

Group 3, one showed a normal output and the others ranged from 1/20 to 1/100 of the average epinephrine output for normal dogs. In Group 4 (5 dogs) a normal output was found in 3 animals, about 1/8 of the normal average in one and 1/50 in the other.

It appeared, at first, that insulin might be responsible for the low epinephrine output, since most of the treated depancreatized animals showed a marked reduction. However, in 3 of the 13 untreated depancreatized dogs there was a definitely reduced epinephrine output. The animals in this group did not live nearly as long as the treated animals, which may explain the smaller number of instances of reduction in output in the untreated dogs. On the other hand, a similar difference is seen in the case of unoperated dogs on a diet rich in sugar, between Groups 3 (receiving insulin) and 4 (untreated). Of course, it is possible that this difference might be less striking in larger series of experiments. Nevertheless, whatever the reason may be for the greater number of instances of reduced epinephrine output in the insulin-treated groups, it is evident that this reduction can occur without the action of insulin. That the liver may play a rôle and other probable factors remain for further investigation.

The evidence indicates that the diabetic state of the animal is primarily responsible for the reduction or suppression of epinephrine secretion from the adrenals. We have found that electrical stimulation of the splanchnic nerve is capable of increasing the epinephrine output up to or above the normal level, in those animals that show a marked reduction in output.

8930 C

Electrocardiographic Changes in Rats Deficient in Vitamin B₁.

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Vitamin B₁ deficiency in rats and pigeons has been found to be associated with bradycardia (Birch and Harris¹; Drury, Harris and Maudsley²; Carter and Drury³; and Méhes and Péter^{4, 5}). Changes

¹ Birch, T. W., and Harris, L. J., *Biochem. J.*, 1934, **28**, 602.

² Drury, A. N., Harris, L. J., and Maudsley, C., *Biochem. J.*, 1930, **24**, 1632.

³ Carter, C. W., and Drury, A. N., *J. Physiol.*, 1929, **68**, i (Proceedings).

⁴ Méhes, J., *Arch. f. Exp. Path. u. Pharm.*, 1934, **176**, 141.

⁵ Méhes, J., and Péter, F., *Arch. f. Exp. Path. u. Pharm.*, 1934, **176**, 226.

in the complexes of the electrocardiograms have not been described. As far as one can ascertain, the electrocardiograms obtained in rats deficient in vitamin B₁ were not standardized.

Because of the discrepancy between electrocardiographic findings in deficiency states attributed to vitamin B in man (beriberi, pellagra, polyneuritis)⁶⁻⁹ and in animals, a study was undertaken on the effect of vitamin B₁ deficiency on the heart of the rat, as indicated by the electrocardiogram. Nine rats were placed on diets deficient in B₁, consisting of Wesson¹⁰ salt mixture 3.5%, starch 55%, butter fat 8.5%, casein 18% and autoclaved bakers' yeast 15%. The casein was washed with alcohol by a method similar to that of Chase and Sherman.¹¹ The yeast was autoclaved for one hour at 20 pounds after the addition of 0.1 normal sodium hydroxid. Standardized electrocardiograms using skin copper leads were obtained. During a period of 7 weeks only moderate loss of weight developed. This, together with the absence of bradycardia and of nervous manifestations, indicated the existence of but partial deficiency. The yeast was therefore autoclaved for 6 hours at 15 pounds at a pH of 8 to 9. After 3 weeks on this modified diet the animals exhibited marked loss of weight, neurological manifestations, bradycardia and changes in the electrical complexes of the cardiogram. The heart rate gradually fell from a normal level of from 564 to 666 per minute (average 581) to from 354 to 134 (average 286). In 5 of the rats T wave changes of high origin were observed. Increase in the height of the T wave developed in 2 animals. Definite inversion of the T wave occurred in one, and questionable inversion in another animal. In one of the deficient animals there were no changes in the complexes. The alterations in the electrocardiographic complexes bore no direct relation to the degree of slowing of the heart.

Subcutaneous administration of from 5 to 25 γ of crystalline vitamin B₁ (Merck) abolished both the bradycardia and the changes in electrocardiographic complexes when the rate was 300 or over, but usually failed to save the animals when the rate was below this level. Elevation of the heart rate and disappearance of the abnormal complexes occurred as early as within 4 hours. In animals in

⁶ Scott, L. C., and Herrmann, G. R., *J. A. M. A.*, 1928, **90**, 2083.

