Bidirectional Placental Transfer of Glucose and Its Turnover in Fetal and Maternal Sheep

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SUMMARY

Glucose biokinetics were assessed simultaneously in the pregnant ewe and its fetus by a primed constant infusion of 2-^{3}H glucose and U-^{14}C glucose. Late in gestation fetal glucose turnover was 27.3 ± 3.7 mg/min; expressed in terms of fetal weight this is 6 to 10 mg/kg/min. In the fed state the results indicated that all of the fetal glucose turnover was derived from the mother via placental transfer and there was no evidence that the fetus was capable of glucose production. Maternal glucose turnover was 145.6 ± 9.3 mg/min (2.8 mg/kg/min). There was a significant amount of glucose (16.3 ± 2.3 mg/min) transferred from the fetus to the mother. This feto-maternal transfer of glucose accounted for 11% of the maternal glucose turnover and approximately 50% of the total glucose coming to the fetus from the mother. This study provides the first *in vivo* simultaneous quantification of the bidirectional glucose transfer across the placenta.

SPECULATION

In the fed state all the fetal glucose is derived from the mother, and the fetus does not produce glucose. A large portion of the glucose coming from the mother to the fetus is returned to the mother, despite glucose concentrations that are threefold higher in the mother than fetus. Thus, the transplacental passage of glucose is bidirectional; this bidirectionality may be responsible for maintaining the concentration gradient that always keeps fetal glucose concentration at a lower level than that of the mother, and thereby facilitates fetal glucose supply.

INTRODUCTION

Glucose is regarded as the primary fuel for the mammalian fetus. In all species examined the glucose concentration in the fetal plasma is considerably lower than that of the mother (13,14,23,27), and there is a close relationship between maternal and fetal glucose concentrations. Therefore, it has been proposed that fetal glucose is obtained principally by placental transfer from the mother (8). The transport mechanism is a rapid, stereospecific facilitated diffusion process; this process is carrier mediated, yet depends upon the existence of a positive concentration gradient between maternal and fetal plasmas (11,28,33).

Placental transfer of metabolites including glucose has been measured using the Fick principle. Measurement of net fetal uptake of glucose by this method has the drawback that it requires measurement of umbilical blood flow and umbilical arteriovenous difference of glucose concentration (10,18). The interpretation of the measurement of the arteriovenous difference on the maternal side is complicated by the effect of glucose utilization by nonplacental maternal uterine tissues and by the problem of non-homogeneity of maternal uterine drainage sampled by a single catheter at a single site. Thus, only net unidirectional changes can be discerned and there are practical limitations to the use of arteriovenous differences of metabolites across the umbilical circulation as a general tool in measuring the bidirectional flux of metabolites in and out of the fetal body (23).

Glucose transport across the placenta, both in the maternal to fetal and fetal to maternal direction, has not been directly measured *in vivo*. Furthermore, the glucose kinetics in the fetus *in utero* have not been quantified (16) and previous studies have failed to establish conclusively the contribution of fetal gluconeogenesis to its glucose supply (8).

The present studies were designed to quantify transfer of glucose across the ovine placenta in both directions. The model used was the fetal sheep preparation with chronically indwelling vascular catheters. This preparation permits the infusion of isotopically labeled glucose into the unstressed ewe and fetus several days after surgery. These studies also provided data on simultaneous measurement of glucose turnover in both mother and fetus and demonstrated that there was no endogenous production of glucose in the fetus of a fed mother.

METHODS

Animals

Twenty date-bred ewes of Rambouillet-Columbia strain with gestational ages between 111-120 days were starved for 24 hours before surgery. The surgical procedure for implantation of chronic indwelling catheters, both in the fetal and maternal blood vessels, has been described previously (24). The fetal catheters were inserted into the pedal artery and pedal vein. In some cases the fetal carotid artery also was catheterized. The maternal catheters were placed in the femoral artery and femoral vein. The animals recovered promptly from surgery; ewes were standing in their pens eating and drinking within 6 hours after surgery. The maternal catheters were flushed daily with a heparinized saline solution (10 heparin units/ml of physiological saline). The fetal catheters were infused with the heparinized saline solution at 1 ml/hr. Fetal pH, pO_2 and pCO_2 were monitored daily using a blood gas analyzer (Radiometer ABL2) and fell within normal range for all animals. The mean ± standard error of the mean values were pH 7.35 ± 0.06, pO_2 23.5 ± 0.93, and pCO_2 40.6 ± 1.09. A minimum of 5 days was allowed for recovery from operative stress before the animals were used for experimental studies. The blood gases and pH were normal on the day of the experiment and the day after. The body weight of the pregnant ewes was 52.0 ± 3 kg and estimated weight of their fetuses 3.9 ± 0.5 kg (mean ± SEM).

