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TRANSFER OF FATTY ACIDS ACROSS THE RABBIT PLACENTA

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SUMMARY

1. Transfer of fatty acids across the placenta was studied in anaesthetized rabbits at 28-days gestation by measuring umbilical venous–arterial differences, by injection of labelled palmitate into the mother and observing its appearance in the foetus, by injection of labelled palmitate into the foetus and measuring its appearance in the mother and the foetal clearance rate.

2. The release of fatty acids and glycerol by foetal adipose tissues was investigated *in vitro* by measuring the effect of addition of noradrenaline to the incubation medium and *in vivo* by measuring the effect of noradrenaline infusion into the foetus on circulating glycerol and free fatty acid concentrations.

3. In anaesthetized rabbits at 28-days gestation the maternal circulating free fatty acid concentrations were high and there was a positive umbilical venous–arterial difference. High maternal free fatty acid concentrations were associated with high umbilical venous–arterial differences.

4. Label was present in the foetus in 2 min and reached a peak in 3 min after injection of labelled palmitate into the mother. Label appeared in the maternal circulation in 1 min after injection into the foetus. The half-life of labelled palmitate was of the order of 30–60 sec in both mother and foetus.

5. Foetal white adipose tissue released both free fatty acids and glycerol into the medium and the rate of release increased four to five fold after addition of noradrenaline. Infusion of noradrenaline in the foetus led to a rise in glucose and glycerol concentrations, but the change in free fatty acid concentrations was not significant.

6. It was concluded that (i) free fatty acids can cross the rabbit placenta in amounts sufficient to provide the fatty acid components of stored

triglyceride and structural lipids; (ii) placental transport of free fatty acids depends in part on maternal blood concentration and on foetal uptake; (iii) foetal circulating free fatty acids are continually exchanging with fatty acid pools in the placenta and with the maternal circulating free fatty acids.

INTRODUCTION

Experiments using labelled palmitate have demonstrated that free fatty acids (FFA) cross the placenta in the rabbit (Van Duyne, Havel & Felts, 1962), sheep (Van Duyne, Parker, Havel & Holm, 1960), guinea-pig (Hershfield & Nemeth, 1968), monkey (Portman, Behrman & Soltys, 1969) and rat (Hummel, Schirrmeister, Zimmermann & Wagner, 1974). However, to date, the weight of evidence suggests that glucose is the main substrate for cellular energy in the foetus and that the foetal stores of triglyceride are formed by lipogenesis from glucose. If this is so, then the flow of fatty acids from mother to foetus is small.

During a recent study in rabbits on the intra-uterine growth of adipose tissue we observed that fasting the doe near term resulted in a large increase in the triglyceride stores in the foetal liver, foetal brown adipose tissue and foetal white adipose tissue (Edson, Hudson & Hull, 1975). This occurred when the maternal blood sugar concentrations were falling and therefore it seemed unlikely that the larger fat stores were secondary to increased transfer of glucose from mother to foetus. On the other hand they could have been secondary to lipid mobilization in the mother induced by the fast. But if this were so, the free fatty acids released from the maternal adipose stores must cross the placenta in considerable amounts for the fat stores in the foetuses of fasted does were greater by 80%. These experiments were designed to investigate this possibility.

Free fatty acids are present in the foetal circulation, usually, although not invariably, in concentrations lower than those in the maternal circulation. There have been few studies on the clearance of free fatty acids from the foetal circulation and the release, if any, of fatty acids from foetal adipose tissue has not been demonstrated. Information in both areas is essential for the understanding and further investigation of the contribution of maternal lipids to the foetal circulation and so to the foetal energy reserves. Therefore, experiments on clearance of fatty acid from the rabbit foetal circulation and the release of fatty acids by rabbit foetal adipose tissue *in vitro* were made and the results included in this report.

