KK mice (same as in Swiss albino), it seems probable that more lipids may have been synthesized and accumulated in the liver during the last days of gestation in order to prepare for the extrauterine life. Consequently, the lipids were increased at birth for later utilization, which resulted in a decrease after 24 h of life.

In liver of the KK fetus, all types of lipids were present in almost equal proportion. In liver of the Swiss albino fetus, however, the concentration of lipids decreased in the following order: Phospholipids, cholesterol esters, triglycerides, and free cholesterol. It is probable that the unequal distribution of lipids in the fetal liver of Swiss albino mice might be due to differences in their turnover rates.

In order to examine whether the changes in lipids in the fetal liver would reflect changes in the fetal weight at birth, the newborn were weighed immediately after spontaneous delivery. There was no significant difference in weight between the 2 groups of the newborn (Figure 2), suggesting that changes in lipids in the liver tissue of the fetus have no effect on the birth weight[17].

In summary, our data suggest that the genetic diabetes influences fetal liver lipids with no effect on birth weight.

Summary. Triglycerides, phospholipids, cholesterol and cholesterol esters were determined by thin layer chromatography in the fetal and neonate livers of normal (Swiss albino) and genetic diabetic (KK) mice. In general, the lipids were elevated in the fetal liver of the KK mice. Despite this elevation in liver lipids, no increase in the weight of the newborn was observed.

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Inhibition of Human Chorionic Gonadotrophin-Induced Ovarian and Uterine Growth in the Mouse by Synthetic Arginine Vasotocin[1]

Arginine vasotocin (AVT), a nonapeptide which has been isolated from the mammalian pineal gland[2,3], has been implicated by PAVEL et al.[4–6] as an antigonadotrophic compound. Previous studies in our laboratory have shown that AVT partially blocked the stimulation of the ovaries due to combined treatment with pregnant mare's serum and human chorionic gonadotrophin (HCG) in the mouse[7]. In the present study, the time course of uterine and ovarian growth in the immature mouse after HCG stimulation was investigated. Additionally, we examined the effect of AVT on the growth response of the reproductive organs.

In a preliminary experiment, 21-day-old Swiss-Webster mice (Hilltop Lab Animals) were given a single i.p. injection of 0.25 IU HCG (Antuitrin S, Parke-Davis) at 09.00 h (lights on 08.30 h, lights off 20.30 h). 1 group of mice received an i.p. injection of AVT (1 μg/injection) at 0, 12, 24, 36 and 48 h post-HCG administration, while the HCG-treated mice received an i.p. injection of Ringer's lactate at 12, 24, 36 and 48 h. The AVT (Schwartz-Mann) was dissolved in Ringer's lactate about 2 min prior to its injection. Necropsy of all mice at 72 h post-HCG injection revealed significantly depressed body weights in AVT-treated mice. Since both absolute and relative ovarian and uterine weights in the AVT-treated mice were significantly depressed, it is clear that the organ weight changes were not merely a reflection of body weight (Table).

In the second study, 1 IU HCG was given i.p. 09.00 h to 150 21-day-old mice. A similar injection protocol as in the previous study was utilized with the addition of a 60 h timepoint for AVT administration. AVT (Bachem Co). was dissolved just prior to injection of 2 μg/0.1 ml/mouse. Representative animals (10 to 12 mice) from each group were necropsied at 0, 12, 24, 36, 48, 60 and 72 h. The ovaries and uterus were cleaned and weighed fresh on a

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Effect of arginine vasotocin (AVT) on the stimulation of absolute (mg) and relative (mg/100 g BW) ovarian and uterine weights (± standard errors) by HCG in Swiss-Webster mice

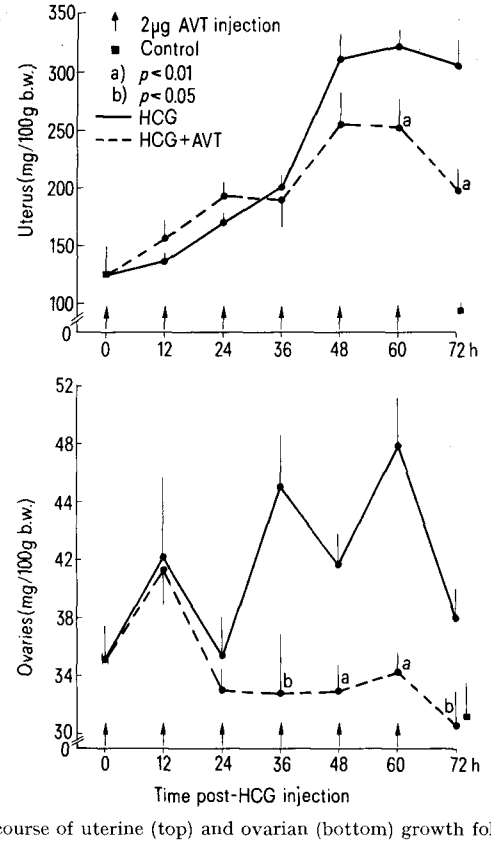
Group	*N*	Body wt. (g)	Ovaries		Uterus	
			mg	mg/100 g	mg	mg/100 g
Untreated Controls	10	15.5 ± 0.5	4.75 ± 0.30	30.9 ± 2.2	18.6 ± 1.5	119.0 ± 8.8
HCG	10	15.1 ± 0.6	6.49[a] ± 0.36	43.2[a] ± 2.3	60.2[a] ± 2.5	402.9[a] ± 19.7
HCG + AVT	10	12.7 ± 0.5	4.16[b] ± 0.17	33.1[c] ± 1.8	21.4[b] ± 2.3	167.9[b] ± 14.8