Measurement of Glucose Kinetics

Glucose kinetics were measured simultaneously in the mother and fetus by a primed constant infusion of radioisotopic tracer (29). Glucose labeled with tritium at position 2 (2-^{3}H-glucose) and uniformly labeled with Carbon-14 (U-^{14}C glucose) were used. The labeled glucose was administered intravenously via the indwelling polyvinyl catheters, (pedal vein in the fetus and femoral vein in the mother). An initial priming dose, approximately 60 times the infusion rate (nCi/min) of the isotope, was followed immediately by a constant infusion lasting for 3-5 hours. In approximately half the experiments the ewe and the fetus were simultaneously infused with tritiated glucose and ^{14}C-glucose, respectively. In the other half of the experiments, the situation was reversed. The infusion rates of isotopes in each animal are shown in Table 1.

At 30 minute intervals during the course of the experiment approximately 7 ml of blood were drawn from the maternal arterial catheter and 2 ml from the fetal arterial catheter. The blood was collected in chilled tubes containing EDTA as anticoagulant and fluoride as inhibitor of glycolysis. The blood samples were immediately centrifuged to separate the plasma, which was frozen and stored at -20°C until ready for laboratory analysis. All analyses were performed within one week of the experiment.

Analytic Techniques

The plasma glucose concentration was measured by a glucose oxidase method. Low glucose concentrations in fetal plasma made it necessary to modify the method described by Krebs et al (22). The glucose oxidase reagent was prepared by mixing 12.5 mg of glucose oxidase and 4.0 mg peroxidase per 100 ml of Tris (0.1mM) phosphate (0.3mM) buffer to which 0.1 ml of 1% aqueous solution of o-dianisidine HCl was slowly added. 0.1 ml of fetal plasma was deproteinized with 0.9 ml of Hycel tungstic acid reagent. 0.5 ml of protein free filtrate was mixed with 3.0 ml of glucose oxidase reagent and incubated in a water bath at 37°C for 1 hour. The optical density was determined at 420 mμ. A water blank and a set of standards were run with each series of samples. This method was sensitive enough to determine glucose concentration as low as 1 to 2 mg per 100 ml.

Glucose was isolated from both maternal and fetal plasma by preparing glucose penta-acetate (19). The specific activity was determined by using a Searle Mark II Scintillation Counter and the channel ratio method was employed for the calculation of efficiency of the counting system. In plasma samples with tritium only, the specific activity of glucose was also determined by evaporating 200 μl of protein free filtrate to dryness at 60°C, redissolving it in 200 μl of distilled water and adding it to 10 ml of scintillation fluid. No significant difference was observed in the results obtained from these two methods.

Calculations

The glucose turnover rate was calculated from the rate of tracer infusion and the steady state specific activity of glucose in plasma (29,30) as follows.

$$(1)\qquad \text{Glucose Turnover (mg/min)} = \frac{\text{isotope infusion rate (nCi/min)}}{\text{steady state specific activity of plasma glucose (nCi/mg)}}$$

The placental transfer of glucose between mother and fetus was calculated as follows.

$$(2)\qquad \text{*Transfer of glucose from mother to fetus (mg/min)} = \frac{\text{steady state specific activity of fetal glucose (nCi/mg)}}{\text{steady state specific activity of maternal glucose (nCi/mg)}} \times \text{fetal glucose turnover (mg/min)}$$

*Mother was infused with labeled glucose.

$$(3)\qquad \text{**Transfer of glucose from fetus to mother (mg/min)} = \frac{\text{steady state specific activity of maternal glucose (nCi/mg)}}{\text{steady state specific activity of fetal glucose (nCi/mg)}} \times \text{maternal glucose turnover (mg/min)}$$

**Fetus was infused with labeled glucose.

These calculations are based on established procedures as described by other investigators (5,6).

