



## Kinetic heterogeneity of non insulin-dependent diabetic patients: stable isotope study

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**Production of glycerol by rat muscles in vivo: demonstration using microdialysis.**

O Peroni, V Large, V Beylot, M Beylot (*Laboratoire de physiopathologie métabolique et rénale et Inserm U 197, Faculté de médecine René-Laennec, 69372 Lyon cedex 08, France*).

It is generally considered that circulating glycerol is produced mostly by the hydrolysis of adipose tissue triglycerides and, for a small part, by the hydrolysis of circulating triglycerides. However, an hormone-sensitive lipase is present in muscles suggesting that this tissue could also produce glycerol. To test this hypothesis, we infused (3 h) rats ( $n = 5$ , 24 h fasted) with  $[6,6-^2\text{H}]$  glucose and  $[2-^{13}\text{C}]$  glycerol. Microdialysis catheters were inserted into subcutaneous abdominal adipose tissue and into hind leg muscles. Blood and dialysate samples, were collected during the third hour to measure isotopic enrichments (IE, MPE) of glucose and glycerol. It had been previously verified in vitro that there was no difference between  $^{12}\text{C}$  and  $^{13}\text{C}$  glycerol for passing through the dialysis membrane. Glucose IE was the same in muscle ( $5.39 \pm 0.32\%$ ) and adipose tissue ( $5.3 \pm 0.31\%$ ) dialysates samples and in blood ( $5.47 \pm 0.24\%$ ). As expected, glycerol IE was lower in adipose tissue dialysate samples than in blood ( $2.3 \pm 0.3$  vs  $6.2 \pm 0.2\%$ ,  $P < 0.01$ ) due to lipolysis in adipose tissue. However, glycerol IE in muscle dialysate samples ( $3.3 \pm 0.5\%$ ), although higher than in adipose tissue ( $P < 0.05$ ), was also lower than in blood ( $P < 0.01$ ).

**Conclusion:** These results strongly suggest that muscles are an active producer of glycerol in vivo.

**Disorder of apolipoprotein AI metabolism in non insulin-dependent diabetes mellitus: a kinetic study.** R Frenais, K Ougueram, C Maugeais, P Mahot, T Magot, M Krempf (*Centre de recherche en nutrition*

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A disorder of High Density Lipoprotein (HDL) metabolism could explain the excess of cardiovascular diseases in non insulin-dependent diabetic (NIDDM) subjects. However, kinetic perturbations of this metabolism have not been clearly shown. A 14 h ( $^2\text{H}_3$ )-leucine primed infusion ( $10.10^{-6}$  mol/kg/h) was given to eight NIDDM patients ( $\text{Hb-A1C} = 8.16\% \pm 1.93$ ) and seven control subjects. A monocompartmental model was used to analyse HDL kinetic data (SAAM II software). For apolipoprotein AI (apo AI) precursor enrichment, it was assumed that the VLDL-apo B100 tracer-to-tracee ratio at plateau, calculated by monoexponential regression, corresponded to the tracer-to-tracee ratio of the leucine precursor pool. Apo AI concentration was lower in NIDDM than in controls ( $96 \pm 12$  vs  $124 \pm 13$  mg.dL $^{-1}$ ,  $P < 0.002$ ). The mean apo AI fractional catabolic rate (FCR) was significantly faster ( $0.39 \pm 0.16$  vs  $0.21 \pm 0.06$  day $^{-1}$ ,  $P = 0.032$ ) and the apo AI absolute production rate (APR) was not significantly greater ( $16.6 \pm 6.1$  vs  $12.0 \pm 4.2$  mg.kg $^{-1}$ .day $^{-1}$ ,  $P = 0.17$ ) in NIDDM. Furthermore, HDL-triglycerides level and apo AI/HDL-cholesterol ratio were higher in diabetic patients (respectively  $14.9 \pm 6.2$  vs  $4.3 \pm 1.5$  mg.dL $^{-1}$ ,  $P < 0.004$  and  $2.78 \pm 0.84$  vs  $2.31 \pm 0.16$ ,  $P = 0.24$ ). The FCR of apo AI was not correlated with Hb-A1C level, but positively correlated with plasma and HDL-triglycerides levels, and inversely correlated with apo AI concentration.

We conclude that decreases in plasma apo AI and HDL cholesterol concentrations are related to the increase in HDL-apo AI FCR in NIDDM.

