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Effect of Artificial Achylia Gastrica and a Diet Restricted in Vitamin B_2 (G) on Hematopoiesis.

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A mechanism implicated in the production of Addisonian (pernicious; macrocytic) anemia, is demonstrated by Castle[1] in the inability of patients to digest properly and obtain from food an antianemic principle in amounts adequate to maintain a normal number of erythrocytes in the circulating blood. As a result of these investigations, many attempts have been made to produce in laboratory animals a disease syndrome similar to that of pernicious anemia.

Ivy, Morgan and Farrell[2] have reported the occasional occurrence of a spontaneous anemia in gastrectomized dogs, and have also noted an increased tendency towards anemia during pregnancy in their

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[1] Castle, W. B., *Am. J. Med. Sc.*, 1929, **178**, 748.

[2] Ivy, A. C., Morgan, J. E., and Farrell, J. I., *Surg., Gyn. and Obst.*, 1931, **53**, 611.

gastrectomized dogs. Gutzeit,[3] Aron and Bauer,[4] and Maison and Ivy,[5] in studies on rats and dogs found that a similar anemia occurred following the surgical removal of the animals' stomachs. Mullenix, Dragstedt and Bradley[6] reported that their dogs after gastrectomy, showed a reduced capacity to form hemoglobin. Mettier, Kellogg and Purviance[7] produced an hypochromic anemia in their dogs by frequent bleeding; and observed, after the surgical removal of the animals' stomachs, that the blood showed a more marked microcytosis.

Miller and Rhoades[8, 9] produced what they interpreted as a macrocytic anemia in dogs and in swine by using a diet deficient in vitamin B.

The present problem, therefore, was undertaken to study blood formation in gastrectomized dogs while on a diet low in vitamin B_2 (G).

Three mongrel German shepherd dogs, 2 males (No. 393 and No. 161) and one female (No. 473), were used for this study. These animals had been gastrectomized at least one year prior to the present experiment, for the purpose of making studies on hypochromic anemia, the results of which have been published elsewhere.[7]

The diet used for the experiment was similar to that used by Miller and Rhoades.[9]

Preceding this study, analysis of the upper intestinal contents of all 3 dogs showed absence of free hydrochloric acid even after the subcutaneous administration of histamine.

After approximately 80 days had elapsed, the animals showed the symptom-complex characteristic of black-tongue. Diarrhea and progressive weakness developed; there was a slight loss of bodyweight; and marked stomatitis with salivation appeared.

During the control period the erythrocyte count of each of the 3 animals was slightly above 6,000,000 cells per cu.mm., and the hemoglobin content was between 60% (8.4 gm.) and 70% (9.8 gm.). The mean corpuscular volume, as shown in Table I, was 62 (No. 473), 50 (No. 393), and 66 (No. 161) cubic microns respectively. [Normal values for man (average): mean corpuscular volume, 87.0 cubic microns; mean corpuscular hemoglobin concentra-

[3] Gutzeit, K., *Verhandl. d. deutsch. Gesellschaft f. inn. Med.*, 1932, **44**, 478.

[4] Aron, E., and Bauer, R., *Compt. rend. Soc. de Biol.*, 1935, **113**, 1065.

[5] Maison, G. L., and Ivy, A. C., PROC. SOC. EXP. BIOL. AND MED., 1934, **31**, 554.

[6] Mullenix, R. B., Dragstedt, C. A., and Bradley, J. D., *Am. J. Physiol.*, 1933, **105**, 443.

[7] Mettier, S. R., Kellogg, F., and Purviance, K., *J. Clin. Invest.* (In press.)

[8] Rhoades, C. P., and Miller, D. K., *J. Exp. Med.*, 1933, **58**, 585.

[9] Miller, D. K., and Rhoades, C. P., *J. Clin. Invest.*, 1935, **14**, 153.

