Circulating Metabolite Utilization by Periuterine Adipose Tissue In Situ in the Pregnant Rat

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To study the use of glucose for lipid synthesis by the periuterine adipose tissue in situ, ^{14}C-glucose was infused through the left uterine artery of anesthetized, fed pregnant and virgin control rats. A greater amount of ^{14}C-lipid always appeared in the adipose tissue from the left uterine horn than in the tissue from the right uterine horn, indicating direct utilization of the infused ^{14}C-glucose by the tissue. Glucose utilization for both glyceride glycerol and fatty acid synthesis increased from day 0 (virgin rats) to day 20 of gestation and then decreased dramatically on day 21. In virgin and 12-day pregnant rats, glucose was incorporated into either lipidic moiety at similar rates, whereas in late pregnant rats glucose utilization for glyceride glycerol synthesis was four to five times greater than for fatty acids. The utilization of circulating fatty acids and the lipoprotein triglyceride-derived fatty acids was studied by infusing ^{14}C-palmitate or ^{14}C-triolein–labeled very–low-density lipoprotein (VLDL) through the left uterine artery in both virgin and 20-day pregnant rats. Incorporation of fatty acids from either one of these plasma sources was significantly higher in the pregnant than in virgin rats. This high amount of fatty acid acquisition did not account for the very active glyceride glycerol synthesis observed in pregnant rats and can only be explained by the intracellular reesterification of some lipolitic fatty acids. The results suggest a highly accelerated triacylglycerol/fatty acid substrate cycle in adipose tissue during late pregnancy, which would allow active esterification (contributing to fat accumulation) and responsive lipolysis (permitting rapid fat mobilization) by the mother.

DURING GESTATION, the maternal body fat accumulation in both humans and rats[1-3] is clearly related to food intake, since it does not occur in food-restricted[2,3] or food-deprived rats.[1] Recent carcass analysis studies showed that this increase starts in the rat in the second half of pregnancy and lasts until the 19th gestational day and then it declines between day 19 and labor.[4] At this stage of late gestation in the rat, maternal metabolic changes tend to favor the depletion rather than the accumulation of fat, as indicated by the reduction in adipose tissue lipoprotein lipase activity[5,6] and the increase in adipose tissue lipolysis.[7,8] Although measuring the rate of ^3H_2O incorporation into fatty acids by the parametrial adipose tissue shows maternal lipogenesis to be reduced,[9] the utilization of different substrates (ie, glucose, glycerol) for lipid synthesis in in vitro preparations has been reported to be reduced,[10,11] unaffected,[12] or slightly enhanced.[7,8] It has therefore been suggested that during the last days of gestation in the rat augmented food intake[3,13] and adipose tissue glyceride-glycerol synthesis[7,8,11] counteract the catabolic tendency of maternal adipose tissue, and protect against greater depletion of fat stores. Redistribution of blood flow to organs, especially the uterus,[14,15] as well as the changes in plasma metabolite concentration that take place during gestation,[16,17] could affect the actual availability of substrates for adipose tissue; therefore, in vivo experiments are required to examine the role of these factors on maternal lipidic modifications throughout gestation.

In the present work, we study the direct incorporation of different metabolites into lipids by periuterine adipose tissue in situ after different days of gestation in the rat, using a technique we have recently described.[18] The technique consists in infusing ^{14}C-labeled substrates through the left uterine artery so that the periuterine adipose tissue on the left side receives the infused substrate directly, whereas the right side receives the substrate after it has been circulated through the entire rat. Comparison of the radioactivity present in periuterine adipose tissue lipids from either side and adequate correction by specific activity and artery blood flow allows estimation of the utilization of the infused substrate by the tissue.[18] In this work, we have determined the utilization of glucose for lipogenesis and glyceride glycerol synthesis, as well as the incorporation of fatty acids from both very–low-density lipoprotein (VLDL)-triglycerides and circulating free fatty acids (FFA) by periuterine adipose tissue in fed virgin, and mid- and late-pregnant rats.