STATISTICS

All results are expressed as statistical mean ± standard error of mean. The difference between means was tested by Student's t test. The linear re-

gression lines and correlation coefficients were calculated using the programmable calculator T158 (Texas Instruments) by the method of least squares.

RESULTS

Figure 1 represents typical experiments showing the specific activity of glucose in the plasma of ewe and fetus following a primed infusion of 2-^{3}H-glucose to the mother. A steady state specific activity was achieved within 90 minutes in both the mother and fetus in all animals. Figure 2 shows the specific activity of maternal and fetal plasma glucose when the ewe was infused with U-^{14}C-glucose. For both isotopes, the specific activity for each experiment is shown in Table 2. This ratio, ranged from 0.72 to 1.23, but was near 1.0 in the majority of the animals. The mean ratio of specific activity of glucose in fetal to maternal plasma was 0.99 ± 0.04 when tritiated glucose was infused to the ewe and 0.99 ± 0.07 when ^{14}C-glucose was infused. These statistical ratios of near unity indicate that the glucose in the mother and fetus behaves as a single pool and that in these experiments all of the fetal glucose was derived from the mother.

Figure 3 shows data from a typical experiment of specific activity of plasma glucose of mother and fetus after primed infusion of 2-^{3}H-glucose to the fetus. In this case again, a steady state specific activity was achieved in the last three hours of the experiment both in the fetus as well as in the mother. It has been demonstrated that when the tritiated glucose is infused in the fetus it is metabolized, the predominant end product being labeled water, which rapidly equilibrates with the large pool of body water (18), so that the reincorporation of tritium into glucose is insignificant. Therefore, the appearance of tritium in the maternal plasma glucose when the fetus was infused with the labeled glucose indicates that there was a transfer of glucose from the fetus to the mother. The ratio of maternal glucose specific activity to fetal glucose specific activity for each experiment is shown in Table 3. This ratio is an estimation of the fraction of the maternal glucose pool derived from the transfer of glucose from the fetus to the mother. The ratio of 0.11 ± 0.03 (Table 3) indicates that 11 ± 3% of the glucose turnover in the mother is due to placental transfer of glucose from fetus back to mother. When ^{14}C-labeled glucose was infused into the fetus, a significant amount of labeled glucose again appeared in the maternal circulation, and the ratio of maternal glucose specific activity to fetal glucose specific activity was 0.14 ± 0.03 (Table 3). A slight overestimation of this ratio with ^{14}C-glucose is expected since the ^{14}C-glucose, unlike the tritiated glucose, is broken down to labeled metabolites, such as lactate, which might be transferred from the fetus to mother and then reincorporated into glucose. However, this recycling of the label has only a minimal effect since the ratio obtained with ^{14}C-glucose is not significantly different from the ratio obtained with ^{3}H-glucose.

Table 4 lists the rate of glucose (mg/min) transferred from the fetus to mother in each animal. The average amount of glucose transferred back to the mother from the fetus was 16.3 ± 2.3 mg/min (n=10). This amount represents 11% of the maternal glucose turnover and 57% of the fetal glucose turnover. Thus, it is evident that approximately half of the glucose coming from the mother to the fetus returns from the fetus to the mother. Since the maternal glucose concentration in the sheep is 3.5 times the glucose concentration in the fetus, this amount of glucose is transported against an apparent concentration gradient. This fetus to mother transfer of glucose is positively correlated with the fetal glucose concentration ($r = 0.89$, $p < 0.001$) (Figure 4).