METHODS

Experiments in vivo

Four series of experiments were performed on anaesthetized pregnant rabbits involving measurement of umbilical venous–arterial difference, injection of labelled palmitate into the maternal circulation, injection of labelled palmitate into the foetal circulation and infusion of noradrenaline into the foetal circulation. For all the experiments the preliminary preparations were the same. All the rabbits studied were reared from birth in our animal colony and kept under known controlled ambient conditions. The time of mating was known and only rabbits with good food intakes during pregnancy were used. All the experiments were performed 28 days after mating. Each pregnant doe was gently removed from her cage and anaesthetized immediately with urethane, 7–10 ml. of 0·2 g/ml. solution given via an ear vein. She was then laid gently on to a warmed table, the thorax and head being laid on the right side. Infusions were given through indwelling needles into a vein of one ear and blood samples were usually taken from the arteries of the other ear. In early experiments blood samples were taken also from the ear veins. Twelve matched samples showed no significant difference between the free fatty acid concentrations in blood from the artery and vein, so the data were pooled.

Along the mid line of the lower abdominal wall 1 ml. lignocaine was injected and further injections of urethane were given I.V. when necessary. Usually a total of 15–25 ml. was required during the induction and initial manipulations and further injections were rarely used. A small mid-line abdominal incision was made.

All foetuses included in the results were within ± 2 S.D. of the mean weight of 28-day foetuses in our colony ($33{\cdot}5 \pm 11{\cdot}2$ g, mean ± 2 S.D., $n = 83$).

Measurement of umbilical venous–arterial difference. Paired umbilical arterial and venous blood samples were obtained from thirty-one foetuses from seven does. The uterus was incised longitudinally along a line opposite to the entry of the vessels and the foetal sacs opened. The foetus was gently displaced to reveal the umbilical vessels, which were supported over the ends of a pair of curved fine forceps allowing the amniotic fluid to drain away. A fine heparinized capillary tube was placed next to an umbilical vein which was then snicked with a pair of fine scissors and a small free flowing venous sample obtained over a maximum period of 5 sec. An arterial sample was obtained immediately in the same way. Whilst two investigators took the umbilical samples, a third collected a simultaneous maternal blood sample from the ear.

Injection of labelled palmitate into the maternal circulation. [1-^{14}C]palmitate, 10 μCi/kg body wt., was injected, over 10 sec, into the ear vein of seven pregnant rabbits and their foetuses were left undisturbed until they were delivered over the following 20 min. Blood samples were collected from each foetus by a deep cut in the neck. The rapid and pulsatile flow suggested that it was mainly arterial, but clearly the main veins were also cut and the final samples were a variable mixture of both foetal venous and arterial blood. Contamination from amniotic and lung fluid did not appear to be a problem. But even if it were, the free fatty acid content of both is small and we were concerned with the transfer of label into the foetal free fatty acid pool. Maternal samples were obtained from the ear vessels at regular intervals as well as concurrently with every foetus delivered. All blood samples were analysed for free fatty acid concentrations and lipid-soluble radioactivity.

Injection of labelled palmitate into the foetus. For these experiments on eleven foetuses from three does, each foetus was gently delivered from the uterus and held in the valley of the maternal wound and surrounded, except for the neck, by warm saline packs. Care was taken not to interfere with the umbilical vessels. Fine

polyethylene catheters (external diameter 0·80 mm, internal diameter 0·40 mm, drawn out at the end to an external diameter of about 0·60 mm) were inserted into the external jugular vein with the aid of a dissecting microscope. A solution of [1-^{14}C]palmitate, dose 6·25 μCi in 0·25 ml., was injected, and the catheter immediately and gently washed in and out with blood and 0·25 ml. saline. Blood samples were collected serially from the foetus via this catheter before and after injection. Studies *in vitro* comparing saline flushed catheters with separate sampling catheters showed that contamination of the injecting catheter would lead to an error of not more than 1 %. Matching maternal blood samples were collected and the foetus delivered and killed 5–10 min after the injection, leaving the placenta in position.

Infusion of noradrenaline into foetuses. Noradrenaline (noradrenaline bitartrate, Winthrop Laboratories) was infused into fourteen foetal rabbits in five does. The experiment technique was the same as that used for injection of labelled palmitate. The dose given, on the assumption that the foetal body wt. was 30 g, was 4 μg base/kg body wt./min for 10 min. This dose is a powerful stimulant to lipolysis in the new-born rabbit. Foetal blood samples were taken immediately before and after the 10 min infusion.