MATERIALS AND METHODS

Perfusion of the Left Uterine Horn

Virgin female Wistar rats were maintained in a light- (12-hour on-off cycles) and temperature- (22 ± 2°C) controlled room and fed a standard chow diet ad libitum (Panlab, Barcelona, Spain). Rats were mated when weighing 170 to 190 g, and studied on days 0, 12, 20, or 21 of gestation (estimated by the appearance of spermatozoids in vaginal smears). Rats were anesthetized with sodium pentobarbital (33 mg/kg body weight, dissolved in 0.9% NaCl, intravenously) and subjected to the surgical procedure already described.[18,19] In short, after laparatomy, the hypogastric trunk, superior gluteal, superior external pudendal, and the deep circunflex arteries of the left side were clamped. A PE-10 cannula (ID 0.011 in, OD 0.024 in, Intramedic, Parsippany, NJ) was introduced countercurrent into the left external iliac artery to the level of the left uterine artery. After surgery, the abdomen was closed and a solution of 0.9% NaCl was immediately infused at the

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Supported by Grants No. 2168/83 and 0451/84 from the Comisión Asesora de Investigación Científica y Técnica, Spain.

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0026-0495/91/4005-0016$03.00/0

rate of 12.5 μL/min by means of a peristaltic pump. After 20 minutes of infusion, the medium was changed to 0.9% NaCl supplemented, with 10 μCi/250 μL of D-(U-^{14}C)-glucose (specific activity, 257 mCi/mmol; Radiochemical Center, Amersham, UK). When ^{14}C-palmitate was the infused tracer, 3 to 4 μCi of (1-^{14}C)-palmitate (sodium salt; specific activity, 51.8 mCi/mmol; Radiochemical Center) was dissolved in 250 μL of 6% fatty acid-poor serum bovine albumin, pH 7.4, and infused to each rat at a rate of 12.5 μL/min for 20 minutes. In other experiments using ^{14}C-VLDL as the infused tracer, human VLDL was obtained from pooled sera by ultracentrifugation at d = 1.006 g/mL in a Beckman 50.2 Ti rotor (Palo Alto, CA), at 40,000 rpm, for 18 hours, at 8°C. The VLDL was labeled by incubation with glycerol tri-(1-^{14}C)oleate (specific activity, 66 μCi/6 mg; Radiochemical Center) previously adsorbed to cellite, and filtered as described.[20] Efficiency of the labeling process was 5% to 8%. Approximately 2 μmol (0.3 to 0.5 μCi) of ^{14}C-labeled VLDL-triglyceride in 500 μL of 0.9% NaCl was infused to each rat in 20 minutes.

After infusion, blood was collected from the abdominal aorta with heparinized syringes. The periuterine adipose tissue from the left and right horns was dissected, thoroughly rinsed with 0.9% NaCl, and frozen in liquid N_2. Weighed aliquots of the tissue from each side were used for lipid extraction with choloroform-methanol 2:1 (by vol)[21] and fractionation as described elsewhere.[22] Radioactivity measurements were performed in a xylene/Triton X-100/PPO/POPOP-based scintillation cocktail, with a counting efficiency that was always greater than 93%. Plasma was separated immediately after blood collection and aliquots were deproteinized with 10% $HClO_4$ and neutralized with saturated $KHCO_3$. Protein-free supernatants were used for glucose.[23] Plasma FFA concentration was estimated by using a colorimetric method,[24] and triglycerides were determined enzymatically with a commercial kit (Menarini, Firenze, Italy) using glycerol as standard. Finally, plasma insulin was determined[25] with a rat-specific radioimmunoassay kit that was generously provided by Novo Industri A/S (Copenhagen, Denmark).