Figure 5 demonstrates the negative correlation ($r = -0.93$, $p < 0.001$) between the fetus to mother transfer of glucose and the materno-fetal glucose concentration difference. Tables 5 and 6 list the rate of glucose turnover (mg/min) in the mother and fetus, respectively. The glucose turnover was determined independently by using 2-^{3}H-glucose or U-^{14}C-glucose. The value of glucose turnover in the mother was 143.4 ± 10.2 mg/min (n=8) with ^{3}H as a tracer and 107.6 ± 11.7 mg/min (n=8) with ^{14}C-glucose as a tracer. The value of glucose turnover obtained using U-^{14}C-glucose was significantly lower than that obtained with 2-^{3}H-glucose. The lower value obtained with ^{14}C-glucose in the mother is most likely due to the recycling of this label as clearly shown in other studies (20,21). The ^{14}C-glucose is catabolized to labeled lactate which is reconverted to glucose and similarly $^{14}CO_2$ produced from ^{14}C-glucose is returned to the glucose pool. Such recycling is likely to cause an underestimation of the glucose turnover, because of a higher specific activity. The maternal glucose turnover was significantly correlated with glucose concentration ($y = 3.05x - 71.5$; $r = 0.916$; $p < 0.01$). Whereas some of the discrepancy in results obtained using 2-^{3}H and ^{14}C can be explained by recycling of ^{14}C, the animals infused with ^{14}C-glucose had somewhat lower glucose concentrations as compared to those infused with tritiated glucose and therefore, these animals would be expected to have lower glucose turnover. Table 6 lists the fetal glucose turnover (mg/min) and metabolic clearance (ml/min). The average value of glucose turnover in the fetus was 27.3 ± 3.7 mg/min using tritiated glucose and 29.3 ± 4.8 mg/min using ^{14}C-glucose, respectively, These independently obtained values were not significantly different. Thus, the statistically same value of glucose turnover in the fetus obtained by either of the two isotopes demonstrates that there was no recycling of C-14 within the fetal compartment. This is a further evidence that there was no gluconeogenesis in the fetus. As shown in Figure 6, the fetal glucose turnover is highly correlated with fetal glucose concentration ($r = 0.91$; $p < 0.001$).

DISCUSSION

The present study provides the first quantification of glucose turnover measured simultaneously in the fetus and the mother. Using tritiated glucose the fetal glucose turnover was 27.3 ± 3.7 mg/min, which is approximately 8.0 mg/kg/min. The glucose uptake by the fetus has been estimated by previous workers by the application of Fick's principle (10,18). Boyd et al reported (10) that in fetal sheep of fed mothers the glucose uptake was 18.0 ± 1.4 mg/min which corresponded to 4.8 mg/kg/min in their animals. However, these investigators encountered wide variations in day-to-day glucose uptake measurements and attributed them partly to the difficulty of measuring accurately small arteriovenous differences of glucose (10). Using the same principle, James et al (18) measured glucose uptake in fetal sheep and reported 1.0 to 6.0 mg/kg/min. More recently, Hodgson and Mellor (16) used labeled glucose either as a constant infusion or single injection to the fetal sheep and reported that the net placental transfer of glucose from mother to fetus was 36 or 55 g/24 hour in one of the two animals studied (16). When expressed as mg/min, these values correspond to 25 mg/min or 38 mg/min and compare favorably with the results obtained from our studies. Glucose turnover has not been measured *in utero* in the fetus of other animal species. However, the rate of glucose production has recently been assessed in premature human infants and term neonates (9). Glucose turnover in premature infants was 5.5 ± 0.3 mg/kg/min and in term neonates it averages 6.1 ± 0.5 mg/kg/min. In this regard, the newborn human infant is similar to the immature rhesus monkey, dog, and sheep, which produce glucose at rates of 4 to 8 mg/kg/min (9), values that are remarkably similar to the fetal values in our present studies.

The maternal glucose turnover averages 145.6 ± 9.3 mg/min using tritiated glucose and 107.6 ± 11.7 mg/min using ^{14}C-glucose. These values correspond to 2.8 and 2.1 mg/kg/min respectively. The glucose turnover measured with tritiated glucose provides a better estimate of "true" glucose production rate since the recycling of this label into glucose is negligible (20,21). The glucose turnover in the pregnant sheep has been measured by previous workers (5,6,7). Bergman et al (7) reported that glucose turnover in pregnant sheep averaged 138.0 mg/min, a value which is similar to that obtained in the present study.