Experiments in vitro

Foetal perirenal white adipose tissue lobes for studies *in vitro* were dissected fresh, rinsed in saline and then in incubation medium, which consisted of Krebs–Ringer phosphate medium with half the Ca^{2+} concentration and containing 4 % fatty acid-free albumin. Paired lobes from individual foetuses were incubated in stoppered 25 ml. flasks containing 5 ml. incubation medium under air in a shaking water-bath at 37° C. After 5–10 min incubation, noradrenaline, as the bitartrate, was added to the experiment flasks to give a concentration 5 μg/ml. and the incubation continued for 5 hr. Samples, 0·2 ml., were removed every hour for glycerol and free fatty acids analysis. At the end of the incubation the tissue lobes were removed, blotted dry and weighed.

Chemical methods

Albumin-bound [1-^{14}C]palmitate was prepared as follows: 250 μCi [1-^{14}C]palmitic acid (specific activity greater than 50 mCi/m-mole, Radiochemical Centre, Amersham, Bucks) was made up to 25 ml. with heptane. This solution, 5 ml., (50 μCi) was evaporated down over 0·1 ml. 0·015 N-NaOH. The sodium palmitate was dissolved in the remaining water by heating and 4·9 ml. 4 % fatty acid-free albumin (Albumin Cohn Fraction V, essentially fatty acid free, Sigma Chemical Co. Ltd) made up in normal saline was added to give a final solution containing 10 μCi/ml. The solution was quite clear, even when stored at 4° C for a week, and lost none of its activity when passed through a 0·2 μm pore filter (Gelman GA.8 membrane). When radiochemical purity was checked with thin-layer chromatography, 98 % of the activity was found in the free fatty acids zone. For foetal injection the labelled fatty acid solution was prepared as above except that the sodium palmitate was taken up to 1 ml. with albumin to give a solution containing 50 μCi/ml.

Glucose was estimated using glucose oxidase (Huggett & Nixon, 1957) and glycerol was analysed by a fluorimetric adaption of the test kit method supplied by the Boehringer Corporation Ltd. Plasma and whole blood free fatty acids were determined in 25 μl. samples using an automated colorimetric system based on the selective transfer of copper soaps into chloroform (Elphick, 1975). A comparison between this method and the titrimetric procedure of Trout, Estes & Friedberg (1960) using pooled foetal and pooled maternal rabbit plasma showed good agreement (0·54 and 1·33 m-equiv/l. for the titrimetric method and 0·56 and 1·39 m-equiv/l. for the automatic method, respectively).

Blood samples from the maternal to foetal label transfer experiments were centrifuged and 300 μl. plasma extracted into chloroform according to the method of Itaya & Ui (1965). The extract was evaporated to dryness and the residue taken up in a xylene based scintillation fluid for ^{14}C counting. The ability of this system to extract free fatty acids from plasma was determined by adding 0·1 ml. albumin-bound [1-^{14}C]palmitate acid (10 μCi/ml., prepared as above) to 9·9 ml. fresh heparinized human plasma. The activity recovered from 300 μl. extracts was compared with the activity of the original heptane solution of label and showed an extraction efficiency of 93 %. During the measurement of foetal plasma labelled palmitate clearance rates, free fatty acid was extracted for radioactivity determination using the same method but with 25 μl. plasma samples and proportionately less chloroform and buffer. Counting efficiency was determined using a channel ratio method and was about 96 % efficient.

In order to determine the distribution of radioactivity between the various lipid classes, thin-layer chromatography was performed on lipid extracts of ten maternal and foetal sample pairs as follows: plasma samples of 500 μl. were extracted with chloroform/methanol 2:1 (v:v) using the system described by Folch, Lees & Sloane-Stanley (1957), which gave a recovery of labelled palmitate from plasma of 82 % (determined as above). The extracts were evaporated down to a volume of about 200 μl. which was then applied to thin-layer chromotography plates coated with silica gel H (E. Merck Ltd). The lipid components were separated in equilibrated tanks with a solvent system consisting of petroleum ether 60–80°, diethyl ether and glacial acetic acid in the volume ratio of 60:40:1. The zones were stained in iodine vapour, scraped from the plates and extracted with three lots of 2 ml. aliquots of the following solvents: glycerides with chloroform methanol 2:1; fatty acids with diethyl ether, petroleum ether 40–60°, formic acid 50:50:1 (v:v); phospholipids with chloroform, methanol, water, glacial acetic acid, 50:39:10:1 (v:v). Zone extracts were evaporated to dryness *in vacuo* and taken up in 5 ml. xylene scintillation fluid for liquid scintillation counting.

