fat ingested in the diet. This, of course, involves an error due to fat secretion by the lower intestinal tract, but in this case, the amount of stool fat from this source is a negligible item.

In experiment 1, our stock diet[5] in the form of a dry mash and in experiment 2, a synthetic paste diet (5, page 183) was fed. As a drinking fluid, a 0.5% NaCl and 0.2% $NaHCO_3$ mixture was allowed *ad lib.* Eight out of 35 adrenalectomized rats did not survive this regime. Data on these are not included in the averages. Evidence of adrenal insufficiency is found in the low weight gain of the adrenalectomized groups and the marked diuresis in these animals (Table I, Exp. 1).

The adrenalectomies and sham operations on the control rats were performed as usual.[5, 6] Food intake and stool collection observations were commenced a day later. The stools were collected over 24-hour periods and dried for analysis. "Fat" refers to the petroleum ether extract dried at 100°C, of either the food or the stools, as the case may be.

The data presented in Table I show very clearly that, under the conditions of these experiments, the absorption of fat is not influenced by adrenalectomy. Nor, if we assume that all of the stool fat is secreted by the intestinal mucosa, is there evidence that this excretion of fat is affected by removal of the adrenal glands.

Summary. Under fairly normal conditions of nutrition, salt solution being supplied as drinking fluid to maintain the adrenalectomized rats, adrenalectomy has no influence on the absorption of fat from the food. With adequate food intakes, the removal of the adrenal glands does not affect the excretion of fat in the stool.

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Effect of Heterologous Antigonadotropic Sera on the Course of Pregnancy in Rats.

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Recently Thompson[1] has reported on abortion produced in dogs with serum of a dog immunized over a period of 3½ years with

5 MacKay, L. L., and MacKay, E. M., *Am. J. Physiol.*, 1927, **83**, 179.

6 MacKay, E. M., and MacKay, L. L., *J. Exp. Med.*, 1926, **43**, 395.

1 Thompson, K. W., *Endocrinology*, 1939, **24**, 613.

sheep pituitaries. Thompson's results which were obtained by intravenous injection were almost 100% positive. It is beyond doubt that certain antigonadotropic sera from pituitaries of animals may exert a strong antigonadotropic effect in a heterologous species as has been shown by the extensive investigations of Rowlands.[2] On the other hand, it has been established by Zondek and Sulman[3] that the antigonadotropic sera produced by immunization with prolan of human origin and prosylan of pregnant mares' blood have a strong species specificity, so that not even 0.5% of the homologous activity could be exerted against prolan of heterogeneous origin. The positive results of Thompson have prompted us to publish a short review of the negative results which were obtained in 1938.

The experiments of Pencharz and Long,[4] Selye, Collip and Thompson,[5] Bergman,[6] *et al.*, have shown that hypophysectomy in rats more than 4 days after mating prevents nidation. Hypophysectomy between the 7th and the 10th day of pregnancy results in the death and absorption of the foetus. Later on, between the 10th and 20th day, hypophysectomy results either in death and absorption of the foetus or in delay of term from 21-22 to 24-26 days.

In comparison with the aforementioned results of hypophysectomy we tried to produce similar effects by the administration of antigonadotropic sera at various stages.

The antigonadotropic sera used were derived from goats immunized during 9 months with daily injections of 1000 RU of pregnancy urine prolan + 25 RU prolan of human retroplacental blood (contained in 50 mg acetone-dry-powder of the serum) + 10 RU of prosylan of human anterior pituitary prepared according to Wallen-Lawrence and v. Dyke.[7] The antigonadotropic sera were stored as an acetone-dry-powder,[8] 60 mg corresponding to 1 cc of serum. Its antigonadotropic activity amounted to 300 PAU,* against pregnancy urine prolan and 40 PSAU,† against human hypophyseal prosylan in 1 cc (60 mg).

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2 Rowlands, I. W., *Proc. Roy. Soc.*, L. Ser. B, 1937, **121**, 517.

3 Zondek, B., and Sulman, F., PROC. SOC. EXP. BIOL. AND MED., 1937, **36**, 712.

4 Pencharz, R. I., and Long, J. A., *Science*, 1931, **74**, 206; *Am. J. Anat.*, 1933, **53**, 117.

5 Selye, H., Collip, J. B., and Thompson, D. L., PROC. SOC. EXP. BIOL. AND MED., 1933, **30**, 689; **31**, 82.

6 Bergman, F., *Act. Brev. Neerl.*, 1934, **4**, 81.

7 Wallen-Lawrence, Z., and v. Dyke, H. B., PROC. SOC. EXP. BIOL. AND MED., 1931, **28**, 956; *J. Pharm. and Exp. Therap.*, 1931, **43**, 93.

8 Zondek, B., and Sulman, F., PROC. SOC. EXP. BIOL. AND MED., 1937, **36**, 708.

* 1 PAU = 1 prolan anti-unit is the minimum amount of anti-prolan which annihilates the gonadotropic effect of 1 RU of prolan (estrus reaction) (*cf.* 8).

