0031-3998/87/2204-0483$02.00/0
PEDIATRIC RESEARCH

Vol. 22, No. 4, 1987
Printed in U.S.A.

Glucose Utilization by the Placenta of Anesthetized Rats: Effect of Insulin, Glucose, and Ketone Bodies

A. LETURQUE, S. HAUGUEL, J. KANDE, AND J. GIRARD

Centre de Recherches sur la Nutrition, 92190 Meudon-Bellevue, France

ABSTRACT. Placental glucose metabolism and its regulation have been investigated *in vivo* in the rat using the radioactive 2-deoxyglucose technique. In the basal state, placental glucose utilization rates were similar on days 19 and 21 of gestation: 139 ± 5 and 155 ± 22 nmol/min/g at maternal blood glucose concentrations of 4.3 ± 0.1 and 4.2 ± 0.1 mmol/1. During hyperglycemic clamps, maternal glycemia was raised to 5.5 mmol/liter, a value similar to that during a meal in the rat. In this condition, the rate of placental glucose utilization at 19 days of gestation was increased by 85%. This was due not only to hyperglycemia but also to glucose-induced hyperinsulinemia. Indeed during hyperinsulinemic euglycemic clamps, placental glucose utilization showed a dose-response relationship to insulin (400 and 5000 μU/ml). At 21 days of gestation, placental glucose utilization was not affected by hyperglycemia or by hyperinsulinemia suggesting that in term placenta, glucose metabolism is no longer regulated. When 19-day pregnant rats were fasted for 48 and 96 h, the resulting low blood glucose and plasma insulin concentrations and the high ketone body concentrations induced, respectively, a 40 and 47% reduction of placental glucose utilization. The decrease in placental glucose utilization probably was due to both maternal hypoglycemia and long term adaptation to hyperketonemia. Indeed, the acute hyperketonemia in fed rats did not alter glucose utilization rate in placenta at 19 days of gestation. These data suggest that glucose metabolism in the preterm rat placenta is modulated *in vivo* by the maternal metabolic environment, particularly by maternal blood glucose and insulin concentrations. The preterm rat placenta is thus an insulin sensitive tissue. (*Pediatr Res* 22: 483–487, 1987)

Abbreviations

^{3}H-2DG, 2 deoxy[1^{3}H]glucose
ip, intraperitoneal

The placenta is an organ that is involved in the uptake and the transfer of energy substrates to the fetus. Both processes are dependent on placental blood flow and maternal substrate availability. The concentration of energy substrates in the maternal circulation affects the rate of fetal growth (1–4). In addition placental metabolism is an important determinant of normal fetal growth. The restriction of placental transfer of nutrients by reduction of placental size or placental blood flow reduces fetal growth (5–8). The function of the placenta in the nutrient transfer to fetuses has been extensively studied (review in Ref. 9). However, the contribution of different fuels to placental metabolism is not entirely clear (10).

The aim of the present study was to measure placental glucose utilization *in vivo* in the rat under various physiological conditions. Placental substrate availability was modified by maternal fasting and by inducing acute maternal hyperglycemia and hyperketonemia. Insulin sensitivity of the placenta was studied by using maternal hyperinsulinemic euglycemic clamps. The experiments were performed in 19- and 21-day pregnant rats to take into account the aging process in the placenta.

MATERIALS AND METHODS

Animals. Female rats of the Wistar strain bred in our laboratory were used. They were housed at 24° C with light from 07.00 to 19.00 h. They had free access to water and food pellets (U.A.R. 103, Epinay, France; carbohydate 65%, fat 11%, and protein 24% of total energy) unless otherwise stated. The rats were studied on day 19 and 21 of pregnancy. The stage of pregnancy was determined as described previously (11). Pregnant rats were anesthetized with pentobarbital (30 mg/kg body weight ip). One carotid artery was catheterized and a tracheotomy was performed. Body temperature was maintained at 38° C. Infusions were made through the maternal saphenous vein. Fetal blood was sampled via axillary vessels after maternal laparotomy (11).

