

ism¹ and to that of invertebrate hearts (Garrey²), seem completely wanting.

The transition to intrinsic automacity on the part of lymphatic hearts is thus shown to involve a radical functional change from skeletal to cardiac muscular properties. Results in detail will appear in a later report.

6624

Studies on the Adrenal. II. Extraction of Cortical Hormone from Urine.

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It is probable from many physiological observations that the active principle of the adrenal cortex is of the nature of a general tissue hormone. If this be the case it should be present, albeit in small quantities, throughout the body and possibly in various secretions. Its presence was therefore sought in the urine. Perla and Gottesman¹ claimed to have extracted the hormone from urine. From each liter of urine they obtained a quantity of hormone comparable to that obtained from about 225 gm. of the fresh beef adrenal glands by the method of Hartman.² Such a high yield would speak either for the excellency of urine as a source of the hormone or for the poor yield obtainable from glands by the method utilized. Unfortunately, Perla and Gottesman used as evidence for the presence of cortical hormone in urine the increased resistance of rats to histamine when the extract was simultaneously injected. The indirect nature of this method of test renders their conclusion open to question.

Our urinary extracts were prepared by extracting the fresh urine with benzene. When other than freshly voided urine was used, the products were less active, having apparently undergone decomposition, as might be readily expected. After washing the benzene with water, it was removed *in vacuo* at 40°C., after adding an

¹ Garrey, W. E., *J. Cell. and Comp. Physiol.*, 1932, **1**, 209.

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¹ Perla, D., and Gottesman, J. M., *Proc. Soc. Exp. Biol. and Med.*, 1931, **28**, 1024.

² Hartman, F. A., *Endocrinol.*, 1930, **14**, 229.

amount of 0.9% saline to make 1 cc. of the final extract correspond to one liter of urine. A yellowish, odoriferous solution was obtained which was capable of prolonging life and permitting growth in one-month-old adrenalectomized rats when administered in doses of a cubic centimeter, twice daily. As compared to the extracts obtained by us from adrenal glands,³ one liter of urine contains an amount of hormone corresponding to approximately only one-half gram of glandular tissue. It is thus much less valuable as a source of the hormone than indicated by Perla and Gottesman's results.

An attempt was also made to prolong life in adrenalectomized dogs and cats by the urinary extracts. As might be anticipated, the results, although indicating the presence of some activity in the extracts, showed the practical impossibility of preparing sufficient hormone from urine to prolong life of adrenalectomized cats or dogs for any considerable length of time. Thus a dog, bilaterally adrenalectomized at one operation, was kept alive for 9 days. Microscopic examination of the adrenal sites revealed the absence of any residual cortical tissue. In our control series of untreated dogs death resulted on an average on the fourth day with a maximum survival of 7 days (one stage operation in each case). The animal cited received an average daily dose of 17 cc. of extract, which corresponds to the amount of hormone obtained from about 8 gm. of cortical tissue as prepared by our method.³

In view of the imputed importance of pregnancy and "heat"⁴ in prolonging the life of adrenalectomized animals it was necessary to prove that the above described results were not due to any effect of the sex-stimulating hormones present in urine. Extracts made from the urine of pregnancy were no more potent than those from male urine. Theelin, Antuitrin, and Follutein[†] were ineffective in prolonging life of adrenalectomized animals; and hence it is doubtful if the observed results are attributable to the presence of sex hormones. On the other hand, it is necessary to consider the presence of a cortical hormone or its decomposition products in urinary extracts as being possibly responsible for certain effects of such extracts on the reproductive system.

³ The rat method of assay and the preparation of active cortical extracts from adrenal glands are described elsewhere (Grollman, A., and Firor, W. M., *J. Biol. Chem.*, 1933, in press).

⁴ Stewart, G. M., and Rogoff, J. M., *Am. J. Physiol.*, 1927, **79**, 508. Firor, W. M., and Grollman, A., *Ibid.*, 1933, **103**, 686.

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