The specific mechanism for the transfer of glucose across the placenta has not been conclusively identified (1). On the basis of data obtained by Huggett et al (17), Widdas postulated facilitated diffusion (33). In this mechanism a carrier of high specificity ensures a faster rate of transfer than would be achieved by simple diffusion. Chinard et al (12) have demonstrated that the placental transfer of fructose is slower than glucose. However, there is no transfer of glucose against a concentration gradient from mother to fetus (4). This implies that the fetus must maintain a lower glucose concentration than the mother if it is to depend on the supply of glucose from the mother. In all species examined, fetal glucose concentration is indeed lower than that of the mother; in the fetal sheep, the glucose concentration is only one-third to one-fourth that of the mother. The mechanism by which the fetus is able to maintain a lower glucose concentration than that of the mother remains unknown. That glucose transport across the placenta is stereospecific has also been demonstrated by Carstensen et al (11) and Stacy et al (28).

It is evident from the results presented here that a significant amount of glucose is also transported from fetus to mother despite the threefold higher glucose concentrations in the mother compared to her fetus. In our studies, approximately 16mg of glucose/min was returned back from fetus to mother; this represents nearly 57% of the fetal glucose turnover and accounts for 11% of the total maternal glucose turnover. There has been no previous study reporting the *in utero* estimate of glucose transport on the feto-maternal side. The mechanism by which glucose is transported across the placenta from fetus to mother is not clear from these studies. However, the amount of glucose transferred back to the mother was positively correlated with the fetal glucose concentration. And fetus to mother glucose transfer continued even at the lower range of fetal glucose concentration. The correlation suggested that the fetal plasma glucose concentration would have to be below 5mg per 100ml before this fetus to mother transfer of glucose would cease. Thus, it would be of interest to determine whether the fetus has a mechanism to protect itself against hypoglycemia. Furthermore, this feto-maternal transfer of glucose is negatively related to the glucose concentration difference between the mother and her fetus (Figure 5); the lower the concentration gradient, the higher is the transfer rate. This indicates that although the transport of glucose from fetus to mother is against a "concentration gradient," the net rate of glucose transfer depends upon the concentration difference between mother and fetus.

When labeled glucose was infused into the mother, a statistically identical specific activity was obtained in both the mother and her fetus. The ratio of specific activity in fetal to maternal plasma glucose was 0.99 indicating that virtually all of the fetal glucose was derived from the mother. If the fetus were producing glucose either through gluconeogenesis or glycogenolysis, the specific activity of labeled glucose coming from the mother would be diluted. Since there was no significant decrease in the specific activity of fetal plasma glucose (Figures 1 and 2), and it remained indistinguishable from that of maternal plasma glucose, there was no endogenous production of glucose in the fetus under our experimental conditions. Recently, Girard et al (15) showed in rats that the infusion of 2-^{3}H-glucose to constant specific activity in the mother resulted in a ratio of maternal to fetal glucose specific activity of 1.0 in fed animals and 1.56 in fasted animals. Thus, they also concluded that glucose measured in the fetus of fed mothers was entirely of maternal origin. In the fetus of the fed mother, the metabolic state may be considered as one of maximal anabolism (14), so that protein synthesis is active, glycogen synthesis proceeds maximally, and hepatic gluconeogenesis and ketogenesis are curtailed, normally appearing only after birth in the rat (15). Our results show that with respect to glucose, the sheep fetus of the fed mother behaves in a similar fashion and displays no evidence of endogenous glucose production. Warnes et al (32) demonstrated that there was no gluconeogenesis from lactate in fetal lambs, although active glucose formation from lactate was demonstrable within a few minutes of birth. Similarly, gluconeogenesis from alanine, lactate, or propionate did not occur in the perfused fetal sheep liver unless glucagon was added in pharmacological amounts to the perfusion medium (26). And gluconeogenesis in the fetus of other animal species has also been shown to be negligible (3,34). A recent study purported to show gluconeogenesis from labeled alanine infused directly into the ovine fetus (25). However, these authors failed to consider the possibility that the labeled alanine or its metabolite, labeled lactate, which accounted for 22% of total fetal lactate production (25), were transferred to the mother. Upon transfer to the mother either substrate could be converted to glucose and transferred back to the fetus. Thus, in those studies, the appearance of labeled glucose in the fetus does not conclusively prove that the glucose was actually produced from alanine by the fetus itself. In fact, the potential pathways for the appearance of labeled glucose in the fetus via gluconeogenesis from substrates transferred to the mother could explain the apparent low rate (2.3%) of glucose production from alanine reported in that study (25).

