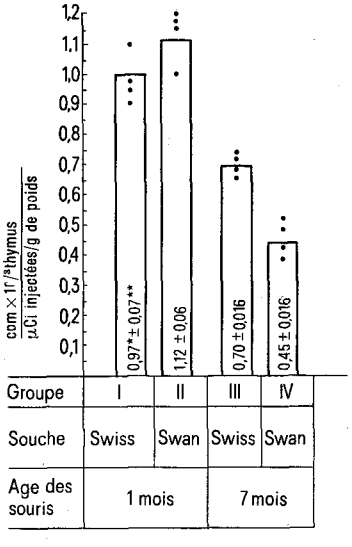
Swan un déficit précoce du thymus et des cellules T objectivé par une chute de l'activité «thymosine like» circulante[4] une mauvaise réponse à un Ag thymodépendant: le GRM, une faible réponse des splénocytes à la PHA, une très faible compétition antigénique (ce phénomène étant normalement thymodépendant[5]).

Matériel et technique. Nous avons utilisé 16 souris Swiss[6] et 16 souris Swan. Dans chacun de ces groupes une moitié des souris est âgée de un mois et l'autre de 7 mois.

Protocole opératoire. Tous les animaux reçoivent le même jour par voie i.p. 10 μCi de sulfate 35 S de sodium par g de poids. 12 h après les souris sont sacrifiées et la totalité du thymus prélevée. Ces organes sont ensuite groupés 2 par 2 dans chaque groupe de souris puis placés dans 1 ml d'eau distillée et homogénéïsés 1 min environ dans un appareil de Poter. L'homogénat est alors centrifugé à 12.000 *g* pendant 30 min à 4 °C, le surnageant limpide est prélevé; un volume de 0,4 ml de ce surnageant est déposé au sommet d'une colonne de gel de polyacrylamide: (Biogel, Calbiochem. P2) de 9 × 550 mm. (La colonne avait d'abord été équilibrée avec du tampon PO_4 0,05 *M*, pH 7,1 selon SORENSEN) puis élué avec le même tampon à une vitesse d'élution de 0,3 ml/min, les fractions recueillies étant de 2 ml. Le soufre marqué de chacune de ces fractions est recherché de la façon indiquée par CLARK[1] à l'aide d'un scintillateur gamma pour échantillons liquides (Nuclear Chicago). Les résultats sont exprimés en

$$\frac{\text{cpm} \times 10^{-3}/\text{thymus}}{\mu\text{Ci injectées/g de poids de l'animal}}$$

qu'on monmera index fonctionnel.



* Moyenne arithmétique; ** erreur standard; ● les points représentent les valeurs individuelles par échantillon. L'étude statistique de la différence entre 2 moyennes est réalisée à l'aide du *t* de Student: I et II, non significative; I et III, $p < 0.025$; II ,III et IV, $p < 0.0005$.

Résultats. Le soufre macromoléculaire de l'extrait correspondant au soufre minéral incorporé dans les cellules réticuloépithéliales du thymus se situe dans les fractions 6 et 7 alors que le soufre minéral libre passe dans les fractions 12, 13, 14 et 15. Le tableau indique les résultats obtenus dans les 4 groupes de 8 souris chacun.

L'index fonctionnel n'est pas significativement différent pour les Swiss et les Swan de 1 mois par contre la différence est significative entre les index fonctionnels des Swiss et Swan de 7 mois ainsi qu'entre ceux des Swiss de 1 et 7 mois et des Swan de 1 et 7 mois (*t* de Student).

Discussion. L'index fonctionnel du thymus des souris normales diminue significativement avec le vieillissement mais cette chute est beaucoup plus nette chez les Swan. Ainsi l'index fonctionnel du thymus des souris Swan âgées de 7 mois est à la fois beaucoup plus bas que celui des témoins Swiss de même âge et que celui des jeunes Swan. Ce résultat va dans le même sens que ceux que nous avons déjà obtenus chez les Swan, c'est à dire une altération précoce du fonctionnement du thymus de ces couris autoimmunes. Le produit macromoléculaire soufré des cellules réticuloépithéliales du thymus n'est pas encore identifié. Il peut représenter soit un des éléments des systèmes enzymatiques des cellules réticuloépithéliales nécessaire à la production de l'hormone thymique, soit l'hormone thymique elle-même (ou son précurseur). Cette dernière interprétation peut s'accorder avec la mise en évidence par GOLDSTEIN, de petites quantités de cystéïne et de méthionine dans sa thymosine.[7]

Summary. A diminution of the incorporation of radioactive S in épithelial cells of the thymus of auto-immune Swan mice is shown. This defect of incorporation seems to be in relation to a thymus deficiency.

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Pre- and Postnatal Distribution of Lipids in the Liver of Genetic Diabetic Mice

It is well established that infants of diabetic mothers are frequently larger than those of non-diabetic mothers. This increase in body weight was accounted for by an increase in total fat content[1]. High fat contents in still born infants of diabetic women were confirmed by direct estimation[2]. Similar observations were reported in the fetuses of streptozotocin diabetic rats[3]. ANGERVALL et al.[4] found an increase in neutral fat with no changes in total lipids in the overweight newborn of alloxan diabetic rats. On the other hand ,SOLOMON[5] observed no increase in body lipids of the overweight fetuses of the subdiabetic (alloxan) rats. The present study was designed primarily to examine the pre- and postnatal changes of lipids in the fetal liver of the normal (Swiss albino) and KK (genetic

diabetic) mice and to correlate these changes with the weight of the newborn.