Determination of Blood Flow to the Uterine Horn

Blood flow to the uterine horn was determined in other animals kept under the same environmental and experimental conditions as above. In addition to the cannula placed in the left external iliac artery, two other polyethylene catheters were inserted to each animal, one in the right carotid artery and the second in the right femoral artery.[15] One hundred thousand ^{99m}Tc-labeled albumin microspheres (23 to 45 μm, Sovin Biomedica, SpA, Saluggia, Italy) in 1 mL 10% dextran, 0.1% Tween-80, were injected via the carotid artery into the heart over a period of 30 seconds by means of a multichannel peristaltic pump. Simultaneously, saline was being infused at 12.5 μL/min via the left iliac artery and blood was withdrawn from the right femoral for 90 seconds at a rate of approximately 0.8 mL/min. The rats were killed, the left uterine horn was excised, and the radioactivity was counted after removing the fetuses (if present). Blood flow to the left uterine horn was calculated by comparing its radioactivity to that present in the blood aliquot obtained from the right femoral artery, as described by Rosso and Kava.[14]

Expression of the Results and Calculations

An aliquot of the tracer solution to be administered was always counted to determine the total radioactivity (TR) given to each animal. All radioactivity values in plasma and tissues were corrected by a factor of 1×10^6/TR to obtain the cpm value for each parameter. In this way, TR was always considered to be 1×10^6 cpm. Results were expressed as mean ± SEM and statistical comparisons between groups were done with the Student's *t* test. The utilization by the periuterine adipose tissue of the infused metabolite for lipid synthesis was calculated by the following formula: Metabolite converted to lipids (nmol/g fresh tissue weight per min) = (Lipids*L − Lipids*R) × (Met) × F/Met*, where Lipids* denotes the labeled lipids (cpm/g) in left (L) and right (R) periuterine adipose tissue, Met is the arterial plasma concentration of the infused metabolite, Met* is the radioactivity of the infused metabolite (always corresponding to 1×10^6), and F is the estimated blood flow to the left uterine horn. An example of calculation to estimate glucose utilization in lipid synthesis by the periuterine adipose tissue in virgin rats has been given elsewhere.[18]

RESULTS

Experiments were conducted to study comparatively the utilization of glucose in lipid synthesis by the periuterine adipose tissue in virgin and 12-, 20-, and 21-day pregnant rats. As shown in Table 1, after the infusion with ^{14}C-glucose through the left uterine artery, the appearance of the ^{14}C-labeled glyceride glycerol and the fatty acids was significantly higher in periuterine adipose tissue from the left side than in the tissue from the right uterine side, as a result of the direct utilization of ^{14}C-glucose by the periuterine adipose tissue as source of α-glycerol phosphate for acylglycerol synthesis and of acetyl-CoA for lipogenesis. The magnitude of the differences in radioactivity between the left and the right uterine sides were higher on days 12 and 20 than on day 0 (virgins) or 21, suggesting an increased utilization of glucose in lipid synthesis on these days of gestation. However, corrections for the dilution of the tracer in the blood irrigating the left uterine horn should be made before making the intergroup comparisons. In the present experimental approach, tracer dilution in the left

Table 1. Levels of ^{14}C-Labeled Lipids in Periuterine Adipose Tissue From Virgin and Pregnant Rats After a 20-Minute Infusion With D-(U-^{14}C)Glucose Through the Left Uterine Artery

	cpm in ^{14}C-Labeled Lipids/g Fresh Tissue			
	^{14}C-Glyceride Glycerol		^{14}C-Fatty Acids	
Rats	Left Side	Right Side	Left Side	Right Side
Virgin	2,810 ± 460	504 ± 218*	2,558 ± 379	342 ± 156†
12-day pregnant	11,516 ± 1,267	1,015 ± 188‡	10,222 ± 3,354	458 ± 104†
20-day pregnant	9,007 ± 2,491	188 ± 46†	1,577 ± 425	25 ± 8*
21-day pregnant	1,304 ± 319	140 ± 38†	319 ± 115	34 ± 8*

NOTE. Values correspond to mean ± SEM of four to six rats per group, and were corrected by considering 1×10^6 as the total radioactivity of each tracer administered to each rat.

