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Reaction of Anterior Pituitaries of Immature Female Rats to Injections of Various Amounts of Oestrin.*

J. M. WOLFE AND C. S. CHADWICK.

From the Departments of Anatomy and Biology, Vanderbilt University, Nashville, Tenn.

It is well established that injection of oestrin in normal female rats induces changes in the anterior hypophysis comparable to those of pregnancy and that such injections in castrated female rats prevent typical castration changes. Daily injection of large amounts of oestrin into normal female rats for 10 days results in a marked but variable weight increase in the pituitaries. The basophiles are markedly degranulated and reduced in relative percentage. The eosinophiles also present loss of granules and a variable reduction in relative percentage. The chromophobes are greatly increased in relative percentage.[1] In the studies recorded below we have attempted to ascertain more exactly the morphologic and quantitative effects of large and small daily injection of oestrin for periods of 5 and 10 days on the various cell types of the anterior pituitaries of immature female rats. We wished to determine if the amounts of oestrin necessary to cause changes in one cell type would induce changes in the other types. Female rats, 21 to 23 days old were used. At autopsy, body, ovary and pituitary weights were obtained. Serial sections of all pituitaries were cut. Five representative sections from each were studied; differential cell counts were made on each; the number of mitoses were also counted.

In the first series, 9 rats received daily injection of 10 units of oestrin† for 5 days; a second group of 8 littermates received daily injection of 200 units for the same period. Eleven littermate controls were available. In the rats receiving 10 units daily the pituitaries were increased in weight to a mean of 3.5 mg.; the mean in the controls was 2.6 mg. The basophiles of the injected rats were moderately degranulated; the result was a decrease in the relative levels of the granular basophiles to a mean of 2.8% while this mean in the controls was 8.3%. A few of the eosinophiles in the

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1 Wolfe, J. M., PROC. SOC. EXP. BIOL. AND MED., 1935, **32**, 1192.

†Dihyroestrin (Progynon-B) was used; a portion of this was furnished gratuitously by Schering Corporation, Bloomfield, N. J.

injected rats were swollen and showed loss of granules. The relative percentages of eosinophiles were not decreased when compared with the controls. This may possibly be explained by the fact that in the injected rats the number of mitoses found in the eosinophiles was much greater than in the controls; the mean number per section in the injected rats was 14.7 while in the controls it was only 3.2. The mean number of mitoses per section in the chromophobes was also increased; in the injected rats it was 18.4 while in the controls it was 7.7. Mitoses were not observed in the basophiles. In the rats receiving daily injections of 200 units of oestrin for 5 days the pituitaries were increased to a mean weight of 3.9 mg. The degranulation of the basophiles was more marked than in the rats which received daily injections of 10 units; the relative level of the granular basophiles was reduced to a mean of 1%. Non-granular basophiles were increased inversely. Numerous eosinophiles in these glands showed loss of granules; as a whole the degree of granular loss from these cells was not much greater than in the animals which received only 10 units of oestrin daily. The relative levels of these cells were not decreased when compared with the controls. The number of mitoses in the eosinophiles was increased to a mean of 11.5, and in the chromophobes to a mean of 13.7.

In a second series, 17 rats received daily injections of 10 units of oestrin for 10 days; a second group of 27 littermate sisters received daily injection of 200 units for 10 days. Nineteen littermate controls were available. In the rats receiving 10 units daily the pituitaries were increased to a mean weight of 4.8 mg.; the mean in the controls was 3.3 mg. The basophiles exhibited marked degranulation; the mean level of the granular basophiles was reduced to 1%. The mean of the granular basophiles in the controls was 6.8%. Many eosinophiles showed loss of granules but this loss was not marked enough except in 2 rats to cause any appreciable decrease in the relative levels of these cells. The mean number of mitoses in both the chromophobes and eosinophiles per section was increased when compared with the controls. In the rats receiving 200 units daily the pituitaries were increased in weight to a mean of 5.8 mg. Degranulation of the basophiles in this group was practically complete; the mean level of the granular basophiles was only 0.3%. Granular loss was marked in the eosinophiles and furthermore the relative percentages of these cells were reduced to a mean of 28.3%, which was far below the mean level of these cells in the controls (38.7%). Many eosinophiles were swollen and showed loss of granules (the granules remaining in the cell took a pale

stain). In many the negative image of the Golgi apparatus was enlarged. The chromophobes were markedly increased in percentage. Many of these cells were enlarged; the cytoplasm was either dense blue or light blue and fragmentary. In many the negative image of the Golgi apparatus was enlarged. In this group the mean number of mitoses per section in the eosinophiles was 7.5; in the chromophobes it was 19.5. In the controls these 2 means were 6 and 9.6, respectively.

These studies indicate that oestrin exerts a definite influence on both the eosinophiles and the basophiles. Small amounts of oestrin apparently induce a very definite degranulation of the basophiles and a reduction in the relative percentages of the granular basophiles in a short time. Our observations further indicate that the non-granular basophiles eventually pass into chromophobes. Mitoses were not observed in the basophiles. In the case of the eosinophiles our data are suggestive that the situation is somewhat different. Injection of oestrin induces degranulation of the eosinophiles and these degranulated cells give rise to chromophobes. However, it seems that it requires more oestrin and a longer period of time to induce degranulation in a sufficient number of eosinophiles to cause a decrease in the relative percentages of these cells in the gland. It seems highly possible that this finding is at least partially due to the fact that injection of oestrin increases the number of mitoses in the eosinophiles, thus introducing a factor which tends to keep the level of these cells near the normal limit regardless of the fact that many of these cells are at the same time losing granules and passing into chromophobes. Since the same factor is apparently not active in the basophiles any degranulation of these cells results in an immediate reduction in the relative percentages of the granular cells.