# Transplantation of a Granulosa Cell Tumor into the Spleen of Castrated Rats, Treated with Gonadotrophin.* (20581)

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Successful production of luteomas and granulosa cell tumors from implanted ovarian tissue into the spleen of ovariectomized rats was first reported by Biskind and Biskind(1,2). Luteomas appeared (at the earliest) 160 days after the implantation of ovarian tissue into the spleen, while granulosa cell tumors did not appear earlier than 300 days after the implantation. No tumors developed when the implantation was made into the kidney nor when fibrous vascular adhesions between the spleen and abdominal wall were present. The estrogen produced by the ovarian transplant in the spleen was inactivated by the liver(3), as proved by the vaginal smear. The Biskinds did not conclude which was the more important factor in the production of the tumors: the disappearance of estrogen from the circulation or the hypophyseal stimulation due to failure of the usual inhibition of the hypophysis by the estrogenic hormone. If hyperproduction of the anterior pituitary gonadotrophin played an important role, it should be possible to enhance the formation of luteomas and granulosa cell tumors by injecting gonadotrophin into the castrated and intrasplenic ovarian grafted rats. Zondek and Laufer(4) succeeded in enhancing the formation of luteomas and granulosa cell tumors in castrated rats with intrasplenic ovarian grafts, by injection of chorionic gonadotrophin, three times weekly 20-100 R.U. The tumors appeared 40-150 days earlier than in Biskind's experiments, in which the rats were not treated with gonadotrophin. The transplantation of such tumors into other animals was difficult and unsuccessful(5). Li(6) was the first to report a successful intrasplenic transplantation of a granulosa cell tumor in a mouse treated with progesterone (4 weekly injections of 1 mgr.). The original tumor developed in castrated mice with homotransplants of ovaries in the spleen, treated with subcutaneous injections of progesterone.

In the present paper the transplantation and growth of granulosa cell tumor in the spleens of castrate female rats is reported.

*Methods.* The original tumor was produced by repetition of Biskind's experiment (castration of rats and implantation of ovarian tissue into the spleen) without any treatment. Ten rats weighing between 110-120 g were castrated and tiny pieces of granulosa cell tumor were grafted beneath the capsule of the spleen. Three weeks later the animals were injected with 20 R.U. of chorionic gonadotrophin (Korotrin) 3 times weekly for 9 months. Of the original 10 rats, 1 died and at autopsy no tumor was found. The remaining animals were sacrificed after additional 4 months, *i.e.*, 13 months after castration and transplantation of the granulosa cell tumor.

*Results.* Two of them developed large splenic tumors and few or no adhesions were found around the spleen. In the other 7 rats fibrous adhesions between the spleen, surrounding organs and abdominal wall were

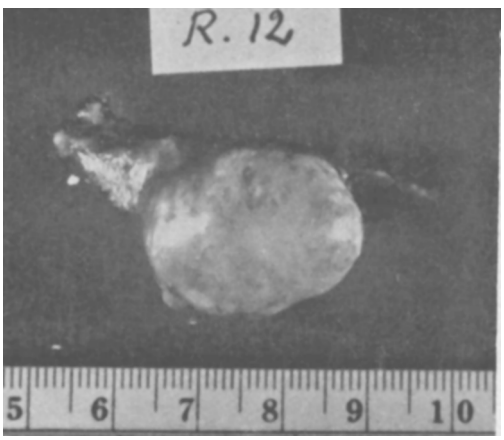


FIG. 1. Ovarian tumor, with characteristics of a granulosa cell tumor and luteoma, in the spleen.

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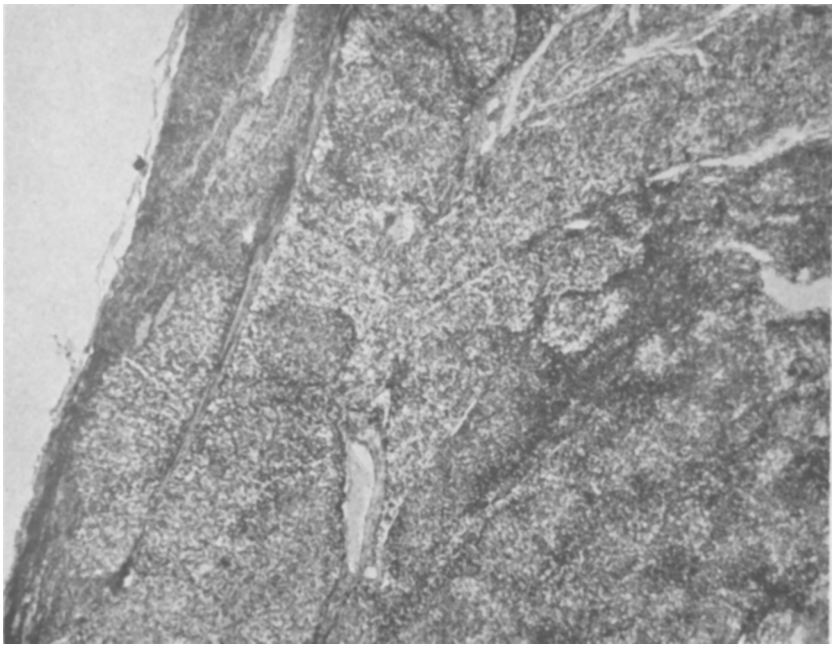

FIG. 2. Tumor nodules. Note the invading nodule into the splenic tissue, × 52.