Statistical comparisons between tissues from the left and the right sides of each parameter: *$P < .05$; †$P < .01$; ‡$P < .001$.

uterine artery is equal to the blood flow through the artery times the arterial concentration of the corresponding metabolite and divided into the amount of infused radioactivity.[18] Blood flow was determined by infusing ^{99m}Tc-labeled microspheres to other rats under the same experimental conditions as those used to infuse ^{14}C-glucose. Blood flow to the left uterine horn in virgin rats was 0.158 ± 0.012 mL/min (n = 10). In 12-day pregnant rats, blood flow to the uterine horn was 0.44 ± 0.04 mL/min (n = 10), which was significantly higher than in virgins ($P < .001$). In late-pregnant rats, blood flow through the uterine artery was found to be a function of the number of fetal-placental units present in the uterine horn (P) as follows: (1.03 ± 0.13) × P mL/min (n = 14) in 20-day pregnant rats and (1.12 ± 0.14) × P mL/min (n = 12) in 21-day pregnant rats. According to these observations, estimated blood flows (in mL/min) through the left uterine artery in the rats infused with ^{14}C-glucose are: 0.158 in virgin rats; 0.44 in 12-day pregnant rats; 1.03 × P in 20-day pregnant rats, and 1.12 × P in 21-day pregnant rats (P represents the number of placentas), respectively. On the other hand, the arterial plasma glucose concentration was significantly lower in both 12-, 20-, and 21-day pregnant rats than in virgin rats (see Fig 1 note). Therefore, we estimate that the ^{14}C-glucose infused in the left uterine artery was approximately 2, 35 or 40 times more diluted in gestating rats on the 12th, 20th, and 21st days, respectively, than in the virgin rats.

Taking into account the dilution of the tracer in the left uterine artery and differences in the amount of radioactivity incorporated into the lipids in the left and the right uterine horns (Table 1), we estimated glucose flux into glyceride glycerol and fatty acids by the periuterine adipose tissue in ng atoms of $C \cdot g^{-1} \cdot min^{-1}$. Results are represented in Fig 1, which shows that the most obvious change in lipid synthesis from glucose during gestation is the tremendous increase in glyceride glycerol production. This parameter was already increased at day 12 as compared with controls and peaked on day 20 when it reached a value over 100 times greater than in virgin rats. After that, on day 21, the utilization of glucose for glyceride glycerol synthesis decreased dramatically. Similarly, glucose utilization for fatty acid synthesis progressively increased from day 0 to 12 and then from day 12 to 20 of gestation before decreasing on day 21.

In both virgin and 12-day pregnant rats, glucose was incorporated into either lipidic moiety at similar rates, whereas in late pregnancy glucose utilization for glyceride glycerol synthesis was four to five times greater than for fatty acids (Fig 1). These data suggest that, during late gestation, fatty acid esterification rather than synthesis is favored. To test this possibility directly, 20-day pregnant rats and age-matched virgin controls were infused through the left uterine artery with either ^{14}C-palmitate or ^{14}C-triolein–labeled VLDL. The appearance of ^{14}C-lipids in periuterine adipose tissue from the left and the right sides, as well as the arterial concentration of fatty acids and triglycerides, were evaluated so as to estimate both palmitate and VLDL-triolein utilization by the tissue. As shown in Table 2, ^{14}C-lipids appearing in adipose tissue from the left side were always higher than in tissue from the right

