hydrazones. Several other ways of preparing reagents with similar properties and suggestions for their practical use will be published elsewhere.

Part of this work was carried out at the Corrosion Laboratory of the late Prof. W. Palmaer.

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[1] *Nature*, **152**, 189 (1943); *Svensk Kem. Tid.*, **53**, 81 (1941); **56**, 295 (1944).

Study of the Gonadotrophic Activity of the Hypophysis *in situ*

IN former years parabiosis of a castrated rat with an intact one has been used in this and other laboratories for the study of the gonadotrophic functional condition of the hypophysis *in situ* freed from ovarian control. In the last four years we have made much use of a new method which allows the study of the gonadotrophic activity of the *castrate* hypophysis on the animal's own ovary.

It is known from the pioneer work of Biskind[1] that œstrogens absorbed from tablets implanted into the spleen of the rat are inactivated in the liver. We have found that this inactivating faculty of the liver may serve in the guinea pig even as a defence against tumorigenic quantities of œstrogens absorbed from the spleen in the course of several months[2,3]. Œstrogens absorbed from an ovary grafted into the portal field are also inactivated[4].

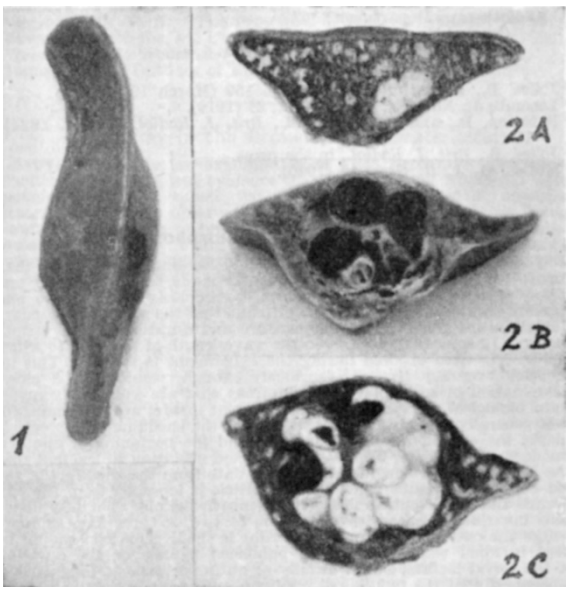

Fig. 1. SPLEEN GREATLY DISTENDED BY AN AUTOPLASTIC OVARIAN GRAFT. TEN MONTHS AFTER TRANSPLANTATION. × 7.

Fig. 2. *A*. PART OF SECOND OVARY HAS BEEN LEFT IN THE BODY. CORPORA ARE PRESENT IN THE GRAFT BUT NO BLOOD FOLLICLES. *B*. SECOND OVARY HAS BEEN REMOVED. SEVERAL BLOOD FOLLICLES (*A* AND *B* AT 2 MONTHS AFTER TRANSPLANTATION). *C*. AT 10 MONTHS AFTER TRANSPLANTATION. THE LUTEINIZATION IS NOW OVERWHELMING, BUT BLOOD FOLLICLES ARE STILL PRESENT. ALL × 3.

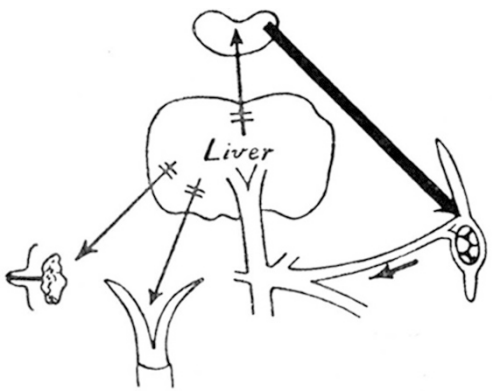

Fig. 3. DIAGRAM SHOWING FUNCTIONAL RELATIONS BETWEEN THE OVARY AND THE HYPOPHYSIS IN EXPERIMENTS WITH INTRASPLENIC GRAFTS.

Œstrogens are destroyed in the liver; the hypophysis is freed from the ovarian control and behaves like that of a castrated animal. Consequently the hypophysis is able to stimulate greatly the follicular development in the intrasplenic graft.

When working with intrasplenic autoplastic ovarian grafts in guinea pigs we have discovered two relevant facts: (1) The ovary 'takes' in the spleen in no less than 90 per cent of animals and survives indefinitely; the graft was found in full follicular development in 150 out of 162 cases, some of which were subjected to necropsy 10 and even 22 months after transplantation. (2) The intrasplenic ovarian graft behaves, when the other ovary is absent, like an ovary which is subjected to the action of injected hypophyseal or placental gonadotrophic hormones.