In vivo measurements of the rate of 2-deoxyglucose accumulation by rat placenta. The method used was derived from the technique of Sokoloff *et al.* (12) and described previously (13). In brief, 30 μCi of ^{3}H-2DG 20 Ci/mmol (CEA, Saclay, France) were injected in a maternal vein. Maternal arterial blood was sampled at 1, 3, 5, 10, 15, 20, 30, 40, and 60 min after the injection. The measurement of specific activity was performed on blood samples (50 μl) deproteinized with $ZnSO_4/Ba(OH)_2$ and centrifuged. ^{3}H-2DG was determined using a scintillation counter Betamatic 2, Kontron, Velizy, France) and blood glucose concentration using glucose oxidase method (Boehringer, Meylan, France). The integral of specific activity ^{3}H-2DG/glucose was calculated over 60 min. Plasma insulin was determined by radioimmunoassay (14) and ketone bodies were measured enzymatically on aliquots of the last blood samples (15). After the last blood sampling, rats were killed by cervical dislocation and placentas were excised. The amount of ^{3}H-2DG-6-phosphate accumulated in the placenta was determined by differential precipitation in Somogyi reagent and in 6% HCl O_4 on aliquots of tissues digested for 1 h at 60° C in 1 M NaOH and neutralized.

In preliminary experiments, the specific activity ^{3}H-2DG/glucose was measured simultaneously in maternal and fetal blood. The difference between maternal and fetal integral of ^{3}H-2DG/glucose specific activity is the result of the discrimination of 2DG against glucose by the placenta because axillary blood of fetus represents efferent blood from placenta (16). The ratio of

Received March 2, 1987; accepted May 27, 1987.
Reprints requests Dr. A. Leturque, Centre de Recherches sur la Nutrition, 9 rue Jules Hetzel, 92190 Meudon-Bellevue, France.

the integral of maternal arterial blood ^{3}H-2DG/glucose to fetal blood ^{3}H-2DG/glucose was 0.87 ± 0.02 (n = 6).

Glucose utilization rate was calculated as the amount of ^{3}H-2DG-6-phosphate accumulated in the placenta divided by the integral of ^{3}H-2DG/glucose specific activity in the blood and by the discrimination constant.

$$\text{Glucose utilization} = \frac{^3\text{H-2DG 6 phosphate in placenta}}{0.87 \times \int_0^{60} \frac{^3\text{H 2DG}}{[\text{glucose}]} \text{ in arterial blood}}$$

The results were expressed in nmol of glucose utilized per min and per g of placenta. Placental glucose utilization rates were measured in steady state conditions for blood glucose concentration and glucose utilization during different metabolic situations, in the fed state and after 48 h or 96 h of maternal fasting and during euglycemic hyperinsulinemic clamps and hyperglycemic clamps as well as during β-hydroxybutyrate infusions to fed pregnant rats. Maternal euglycemic hyperinsulinemic clamp experiments (14, 17) were performed at two different insulin infusion rates: 0.4 and 3 U/kg/h, the euglycemia was maintained by an appropriate glucose infusion: 22 ± 3 and 49 ± 2 μmol/min, respectively, in 19-day pregnant rats. In 21-day pregnant rats infused with insulin at the rate of 3 U/kg/h an exogenous infusion of glucose at the rate of 41 ± 3 μmol/min was necessary to maintain euglycemia (Tables 1 and 2). The plateau of exogenous glucose infusion was achieved by 30–40 min and was maintained during the measurement of glucose utilization by ^{3}H-2DG technique. Maternal hyperglycemic clamp experiments were performed by infusing exogenous glucose at a rate of 37 ± 3 μmol/min in 19-day and 29 ± 3 μmol/min in 21-day pregnant rats in order to reach a steady state blood glucose concentrations of 5.5 mmol/liter. Plasma glucose concentrations were recorded every 5 min with a Yellow Springs Glucose Analyzer YSI 23A (Yellow Springs, OH). Steady state glucose concentrations and glucose infusion rates were reached within 15 min onward.