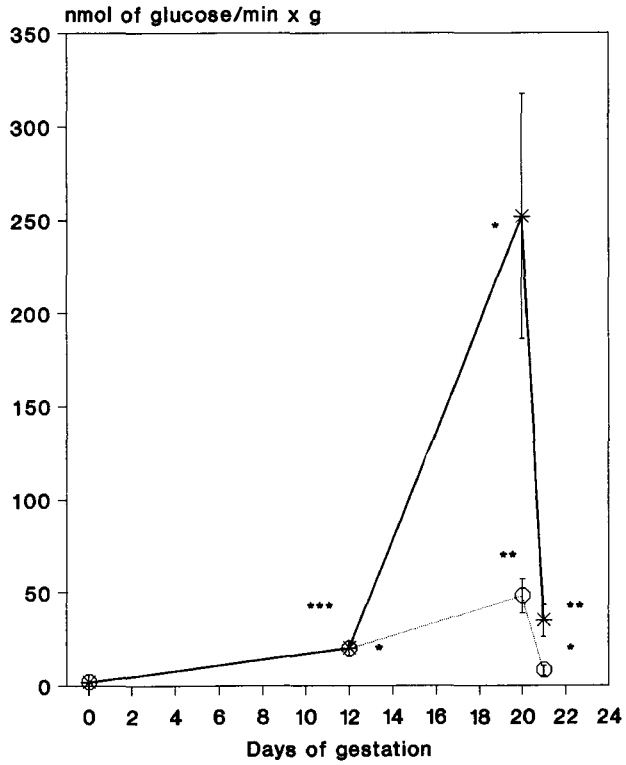

Fig 1. Glucose utilization for fatty acid (○ · · · · · · · · ○) and glyceride glycerol (✱——✱) synthesis by periuterine adipose tissue during gestation in the rat. Values correspond to mean ± SEM of four to six rats per group. The estimation of glucose utilization for glyceride glycerol or fatty acid synthesis takes into account the tissue ^{14}C-lipid values and the arterial plasma glucose concentrations shown in Table 1, as well as the estimated blood flow through the left uterine artery. Statistical comparisons between virgin and pregnant rats: *$P < .05$; **$P < .01$; ***$P < .001$. Arterial plasma concentrations of glucose (mmol/L) were: virgins, 5.8 ± 0.2; 12-day pregnant, 4.3 ± 0.1; 20-day pregnant, 5.0 ± 0.3; and 21-day pregnant, 4.7 ± 0.3. Estimated blood flow values used were: 0.158 mL/min in virgin rats; 0.439 mL/min in 12-day pregnant rats; 6.4 ± 0.7 mL/min in 20-day pregnant rats; and 7.6 ± 0.9 mL/min in 21-day pregnant rats.

side, indicating that in our in vivo preparation circulating palmitate, as well as VLDL-triolein, was efficiently incorporated by the tissue. Fatty acid incorporation by the tissue was estimated by considering the dilution of the tracer and the differences in ^{14}C-lipids in the left and the right uterine horns, as before. Plasma concentration and blood flow values are indicated in the note to Table 2. As shown in Table 2, the incorporation of circulating free palmitate into the lipids in the periuterine adipose tissue was significantly higher (approximately eight times) in the 20-day pregnant rats than in the virgin ones. The utilization of lipoprotein-triolein was also estimated to be over 15 times greater in pregnant than in virgin rats (Table 2). It is worth mentioning that the last results are expressed in nmol of triolein, and so, if one considers that three fatty acids can result from the hydrolysis of one triglyceride molecule, actual fatty acid incorporation from circulating VLDL is numerically three times greater than what is shown in Table 2. These data suggest that both circulating FFA and fatty

Table 2. Utilization by the Periuterine Adipose Tissue of ^{14}C-Palmitate or ^{14}C-Triolein–Labeled VLDL Infused Through the Left Uterine Artery in Virgin and 20-Day Pregnant Rats

	^{14}C-Total Lipids (cpm/g Fresh Tissue)		Plasma FFA Concentration (μmol/L)	Palmitate Utilization (nmol/g · min)
	Left Side	Right Side		
^{14}C-palmitate infusion				
Virgin	68,984 ± 12,948	1,351 ± 110†	517 ± 149	5.2 ± 1.1
20-day pregnant	20,333 ± 9,406	4,136 ± 2,024*	947 ± 243	42.1 ± 9.7‡
			Plasma TG Concentration (μm)	Triolein Utilization (nmol/g · min)
^{14}C-triolein–labeled VLDL infusion				
Virgin	23,825 ± 5,122	3,283 ± 1,534†	1,071 ± 144	3.4 ± 0.6
20-day pregnant	6,560 ± 1,325	1,112 ± 312*	2,738 ± 568‡	57.1 ± 16.2‡

