several interesting possibilities. Further studies under similar conditions with the removal of other endocrine glands are being done.

While these studies were in progress the interesting reports of Dodds and his associates^{4, 5} were published. They have noted the development of an anemia and a marked reticulocytosis in association with gastric lesions upon the injection of pituitary extract. They conclude that a hormonal connection may possibly exist between the posterior lobe of the pituitary gland, the stomach, and the blood.

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Effect of Vitamins B and G Deficient Ration on a Coccidian Infection.

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Fifteen half-grown rats were put on the following diet, in order to develop in them the early symptoms of vitamins B and G deficiency: extracted casein, 18 pts.; starch, 73 pts.; butter, 4 pts.; salt mixture, 4 pts.; cod liver oil, 1 pt. The 15 controls received the same mixture made up to 8.0% with Fleischmann's powdered yeast. After 9 days on these rations each rat was infected *per os* with 1500 sporulated oocysts of *Eimeria miyairii* daily for 5 successive days. The oocysts eliminated during the infections were collected during the patent period in pans beneath the wire cages, and counts were made by the counting and dilution method.

The rats on the deficient diet eliminated from 2 million to 91 million oocysts each; mean, 35.8 ± 4.5 million. The controls on the normal diet eliminated from 106 million to 275 million oocysts each; mean 167.27 ± 7.15 million. It appears that the deficient rats developed infections only from a fourth to a fifth as heavy as the control rats. Both series were refractory to subsequent reinfection when restored to the growing diet (Steenbock's).

No explanation is offered at present, but it appears that the yeast contains something that favors the development of a coccidian infection. Work is now in progress to separate the influence of vitamins B and G.

⁴ Dodds, E. C., Hills, G. M., Noble, R. L., and Williams, P. C., *Lancet*, 1935, 1099.

⁵ Dodds, E. C., and Noble, R. L., *Nature*, 1935, **135**, 788.