Our studies demonstrate that the entire fetal glucose supply is provided by placental transfer from the maternal circulation under normal conditions of fetal life. These data again support the concept that glucose transport across the placenta involves facilitated transport, which implies bidirectional transfer. Our data provide a measure of the relative transport constants and imply that under physiological conditions, fetal glucose concentration is maintained lower than maternal, thereby facilitating net glucose transfer to the fetus. It remains to be determined whether the fetus can initiate glucose production during maternal starvation or hypoglycemia.

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TABLE 1 EXPERIMENTAL ANIMALS AND THE RATE OF ISOTOPE INFUSION

Expt. No.	Gestational Age (Days)	Mother Infusion Rate	Isotope	Fetus Infusion Rate	Isotope
		(μ ci/min)		(μ ci/min)	
FG I	128	0.96	2-(^{3}H)gluc.	0.16	(U-^{14}C)gluc.
FG II	133	-	-	1.05	2-(^{3}H) gluc.
FG III	130	1.61	2-(^{3}H) gluc.	-	-
FG IV	130	3.84	2-(^{3}H) gluc.	0.46	(U-^{14}C) gluc.
FG V	131	3.76	2-(^{3}H) gluc.	0.46	(U-^{14}C) gluc.
FG VI	139	1.12	(U-^{14}C) gluc.	0.97	2-(^{3}H) gluc.
FG VIII	127	-	-	0.94	2-(^{3}H) gluc.
FG IX	132	0.94	(U-^{14}C) gluc.	0.90	2-(^{3}H) gluc.
FG X	129	0.74	(U-^{14}C) gluc.	0.85	2-(^{3}H) gluc.
FG XII	129	0.76	(U-^{14}C) gluc.	0.87	2-(^{3}H) gluc.
FG XIII	130	0.71	(U-^{14}C) gluc.	0.96	2-(^{3}H) gluc.
FG XIV	128	1.68	2-(^{3}H) gluc.	0.38	(U-^{14}C) gluc.
FG XV	130	2.03	2-(^{3}H) gluc.	0.35	(U-^{14}C) gluc.
FG XVI	133	1.74	2-(^{3}H) gluc.	0.30	(U-^{14}C) gluc.
FG XVII	121	1.74	2-(^{3}H) gluc.	0.30	(U-^{14}C) gluc.
FG XVIII	132	1.56	2-(^{3}H) gluc.	-	-
		0.56	(U-^{14}C) gluc.		
FG XX	126	1.34	2-(^{3}H) gluc.		
		0.47	(U-^{14}C) gluc.		

TABLE 2 RATIO OF STEADY STATE SPECIFIC ACTIVITY OF PLASMA GLUCOSE OF FETUS (F) TO ITS MOTHER (M)

Infusions of 2-(^{3}H) glucose to mother				Infusions of (U-^{14}C) glucose to mother			
Specific Activity (nci/mg)				Specific Activity (nci/mg)			
Expt. No.	M	F	Ratio F/M	Expt. No.	M	F	Ratio F/M
FG I	5.36	6.41	1.19	FG VI	7.4	9.1	1.23
FG III	14.60	14.40	0.98	FG X	9.8	9.6	0.98
FG IV	23.70	21.90	1.08	FG XII	8.3	6.0	0.73
FG V	22.20	22.50	1.01	FG XIII	8.3	7.4	0.89
FG XIV	14.10	14.00	1.00	FG XVIII	4.4	4.5	1.03
FG XV	18.50	13.40	0.72	FG XX	3.3	3.5	1.05
FG XVII	11.80	12.10	1.03				
FG XVIII	11.30	10.40	0.92				
FG XX	8.20	8.00	0.98				
F/M Mean ± SEM = 0.99 ± 0.04				F/M Mean ± SEM = 0.99 ± 0.07			

TABLE 3 RATIO OF STEADY STATE SPECIFIC ACTIVITY OF PLASMA GLUCOSE OF MOTHER (M) TO ITS FETUS (F)