RESULTS

The plasma free fatty acids concentration in venous blood from the ear veins of well-fed anaesthetized rabbits at 28 days gestation and between 9 and 10 o'clock in the morning is 0·45 ± 0·04 m-equiv/l. (mean ± S.E. of mean, n = 26). In six rabbits venous blood was taken 5–10 min after anaesthetic induction and then again 5–15 min after laparotomy; the results were 0·42 ± 0·01 and 0·99 ± 0·04 m-equiv/l. (mean ± S.E. of mean) respectively. It appears that laparotomy led to a large increase in circulating concentrations of free fatty acids.

Paired samples of umbilical arterial and venous blood were obtained for whole blood free fatty acid estimation from thirty-one foetuses from seven does; maternal blood was taken simultaneously. High maternal blood concentrations of free fatty acids were associated with high concentrations in the umbilical venous blood, the relation with arterial concentrations was less marked (Fig. 1). There was a significant correlation between the maternal blood concentration and the umbilical blood venous–arterial difference (Fig. 2).

Infusion of noradrenaline (4 μg/kg/min for 10 min) into fourteen foetuses

led to a significant rise in plasma glucose from 80 ± 16 to 94 ± 18 mg/100 ml. ($P < 0{\cdot}01$ calculated using a paired t-test). In eight foetuses, blood samples large enough to measure glycerol concentrations were obtained and these also increased from $0{\cdot}19 \pm 0{\cdot}02$ to $0{\cdot}25 \pm 0{\cdot}04$ mM/l. ($P < 0{\cdot}01$). There was not a significant rise in free fatty acid concentrations. In eight foetuses from five does the umbilical venous–arterial difference was

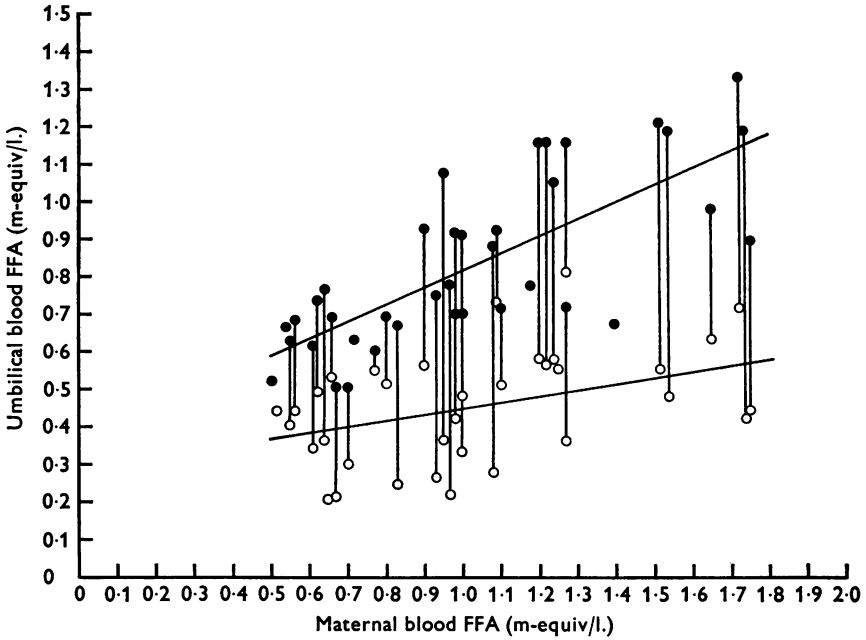

Fig. 1. Levels of free fatty acid, FFA, in the umbilical vessels of 28-day foetuses (y) compared with those in their mother's blood (x). The regression lines shown are for cord venous blood (●), $y = 0{\cdot}453x + 0{\cdot}37$ ($n = 38$, $r = 0{\cdot}750$, $P < 0{\cdot}001$), and cord arterial blood (○), $y = 0{\cdot}162x + 0{\cdot}29$ ($n = 35$, $r = 0{\cdot}410$, $P < 0{\cdot}02$). Free fatty acid levels were measured in whole blood.

measured after noradrenaline (4 μg/kg/min for 10 min) infusion. The free fatty acid concentration venous–arterial difference (whole blood) varied from $-0{\cdot}05$ to $+0{\cdot}63$ m-equiv/l. and fell within the range of values shown in Fig. 2.

