jects (4M/4F, 23.1 ± 2.4 years, 23.7 ± 3.5 kg/m^2 of BMI) were studied i) during hourly ^{13}C fructose ingestion (0.3 g/kg fat free mass/h) for 3 h (F); ii) during ^{13}C fructose ingestion and glucagon infusion (F + G); iii) during glucagon infusion alone (G). EGP levels were assessed by 6.6 ^{2}H glucose and the contribution of fructose gluconeogenesis to EGP from ^{13}C plasma glucose. Basal levels of glucagonaemia were similar in F, F + G and G and remained unchanged during fructose ingestion (F); F + G and G significantly increased glucagonaemia (from 112 ± 5 to 233 ± 9 ng/L with F + G, from 107 ± 4 to 210 ± 26 ng/L with G). EGP increased by 19.8 ± 1.5% with F + G (from 9.7 ± 1.2 to 11.8 ± 2.2 µmol/kg/min, $P < 0.001$) but remained unchanged during F or G. Gluconeogenesis from fructose represented about 80% of EGP with F + G. Plasma ^{13}C glucose levels were identical with F and F + G, indicating a similar relative contribution of fructose gluconeogenesis to the glucose-6 phosphate pool. It was concluded that i) both an increased glucagonaemia and an enhanced supply of gluconeogenic precursors are required to increase EGP; ii) F + G increase EGP without changing the relative proportion of glucose-6 phosphate production from fructose and from other sources (ie, glycogenolysis + gluconeogenesis from non-fructose precursors). This suggested that alterations in the rates of glycogen synthesis or glucose-6 phosphate hydrolysis are involved.

Role of glucose-6 phosphatase and glucokinase in the regulation of hepatic glucose production in insulin-resistance.
C Minassian, G Mithieux *(Faculté de médecine René-Laënnec, Inserm, Unité 449, rue Guillaume-Paradin, 69372 Lyon cedex 08, France)*

We assessed the insulin sensitivity of hepatic glucose production (HGP) and the components of the glucose–glucose-6 phosphate (Glc6P) cycle in rats fed a standard hyperglucidic diet (S) or a high-fat diet for 3 weeks, supplemented (HFM) or not (HF) with oral metformin (50 mg/kg/day) during the last week. HGP was assessed by [3-^{3}H]glucose dilution after saline or insulin infusion during 45 min euglycemic clamps.

Basal HGP was similar in the three groups: 75 ± 8, 65 ± 9.5 and 71 ± 3 µmol/kg/min (mean ± SEM, $n = 5$) for S, HF and HFM rats, respectively. Upon insulin infusion (35 mU/h), HGP decreased by 35% in S rats (49 ± 4.5 µmol/kg/min, $P < 0.05$ vs basal), did not decrease in HF rats (60 ± 12 µmol/kg/min, NS vs basal) and decreased by 68% in HFM rats (22.5 ± 10 µmol/kg/min, $P < 0.01$ vs basal). Upon insulin infusion at 70 mU/h, HGP was similarly suppressed in the three groups: 5.5 ± 7, 6.5 ± 8 and 14 ± 7 µmol/kg/min, respectively.

Total Glc6Pase activity levels, assayed in intact microsomes isolated from fresh livers, were 30% lower ($P < 0.01$) in HF and HFM rats (0.15 ± 0.01 and 0.16 ± 0.01 µmol/min/mg prot) than in S rats (0.23 ± 0.02 µmol/min/mg), with similar Kms (≈ 2 mM). Glucokinase (GK) activity was 65% lower ($P < 0.01$) in HF and HFM rats (0.54 ± 0.13 and 0.60 ± 0.17 U/g wet weight) than in S rats (1.63 ± 0.4 U/g), with similar Kms (≈ 8 mM). Insulin had no effect on Glc6Pase and GK. Glc6P, assayed in a freeze-clamped liver lobe, was similar in the three groups after saline or insulin perfusions. Plasma Glc was similar in the three groups, before and after the perfusions. Insulin had no significant effect on the theoretical glucose output, calculated from the enzyme kinetics and the substrate concentrations, in any of the three groups.