**Kinetic heterogeneity of non insulin-dependent diabetic patients: stable isotope study.** C Maugeais, P Mahot, K Ougueram, M Krempf, T Magot (*Centre*

*de recherche en nutrition humaine, Hôpital Laënnec, 44035 Nantes cedex 01, France).*

Cardiovascular diseases are the most prevalent of mortality in non insulin-dependent diabetics (NIDDM). These patients are often hypertriglyceridemic while cholesterol of LDL was in normal range. The apoB100 metabolism was explored in NIDDM subjects by endogenous labeling in large VLDL, small VLDL, IDL and LDL.

Ten NIDDM patients were studied (HbA1C 6.7; 10.3%; BMI 30–33 kg/m<sup>2</sup>). They were hypertriglyceridemic (TG 1.8; 3.6 mmol/L). Each patient received a 14 h-intravenously infusion (10.10<sup>-6</sup> mol/kg/h) in fasting state. Large-VLDL, small-VLDL, IDL and LDL were isolated by density gradient ultracentrifugation and apoB100 by SDS-PAGE. The apoB100 was hydrolyzed and tracer-to-tracee ratio curves were analyzed by compartmental modeling.

Kinetic analysis showed that NIDDM patients had a production rate of 75 ± 50 mg/kg/day and 2.61 ± 1.1 mg/kg/day for large-VLDL and small-VLDL respectively. Fractional catabolic rates (FCRs) of large-VLDL, small-VLDL, IDL and LDL were 0.29 h<sup>-1</sup> ± 0.15, 0.44 h<sup>-1</sup> ± 0.15, 0.21 h<sup>-1</sup> ± 0.02 and 0.025 h<sup>-1</sup> ± 0.004 respectively. Direct uptake was in NIDDM patients, 0–81% of large-VLDL metabolic fate.

This study pointed out the heterogeneity of the apoB100 metabolism in NIDDM, mainly from the metabolic fate differences of large-VLDL.

**Insulin resistance in Vietnamese subjects with essential arterial hypertension.** VH Minh, LC Thanh, PTB Ngoc, TD Trinh, TD Tho, P Valensi (*Medical School of Hue and Bach Mai Hospital, Hanoi, Vietnam; Jean Verdier Hospital, 93140 Bondy, France*).

Several studies suggest that essential arterial hypertension is associated with insulin resistance in obese and non obese subjects. Malnutrition remains frequent in Vietnam and mean body mass index (BMI) in Vietnamese adults is around 18.5 kg/m<sup>2</sup>.

This study aimed to look for an insulin resistance state in Vietnamese subjects with hypertension. One hundred and eight hypertensive patients (51 men and 57 women) over 40 years (mean = 65.4) were compared with 40 healthy subjects (23 men and 17 women) also over 40 years (mean = 61.0). Hypertensive patients had a BMI significantly higher (mean ± SD = 20.4 ± 1.15 kg/m<sup>2</sup> vs 18.3 ± 2.13 kg/m<sup>2</sup>,  $P < 0.01$ ), a thicker tricipital skinfold (12.7 ± 6 mm vs 7.0 ± 3.7 mm,  $P < 0.001$ ), no significant difference in waist/hip ratio (0.88 ± 0.06 vs 0.85 ± 0.06). Blood glucose during fasting and 2 h after 75 g glucose taken orally were similar. Plasma insulin measured during fasting and 2 h after glucose ingestion were significantly higher in hypertensives (44.4 ± 5.1 vs 21.6 ± 3.2 pmol/L,  $P = 0.026$  and 271.1 ± 21.6 vs 139.1 ± 15.2 pmol/L,  $P = 0.00001$ ). These differences were still significant after excluding subjects with BMI > 22 kg/m<sup>2</sup>.

In conclusion this study shows that healthy Vietnamese adults have a BMI lower than in occidental countries. Hypertension was shown to be associated with a slight but significant increase in: i) BMI which however remains far from the definition of obesity in western countries; ii) fat mass without predominant abdominal adiposity; iii) an insulin resistance state despite the modest overweight.

**Influence of dairy protein on cholesterol synthesis in humans.** A Avignon, JM Didelot, TC Pham, C Colette, B Descomps, L Monnier (*Department of Metabolic Diseases, University Hospital, 34000 Montpellier, France*).