Injection of labelled palmitate into the mother

Seven pregnant rabbits were injected with [1-^{14}C]palmitate 10 μCi/kg. The initial clearance rates at 2 and 4 min after injection were high with a half-life between 30 and 60 sec. An accurate half-life is difficult to calculate because of initial mixing in the circulation and possible rapid

recycling of the label. The label appeared in the foetal blood free fatty acids pool within 2 min and reached its peak within 3 min. Thereafter the activity fell at the same rate as that in the mother (Fig. 3). Separation by thin-layer chromatography of ten pairs of maternal and foetal plasma lipid extracts, taken 10 min after injection of label, showed that in both foetal and maternal plasma less than 2% of the label had entered the non-free fatty acid lipid fractions. The mean ± S.E. of the mean of the maternal and foetal plasma free fatty acid concentrations during these experiments were 1·49 ± 0·08 and 0·39 ± 0·02 m-equiv/l. respectively.

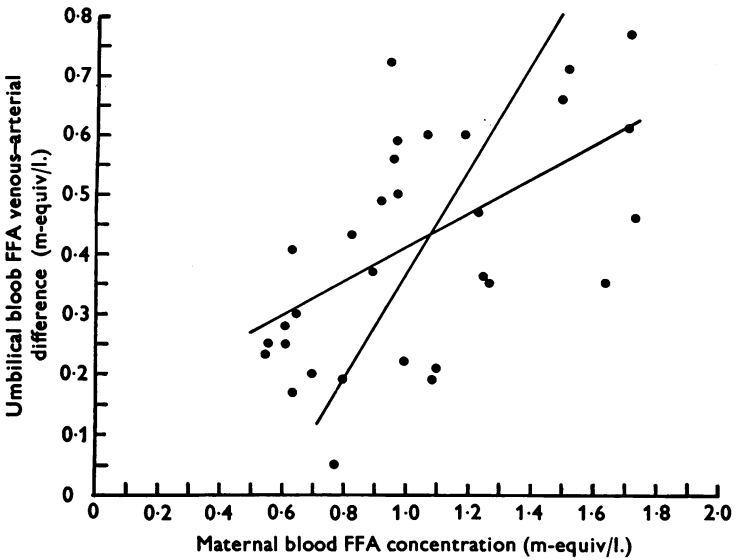

Fig. 2. Umbilical venous–arterial differences in whole blood free fatty acid levels in 28-day foetuses (y) compared with maternal venous levels (x). The two regression lines are given by the formulae: $y = 0{\cdot}305x + 0{\cdot}12$, $x = 1{\cdot}13y + 0{\cdot}58$ ($r = 0{\cdot}588$, $n = 31$, $P < 0{\cdot}001$).

Injection of labelled palmitate into the foetus

Six foetal rabbits from two does were injected with 12·5 μCi of labelled palmitate. The label rapidly appeared in the maternal circulation (Fig. 4). The amount of palmitate given in these as in the other experiments was not sufficient to significantly alter the circulating levels. The free fatty acid concentration in plasma obtained through the catheters of the foetuses was 0·69 ± 0·05 m-equiv/l. (mean ± S.E. of mean) and in the two does ranged between 1·17 and 1·95 m-equiv/l. In all instances the concentration of free fatty acids in the does was higher than that in her foetuses. In three of these foetuses venous–arterial differences were

obtained within 10 min of the injection. In all the free fatty acid concentration in the venous whole blood was higher than that in the arterial cord blood. The venous–arterial differences were: 0·17, 0·25 and 0·58 m-equiv/l.

