17081. Effect of Pregnancy on the Rat Ovary Transplanted to the Spleen.*

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The response of the ovary of rats to endogenous hormones, when it is placed in the portal circulation by means of intrasplenic transplantation, differs greatly from that of the ovary that is in its normal position. If the animal is a castrate, the intrasplenic ovary shows a continuous formation of new follicles which luteinize. The corpora lutea do not involute, and from them a neoplasm may ultimately develop.[1,2] If the animal is a unilateral castrate, the intrasplenic ovary atrophies after a period of 24 days, but this atrophic ovary assumes active growth as soon as the normal ovary is removed.[3] It is probable that when one ovary is intact and the other is transplanted to the spleen both are receiving the same hormonal influences through the systemic circulation. The normal ovary shows the compensatory hypertrophy that customarily follows unilateral castration, while the intrasplenic ovary simultaneously is undergoing severe atrophy. That the splenic pulp does not interfere with growth is proved by the appearance of follicles and corpora lutea in the intrasplenic ovary and its progressive enlargement, immediately following the removal of the normal ovary.[3]

The present investigation is a related study on the effect of the endogenous chorionic gonadotrophic hormones of the rat on the normal and on the intrasplenic ovary. Young adult female rats of the Long-Evans strain were employed. The left ovary was removed under ether anaesthesia through a lumbar approach and cleaned of fat and the tube. The spleen was delivered into the wound, and the left ovary was placed in a pocket made by incising the splenic capsule. After an interval of from 40 to 50 days, the rats during estrus were placed with males, and all became pregnant. Six animals were sacrificed as soon as possible after the litter was delivered; nine additional animals were permitted to live between 9 and 60 days after the termination of pregnancy. Another group of nine animals was ovariectomized as soon as possible after the litter was delivered and subsequently three of these were sacrificed on each of the following days after the birth of the litter: 10, 31, and 62.

Pregnancy had occurred only in the right horn of the uterus of each animal. The litters were composed of normal young which were removed from the mother at birth. In the group ovariectomized post partum, the right ovary was removed through a right lumbar incision, and the spleen was carefully examined for adhesions between it and the parietal abdominal wall or other organs. A complete autopsy was performed on each animal. The tissues were prepared in the usual manner for histologic study and multiple sections at several levels of the transplanted ovary were studied.

The 6 animals that were sacrificed at the termination of pregnancy showed a slight increase in the size of the transplant. Histologic examination revealed that this was due to an increase in the size and number of follicles. Many of the follicles were large and contained an ovum that was compactly surrounded by as many as ten rows of follicular cells. A single cross section through a transplant often contained as many as 10 to 15 follicles of varying size. In one transplant, there was a single small corpus luteum; serial sections of the remaining transplants did not disclose a corpus luteum. The control

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1 Biskind, M. S., and Biskind, G. R., PROC. SOC. EXP. BIOL. AND MED., 1944, **55**, 176.

2 Biskind, G. R., and Biskind, M. S., *Am. J. Clin. Path.*, in press.

3 Biskind, G. R., and Biskind, M. S., *Science*, 1948, **108**, 137.

transplants in non-pregnant animals rarely contained as many as 5 minute atrophic follicles.[3]

Animals sacrificed at intervals after the termination of the pregnancy showed that the transplants decreased in size and became atrophic. In 7 instances, they resembled the transplants in the animals with one normally situated and one intrasplenic ovary.[3] The ovarian stroma of each of these groups was composed of clusters of small cells that may have been thecal cells. Small follicles were scattered in the stroma. In 2 transplants small corpora lutea were present.

The animals in the last group had one ovary removed at the termination of pregnancy and subsequently were sacrificed at the intervals mentioned. The intrasplenic ovary grew rapidly and increased in size as early as ten days after the operative procedure. It was composed of developing follicles and corpora lutea. At 31 and 62 days after ovariectomy, some ovaries seemed larger than the corresponding intrasplenic ones described previously.[2] It is apparent that when the normally situated ovary is removed, the hormonal factors originally described are permitted to influence the follicular and luteal growth. In this instance there may be a slightly greater degree of growth of the intrasplenic transplant because of the extent of follicular growth during pregnancy.

The results suggest that in pregnant rats there is a decided difference in the response of the intrasplenic compared to the normal ovary. In the non-pregnant rat, the normal ovary is hypertrophied, the intrasplenic ovary is atrophic. Pregnancy produced the usual large corpora lutea in the hypertrophied normally situated ovary, follicular growth in the intrasplenic ovary of 5 rats, and corpora lutea in 1 rat. Several hypotheses can be adduced to account for these unusual responses of the same gonadal tissues in different sites in the body. The action of the liver in inactivating the estrogenic hormones elaborated by the intrasplenic ovary may play a role. Consideration must be given to the effect of the estrogen secreted into the systemic circulation by the normally placed ovary and its probable limitation of growth on the intrasplenic ovary, either directly or by influencing the hypophysis. In addition, there is an increase in estrogens as well as in progesterone during pregnancy which may act on the intrasplenic ovary. The production of follicular growth only in the intrasplenic ovary in five out of six animals may be due to the increased amounts of chorionic gonadotrophins from the placenta, or to increased hypophyseal stimulation. Further studies to elucidate this unusual effect are being performed.

Summary. In 24 rats the left ovary was transplanted to the spleen, and between 40 and 50 days later they were permitted to become pregnant. Six animals were sacrificed at the termination of pregnancy, and in all the intrasplenic ovary showed distinct proliferation of new follicles, and only one of these in addition contained a corpus luteum. Nine animals were sacrificed at intervals up to 60 days post partum, and in these the intrasplenic ovary showed progressive atrophy. In another series, the normal right ovary was removed at the termination of pregnancy and groups of 3 animals were sacrificed 10, 31, and 62 days later. The intrasplenic ovary of this series showed progressive enlargement with the continuous formation of new follicles and corpora lutea, and there was no evidence of involution of the latter. In this experiment, the gonadotrophic hormones of pregnant rats produced primarily follicular activity in the intrasplenic ovary, while simultaneously in the normally situated ovary corpora lutea were formed and maintained.

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