Infusion of 2-(^{3}H) glucose to fetus				Infusions of (U-^{14}C) glucose to fetus			
Specific Activity (nci/mg)				Specific Activity (nci/mg)			
Expt. No.	M	F	Ratio M/F	Expt. No.	M	F	Ratio M/F
FG II	2.8	69.9	0.04	FG I	0.07	6.4	0.11
FG VI	3.0	37.0	0.08	FG IV	1.06	30.1	0.04
FG VIII	4.6	29.7	0.15	FG V	2.40	15.0	0.16
FG X	2.8	48.3	0.06	FG XIV	1.50	10.7	0.14
FG XIII	5.3	23.2	0.22	FG XV	1.80	7.3	0.25
				FG XVII	1.08	9.7	0.11
M/F Mean ± SEM = 0.11 ± 0.03				M/F Mean ± SEM = 0.14 ± 0.03			

TABLE 4 FETAL TO MATERNAL TRANSFER OF GLUCOSE

Experiment Number	F → M Transfer (mg/min)
FG I	20.3
FG IV	7.0
FG V	26.0
FG VI	12.0
FG IX	13.9
FG X	4.6
FG XIII	18.7
FG XIV	16.7
FG XV	27.5
FG XVII	16.3

Mean ± SEM = 16.3 ± 2.3

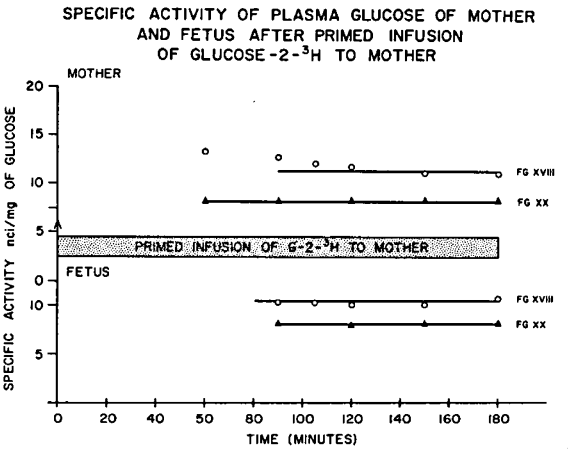

Figure 1

TABLE 5 MATERNAL GLUCOSE TURNOVER AND METABOLIC CLEARANCE RATE (MCR)

Using 2-(^{3}H) glucose as tracer				Using (U-^{14}C) glucose as tracer			
Expt. No.	Turnover (mg/min)	MCR (ml/min)	Glucose Conc. (mg/dl)	Expt. No.	Turnover (mg/min)	MCR (ml/min)	Glucose Conc. (mg/dl)
FG I	179.3	236	76	FG VI	151.1	201	75
FG III	110.0	177	62	FG IX	60.5	159	38
FG IV	175.0	225	78	FG X	76.2	149	51
FG V	169.3	235	72	FG XI	122.7	201	61
FG XIV	118.9	167	71	FG XII	93.9	162	58
FG XV	109.7	196	56	FG XIII	85.1	147	58
FG XVII	147.7	214	69	FG XVIII	130.1	186	70
FG XVIII	137.3	196	70	FG XX	141.5	211	67
Mean	143.4*	206**	69.3		107.6*	177**	59.8
SEM	10.2	9.2	2.5		11.7	9.0	4.1

* Significantly different from each other ($p<0.05$)

** Significantly different from each other ($p<0.05$)

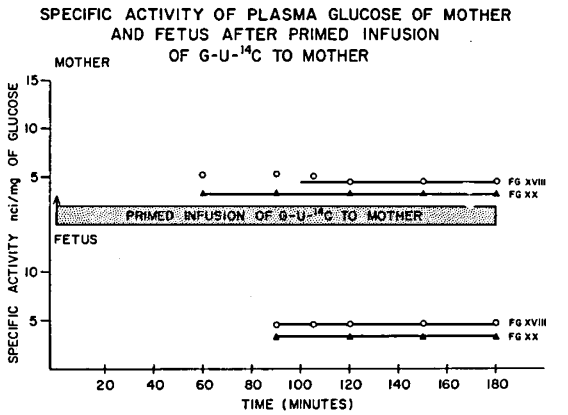

Figure 2

TABLE 6 FETAL GLUCOSE TURNOVER AND METABOLIC CLEARANCE RATE (MCR)