Sodium D-L β-hydroxybutyrate (Sigma, St Louis, MO) was infused during 2 h to fed pregnant rats at a rate of 5 μmol/h/g in order to raise the β-hydroxybutyrate concentration two-fold over basal values. Steady state maternal β-hydroxybutyrate concentrations (2–3 mmol/liter) were reached after 30 min onward (results not shown). The glucose utilization index was measured during the last hour of β-hydroxybutyrate infusion. This rate of β-hydroxybutyrate infusion was chosen since it did not increase lactatemia. In preliminary experiments maternal lactatemia was increased two-fold when β-hydroxybutyrate was infused at the rate of 10 μmol/h/g (result not shown).

Statistics. Results are presented as means ± SEM of six to nine pregnant rats. Statistically significant differences were assessed using non parametric Mann-Whitney test.

RESULTS

Effects of hyperglycemic clamp. In the basal state, placental glucose utilization was 139 ± 5 nmol/min/g on day 19 and 155 ± 22 nmol/min/g on day 21 of gestation (Fig. 1). Hyperglycemic clamps were performed to produce an increase of glycemia and insulinemia similar to that observed during a meal in the rat (18) (Tables 1 and 2). During hyperglycemic clamps a 85% increase in placental glucose utilization rate was observed in placenta from 19-day pregnant rats ($p < 0.01$) whereas no significant modification was obtained in placenta from 21-day pregnant rats (Fig. 1). The changes of fetal blood glucose and plasma insulin levels (Tables 1 and 2) could not explain the difference observed between 19- and 21-day placenta in the basal state as well as during clamp experiments.

Effects of insulin. The effect of two different plasma insulin levels were investigated during hyperinsulinemic euglycemic clamps performed in 19-day pregnant rats. The rate of placental glucose utilization was increased by 35% ($p < 0.05$) at physiological hyperinsulinemia (Table 1) and by 100% ($p < 0.01$) at maximal plasma insulin levels (Fig. 2; Tables 1 and 2). By contrast, placental glucose utilization rate was not significantly stimulated by maximal plasma insulin level during euglycemic hyperinsulinemic clamps in 21-day pregnant rats (Fig. 2; Tables 1 and 2).

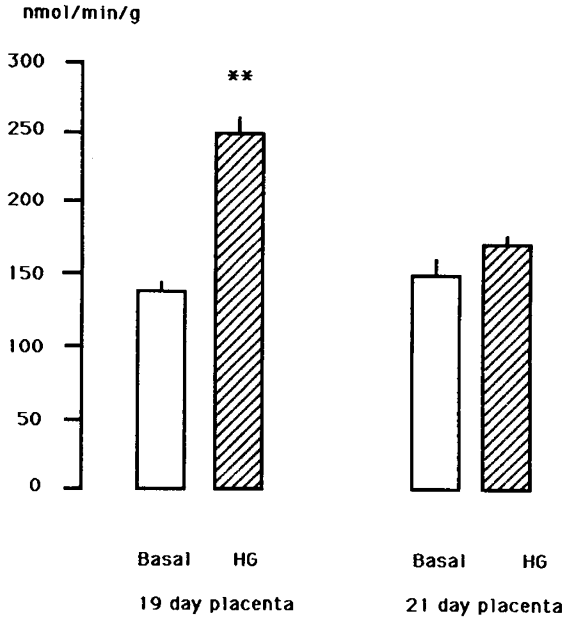

Fig. 1. Placental glucose utilization rate measured by the 2DG technique in 19-d and 21-day pregnant rats in the basal state ▨ and during hyperglycemic clamp experiments (*HG*) ▨. Values are the mean ± SEM of six rats. **$p < 0.01$ when compared with basal values.

Effect of fasting. Fasting was characterized by low blood glucose and by high blood ketone body concentrations in maternal and fetal circulations, whereas plasma insulin concentration was decreased only in the mothers (Table 3). After a fast of 48 or 96 h (Fig. 3), placental glucose utilization rates were decreased by 40% ($p < 0.01$) and 47% ($p < 0.01$) respectively.

