

discarded in the preparation of the ovary-stimulating hormone described in this paper.*

We are greatly indebted to Dr. H. B. Van Dyke, of the University of Chicago, for making tests to determine the effect of the placental extract (85 per cent alcohol soluble) upon completely hypophysectomized rats. He has very kindly permitted us to quote his results, which he will doubtless publish in detail later. After two weeks of daily injections with known potent extracts, he obtained œstrus in five hypophysectomized animals. He also confirmed our results as to the absence of œstrin from the extract.

The fact that the ovary of the hypophysectomized rat has been activated by the placental extract, even though the time required was much greater than in the case of immature normal animals, is a matter of great importance. It may be viewed as evidence against the theory of placental origin of the hormone suggested in this communication. A practical point which the experiment indicates is in relation to the time required to produce the result. It is possible, therefore, that certain clinical cases of ovarian hypofunction of pituitary origin may be found to respond to treatment with the extract if the treatment is continued over some months.

The problem of standardization of the extract is a very formidable one. Lately we have found that spontaneous œstrus may occur in untreated control animals as early as twenty-six days of age. It becomes necessary, therefore, to use animals in assay work which are of such an age and weight as practically to exclude the possibility of obtaining positive results in controls. Very young rats are relatively insensitive to the hormone in our experience. Also, it has been very difficult at times to obtain clear, positive œstrus smears in rats of less than twenty-five days of age and weighing under 35 grm., even when they have been injected with known potent extracts. A phase of cornification may be obtained, but leucocytes are usually present. It is necessary, then, in many instances to confirm by post mortem and sectioning of the vagina what might be termed doubtful vaginal smears. It is possible that one may be dealing with a seasonal condition. We are desirous, however, of emphasizing the pitfalls in the biological assay, because we

doubt if all who have worked in this field fully appreciate the conditions.

It is to be hoped that some satisfactory solution of the problem may be arrived at by the use of special diets or by the removal of the pituitary or thyroid gland from adult animals, with a view to rendering them acyclic.

For the moment we feel that extracts prepared by rigidly followed methods present a lesser degree of variability than does the rat assay test. The extracts which have been used clinically have therefore been appraised in terms of grams of placenta per cubic centimetre. The rat tests on these extracts have shown a variation of from one to three units per gram of original placenta.

The ultimate solution of the problem would seem to depend on the production of large amounts of final product, and a rigorous assay of this material by the use of a large number of standard animals.

The name "Emmēnin", suggested by Prof. A. B. Macallum, is proposed for the placental hormone described in this paper.

SUMMARY

1. Methods of preparing active extracts of an ovary-stimulating hormone derived from placental tissue are described.
2. Physiological studies with the hormone are described and a theory is suggested that the hormone is of placental origin.
3. The name "Emmēnin" is proposed for the hormone.

It is a great pleasure to acknowledge the great help that my colleague, Dr. D. L. Thomson, has given. I am deeply indebted to him for the survey of the literature which forms an integral part of this paper. I wish also to acknowledge the technical assistance of Mr. M. McPhail and Miss J. Williamson, who were responsible for the daily examinations of large numbers of the experimental animals. Prof. F. E. Lloyd has very kindly allowed us to use his photographic apparatus and has given us his personal assistance, for which we wish to thank him.

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* See special note on p. 774.