⁷ Keefer, C. S., *Arch. Int. Med.*, 1930, **45**, 1.

⁸ Feil, H., *Am. Heart. J.*, 1936, **11**, 173.

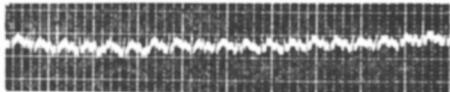
⁹ Weiss, Soma, and Wilkins, R. W., *Tr. Assn. Am. Phys.*, 1936, **51** (in press).

¹⁰ Wesson, L. G., *Science*, 1932, **75**, 339.

¹¹ Chase, E. F., and Sherman, H. C., *J. Am. Chem. Soc.*, 1931, **53**, 3506.

VITAMIN B₁ DEFICIENCY IN RATS
(RAT NO. 9)

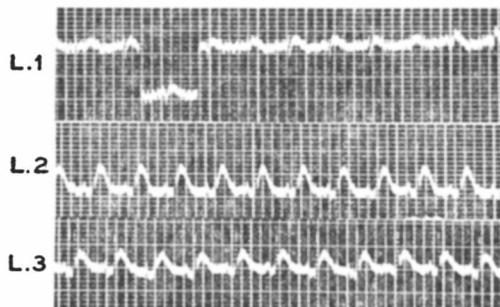
7/6/36
RATE 582



8/28/36
RATE 408



9/1/36
RATE 354



0.025 MG. VITAMIN B₁ INJECTED

9/2/36
RATE 498

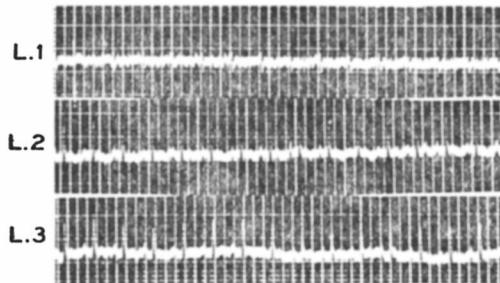


FIG. 1

The effect of diet deficient in vitamin B₁ on the electrocardiogram of the rat. Note progressive slowing of the cardiac rate and changes in the S-T complexes. Subcutaneous injection of crystalline B₁ abolished the changes in the electrocardiographic complexes within 12 hours.

which the deficiency was abolished with crystalline B₁ and was repeatedly induced again, the changes in the electrocardiographic complexes during the subsequent deficiency state were not always identical. The fact that the changes in the electrocardiographic

complexes could be abolished with crystalline vitamin B₁ in animals kept in a fasting state indicates that the cardiac changes are directly related to B₁ deficiency rather than to malnutrition. The latter factor may nevertheless play a secondary rôle. Fig. 1 represents the result of an experiment on the effect of vitamin B₁ deficiency and of the administration of crystalline B₁.

Two rats, used as controls, were kept on an identical diet with the single exception that the yeast was not autoclaved. These animals gained weight and exhibited no cardiac slowing, changes in the electrocardiographic complexes nor nervous manifestations. Further experiments are in progress to elicit the relationship between the cardiac changes here described and vitamin B₁ deficiency.

The results of the experiments here reported and the character of the electrocardiographic changes described are in harmony with the electrocardiographic changes observed in human deficiency states (pellagra, polyneuritis, beriberi). The essential difference is that in man tachycardia rather than bradycardia is present in deficiency states attributed to vitamin B. Transient bradycardia has been observed during recovery from severe "beriberi heart".⁹

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A Comparative Assay of Black Widow Anti-Sera.

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This paper reports the results of a comparative assay of the recently perfected super-immune serum from sheep* and a sample of convalescent human serum supplied through the courtesy of Dr. Emil Bogen of Olive View, California. Some success has been reported in the treatment of arachnidism (of which there were 615 reported cases with 38 deaths in 1935) with human serum and it seemed desirable to compare its potency with that of a carefully assayed super-immune animal serum.

The assay was carried out as follows: A solution of venom was prepared by dissecting the venom-glands from spiders, macerating and dissolving in saline. The average lethal dose (A.L.D.), that is, the dose required to kill 50% of the test animals, was determined. Varying amounts of the sera were added to solutions of the venom,

* Anti-Black Widow Spider Serum—Squibbs.