Effect of acute hyperketonemia. To know whether the decrease in placental glucose utilization observed during maternal fasting could be due to the rise in blood ketone bodies, an acute elevation of maternal and fetal blood ketone body concentrations was performed. During β-hydroxybutyrate infusions to fed pregnant rats, placental glucose utilization rate remained unaltered 133 ± 22 nmol/min/mg (n = 6) (Table 3).

DISCUSSION

The 2DG-6-P accumulated in the placenta represents the amount of glucose utilized by the tissue since every moleculer of glucose which enters the cell is phosphorylated before its incorporation into glycogen or its oxidation. Nevertheless, this technique does not allow identification of the metabolic fate of glucose within the placenta. The rate of glucose metabolism in the placenta is highly dependent on simultaneous variations of uterine blood flow and maternal glucose concentration (19), and these two parameters are taken into account in the measurement of glucose utilization rate by the 2DG technique.

During a meal in the adult rat, the mean blood glucose concentration increases by 1.4 mmol/liter (18). This slight postprandial hyperglycemia could be sufficient to induce an increase in placental glucose utilization because of the high Km of glucose transport in the placenta (4, 20, 21). To test this hypothesis maternal hyperglycemic clamps were performed to increase maternal blood glucose by 1.4 mmol/liter. Indeed, the measurement of glucose utilization requires a steady state for glucose concentration and utilization achieved only during clamp experiments.

Table 1. *Blood glucose and plasma insulin concentrations in 19-day pregnant rats and their fetuses during various clamp experiments (maternal body wt: 332 ± 7, n = 24; fetal body wt: 2.05 ± 0.05 g, n = 24; placental wt: 0.39 ± 0.05, n = 24)**

	Basal state ($n = 6$)	Hyperglycemic clamp ($n = 6$)	Hyperinsulinemic clamp ($n = 6$)	
Maternal values				
Blood glucose (mmol/liter)	4.3 ± 0.1	5.8 ± 0.1†	4.2 ± 0.1	4.3 ± 0.1
Plasma insulin (μU/ml)	81 ± 15	397 ± 85†	450 ± 30†	4900 ± 500†
Fetal values				
Blood glucose (mmol/liter)	2.9 ± 0.3	4.1 ± 0.2†	2.9 ± 0.3	2.9 ± 0.3
Plasma insulin (μU/ml)	116 ± 10	215 ± 27†	116 ± 17	180 ± 32†

* Values are the mean ± SEM of n different rats.
† Difference significant for $p < 0.01$ when compared to basal state.

Table 2. *Blood glucose and plasma insulin concentrations in 21-day pregnant rats and their fetuses during various clamp experiments (maternal body wt: 360 ± 6 g, n = 24; fetal body wt: 5.01 ± 0.05 g, n = 24; placental wt: 0.42 ± 0.04 g, n = 24)**

	Basal state ($n = 9$)	Hyperglycemic clamp ($n = 8$)	Hyperinsulinemic clamp ($n = 7$)
Maternal values			
Blood glucose (mmol/liter)	4.2 ± 0.1	5.6 ± 0.2†	4.3 ± 0.1
Plasma insulin (μU/ml)	50 ± 10	164 ± 34†	5400 ± 600†
Fetal values			
Blood glucose (mmol/liter)	3.2 ± 0.2	4.6 ± 0.2†	3.2 ± 0.2
Plasma insulin (μU/ml)	380 ± 45	774 ± 94†	390 ± 120

* Values are the mean ± SEM of n different rats.
† Difference significant for $p < 0.01$ when compared to basal state.