We concluded that: i) mechanisms additional to total enzyme activities and substrate concentrations control the Glc–Glc6P cycle; ii) HF rats exhibited insulin resistance to HGP and that normal insulin sensitivity

of HGP was restored by metformin; iii) the mechanisms of control of the Glc–Glc6P cycle were impaired in insulin-resistant HF rats and were restored by metformin.

Role of the abundance of messenger RNA in the expression of hepatic and renal glucose-6 phosphatase in fasted and diabetic rats. G Mithieux, H Vidal, C Zitoun, C Minassian, N Daniele *(Faculté de médecine René-Laënnec, Inserm U 449, 69372 Lyon cedex 08, France)*

In this study we cloned and sequenced a rat glucose-6 phosphatase (Glc6Pase) complementary DNA (cDNA). The complete cDNA (1 071 bp) was amplified by RT-PCR using total liver RNA and oligonucleotide primers derived from murine species. The rat enzyme, deduced from the cDNA sequence, is a 95% homologue with the murine enzyme and 90% with the human enzyme. This cDNA was used to probe the abundance of Glc6Pase mRNA by Northern blot in vivo in fasted and diabetic rats (streptozotocin-induced).

In the liver, as compared with the fed rat, the Glc6Pase mRNA level increased 3.6 ± 0.4 and 3.6 ± 0.4 fold (arbitrary densitometric unit) after 24 and 48 h of fasting. It then returned to the fed rat level after 72 and 96 h of fasting (1.0 ± 0.3 and 1.4 ± 0.6 fold, mean ± SEM, $n = 5$). This agreed with the increase in Glc6Pase activity after 24 and 48 h of fasting and its later decrease at 72 and 96 h. In the kidney, the Glc6Pase mRNA level increased 2.7 ± 1.0 and 5 ± 1.2 fold after 24 and 48 h of fasting, it then plateaued at 72 and 96 h (4.5 ± 1.0 and 4.3 ± 1.0 fold). This is in agreement with the gradual increase in renal Glc6Pase activity throughout fasting. The liver Glc6Pase mRNA level in fasted rats rapidly decreased (92%) after refeeding for 90 min, 95% after 180 min and 97% after 420 min ($n = 3$ by time). The Glc6Pase mRNA abundance decreased less rapidly in the kidney. A significant 50% decrease was observed only after 3 h refeeding. However, Glc6Pase activity did not return to normal levels in either the liver or in the kidney during the 7 h refeeding period.

Glc6Pase mRNA abundance increased 4.5 ± 0.4 and 4.3 ± 0.1 fold in the liver and kidney of streptozotocin-diabetic rat, respectively. This correlated with similar increases in the Glc6Pase activity in both tissues. Glc6Pase mRNA level was partially compensated for by 12 h insulin treatment (2.4 ± 0.4 and 1.6 ± 0.2 fold in liver and kidney, respectively). Glc6Pase activity did not return to normal levels during the 12 h insulin treatment, in either of the tissues.

In conclusion, the Glc6Pase mRNA abundance was closely controlled at the pretranslational level in both the liver and kidney during nutritional transitions and diabetes. Our data suggested that insulin might play an important role in this control, and that additional mechanisms take place in the liver during the course of fasting.

The relationship between breakfast caloric intake and late morning blood glucose levels and cognitive capacities in a population of students. L Meynard-Rouard [1], C Jaffiol [2], JC Manderscheid [3], A Borderies [2] *([1] Lycée Victor-Hugo, Carpentras; [2] Service d'endocrinologie et Semhap; [3] Hôpital Lapeyronie, Montpellier, France)*

Several authors have stressed the problem of low breakfast caloric intake in France with its possible deleterous effects on scholastic results. However, discrepancies exist concerning the real effect of proteins and other nutriments on cognitive capacities and behaviour.

Two groups of 50 randomly selected young women (aged 15–21 years) received either a high carbohydrate (glucids 66%,