A striking feature of the autoplastic ovarian graft in the castrated guinea pig is its enormous increase; the spleen appears greatly distended by the graft (Fig. 1). The increase is due, at the beginning, to cystic blood follicles (Fig. 2*B*) which can be recognized by the naked eye when cutting through the spleen fixed in Bouin's fluid. The blood follicles may attain a diameter of about 2·8 mm. (average of a normal tertiary follicle is 1 mm.). Blood follicles are absent in the normal ovary of the guinea pig; they may be found very exceptionally in an intrarenal graft. On the contrary, they are almost always present in the intrasplenic graft.

The functional relations between the ovary and the hypophysis in similar experiments can best be expressed in a diagram (Fig. 3). It is, so to say, the Aschheim–Zondek or Friedman test in the guinea pig, but made with the hormones of the animal's own hypophysis *in situ*.

If one of the ovaries, or part of an ovary, is left at its normal place and the other is grafted into the spleen, the graft also 'takes', but no blood follicles are produced (Fig. 2*A*). If œstrogen is administered to a castrated animal with an autoplastic intrasplenic ovarian graft, production of blood follicles is also inhibited.

At 61–70 days after transplantation, blood follicles were found in 21 out of 22 grafts, while at 303 and 654 days they were present in 6 out of 9 cases. On the contrary, luteinization was in the beginning considerably inhibited, but overwhelming in older grafts (Fig. 2*C*).

Our experiments show definitely that the gonadotrophic hyperfunction of the hypophysis freed from the ovarian control persists for twenty-two months. It is for the moment not possible to give a plausible explanation for the remarkable change of the ovarian picture occurring with time. If this change is not due to an intrinsic ovarian factor, it would mean that the functional pattern of the hypophyseal gonadotro-hyperactivity may change, though always persisting, in this long period of time—twenty-two months is about a third of the life-span of a guinea pig. Our results are thus contrary to the conception of the gonadotrophic antihormones.

A detailed description of our results will be given in a joint paper with Drs. H. Ponce de Léon, E. Woywood and O. Gay in *Revue Canadienne de Biologie*. I acknowledge the support of the Jane Coffin Childs Memorial Fund for Medical Research and the Ella Sachs Plotz Foundation for the Advancement of Scientific Investigation.

Other problems referring to the hypophyseal and gonadal relationship are also under investigation with intrasplenic ovarian grafts.

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[1] Biskind, G. R., *Endocrin.*, **28**, 894 (1941).
[2] Lipschütz, A., and Acuña, L., *Revue Canad. de Biol.*, **3**, 96 (1944).
[3] Lipschütz, A., Quintana, U., and Bruzzone, S., *Proc. Soc. Exp. Biol. Med.*, **55**, 43 (1944).
[4] Golden, J. B., and Sevringhaus, E. L., *Proc. Soc. Exp. Biol. Med.*, **39**, 361 (1938).

Resorption of Glucose from the Small Intestine of Alloxan-diabetic Rats

HITHERTO it has been very difficult for technical reasons to observe the resorption of sugar from the intestine of diabetic animals with and without insulin. Such investigations are now much facilitated by the possibility of producing diabetes in animals simply by injecting them with alloxan. As we know already a lot about sugar resorption from the small intestine, it may thus be possible to get a deeper insight into diabetic disturbance of the metabolism.

We produced diabetes in our animals (rats) by a single injection of 15 mgm. alloxan per 100 gm. body-weight[1]. The resorption was observed 7–10 days later. The degree of diabetes was measured by the quantity of urine and sugar (10–110 c.c. urine corresponding to 0·2–9·0 gm. sugar) daily secreted. Some of the animals with the highest secretion of sugar received 24 units of insulin each three days before the resorption experiment was carried out, and on the day of the experiment only 8–12 units three hours before. In order to avoid a hypoglycæmic shock, we injected 1·5–2 c.c. of an isotonic solution of glucose subcutaneously an hour and a half before the experiment. In order to have still a high glycosuria or hyperglycæmia at the moment of the experiment, we withheld food from the animals only for 16 hours before the experiment instead of the usual 24 hours. Then we injected 3 c.c. of a 10 per cent glucose solution into a rinsed part of the small intestine, 30 cm. long, under urethane narcosis. After 30 minutes we measured the quantity of sugar still present in the intestine by Bertrand's method.

Under these conditions normal rats resorbed on the average 115 mgm. of the injected 300 mgm. of glucose. In the rats made diabetic by alloxan, the quantity of sugar resorbed fluctuated between 115 mgm. in the animal with the least secretion of sugar to 245·5 mgm. in the most diabetic animal. The diabetic rats treated with insulin resorbed on the average, however, only 127·5 mgm. The acceleration of sugar resorption produced by diabetes is thus cancelled by insulin. Rats with diabetes through dialuric acid showed similar conditions of resorption as the rats treated with alloxan.