NOTE. Radioactivity values were corrected by considering 1×10^6 cpm as the radioactivity of each tracer administered to each rat. Values correspond to mean ± SEM of four virgin and seven 20-day pregnant rats. Statistical comparisons between tissues from the left and the right side: *$P < .05$; †$P < .01$. Statistical comparisons of the plasma substrate concentration or of substrate utilization between the virgin and the 20-day pregnant rats: ‡$P < .05$. Estimated blood flows through the left uterine artery were 0.158 mL/min in virgin rats and 4.8 ± 0.3 mL/min in 20-day pregnant rats. Palmitate or triolein utilization by the tissue was estimated using the ^{14}C-lipid values, blood flow, and arterial plasma concentration as described in Materials and Methods.

acids from VLDL-triglycerides are major contributors to active periuterine adipose tissue esterification in the rat during late pregnancy. In an attempt to compare the relative importance of endogenously synthesized fatty acids versus exogenous fatty acids in esterification, we could express the amount of glucose use for esterified fatty acid synthesis as nmol of 16-C fatty acid, which gives values of 0.7 nmol/g · min in virgin rats and 16 nmol/g · min in 20-day pregnant rats.

Finally, and to better understand the changes in the utilization of lipogenic substrates and the incorporation of circulating lipids by the periuterine adipose tissue during gestation, we measured the plasma radioimmunoassay-insulin concentration in our rats. It was found to be 14.9 ± 1.4 μU/mL in virgin rats and 27.7 ± 4.7, 34.5 ± 4.8, and 20.9 ± 1.4 μU/mL in 12-, 20- and 21-day pregnant rats, respectively. All these values were significantly higher than in virgin rats ($P < .05$).

DISCUSSION

Infusion through the left uterine artery of radioisotopic-labeled substrates at high specific activity permits demonstration of direct metabolic utilization by the periuterine adipose tissue of any substrate for lipid synthesis.[18] This experimental approach has been also used by us to study the placental transfer of metabolites from mother to fetus.[19,26-29] The higher amount of radioactivity present in lipids extracted from the adipose tissue from the left horn rather than from the right uterine horn after infusion of ^{14}C-labeled substrate through the left uterine artery, reflects the direct utilization of the substrate by the tissue for lipid synthesis. Therefore, correcting the data by the dilution of the tracer in blood circulating through the left uterine artery (by multiplying by the arterial concentration of the tracer times the blood flow through the artery), an estimation of the actual utilization of the infused substrate (in mol/min) by the tissue can be obtained.[18] The technique has been validated in virgin rats[18] and, in the present study, it has been used to study the utilization of glucose and fatty acids by periuterine adipose tissue in pregnant rats.

Besides directly demonstrating that periuterine adipose tissue utilizes significant amounts of glucose for lipid synthesis during gestation, one major observation of the present study is the steep increase in glyceride glycerol formation in the adipose tissue of late pregnant rats as compared with that seen in virgins. Glucose utilization for this purpose was 100 times higher in 20-day pregnant rats than in the virgin controls (Fig 1). Globally, there was a progressive increase in glyceride glycerol formation from glucose during pregnancy until day 20, followed by a dramatic decrease on day 21, although glyceride glycerol formation still maintained a level that was much greater than the one found in virgin rats. These observations agree with previous results showing accelerated incorporation in vitro of the glucose or the glycerol into glyceride glycerol by lumbar fat from late-pregnant rats.[7,8]