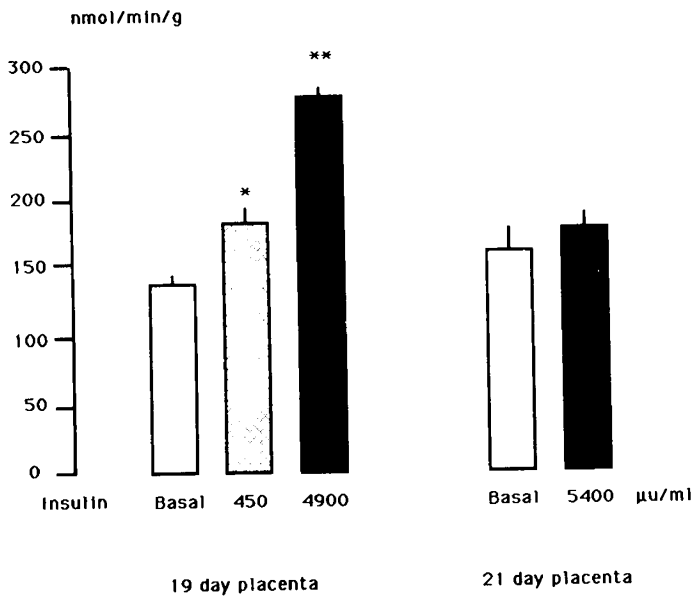

Fig. 2. Placental glucose utilization rate measured by the 2DG technique in 19-d and 21-day pregnant rats in the basal state □ and during euglycemic hyperinsulinemic clamp experiments performed at physiological ▨ and at maximal plasma insulin concentration ■. Values are the mean ± SEM of six rats. *$p < 0.05$, **$p < 0.01$ when compared with basal values.

Placental glucose utilization during hyperglycemic clamp was increased significantly on day 19 of pregnancy as a result of the enhanced blood glucose and plasma insulin concentrations.

Because during hyperglycemic clamps the effect of glucose and insulin cannot be discriminated, hyperinsulinemic euglycemic clamps were performed to test the effect of insulin per se. The effects of hyperinsulinemia on placental glucose utilization were characterized on day 19 of pregnancy by a 30% increase of physiological hyperinsulinemia (16) and by a 100% increase at the maximal concentration of insulin. Nevertheless, the stimulation of placental glucose utilization by insulin is relatively modest when compared to other insulin-sensitive tissues (13, 22, 23). The small proportion (10–20%) of trophoblast in the placenta (24) which represents the metabolically active cells could explain the relatively modest effect of insulin when expressed per unit weight of placenta. The effect of exogenous insulin on placental glucose uptake is observed only when blood glucose is maintained at basal levels since, when blood glucose is allowed to decrease, placental glucose uptake was not modified by insulin (25).

It has been shown that the placenta is endowed with numerous insulin receptors (26) and term human placentas are now commonly used to extract large amounts of insulin receptors (27). The placental receptors resemble insulin receptors of other insulin-sensitive tissues such as adipose tissue or liver (27) suggesting that insulin may play a role in the regulation of placental metabolic function. Furthermore the rat is a species with an hemochorial placenta in which the microvilli come into direct contact with maternal blood. Thus, a control of placental glucose metabolism by insulin is more likely to occur in a hemochorial placenta than in a epitheliochorial placenta such as is present in the sheep (28). It is noteworthy that on day 19 of gestation, the effect of insulin on placental glucose utilization is related to the maternal hyperinsulinemia since fetal insulinemia was not modified under the experimental conditions tested.

By contrast, on day 21 of pregnancy the placental glucose utilization rate was not stimulated during hyperglycemic clamps despite increases in blood glucose and plasma insulin levels. It should be noted that maternal plasma insulin concentration was increased by only 2-fold at this stage of pregnancy compared with the 6.5-fold increase on day 19 of pregnancy (29). Furthermore insulin had no significant effect on placental glucose utilization, as evidenced by the results observed in the presence of high insulin concentrations in both maternal and fetal circulations. These results are in agreement with data obtained in perfused human term placenta in which insulin has no effect on

Table 3. *Blood glucose, plasma insulin and blood ketone body concentrations in 19-day pregnant rats and their fetuses during fasting and during infusion of* DL *β-hydroxybutyrate (5 μmol/min/kg) to fed pregnant rats**

