

to interpret these experiments on the basis of the hypothesis of Fromherz¹ and of Hill⁵ that veratrine is unable to penetrate the myelin sheath until after the sheath has been rendered permeable by a temporary lack of oxygen.

According to Hill the heat production following stimulation of veratrinized nerve in oxygen is not materially greater than normal unless the nerve has been previously asphyxiated. In this condition the heat production following a single shock may be a thousand times normal. Stimulation at a rate of 30 shocks per minute gave a heat production more than 30 times normal in one experiment. Under the conditions of our experiments this would correspond to an excess oxygen consumption of at least 15%. Schmitt and Gasser⁴ have already observed definite increases in oxygen consumption of veratrinized nerves when stimulated at a rate of 2 per second. Preliminary experiments with an improved respirometer have demonstrated increases of 1-3% above the resting level with rates of stimulation of 16-30 shocks per minute, whether or not the nerve has been subjected to previous asphyxiation. The possibility therefore exists that a portion of the large heat production reported by Hill may have no counterpart in processes involving oxygen consumption.

7314 P

Normal and Experimentally Modified Mitotic Activity of Adrenal Gland in Guinea Pig.*†

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The mitotic activity of the thyroid gland in the guinea pig can be used as a quantitative measure of the stimulating effect exerted by various agencies on this organ.¹ In the following investigations we extended this method to the adrenal gland of the guinea pig and we determined the number of mitoses in this gland in the normal animal

⁵ Hill, A. V., *Proc. Roy. Soc.*, 1933, **113**, 386.

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¹ Gray, S. H., and Loeb, Leo, *Am. J. Path.*, 1928, **3**, 257.

and under various experimental conditions. We soon found that there is a remarkable similarity in the mitotic activity in various sections through this organ at the same time, so that it is possible to obtain the measure of the mitotic activity of a gland by counting the mitoses found in 3 longitudinal sections through the center of this organ, each section being approximately 6 mikra thick. Counting the number of mitoses in a larger number of sections does not cause a significant alteration in the figures. The large majority of all mitoses are found either in the *zona glomerulosa* or in the outer portion of the *zona fascicularis* and it seems that, in the former area, mitoses occur especially in younger individuals. In these investigations, we excluded all animals which showed any sign of infection. In normal guinea pigs weighing 190-200 gm. the average number of mitoses per section is about 5; this number declines with increasing weight and age. In guinea pigs weighing 400-600 gm. it is about 1.5 mitoses per section. This series of normal animals includes 87 cases. There is no appreciable difference between males and females. The total number of mitoses in one adrenal gland of a guinea pig weighing 195 gm. was 1340, in the adrenal gland of a guinea pig weighing 340 gm., 930, and in a guinea pig weighing 515 gm., 165. Canalis stated that in sections of suprarenals from normal guinea pigs there might be 5 mitoses, in others as many as 12 per section.² Hoerr states that in sections cut 3 to 4 μ one may expect to find on the average 2 to 8 mitoses in a longitudinal section through the center of a gland of a young adult guinea pig (350-450 gm.).³

Keeping guinea pigs in a room with a temperature varying between 7° and 9°C. for from 8-25 days increased the number of mitoses to 15. The average of 3 controls was 3.6. An almost equal increase in mitotic activity was induced by underfeeding guinea pigs for periods of from 4-7 days, with a daily loss in weight varying between 2.5 and 9 gm. The average number of mitoses per section was 13. Average in 6 controls was 4.5.

Daily intraperitoneal injections of acid extract of anterior pituitary of cattle cause an increase in mitotic activity, which is most marked if, in the course of 6 days, increasing amounts of extract are injected on successive days. The average number of mitoses of 6 guinea pigs thus treated was 50.5. If daily injections of 1 cc. acid extract are given, the increase is much less marked and the number returns almost to normal, if the injections are continued

² Canalis, P., *Internationale Monatsschr. f. Anat. und Physiol.*, 1887, 4, 312.

³ Hoerr, W., *Am. J. Anat.*, 1931, 48, 139.

over a long period of time; this corresponds to an analogous effect in the case of the thyroid gland.⁴ Also inoculations of anterior pituitary glands from guinea pig and rabbit caused a marked increase in the number of mitoses. Daily inoculations of one or 2 anterior pituitary glands from guinea pigs led to a rise in the average number of mitoses to 38. A similar increase was induced by daily inoculations of rabbit anterior pituitary. This figure was still higher (an average of 69 mitoses) in a series in which the administration of rabbit anterior pituitary was preceded by a short period of underfeeding. On the other hand, if in a first period, acid extract was injected daily and, in a subsequent period, guinea pig or rabbit anterior pituitary glands were inoculated, the rise in the mitotic activity was much less. This is perhaps due to an antagonism that exists between the hormones predominant in the anterior pituitary glands of rabbits, rats and guinea pigs on the one hand and in extract of cattle anterior pituitary on the other hand. To our surprise we noted that after inoculation of rat anterior pituitary into guinea pigs, only an exceptional rise in mitotic activity was induced in the adrenal gland of the guinea pig. This apparent relative ineffectiveness of rat anterior pituitary needs further analysis.

We may then conclude that various hormones of the anterior pituitary cause a rise in the mitotic activity of the adrenal gland of the guinea pig, and that this effect seems to be independent of the action of these hormones on the thyroid gland, as evidenced by the fact that the guinea pig anterior pituitary, which has no or only a very slight effect on the thyroid gland,⁵ may have a very marked effect on the adrenal gland.

⁴ Loeb, Leo, and Friedman, Hilda, *PROC. SOC. EXP. BIOL. AND MED.*, 1931, **29**, 172.

⁵ Loeb, Leo, *Endocrinology*, 1932, **16**, 129.