† 1 PSAU similarly defined (*cf.* 8).

The female rats were kept in separate cages and vaginal smears were taken daily. A regular cycle established during one month, the animals were mated and the development of impregnation and pregnancy determined according to Evans' technic for vitamin E test: (a) Impregnation was verified by the presence of spermatozoids in the smear and the formation of the typical vaginal plug. (b) Nidation was verified by the presence of red blood corpuscles in the smear 10-13 days later. (c) The progress of pregnancy was verified by the increase of the weight curve recorded daily.

First Series. (Table I.) The pregnant rats received 1 cc of multivalent antigonadotropic sera daily, starting on the 10th-13th day of pregnancy. The total amount of antigonadotropic sera given varied between 3000 PAU + 400 PSAU and 4500 PAU + 600 PSAU. In no case could we observe any symptoms due to the exclusion or inhibition of the pituitary system, as brought about by hypophysectomy; delivery was at term, the animals born were normal and developed normally. Since the objection might be raised that the injections were started too late to prevent the pregnancy from running its normal course we performed another series of experiments beginning the injections earlier and using double doses of antiprolan.

TABLE I.
First Group of Rats Receiving 300 PAU+40 PSAU Daily During Pregnancy.

No. of rat	Date of impregnation	First injection	Term of delivery	Duration of pregnancy days	Total of antigonadotropic sera given
R 1	10-1-38	20-1-38	1-2-38	22	3,600 PAU + 480 PSAU
R 2	11-1	23-1	2-2	23	3,300 " + 440 "
R 3	10-1	22-1	1-2	22	3,000 " + 400 "
R 4	13-1	23-1	3-2	22	3,600 " + 480 "
R 5	8-1	18-1	30-1	22	3,600 " + 480 "
R 6	8-1	18-1	30-1	22	3,600 " + 480 "
R 7	21-1	23-1	died		
R 8	15-1	23-1	6-2	23	4,500 " + 600 "

Second Series. (Table II.) Female rats with normal cycles were given daily injections of 2 cc of antigonadotropic sera corresponding to 600 PAU + 80 PSAU. This considerable amount of antigonadotropic factor was unable to interfere with the normal course of the cycle which regularly returned after periods of 4-6 days. A period of antigonadotropic treatment of 6 to 38 days having elapsed, the rats were mated and the injections continued. In spite of the considerable amounts of antigonadotropic serum injected, varying between 16,200 PAU + 2,160 PSAU and 36,800 PAU + 4,800 PSAU in all, the course of pregnancy was normal, no abortion occurred, the litters were born and developed normally.

TABLE II.
Second Group of Rats Receiving 600 PAU + 80 PSAU Daily Before and During Pregnancy.

No. of rat	Date of impregnation	First injection	Term of delivery	Period of treatment preceding impregnation (days)	Duration of pregnancy (days)	Total of antigonadotropic sera given			
R 1	6-3-38	28-2-38	27-3-38	6	21	16,200	PAU	+ 2,160	PSAU
R 2	14-2	8-2	7-3	6	21	16,200	"	+ 2,160	"
R 3	6-3	8-2	28-3	26	22	28,800	"	+ 3,840	"
R 4	18-3	8-2	9-4	38	22	36,800	"	+ 4,800	"
R 5	9-3	15-2	29-3	22	20	26,400	"	+ 3,520	"
R 6	24-3	18-2	died	36	—		—		
R 7	sterile	15-2	—	—	—		—		
R 8	6-3	8-2	28-3	26	22	28,800	"	+ 3,840	"

These experiments are a striking proof of the essential part which species specificity plays in the treatment with antigonadotropic sera. Relatively astonishing amounts of antigonadotropic rat units were unable to interfere with the normal course of cycle and pregnancy in rats, because heterologous sera were used which were directed against human prolan and prosylan. There is no doubt that positive results would have been obtained if homologous sera against prosylan of rat pituitaries had been used. It may be possible that antigonadotropic factor directed against the pituitaries of sheep, ox, etc., would have acted in the rats. Antifactor against human gonadotropic hormone, however, has an extremely high species specificity and does not exert any effect except as against homologous human prolan. According to our experience and compared with the results of Rowlands[2] the species specificity of the antigonadotropic sera is not governed by the same rules prevailing in serology, and mammalian relationship reactions established there do not apply to the antigonadotropic reaction. With regard to Thompson's[1] results we have to stress the fact that he injected his dogs with antigonadotropic sera intravenously, whereas we did ours subcutaneously.

Summary. Large amounts of antigonadotropic sera against human prolan and prosylan were daily injected into normal rats. This treatment neither interfered with the normal cycle nor with impregnation, nidation, delivery and normal breeding of the animals. These negative results are to be explained by the high species specificity of antigonadotropic sera directed against prolan and prosylan of human origin.