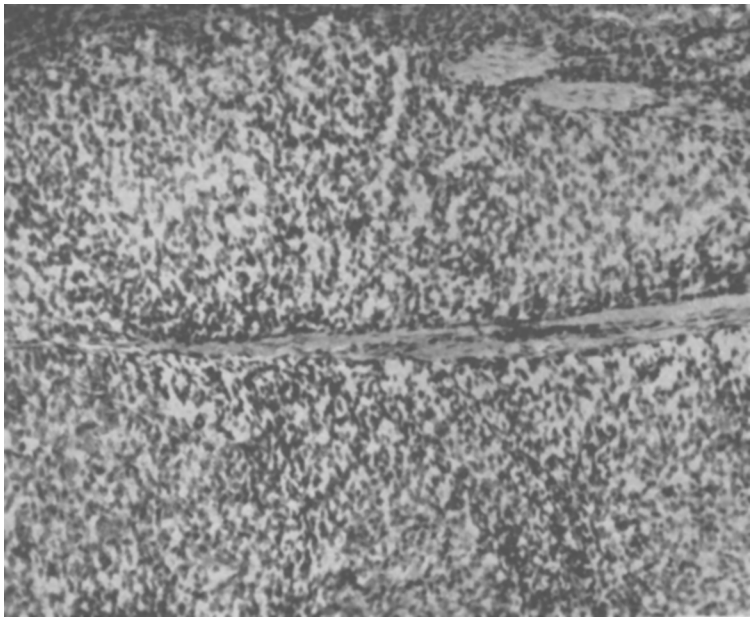

FIG. 3. Granulosa cell elements of the tumor, × 160.

numerous and vascular, and only small scars were found at the site of the transplantation.

Gross and microscopic examination of the two successful transplants revealed the characteristics of both granulosa cell tumor and luteoma. In each case the tumor was over 2 cm in diameter (Fig. 1), somewhat firm, red-yellow, lobulated, and in scattered areas showed small cysts. The tumors were in general well demarcated from surrounding splenic tissue without being encapsulated, but at one point in one of the tumors a nodule invaded

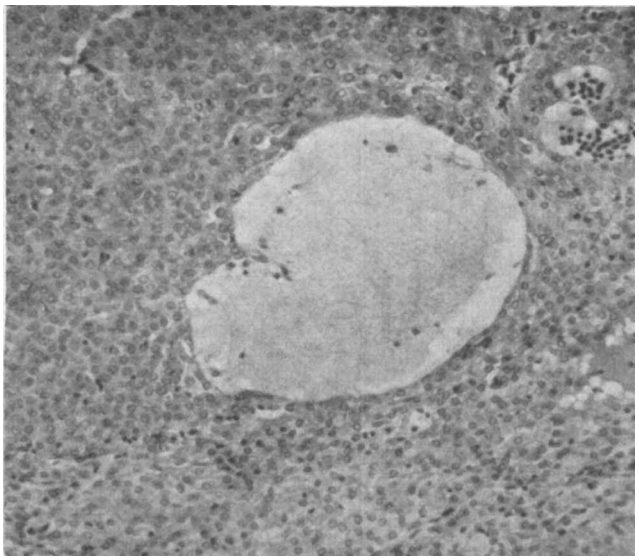

FIG. 4. Lutein elements of the tumor lining cystic spaces, × 225.

the splenic tissue (Fig. 2). Histologically there were two cell types embedded in a fine network of reticulum. One cell type corresponded to typical granulosa cells (Fig. 3) and the other was characteristic of luteum elements (Fig. 4). The two cell types were arranged in broad sheets or clusters, occasionally intermingled, and lined large cystic spaces. The tissue was well vascularized. Mitoses were easily found.

No tumor was found in 5 control rats which did not receive gonadotrophin and in which the granulosa cell tumor was transplanted into the spleen.

*Conclusion and summary.* The results of the present experiments indicate: 1) Ovarian tumors which develop from splenic transplanted ovarian tissue can be successfully retransplanted. 2. The retransplanted tumor resembles both a granulosa cell and luteum cell neoplasm. 3. Administration of gonadotrophin promotes the successful take. 4. It is assumed also that the prolonged stimulation by augmented amounts of gonadotrophic hormones of the hypophysis, to which the spleen grafted animals are subjected, is responsible for the development of the neoplastic growth. Additional subcutaneous injections with gonadotrophin enhance the formation of the tumors. 5. Estrogen produced by the graft must be inactivated by the liver, otherwise tumors do not develop. 6. The presence of adhesions between the spleen and surrounding tissues prevents the growth of the transplant.

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