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The Reproductive System and Its Responses to Ovarian Hormones in Hypophysectomized Rhesus Monkeys.*

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This report is based on 17 adult or subadult Rhesus monkeys which were hypophysectomized at varying stages in the sex cycle and have post-operative periods varying from 4 to 111 days. Eighteen 10-day periods of injection with oestrin (Progynon B, dihydrotheelin, Amniotin) were given and in 3 cases this was followed by progestin for 10 days (1 or 2 Rab. U./day).† Fourteen of these animals have been autopsied and the completeness of the ablation verified by a study of serial sections of the hypophyseal capsule.

The hypophysectomies were performed by the oral approach. The soft palate was incised and the hypophysis exposed by an opening through the sphenoid. The exposure of the gland with this approach is excellent, a clear view of all but the most lateral parts of the gland being secured. The penetration of the pituitary stalk through the diaphragma is clearly seen. The pars tuberalis is not removed. It is quite extensive in the monkey. The incidence of infection is low, 2 animals out of approximately 30 operated on having developed serious infection at the site of operation.

Hypophysectomy during menstruation did not prolong bleeding nor did it induce bleeding if done shortly after menstruation. Animals hypophysectomized in the middle of the cycle and showing a well developed sex-skin color showed on 2nd to the 4th day thereafter grossly evident uterine bleeding which lasted for 3 to 6 days. Bleeding was prevented by the injection of oestrin (400-500 R.U./day was given). If untreated the endometrium and the vaginal epithelium showed an involution as great or greater than after castration.

A 10-day treatment with oestrin (400-500 R.U./day) developed the involuted endometrium into the typical proliferative type

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and the vaginal epithelium became greatly thickened and cornified. In 8 cases bleeding followed cessation of treatment and in 2 cases no bleeding occurred. In those animals which bled it was always greatly delayed over non-hypophysectomized castrates, bleeding beginning on the 11th to 21st days in our series. The remaining 8 cases of oestrin treatment were either killed at the end of treatment or it was followed by progestin so that they gave no data on bleeding from oestrin withdrawal.

Following the oestrin injections 3 treatments of 10 days each with progestin have been given to 2 animals. In 2 of these treatments, given 2 Rab. U./day, bleeding occurred on the 3rd day following cessation of the injections. In the other treatment 1 Rab. U./day was given and bleeding did not follow progestin withdrawal. A typical progravid endometrium resulted from the injections.

The size of the ovaries is not greatly reduced by hypophysectomy. This we attribute to the large amount of stroma present. There is, however, a profound atresia of the follicles. As in hypophysectom-

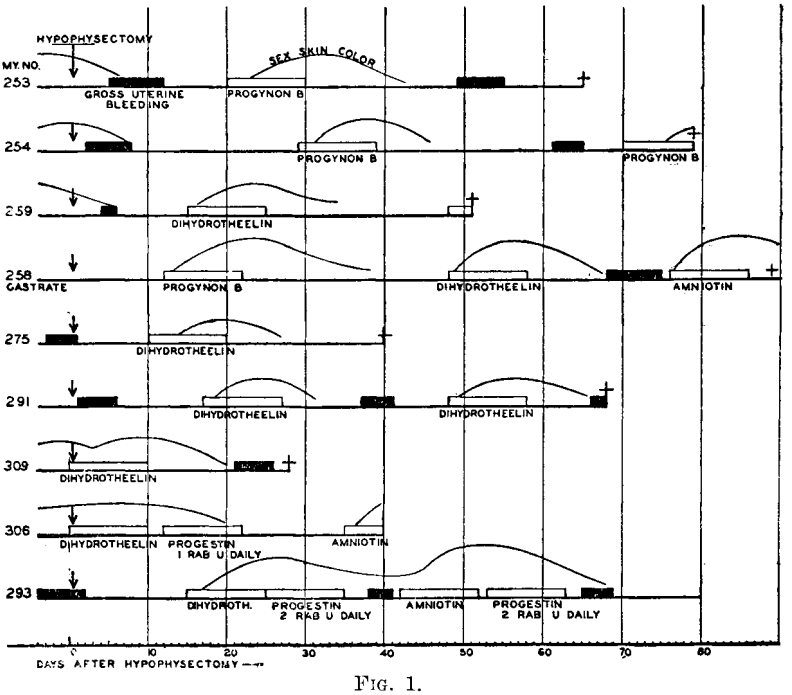

FIG. 1.

Figure showing relation of time of hypophysectomy to menstrual cycle or sex-skin color and the post-operative treatments and responses. Solid squares indicate grossly evident uterine bleeding, the open squares the time of treatment and the curved lines the color response of the sex-skin. Four hundred R.U./day of Amniotin and Progynon B was given and 500 R.U./day of dihydrotheelin.

ized rats, follicles with small antra may develop, but usually show atresia. Large follicles quickly show atresia following the pituitary ablation.

The proneness of the hypophysectomized animals to collapse from hypoglycemia makes it necessary to follow their feeding closely and injections of glucose may not infrequently be necessary as is pointed out elsewhere.

The disabilities following hypophysectomy are so widespread that it is difficult to refer the delay in bleeding after oestrin withdrawal to any specific factor. There occurs the usual atrophy of the other endocrine organs and reproductive organs, a pronounced and constant drop in blood sugar and also a pronounced drop in blood pressure and in heart rate.

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Effect of Hypophysectomy on Blood Sugar of Rhesus Monkeys.*

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It has been demonstrated that hypophysectomy lowers the blood sugar in fasting dogs and rabbits. In dogs—the form in which sugar values are most extensive—the fasting blood-sugar values overlap those of normal animals and prolonged starvation is necessary to lower them to convulsive levels. Moreover, as recently demonstrated, the exposure of the hypophysis by the temporal approach, even though rapid, lowers the blood sugar nearly as much as does the removal of the gland (Chaikoff *et al.*[1]) The temporal approach has been used in the studies reported on blood sugar in hypophysectomized dogs.

The hypophysectomies here reported were done by the oral approach. The possibility of brain injury with the technique used is extremely remote due to the toughness of the diaphragma which is uninjured in the operation. In the animals reported as hypophysectomized the complete removal of the anterior and posterior lobes

* Aided by a grant from the Committee for Research in Problems of Sex, the National Research Council.

1 Chaikoff, I. L., Reichert, F. L., Larson, P. S., and Mathes, M. E., *Am. J. Physiol.*, 1935, **112**, 493.