	Fed ($n = 6$)	48-h fasted ($n = 9$)	96-h fasted ($n = 7$)	β-hydroxybutyrate infusion ($n = 6$)
Maternal body wt (g)	340 ± 9	281 ± 6†	257 ± 6†	345 ± 12
Fetal body wt (g)	2.05 ± 0.05	1.75 ± 0.05†	1.70 ± 0.06†	2.04 ± 0.08
Placental wt (g)	0.39 ± 0.05	0.37 ± 0.04	0.38 ± 0.03	0.42 ± 0.02
Maternal values				
Blood glucose (mmol/liter)	4.3 ± 0.2	2.9 ± 0.2†	3.0 ± 0.2†	4.1 ± 0.1
Plasma insulin (μU/ml)	81 ± 15	39 ± 3†	35 ± 3†	91 ± 9
Blood ketone bodies (mmol/liter)	0.51 ± 0.12	3.6 ± 0.7†	3.7 ± 0.7†	2.5 ± 0.6†
Fetal values				
Blood glucose (mmol/liter)	2.9 ± 0.3	1.3 ± 0.2†	1.2 ± 0.2†	2.8 ± 0.3
Plasma insulin (μU/ml)	116 ± 10	101 ± 12	115 ± 12	95 ± 18
Blood ketone bodies (mmol/liter)	0.4 ± 0.1	4.3 ± 0.6†	3.6 ± 0.4†	1.5 ± 0.1†

* Values are the means ± SEM of n different rats.
† Difference significant for $p < 0.01$ when compared with fed state.

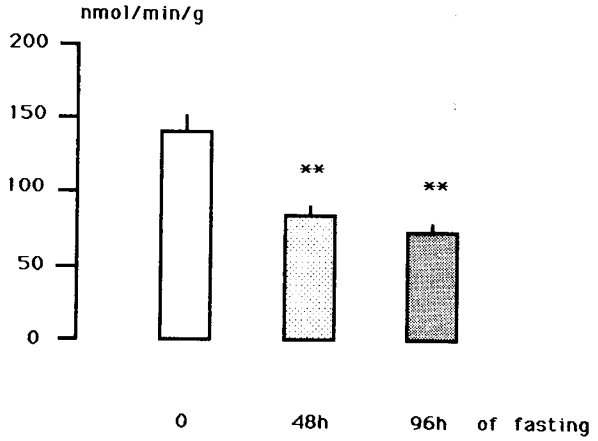

Fig. 3. Placental glucose utilization rate in 19-day pregnant rats in the basal state □ and after 48 h fasting ▨ or 96 h fasting ■. Values are the mean ± SEM of six to nine rats. **$p < 0.01$ when compared with basal value.

glucose transport and metabolism (30). These data suggest that term human and rat placentae are not appropriate models for studying the control of glucose metabolism, either because of an aging process or because of interference by the endocrine environment with placental metabolism at the time of parturition. A down regulation of glucose transport by steroid hormones has been observed *in vitro* in human microvillous placental membranes (21).

After a fast of 48 to 96 h placental glucose utilization decreased by 40–50%. This dramatic fall could be attributed to the 30% decrease in maternal blood glucose concentration (31), to a 50% reduction in placental blood flow (32), or to both factors. In addition, the 50% decrease in fetal blood glucose concentration also could contribute. It has been demonstrated in the sheep that umbilical glucose contributes to placental glucose utilization (33). The reduced placental glucose utilization was not associated with a decrease in placental weight. This is in agreement with the observation that there is a steady state of DNA synthesis in rat placenta from day 16 of pregnancy onward (34).

The availability of ketones also is important during fasting and ketones can be used as alternative energy substrates in various tissues. Indeed the placenta is well equipped with the enzymes necessary to oxidize ketones (35). It has been shown that slices of placenta can oxidize radioactive β-hydroxybutyrate into CO_2 in a medium containing low glucose and high β-hydroxybutyrate concentrations leading to a decreased glucose oxidation (35, 36). The perfusion of β-hydroxybutyrate into 19-day pregnant rats acutely increased blood ketone body concentrations to a level slightly lower than those observed after fasting and this increase induced no modification of placental glucose utilization. Thus, in conditions of normoglycemia, the placenta utilizes glucose as a primary energy substrate rather than ketone bodies.

