



# Endogenous labelling of cholesterol using $^{13}\text{C}$ -acetate perfusion: development of an in vivo study protocol for cholesterol reverse transport in humans

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LDL to determine the relative quantity of each fraction.

Triglyceride concentrations were significantly higher in the NIDDM group. Total cholesterol and LDL apoB were not statistically different between the two groups. Fractions 2 and 3 were significantly decreased and fraction 4 significantly increased in the NIDDM group compared to controls (fig 1).

LDL repartition showed an atherogenic profile in the NIDDM hypertriglyceridemic group. Total cholesterol and LDL apoB were not different but dense LDL were predominant in the NIDDM group.

**Endogenous labelling of cholesterol using  $^{13}\text{C}$ -acetate perfusion: development of an in vivo study protocol for cholesterol reverse transport in humans.**

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Three normocholesterolemic subjects were submitted to  $^{13}\text{C}$ -acetate continuous administration ( $1.5 \mu\text{mol/kg/min}$ ) for 7 h after one bolus of  $90 \mu\text{mol/kg}$ . During the study, blood samples were drawn at 30 min, 1 h, 1 h 30, 2 h and then hourly for 7 h. Samples were used for separation of very low density lipoproteins (VLDL), low density lipoproteins (LDL) and high density lipoproteins (HDL) by ultracentrifugation. Lipids were extracted by the Folch method. They were subjected to chromatography on a silicic acid micro-column to separate the cholesteryl esters from unesterified cholesterol. Samples were derivatized with acetic anhydride-pyridine and enrichments were measured by gas-liquid chromatography coupled to spectrometry (GC-C-IRMS). The enrichment curves of lipoprotein unesterified cholesterol were similar, attesting to rapid exchanges of unesterified cholesterol between lipoproteins. At the end of the

experiment, the isotopic enrichment of free cholesterol was 0.07%, that of esterified cholesterol was 0.016, 0.007, 0.003%, respectively, for HDL, VLDL and LDL.

The order of labelling apparition in lipoprotein esterified cholesterol (HDL, VLDL and LDL) was in agreement with previous data: esterification of cholesterol in HDL and its delivery to apolipoprotein B-containing lipoproteins. A multicompartimental model of cholesteryl ester metabolism was previously developed in normocholesterolemic subjects using radioisotopes. This model integrated the essential role of cholesteryl ester movement from HDL to apoB-containing lipoproteins (about 50% of HDL cholesteryl ester/h) in reverse cholesterol transport. In this model cholesteryl ester appeared essentially by esterification (6%/h of unesterified cholesterol) and disappeared exclusively by LDL uptake (about 3%/h). The simulation of this model under these new labelling conditions led to curves very similar to our experimental data.

This protocol, using stable isotopes permitted us to quantify cholesterol movement involved into reverse cholesterol transport.

**Kinetic study of HDL2 and HDL3 metabolism using endogenous labelling of apolipoprotein AI by stable isotopes in normolipidemic subjects.** K Ouguerram, C Collober, C Maugeais, M Krempf, T Magot (*Laboratoire de nutrition humaine, hôpital Laënnec, 44035 Nantes cedex 01, France*)

Apolipoprotein AI plays a major role in cholesterol efflux from extrahepatic tissues to the liver. It was therefore considered interesting to measure the characteristics of the high density lipoprotein (HDL) apolipoprotein AI turnover.

The endogenous labelling of apolipoprotein AI was carried out in six normolipidemic subjects through the administration of D3 leucine. Four volunteers were perfused for