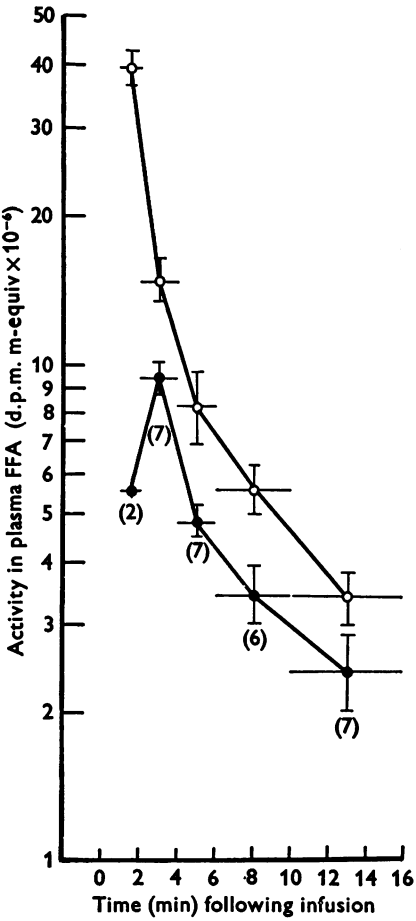

Fig. 3. Radioactivity of maternal (○) and foetal (●) plasma free fatty acids plotted against time following the rapid injection into seven 28-day pregnant rabbits of 10 μCi/kg body wt. albumin-bound [1-^{14}C]palmitate. Each point represents the mean activity of plasma free fatty acids during the various sampling times as indicated by the horizontal line. The vertical bars represent S.E. of the mean values and the figures in parentheses show the number of foetuses studied in each group.

Another eleven foetuses were infused with labelled palmitate, dose 6·25 μCi in 0·25 ml. and serial foetal samples taken. The initial half-life (from 2 to 4 min) ranged between 30 and 70 sec (Fig. 5). The mean foetal

plasma free fatty acid level in blood drawn through the catheters was 0·70 ± 0·04 m-equiv/l. (± S.E. of mean).

In another series of experiments paired umbilical arterial and venous samples were obtained from nine foetal rabbits from two does 7–12 min

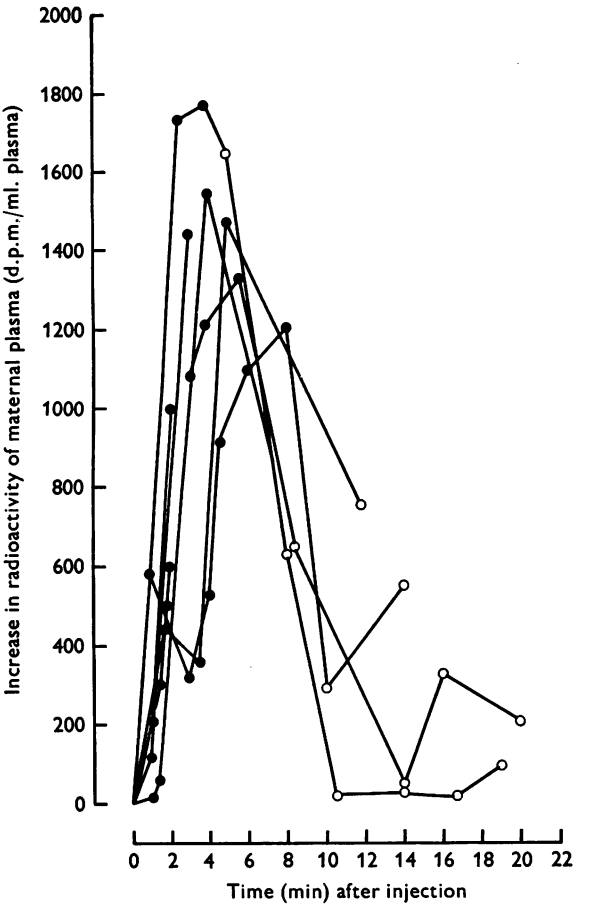

Fig. 4. Appearance of radioactivity in maternal plasma following the injection of 12·5 μCi [1-^{14}C]palmitate into the foetal circulation. The open circles represent measurements taken after severing the umbilical vessels.

after foetal injection of labelled palmitate (12·5 μCi in 0·25 ml.). The means ± S.E. of the mean of the free fatty acid concentrations in whole blood obtained from the vein and artery were 1·09 ± 0·06 and 0·65 ± 0·05 m-equiv./l. respectively. The mean ± S.E. of the mean of the ratio of the lipid-soluble radioactivity in the vein over the activity in the artery was 74 ± 5 % with a range 50–93 %.

