

adults ( $117.2 \pm 6.12$  versus  $144.0 \pm 20$  min,  $P < 0.01$ ).

2) The levels of anti-oxLDL autoantibodies, detected with an ELISA method. Anti-oxLDL IgG titers were higher in children ( $1.67 \pm 0.41$  versus  $1.28 \pm 0.41$  ratio,  $P < 0.01$ ).

3) Vitamin E levels after extraction with hexane by HPLC. No significant difference was present between children ( $3.70 \pm 0.62$ ) and adults ( $3.20 \pm 0.9$  nmol/mgLDL).

The increased susceptibility to oxidation of LDL in vitro and the high antibodies titers detected demonstrates that LDL oxidation occurs already during childhood. The possible pathophysiological relevance of these findings is, at the present, obscure and additional work is required.

**Neonatal pig enterocytes develop the capacity to oxidize long chain fatty acids.** M.T. Morel<sup>a</sup>, P. Guesnet<sup>a</sup>, C. Kohl<sup>b</sup>, C. Prip-Buus<sup>b</sup>, B. Darcy-Vrillon<sup>a</sup>, J.P. Pégurier<sup>b</sup>, P.H. Duée<sup>a</sup> (LNSA, Inra, 78350 Jouy-en-Josas; <sup>2</sup>CEREMOD, CNRS, Meudon-Bellevue).

The post-natal period is critical for intestinal development. At that time, neonates are fed maternal milk, which is a high-fat diet. The aim of the present work was to investigate the metabolic fate of oleate – a monounsaturated long chain fatty acid – in neonatal pig enterocytes.

Experimental: Enterocytes isolated from the jejunum-ileum of newborn (0 d) or suckling (2 and 13 d) pigs were incubated with 1-<sup>14</sup>C]oleate (1 mM) and carnitine (1 mM), with or without glucose (5 mM). The amount of oleate oxidized versus incorporated into triglycerides (TG), phospholipids (PL), and cholesterol esters was measured. The specific activity of the oleate precursor pool was estimated by taking into account the radioactivity present in triglycerides.

Results: Whatever the age, esterification (TG + PL synthesis) was the main metabolic pathway of oleate metabolism, accounting for  $89 \pm 1$  % at 0 and 2 d, and for  $86 \pm 1$  % at 13 d. In all cases, the capacity to esterify oleate was stimulated ( $P < 0.05$ ) by adding glucose to the incubation medium. Taking into account isotopic dilution by endogenous fatty acids, the flux of oleate oxidized was found to increase dramatically after 2 d of suckling ( $6.6 \pm 2.0$  versus  $1.3 \pm 0.2$  nmol/30 min/10<sup>6</sup> cells;  $P < 0.05$ ). This was paralleled by a 2.5-fold increase in mitochondrial carnitine palmitoyl transferase I (CPT I) activity; at the same time, the sensitivity of the enzyme to inhibition by malonylCoA strongly decreased (IC<sub>50</sub>:  $229 \pm 40$  nM at 2 d versus  $8 \pm 4$  nM at 0 d). This was also accompanied by a significant increase of the CPT I protein.

Conclusions: Although oxidation represents a minor pathway of oleate metabolism in enterocytes, expression of CPT I is required to allow this oxidative capacity to develop after birth.

**Treatment effect of growth hormone substitution in adults on body composition and on dynamic parameters of carbohydrate and energy metabolism.** Y. Khalifallah, C. Louche Pelissier, M. Laville, J.P. Riou, G. Sassolas (Inserm U449, Faculté de Médecine R.T.H. Laënnec, 69572 Lyon cedex 08, France).

Growth hormone (GH) action on carbohydrate, lipid and protein metabolisms and on body composition is well known. However, most of these effects were obtained with pharmacological dose of GH during short term trials.

The aim of our study was to determine the metabolic status of 11 secondary GH deficient adults (GHD) before and 1 year after 'physiological' doses of substituted GH. All these patients had a body composition measured by impedancemetry and a

plasma leptin determination. Five of the 11 patients were studied by a hyperinsulinic euglycemic clamp with [6,6-2H<sub>2</sub>]glucose used as tracer, and substrate oxydation measured by indirect calorimetry (IC).