The present studies indicate that the rat placenta changes its rate of glucose utilization when exposed *in vivo* to conditions of mild hyperglycemia or to fasting. These alterations depend mostly on changes in maternal blood glucose concentrations. In addition, the hemochorial rat placenta is an insulin-sensitive organ before term.

Acknowledgments. The authors are indebted to D. Chamereau for the care of the animals and to I. Coquelet and M. Fernandez for preparing the manuscript.

REFERENCES

1. Pedersen J 1977 Placenta in diabetics. In: The Pregnant Diabetic and her Newborn. Williams & Wilkins, Baltimore, pp 106–122
2. Meschia G 1978 Substrate availability and fetal growth. In: Naftolin F (ed) Abnormal Fetal Growth: Biological Bases and Consequences. Dahlem Konferenzen, Berlin, pp 221–228
3. Lederman SA, Rosso P 1981 Effects of fasting during pregnancy on maternal and fetal weight and body composition in well nourished and undernourished rats. J Nutr 111:1823–1832
4. Simmons MA, Battaglia FC, Meschia G 1979 Placental transfer of glucose. J Dev Physiol 1:227–243
5. Alexander G 1964 Studies on the placenta of the sheep (ovis aries L.): placental size. J. Reprod Fertil 7:289–305
6. Wiggleworth JS 1964 Experimental growth retardation in the fetal rat. J Pathol Bacteriol 88:1–13
7. Creasy RK, Barrett CT, DeSwiet M, Kahanpää VV, Rudolph AM 1972 Experimental intrauterine growth retardation in the sheep. Am J Obstet Gynecol 112:566–573
8. Robinson JS, Hart IC, Kingston EJ, Jones CT, Thorburn GD 1980 Studies on the growth of fetal sheep. The effects of reduction of placental size on hormone concentration in fetal plasma. J Dev Physiol 2:239–248
9. Munro HN 1983 The placenta in nutrition. Ann Rev Nutr 3:97–124
10. Meschia G, Battaglia FC, Hay WW, Sparks JS 1980 Utilization of substrates by the ovine placenta in vivo. Fed Proc 39:245–249
11. Girard JR, Cuendet GS, Marliss EB, Kervran A, Rieutort M, Assan R 1973 Fuels, hormones and liver metabolism at term and during the early postnatal period in the rat. J Clin Invest 52:3190–3200
12. Sokoloff L, Reivich M, Kennedy C, Des Rosiers MH, Patlak CS, Pettigrew KD, Sakurada O, Shinohara M 1977 The [^{14}C] deoxyglucose method for the measurement of local cerebral glucose utilization: theory procedure and normal values in the conscious and anesthetized albino rat. J Neurochem 28:897–916
13. Ferré P, Leturque A, Burnol A-F, Girard J 1985 A method to quantify glucose utilization *in vivo* in skeletal muscle and white adipose tissue of the anesthetized rat. Biochem J 228:103–110
14. Leturque A, Burnol A-F, Ferré P, Girard J 1984 Pregnancy-induced insulin resistance in the rat: assessment by glucose clamp technique. Am J Physiol 246:E25–E31
15. Williamson DH, Mellanby J, Krebs HA 1962 Enzymic determination of 3-hydroxybutyrate and acetoacetate in blood. Biochem J 82:90–96
16. Leturque A, Ferré P, Burnol A-F, Girard J 1986 Glucose utilization rates and