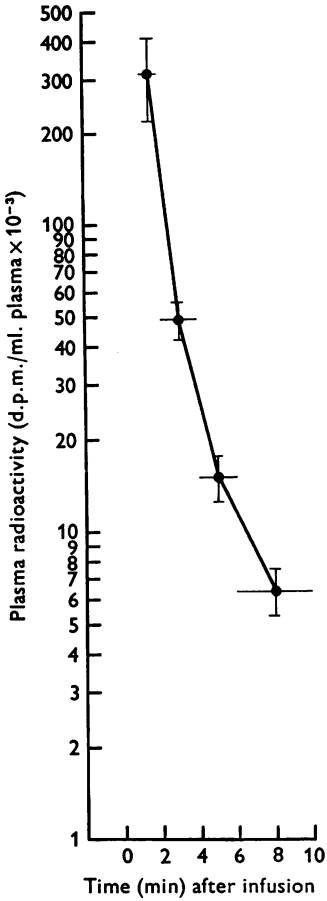

Fig. 5. Clearance rates of [1-^{14}C]palmitate injected into foetal rabbits (6·25 μCi). Blood samples were obtained following the injection, extracted for free fatty acids and the extract analysed for radioactivity. Each point represents the mean plasma radioactivity level found during the times following the injection as indicated by the horizontal lines. The vertical bars represent S.E. of the means.

Thus the label passed into and through the placenta although the net flow of fatty acids was from the placenta to the foetus.

Lipolysis in white adipose tissue of foetal rabbits in vitro

Hourly sampling of the incubation medium of foetal perirenal white adipose tissue showed glycerol and free fatty acids release throughout a 5 hr period. Addition of noradrenaline to the medium stimulated a four- to fivefold increase in the rate of glycerol release. Lowering the

glucose concentration of the medium from 180 mg/100 ml. to 40 mg/100 ml. did not affect the rate of glycerol release, either in control or stimulated tissues, while the rate of free fatty acids release in stimulated tissues was increased at the lower glucose concentration (Table 1). In stimulated tissues the ratio of free fatty acids release to glycerol release almost doubled when the medium glucose concentration was reduced.

TABLE 1. Glycerol and free fatty acids release (mean ± S.E. of mean) from perirenal white adipose tissue lobes of 28-day gestation rabbit foetuses and the effect of noradrenaline at two different medium glucose concentrations

	Glucose concentration			
	40 mg %		180 mg %	
	Control $n = 6$	+NA $n = 16$	Control $n = 5$	+NA $n = 15$
Glycerol release (μmole/g wet wt./hr)	0·69 ± 0·19	3·66 ± 0·35	0·87 ± 0·13	4·16 ± 0·51
			n.s.	
Free fatty acids release (μ equiv/g wet wt./hr)	0·91 ± 0·29	5·43 ± 0·46	0·84 ± 0·19	3·74 ± 0·38
			$P > 0{\cdot}001$	

In every experiment there was an increase in the release of both free fatty acids and glycerol after noradrenaline stimulation. n.s. = not significant.

DISCUSSION

Van Duyne, Havel & Felts (1962) injected labelled palmitate into pregnant rabbits and showed that the label appeared within 2–5 min in pooled samples of foetal blood. Our experiments confirm and extend these observations. The highest levels of activity in the circulating free fatty acids were found in foetuses taken 3 min after injection of label into the mother showing that the label passed rapidly from the maternal to foetal circulation. Even after 10 min over 98% of the label in the blood lipids was found in the free fatty acids fraction. The rapid transfer of label across the placenta suggests that the palmitate passed through the placenta unchanged.