The pattern of fatty acid synthesis from glucose was similar, but not identical, to the pattern of glucose use for glyceride glycerol synthesis, with a slow increase until day 20 and then a rapid decrease on day 21. These results accord with the variation of fat mass[4,30,31] and with the two phases of adipose tissue metabolism during gestation described by others.[9,11] The lipid synthesis from glucose in the adipose tissue observed here parallels the changes in plasma insulin that take place during gestation, so it could be simply considered as an insulin effect on glucose disposal by the tissue.[32] However, other factors must be examined to explain the faster incorporation of glucose into glyceride glycerol than into fatty acids that was clearly seen during mid and late gestation. Actually, and although both the virgin and the 12-day pregnant rats used glucose at similar rates for glyceride glycerol and fatty acid synthesis, the rates were highly altered at late gestation, above all on day 20 (Fig 1), when glucose utilization for glyceride glycerol synthesis was about five times higher than for fatty acids. Assuming complete esterification of sn-glycerol 3-phos-

phate with 3 fatty acids, even in the case that other substrates could contribute to lipogenesis as much as glucose, the imbalance between the fatty acid and glyceride glycerol synthesis rates is still patent in the 20-day pregnant rat. Where do the rest of the fatty acids that are needed for esterification come from? We have found that plasma-derived fatty acids account for at least part of the increased esterification. In fact, periuterine adipose tissue uptake of both palmitic acid and VLDL-triolein were much higher in the 20-day pregnant rat than in the virgin rat. Enhanced fatty acid uptake from circulating VLDL-triglycerides apparently contrasts with the reduced lipoprotein lipase activity previously found in adipose tissue from late pregnant rats.[5,6,33] However, the physiologically high VLDL concentration in the pregnant rat may overcome low lipoprotein lipase activity, since the enzyme is not saturated at this triglyceride concentration.[34] In fact, Humphrey et al[35] observed that the flux of plasma triglycerides was two times greater in the 21-day pregnant rat than in the virgin rat, even when the fractional catabolic rate of infused ^{14}C-labeled chylomicrons was halved[35] and postheparin plasma lipoprotein lipase activity was diminished in the pregnant as compared with the virgin rat.[13] Thus, hypertriglyceridemia in the pregnant rat probably favors a higher absolute triglyceride hydrolitic rate in the periuterine adipose tissue, even when the lipoprotein lipase activity is slightly diminished.

The analysis of our quantitative results indicates that, in the virgin rat, the esterification process as determined by the synthesis of glyceride glycerol could be fully satisfied by the uptake of plasma-derived fatty acids. However, in the 20-day pregnant rat the mentioned imbalance still remains and could only be explained by partial esterification of sn-glycerol 3-phosphate with one or two fatty acids, or by the increase in reesterification of fatty acids derived from intracellular lipolysis. Interestingly, late pregnancy is characterized by a stimulation of the lipolytic process in adipose tissue,[8] and therefore provides potential acyl groups for esterification. In fact, the functionality of the triacylglycerol/fatty acid substrate cycle has been recognized previously by others in human[36] and rat[37] adipose tissue, and the rate of this cycle varies with the hormonal environment of the cells.[36,37] In this respect, it is worth mentioning that the triacylglycerol/fatty acid cycle is highly stimulated by norepinephrine,[36,37] which also stimulates hormone-sensitive lipase,[38] whereas insulin, although not affecting the substrate cycle when added to the medium alone, does increase the response to catecholamines.[37] For obvious reasons, it has not been possible to study the rate of this substrate cycle in our experimental in vivo conditions with the classical method, which is based on the comparative measurement of the exit of glycerol versus fatty acids to the medium.[36,37] However, our results strongly support the contention that the triacylglycerol/fatty acid substrate cycle in periuterine adipose tissue is highly accelerated in late pregnancy, probably as the result of the combined effects of catecholamine-stimulated lipolysis and insulin-activating esterification at the glycerol phosphate acyltransferase level. On day 20 of gestation, for example, when lipolysis is already stimulated,[7,8] the accelerated reesterification of fatty acids may represent a counteracting mechanism to avoid the depletion of fat stores in the fed state, thereby favoring rapid fat mobilization when the recycling process is interrupted. The physiological significance of this metabolic adaptation is uncertain, although it may be important for increasing the hormone sensitivity of lipolysis and/or esterification, and even represent a thermogenic mechanism for the mother.

ACKNOWLEDGMENT

We thank Carol F. Warren for editorial help and A. Murúa and M. Morante for technical assistance.

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