Using 2-(^{3}H) glucose as tracer				Using (U-^{14}C) glucose as tracer			
Expt. No.	Turnover mg/min	MCR ml/min	Glucose Conc. mg/dl	Expt. No.	Turnover mg/min	MCR ml/min	Glucose Conc. mg/dl
FG II	15.0	110	14	FG I	25.4	149	17
FG VI	26.2	163	16	FG IV	15.4	178	9
FG VIII	31.7	167	19	FG V	20.6	86	24
FG IX	36.8	230	16	FG XIV	35.7	170	21
FG X	17.6	195	9	FG XV	48.4	194	25
FG XII	22.6	84	27	FG XVII	30.6	170	18
FG XIII	41.5	160	26				
Mean	27.3	158.4	18.1		29.3	157.8	18.9
SEM	3.7	18.5	2.4		4.8	15.5	2.4

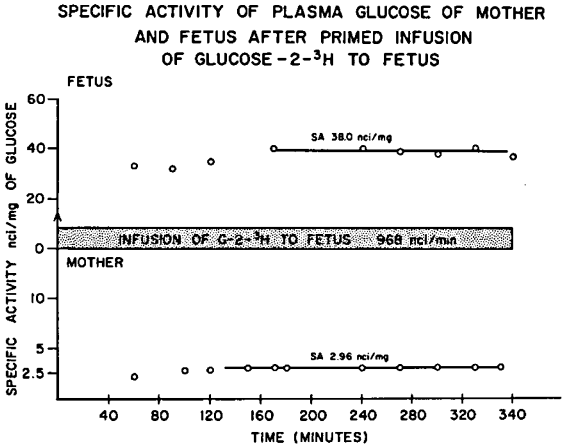

Figure 3

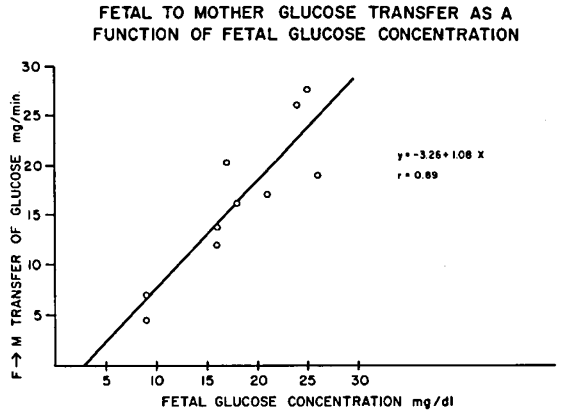

Figure 4

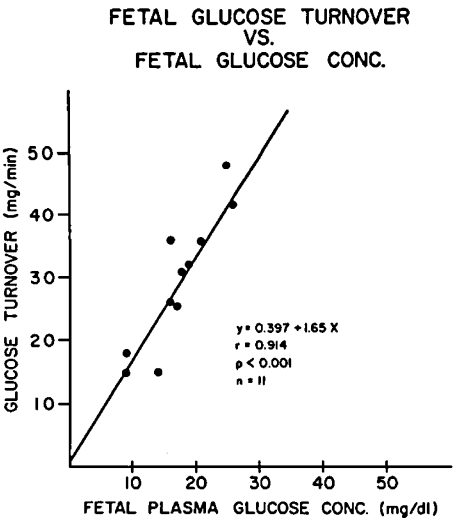

Figure 6

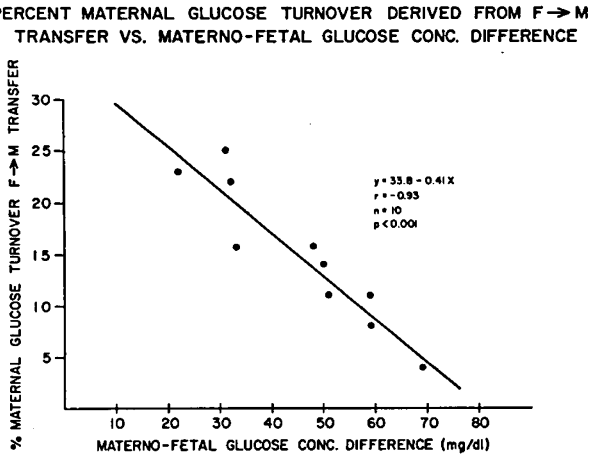

Figure 5

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