It can be appreciated from Fig. 3 that the level of radioactivity per m-equivalent of free fatty acids reaches surprisingly high values in the foetuses. The labelled palmitate is rapidly cleared from both maternal and foetal circulation so the relationship between any single pair of maternal and foetal samples will be complex. Notwithstanding, even if the foetal values reflect exchanges which occurred *two* min earlier, they still suggest that under the conditions of the experiment a substantial portion of the fatty acids in the foetal circulation are derived from the doe.

A large flow of fatty acids from placenta to foetus in our experimental conditions was also demonstrated by the measurements of umbilical cord venous–arterial differences. As might be expected, the differences varied from one foetus to another. However, in many the venous concentration was over 50% higher than the arterial free fatty acid concentration.

In the foetal rabbit the daily increment of triglyceride stores in brown and white adipose tissue and liver over day 28 is approximately 0·2 g. The average foetal body wt. is 33 g, thus the increment is about 6 g/kg/day or 0·014 m-equiv/kg.min. If it is assumed that the placental blood flow is 250 ml./kg.min (Dawes, 1968), then the venous–arterial difference in free fatty acid concentration to provide all the stored fatty acid is less than 0·1 m-equiv/l. Values much higher than this were recorded in these experiments (Fig. 1).

The plasma concentration of free fatty acids in both man and rabbit rises during pregnancy. Towards the end of gestation the maternal metabolism is set toward lipolysis. In the maternal rabbit the free fatty acid concentrations rise on average to 0·5 m-equiv/l. (Edson *et al.* 1975). Anaesthesia, restraint and surgical procedures may all lead to a rise in circulating concentrations. They did so in the majority of our experiments which were performed on well-nourished rabbits which were not fasted before anaesthesia. Thus our studies were performed in the presence of high circulating concentrations of free fatty acids. In general, high maternal circulating concentrations of free fatty acids were associated with high umbilical venous concentrations and they were also associated with high umbilical venous–arterial differences. The high venous–arterial differences not only showed that more free fatty acid was being released into the foetal circulation from the placenta, but also that more free fatty acid must be being taken up by the foetus, and this is reflected by low cord arterial concentrations. Thus it would seem an increase in maternal levels would lead to rapid deposition of fatty acids in the foetal stores until a new equilibrium is reached.

Clearly, many factors other than maternal plasma free fatty acid concentration influence the rate of release free fatty acids by the placenta into the foetal circulation. Nevertheless, it would seem that the maternal concentrations are one factor which determine the size of the foetal triglyceride stores.

The studies on foetal white adipose tissue *in vitro* indicated that foetal tissue could release free fatty acids into the foetal circulation. A number of investigators have infused catcholamines into foetal lambs (Dawkins, 1964; Comline & Silver, 1972) and found no evidence of fatty acid release into the circulation following noradrenaline, but some variable response to adrenaline. Our own studies with noradrenaline infusion are also

inconclusive, although there was a consistent rise in glycerol suggesting that lipolysis was taking place (Table 1).

In these studies there was no evidence to suggest that the net flux of free fatty acids was ever from the foetus to the placenta or from the placenta to the mother. Presumably, this might occur when maternal plasma free fatty acid concentrations are low. That foetal fatty acids can cross from the foetal to the maternal circulation has been shown by others (Portman *et al.* 1969; Kayden, Dancis & Money, 1969; Dancis, Jansen, Kayden, Schneider & Levitz, 1973) and is further demonstrated in the experiments when labelled palmitate was injected into the foetuses. The rapid appearance of label in the maternal free fatty acids plasma fraction again suggests that it passed through the placenta unchanged. These experiments took place when the maternal free fatty acids concentration was high and when it might be expected that the net flow of free fatty acids would be to the foetus. Measurement of activity in cord samples showed that between 10 and 15% of the label was removed as it passed through the placenta but the total concentration of free fatty acids in the venous blood was always higher than in the arteries. Only 20% of the labelled palmitate injected into the foetus was found after 5 min in the foetal triglyceride stores (M. C. Elphick, D. G. Hudson & D. Hull, unpublished observations). The half-life of palmitate in the foetus was very short, between 30–70 sec. Taken together this information supports the possibility that foetal circulating free fatty acids are continually exchanging with pools in the placenta and in the maternal circulation.

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