insulin sensitivity in tissues of virgin and pregnant rats. Diabetes 35:172–177
17. De Fronzo RA, Tobin JD, Andres R 1979 Glucose clamp technique: a method for quantifying insulin secretion and resistance. Am J Physiol 237:E214–E223
18. Berthoud HR 1984 The relative contribution of the nervous system, hormones and metabolites to the total insulin response during a meal in the rat. Metabolism 33:18–25
19. Longo LD 1981 The interrelations of maternal fetal transfer and placental blood flow. Placenta 2 (suppl):45–64
20. Hauguel S, Challier JC, Desmaizieres V 1986 Placental glucose uptake transfer and utilization as functions of maternal glucose concentration. Pediatr Res 17:729–732
21. Johnson LW, Smith CH 1980 Monosaccharide transport across microvillous membrane of human placenta. Am J Physiol 238:C160–C168
22. Kraegen EW, James DE, Jenkins AB, Chisholm DJ 1985 Dose response curves for *in vivo* insulin sensitivity in individual tissues in the rat. Am J Physiol 248:E353–E362
23. Hom FG, Goodner CJ 1984 Insulin dose-response characteristics among individual muscle and adipose tissues measured in the rat in vivo with ^{3}H-2-deoxyglucose. Diabetes 33:153–159
24. Munro HN 1980 Placenta in relation to nutrition. Fed Proc 39:236–238
25. Testar X, Lasuncion MA, Chieri R, Herrera E 1985 Effects of exogenous insulin on placental transfer of maternal glucose to the rat fetus. Diabetologia 28:743–748
26. Posner BI 1974 Insulin receptors in human and animal placental tissue. Diabetes 23:209–214
27. Khan RC, Crettaz M 1985 Insulin receptors and the molecular mechanism of insulin action. Diabetes Metab Rev 1:5–32
28. Hay WW, Spark JW, Gilbert M, Battaglia FC, Meschia G 1984 The effect of insulin on glucose uptake by the maternal hindlimb and uterus and by the fetus in conscious pregnant sheep. J Endocrinol 100:119–124
29. Kervran A, Randon J, Girard JR 1979 Dynamics of glucose induced plasma insulin increase in the rat fetus at different stages of gestation. Biol Neonate 35:242–248
30. Challier JC, Hauguel S, Desmaizieres V 1986 Effect of insulin on glucose uptake and metabolism in the human placenta. J Clin Endocrinol Metab 62:803–807
31. Girard J, Ferré P, Gilbert M, Kervran A, Assan R, Marliss EB 1977 Fetal metabolic response to maternal fasting in the rat. Am J Physiol 232:E456–E463
32. Gilbert M, Leturque A 1982 Fetal weight and its relationship to placenta blood flow and placental weight in experimental intrauterine growth retardation in the rat. J Dev Physiol 4:237–246
33. Hay WW, Sparks JN, Battaglia FC, Meschia G 1984 Maternal-fetal glucose exchange: necessity of a three-pool model. Am J Physiol 246:E528–E534
34. Gewold IH, Barrett C, Warshaw JB 1983 Placental growth and glycogen metabolism in streptozotocin-diabetic rats. Pediatr Res 17:587–591
35. Shambaugh GE, Mrozak SC, Freinkel N 1977 Fetal fuels. I. Utilization of ketones by isolated tissues at various stages of maturation and maternal nutrition during late gestation. Metabolism 26:623–635
36. Shambaugh GE, Koehler RA, Freinkel N 1977 Fetal fuels II: contributions of selected carbon fuels to oxidative metabolism in rat conceptus. Am J Physiol 233:E457–E461

Announcements

Annual Meetings

The Society for Behavioral Pediatrics will hold its 6th Annual Meeting in Washington, D.C., on May 1–2, 1988, in conjunction with the SPR/APS/APA meetings. We invite you to submit abstracts of research papers for consideration for presentation at the scientific sessions. ABSTRACTS MUST BE RECEIVED BY DECEMBER 15, 1987. *For further information and abstract forms, please contact:* Ms. Noreen Spota, SBP Business Administrator, 241 East Gravers Lane, Philadelphia, PA 19118, (215) 248-9168.

The annual meeting of the Southern Society for Pediatric Research will be held February 3–5, 1988, at New Orleans Hyatt Regency Hotel, New Orleans, LA. *For information contact:* Richard F. Jacobs, M.D., Secretary-Treasurer, Southern Society for Pediatric Research, Arkansas Children's Hospital, 800 Marshall Street, Little Rock, AR 72202, (501) 370-1416.