Material and methods. The KK and Swiss albino mice were inbred in our laboratory. They were maintained under similar laboratory conditions and were fed ad libitum the Old Guilford mouse laboratory chow containing 11% fat. Brothers and sisters of the same parents were mated and the presence of the vaginal plug was considered day 1 of gestation.

Pregnant mothers were sacrificed under ether anesthesia on days 10 and 17 of gestation and the fetuses were delivered by laparatomy. The fetuses were killed by cervical dislocation and the livers were excised under magnifying lenses and placed immediately on dry ice. They were kept frozen at −40 °C until analyzed.

Some pregnant mothers were allowed to deliver spontaneously and the liver samples were obtained from the newborn at birth (from 30 min to 5 h) and after 24 h of life. The weight of the newborn was recorded at birth.

Lipid extractions were made in chloroform: methanol (2:1) according to the method of FOLCH et al.[6] Triglycerides, phospholipids, free cholesterol and cholesterol esters were determined using thin layer chromatography as described by AMENTA[7].

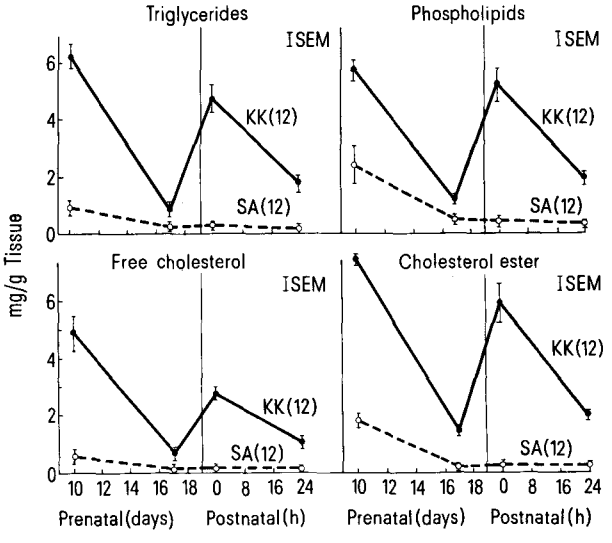

Fig. 1. Distribution of lipids in the liver of the fetus and neonate of KK and Swiss albino (SA) mice.

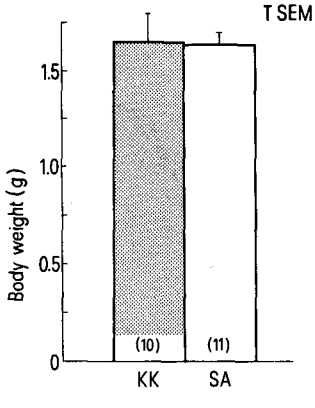

Fig. 2. Body weight of the newborn of KK and Swiss albino (SA) mice.

Results. As shown in Figure 1, all types of lipids were greater in both pre- and postnatal livers of the KK mice compared to those of the Swiss albino mice. While there was a gradual decrease in lipid contents from the early prenatal to the late postnatal life in Swiss albino mice, a different pattern was observed in the KK mice. There was an increase in lipid contents on the 10th day followed by a decrease on the 17th day of gestation. A remarkable increase in the liver fat was observed at birth followed by a decrease during 24 h of life.

Figure 2 shows the weight of the newborn at birth. There was no significant difference between the newborn of the KK and Swiss albino, when equal litter or total litter size were compared.

Discussion. The KK mice are an inbred strain of Japanese mice with a genetic disposition for spontaneous diabetes. Based on the metabolic disturbances at 2 months of age or later, the diabetic syndrome in these mice has been described as chemical diabetes[8,9]. Before this period, they have a normal tolerance to glucose as compared with those of Swiss albino mice[10,11]. Since the KK mice showed relatively elevated levels of serum triglycerides and normal cholesterol[12], it was of interest to examine the distribution of various lipid fractions in the fetal liver of these mice. The lipid fractions, in general, were greater in the fetal liver of the KK mice than in those of Swiss albino mice. It seems that the elevation of triglycerides in the fetus of the KK mice might be a reflection of elevated levels in the mother. However, it appears different in the case of cholesterol levels. The fetal liver had increased concentrations of free cholesterol despite normal levels in the adult mouse. These data suggest that the increased concentrations of the lipid fractions in the fetal liver of the KK mice might be due to genetic diabetes.

It has been reported that the percentage of lipids in liver of the rat fetus remains low throughout pregnancy[13,14] and increases rapidly after birth[13,15]. Similar results were obtained in mice[16]. In our study, however, the lipids in liver of the Swiss albino fetus remained low both in pregnancy and after birth. The situation was different in the KK fetus. Although the fetal liver lipids were low on the 17th day of gestation, they were elevated in the newborn. Since the gestation period is 21 days in the

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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.