[a] $p < 0.001$ vs. control. [b] $p < 0.001$ vs. HCG. [c] $p < 0.01$ vs. HCG.

Cahn DTL electrobalance. Results at each timepoint were analyzed by a Student's t-test.

A diurnal rhythm in ovarian weight in mice treated with HCG only was observed during the 3 day course of the experiment (Figure, bottom). AVT treatment blocked this rhythm in ovarian weight during the last 2 days of the study. A significant reduction in ovarian weight was observed at 36 h and at all subsequent timepoints. In the case of the uterus, the initial phase of growth was not blocked by AVT although the latter phase was significantly attenuated (Figure, top). AVT treatment did not cause a reduction in body weight in this experiment since the final body weight of HCG-treated mice was 16.8 $\pm$ 0.6 g while that of the HCG + AVT treated mice was 15.6 $\pm$ 0.6.

A single injection of HCG causes estrogen release and uterine growth in the immature mouse within a few hours[8]. Our results indicate that AVT probably did not block the initial growth of the ovaries and uterus which is due to the peripheral action of HCG. However, endogenous gonadotrophin secretion contributes significantly during the latter stages to HCG stimulation of the ovaries and uterus in mice and rats[9,10]. Thus, the inhibition of ovarian and uterine growth reported here could be the result of the action of AVT on the hypothalamus where it may modify the discharge of gonadotrophin releasing hormones or directly on the pituitary where it may modulate the synthesis and/or release of gonadotrophic hormone. PAVEL et al.[5] favor the central gonadotrophin inhibiting action of AVT in that they found that the injection of the nonapeptide into the 3rd ventricle was more effective in inhibiting compensatory ovarian hypertrophy than AVT administered by other routes.



Time course of uterine (top) and ovarian (bottom) growth following a single injection of 1 IU HCG. AVT was administered every 12 h for a total of 6 injections. Solid blocks indicate untreated control animals necropsied at 0 and at 72 h. Standard errors are indicated. [a] $p < 0.001$; [b] $p < 0.05$ vs HCG.

Other pineal compounds such as melatonin[11], 5-methoxytryptophol[12] and crude pineal extracts[13] also reportedly inhibit HCG-induced stimulation of uterine growth. Whether the actions of these substances are similar to those of AVT remain unknown. Of particular interest is that although a direct effect of the methoxyindoles on the hypothalamo-hypophyseal-gonadal axis cannot be discounted, recent evidence has shown that melatonin injected into the 3rd ventricle of cats released into the cerebrospinal fluid 50% of the AVT normally present in the pineal[14]. Thus, melatonin may inhibit HCG-induced uterine stimulation by promoting the release of endogenous AVT from the pineal gland.

Summary. 21-day-old Swiss-Webster female mice were injected with 1 IU HCG at 09.00 h. Injection of freshly prepared arginine vasotocin (2 µg/0.1 ml/injection) every 12 h inhibited the HCG-induced hypertrophy of the ovaries at 36, 48, 60 and 72 h after HCG-treatment while the uterine weight was depressed at 60 and 72 h.

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Increased Responsiveness of the Thyroid to Thyrotropin by Pretreatment with Thyroid Hormones in Intact Mice

In the MCKENZIE-assay[1,2] for the detection and quantitation of thyrotropin (TSH) and long-acting thyroid stimulator (LATS), iodine-depleted mice are labelled with radioactive iodide and afterwards treated with thyroid hormones, in order to suppress endogenous TSH secretion before stimulators are injected and the change of radioiodine in blood is measured. It has been shown that large suppressive doses of thyroid hormone reduce the response of the animal to TSH and LATS[3,4]. In studying the inhibition of TRH-induced TSH release of the pituitary by L-thyroxine (L-T4), L-triiodothyronine, and

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