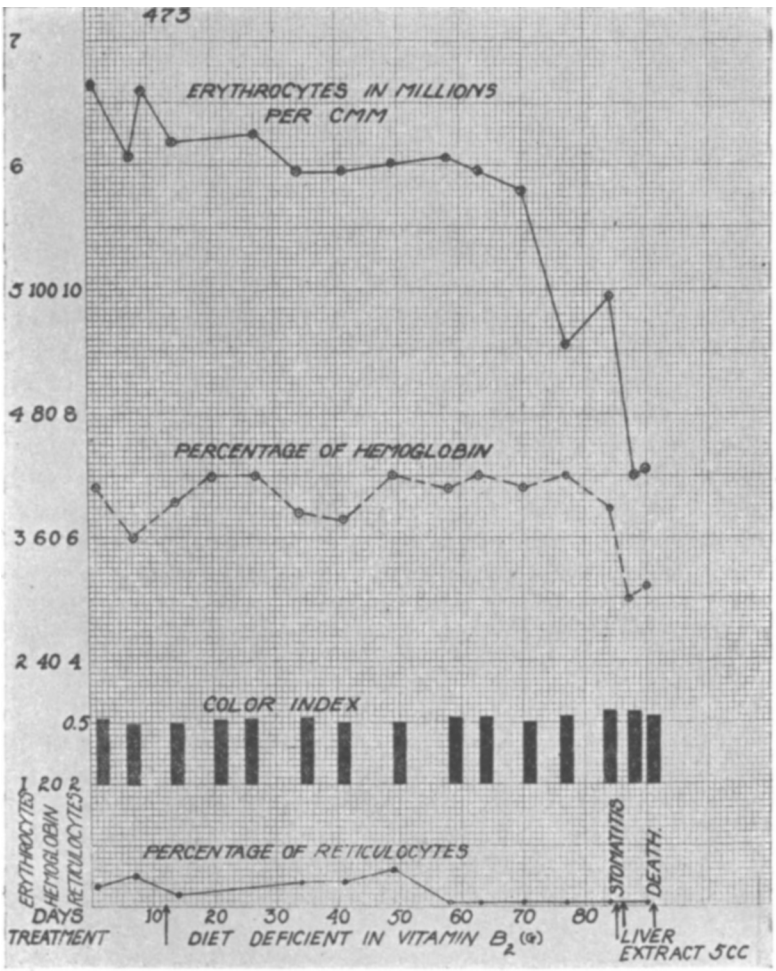

FIG. 1.

Shows a slight drop in the erythrocyte and hemoglobin levels in a gastrectomized dog (No. 475) during the first 15 days on a diet restricted in vitamin B_2 (G) and a more precipitous drop after the animal developed black-tongue. Note the slight terminal rise in color index but the persistence of hypochromic anemia.

tion, 35% (Wintrobe). For dogs: mean corpuscular volume 78.0 cubic microns; mean corpuscular hemoglobin concentration, 25.2% (unpublished data).]

During the first 15 days on the diet restricted in vitamin B_2 (G), there was an average drop of 1,250,000 in the number of red blood cells per cu.mm., and a slight decrease in hemoglobin. For the next 60 days the erythrocytes and their hemoglobin content remained at fairly constant levels.

The blood counts of 2 animals (No. 473 and No. 393) that were

continued on the diet until exitus, were noteworthy during the last 2 weeks of the experiment in that there was a precipitous drop in both the erythrocyte and hemoglobin levels. The final red blood-cell counts were 4,260,000 (No. 473) and 3,900,000 (No. 393) cells per cu.mm., and the hemoglobin determinations were 52 (7.4 gm.) and 36 (5 gm.) % respectively. It is to be emphasized that, throughout the experiment, the color indices remained between 0.5 and 0.7 and the cell-volume less than normal. The anemia, therefore, continued to be hypochromic and microcytic in character.

In these 2 dogs parenteral injections of liver extract† failed to alleviate symptoms, or to alter the progress of the anemia.

The third dog (No. 161) showed a reduction in the number of erythrocytes after 75 days of restricted diet. Progress of the anemia stopped, however, with the daily feeding of raw beef which is rich in vitamin B_2 (G), and subsequently there was a rise in the erythrocyte level.

Conclusion. A diet restricted in vitamin B_2 (G) when fed to dogs with an artificial achylia gastrica did not produce macrocytic anemia.

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Cortico-Adrenal Insufficiency in Rats Under Reduced Pressure.

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This report concerns one of the aspects of a broader research project in which a fairly comprehensive study was made of the response of rats to reduced pressure, inclusive of the relation of such response to some pathological conditions both in rats and other animals. By experiments carried out under a variety of standardized levels of low pressure and for a series of standardized periods of exposure to such pressures, it has been shown that various functional factors respond in a uniform and typical manner to these environments. On this evidence 3 stages could be distinguished with respect to the total exposure period of a rat to the low pressure environment: (a) a pre-adaptive stage during which most deviations of values indicate an unfavorable effect, (b) an adaptive stage during which deviations occur in the opposite direction and are indicative of adaptive adjustments, and (c) a post-adaptive stage during

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