The Wilcoxon test was used to compare results (mean  $\pm$  SEM) before and 12 months after GH treatment. These results showed that in spite of a significant IGF1 increase ( $158 \pm 17$  versus  $77 \pm 9$  ng/ml), neither the body weight ( $70 \pm 6$  versus  $71 \pm 6$  kg), nor the fat mass percentage ( $30 \pm 2$  versus  $31 \pm 2$  %) nor the leptinemia ( $12 \pm 3$  versus  $13 \pm 3$   $\mu$ g/L) were modified. Post-prandial endogenous glucose production ( $10.9 \pm 0.6$  versus  $11.3 \pm 0.4$  mg/kg/min) and insulin stimulated glucose disappearance ( $40 \pm 3$  versus  $47 \pm 3$  mg/kg/min) were not significantly modified by GH treatment. The IC measures showed a more pronounced ( $P < 0.05$ ) protide oxydation inhibition under insulin perfusion ( $0.7 \pm 0.1$  versus  $1.0 \pm 0.1$  mg/kg/min). Glucose and lipid oxydation were not significantly changed.

In conclusion, a complete GH substitution of GH deficient patients had no effect on body composition and did not seem to have any deleterous effect on glucose metabolism and insulinosensitivity.

**Control of glucose-6-phosphatase in the small intestine of fasted and diabetic rats.** N. Bruni, F. Rajas, S. Tarpin, C. Zitoun, G. Mithieux (Inserm U. 449, Faculté de Médecine RTH Laënnec, 69372 Lyon cedex 08, France).

Glucose-6-phosphatase (Glc6Pase) is the last enzyme of gluconeogenesis and glycogenolysis. In agreement with the concept that only the liver and kidney express Glc6Pase, it has been recently reported, using a RT-PCR approach, that Glc6Pase mRNA was not detectable in nine other tissues. Using the same approach, we demonstrated the presence of Glc6Pase mRNA in the duodenum (DUO) and

jejunum (JEJ) of adult rats (10–12 weeks), while Glc6Pase mRNA was not detected in the stomach, ileum, colon, brown adipose tissue, adrenals and bladder. We studied the effect of fasting and diabetes on Glc6Pase mRNA (by northern blot) and specific Glc6Pase activity in the small intestine in rats. The amount of Glc6Pase mRNA increased by eight times and six times ( $P < 0.01$ ) in DUO and JEJ in streptozotocin diabetic rats. It returned to normal levels after insulin treatment for 10 h. Glc6Pase activity was increased by 300 % in DUO ( $2.6 \pm 0.8$  versus  $0.83 \pm 0.09$  U/g wet tissue, mean  $\pm$  S.E.M.,  $n = 4$ ,  $P < 0.05$ ) and JEJ ( $1.9 \pm 0.3$  versus  $0.63 \pm 0.03$  U/g,  $P < 0.01$ ) in diabetic rats as compared to normal rats. The amount of Glc6Pase mRNA increased by eight and seven times in DUO and JEJ of 48-h-fasted rats. It returned to normal levels in both tissues after refeeding for 7 h. Glc6Pase activity was significantly increased in fasted rats ( $2.5 \pm 0.6$  and  $1.3 \pm 0.2$  U/g in DUO and JEJ, means  $\pm$  S.E.M.,  $n = 5$ ,  $P < 0.05$  versus normal fed rats). In addition, Glc6Pase mRNA and activity were also expressed in ileum during fasting ( $1.3 \pm 0.4$  U/g). Glc6Pase mRNA and activity were also demonstrated in the human small intestine. In the human colon carcinoma cell line Caco-2, Glc6Pase is only expressed 15 days after the confluence of cells, in agreement with the state of differentiation of Caco-2 cells in the enterocytes for glucose metabolism. Thus, the small intestine might possess the capacity to produce endogenous glucose in portal blood. This should have important implications in various metabolic situations.

**Assessment of insulin sensitivity from plasma insulin and glucose in the fasting or post oral glucose-load state.** A. Avignon, A. Radauceanu, L. Monnier (Metabolic disease department, Lapeyronie hospital, 34295 Montpellier cedex 5, France).