

more effective than either alone. The prophylactic effect of this combined treatment in raising resistance of rats and mice to histamine shock is much more pronounced than the therapeutic effect after histamine is administered. Application of these experimental observations to the prevention of surgical shock in human beings is reported.

11212

**Are Gonadotropic Hormones Destroyed While They Exert
Their Action on the Ovary?**

HANS SELYE.

From the Department of Anatomy, McGill University, Montreal, Canada.

The question whether hormones are inactivated by the organs on which they act is of fundamental importance for the interpretation of hormone action in general. Some authors regard hormones as catalysts, which would imply that they are not used up during their activity, while others believe that they are destroyed while they exert their action. This latter view appears to receive some support from observations showing that if hormone preparations are administered parenterally only a fraction if any of the injected material may be recovered from the excretions. The fact that removal of one ovary causes compensatory hypertrophy of the remaining gonad has likewise been looked upon as "an expression of the effect of the total amount of anterior pituitary hormone being available for one ovary."¹ However, neither one of these arguments is conclusive and little effort has been made, up to the present, to solve this problem by experimental investigation.

It is doubtless true that hormones are destroyed in the organism but this does not prove that they are used up by the organs upon which they act. Furthermore, the compensatory hypertrophy of an organ such as the ovary may not only be explained by assuming that more gonadotropic hormone is available for the ovarian remnant but might also be looked upon as resulting from increased gonadotropic hormone secretion by the hypophysis of the partially spayed animal.

In order to elucidate this problem, the following experiment was

¹ Adams, A. Elizabeth, *Proceedings of the Second International Congress for Sex Research*, 1930, p. 190.

performed. Twenty "hooded" female rats were hypophysectomized at the age of 4 weeks. Ten of them were unilaterally ovariectomized at the same time. Immediately following the operation, one animal of each group received subcutaneous injections of one R.U. of a follicle-stimulating preparation (F.S.H.) and one R.U. of a luteinizing preparation (L.H.).* The second animal of each group received 2, the third, 3 units of each of these preparations and so on, each animal receiving one more unit so that the last animal in each group received 10 units of F.S.H. and 10 units of L.H. This treatment was repeated once daily for 5 days. On the sixth day, the animals were sacrificed and their ovaries were weighed.

It is obvious that the ovarian weight in these animals could only be determined by the amount of the injected gonadotropic hormone available for each ovary since in the absence of pituitary tissue, no compensatory gonadotropic hormone production was possible. If the ovary destroys gonadotropic hormone during maturation, the weight of one ovary in the unilaterally spayed females should be higher than that of one of the 2 ovaries in the animals possessing both their gonads. Table I shows, however, that this is not the case.

Since there are marked individual variations in the sensitivity to gonadotropic hormones, the parallelism between the dose administered and the resulting ovarian weight is not very close but it is easy to see that half of the combined weight of the 2 ovaries in the non-castrates corresponds approximately to the weight of the remaining ovary in the unilaterally spayed group at the various dose levels. Between one and 3 units, the increase in weight was not significant enough to draw conclusions although histologically some stimulation

TABLE I.

Units of F.S.H. and L.H. injected	Half of the wt of the 2 ovaries in non-spayed, mg	Wt of one ovary in uni- laterally spayed, mg
1	7.5	7
2	8.5	7
3	9	7.5
4	14	12
5	8.5	11.5
6	12.5	12
7	18	13
8	17.5	17
9	14.5	18
10	22.5	22

* We are greatly indebted to the Løvens Kemiske Fabrik for the follicle-stimulating mare serum preparation "Antex Leo" and to the Ayerst, McKenna and Harrison Ltd. for the luteinizing human pregnancy urine extract "APL."

was quite obvious. However, if we compare the animals receiving 3 units with those receiving 6 or the group injected with 4 and 5 units with those injected with 8 and 10 units respectively, it becomes clear that if a certain amount of gonadotropic hormone is present, the resulting ovarian weight is considerably greater than if half of that dose is administered. From this it appears that if each ovary would use half of the injected hormone, the weight of a single ovary should be considerably larger in the group having but one gonad. This, however, is certainly not the case, in fact if we calculate the average weight of one ovary for the 10 different dose levels, it proves to be 13.3 mg in the non-spayed as compared with 12.7 mg in the spayed group which shows that there is no significant difference between the 2 series.

From these experiments it appears that the ovarian weight is determined by the mere presence of a certain concentration of gonadotropic hormones in the body fluids and that no significant destruction of this hormone takes place while it exerts its gonad-stimulating effect. Further experiments will have to show whether other hormones act in a similar manner. Great caution will have to be used, however, in extending such studies to the gonadal hormones. Hertz and Meyer² noted that removal of parts of the male genital tract does not increase the response of the remaining parts to testosterone nor does partial hysterectomy increase the response of the remaining uterine tissue to a standard dose of estrin. In view of the fact that these sex hormones act on many organs other than the genital tract,³ it is difficult to draw any definite conclusions from these experiments because extirpation of part of the genital tract removes only an insignificantly small portion of the tissues upon which these hormones act.

Summary. In hypophysectomized and unilaterally ovariectomized rats, a certain dose of the gonadotropic hormones causes the same increase in the weight of the single ovary as this same amount causes in hypophysectomized animals possessing both their gonads. It is concluded that no significant destruction of the gonadotropic hormones takes place while they exert their action on the ovary.

² Hertz, Roy, and Meyer, Roland K., *Am. J. Physiol.*, 1938, **124**, 259.

³ Selye, Hans, *Canad. Med. Assn. J.*, February, 1940, **42**, 113.