Glucose metabolism and leptin in obese women. C. Percheron[a], C. Colette[a], J. Galitzky[b], P. Barbe[b], L. Monnier[a] ([a]Human Nutrition Laboratory, IURC Montpellier, 75, rue de la Cardonille, 34093 Montpellier cedex 05; [b]U 317 Toulouse, France).

Plasma leptin concentrations (PL) have been found to be associated with insulin resistance in men but not in women. We searched for an association between PL (radioimmunoassay) and insulin sensitivity (S_I, FSIVGTT, minimal model) in obese women. Twenty-seven non-diabetic obese women were included: age 39 ± 3 years, body mass index 33.2 ± 4 kg/m^2, fat mass (FM) 33.7 ± 6.3 kg, FM percentage 38.1 ± 3.3 (mean ± SD). PL (35 ± 13 ng/mL) were significantly correlated with FM ($r = 0.72$, $P < 0.0001$) and FM % ($r = 0.72$) but not with S^I (10^{-4} min^{-1} μU^{-1}.mL, $r = 0.02$). Patients were divided into two subgroups using the S_I median (2.35). The PL concentrations were not significantly different: 36 ± 17 (group 1, S_I = 1.3 ± 0.6) and 33 ± 8 (group 2, S_I = 4.2 ± 1.7). In univariate analysis, PL were positively correlated to FM ($r = 0.8$, $P = 0.0003$), to FM % ($r = 0.83$, $P < 0.0001$) and to S_I ($r = 0.57$, $P = 0.04$) in group 1. In group 2, PL were positively correlated to FM ($r = 0.70$, $P = 0.006$), to FM % ($r = 0.70$), to fasting glucose ($r = 0.66$, $P = 0.03$) and negatively correlated to SI ($r = -0.57$, $P = 0.04$). In stepwise multiple regression analysis, FM % was the only predictor of PL in group 1 ($R^2 = 0.66$). In group 2, PL were positively associated with FM % (step 1), with fasting glucose (step 2), and with S_I (step 3). 79.3 % of leptin variation could be predicted by these three variables. S_I was positively associated with fasting insulinemia (step 1) and leptinemia (step 2). This preliminary data suggested a relation between leptin and glucose metabolism in obese women.

A polymorphism in the 5' untranslated region of the human *ob* gene is associated with lower leptin levels in morbid obesity. K. Clément[a,b], J. Hager[a,c], S. Francke[a], C. Dina[a], J Raison, N. Lahlou[c], A. Basdevant[b], P. Froguel[a], B. Guy-Grand[b] ([a]CNRS EP10/Institut Pasteur de Lille, Lille; [b]Hotel-Dieu Hospital, Paris; [c]Inserm U342/Saint-Vincent de Paul Hospital, Paris, France).

Many studies have shown that obesity has a considerable inherited component. Recent successes in the identification of genetic loci (particularly the *ob* gene responsible for the synthesis of leptin) in mice have resulted in a dramatic increase in information about the mechanisms controlling energy metabolism. In humans, rare cases of leptin deficiency due to a mutation in the leptin gene are associated with early onset obesity. We and others have recently reported evidence that the *ob* gene region is linked to a more common form of morbid obesity (BMI > 35 kg/m^2) in humans. In this study, we screened the human *ob* gene for mutations and evaluated their putative role in obesity by a case-control association study in two independent populations of obese Caucasians. We found a DNA variant in exon 1 of the human *ob* gene (A → G substitution, base +19). This variant was found in 62 % of our study population. Association analyses under different genetic models (dominant, co-dominant, recessive) showed no significant evidence for an association of this variant with BMI. However, obese individuals homozygous for the G-allele showed significantly lower leptin levels (51.4 ± 24 ng/mL) compared to obese patients either heterozygous or homozygous for the A-allele (60.0 ± 26, $P = 0.02$ after correction for BMI). This result was replicated in an independent population of moderately obese French women. Our study provides further evidence that a defect in the *ob* gene in linkage disequilibrium with the G-allele of