

terregulating HSL content in order to limit fatty acid depletion from the stored triglycerides.

**Role of endogenous oleic acid produced by  $\Delta 9$ -desaturase on triacylglycerol secretion in cultured chicken hepatocytes.** P Legrand, D Catheline, M Fichot, P Lemarchal (*Laboratoire de biochimie, Inra-Ensa, Rennes, France*)

The relationship between endogenous oleic acid produced by hepatic  $\Delta 9$ -desaturase, and the rate of secretion of very low density lipoprotein (VLDL)-triglycerides was investigated in a primary culture of chicken hepatocytes. This culture system exhibited a high level of  $\Delta 9$ -desaturase activity and triglyceride (TG) secretion, which both peaked in the interval between 30 and 60 h of culture. Oleic acid added to the culture medium of the secreting cells slightly increased the TG secretion rate, but significantly enhanced the total rate of TG synthesis in these cells. The comparison of the fatty acid composition of the secreted and intracellular TG showed an imbalance in the ratio of monoenes and saturated fatty acids, the secreted TG being significantly more unsaturated than the intracellular TG.

Cyclopropenic fatty acids (sterculic and malvalic acids, 0.5 mM, specific inhibitors of fatty acid desaturation) were added to the culture medium 24 h before measurements of  $\Delta 9$ -desaturase activity and TG secretion rate of the hepatocytes. This led to an almost complete suppression of both desaturase activity and TG secretion, measured in the absence of exogenous fatty acid in the culture medium, but did not affect total TG synthesis. However, the addition of 0.5 mM oleic acid to the culture medium of cells treated with cyclopropenic fatty acids was able to restore the TG secretion rate. Linoleic acid was less efficient than oleic acid and palmitic acid was inefficient. Finally,

even in the presence of 0.5 mM oleic acid in the culture medium of secreting cells, hepatocytes treated with cyclopropenic fatty acids showed a significant ( $P < 0.05$ ) decrease in TG secretion rate compared to nontreated cells ( $3.33 \pm 0.77$  and  $6.20 \pm 0.95$  nmol/mg•h, respectively). Taken together, these results demonstrated that the secretion of TG containing fatty acids produced de novo by chicken hepatocytes is highly dependent on the level of hepatic  $\Delta 9$ -desaturase activity as has been already suggested by previous results in our laboratory. These results suggest that the over-secretion of VLDL-TG in the chicken leading in turn to higher fattening could originate in high desaturation of saturated fatty acids by  $\Delta 9$ -desaturase.

**Effect of 17  $\beta$ -estradiol on hepatic lipid desaturation and secretion in the chicken.** D Hermier <sup>1</sup>, D Catheline <sup>2</sup>, P Legrand <sup>2</sup> (<sup>1</sup> *Inra, 37380 Nouzilly*; <sup>2</sup> *Inra-Ensa, 35042 Rennes cedex, France*)

Hepatic  $\Delta 9$  desaturation of de novo synthesized fatty acids (FA) facilitates the synthesis of triglycerides (TG) and their subsequent secretion as very low density lipoproteins (VLDL) [Jeffcoat (1979) *Assays Biochem* 15, 1-36 in the rat; Legrand and Lemarchal (1992) *Comp Biochem Physiol* 102B, 371-375 in the chicken]. In the laying hen, the dramatic increase in the hepatic lipogenesis by estrogens is frequently paralleled with a hepatic steatosis that may compromise egg production and even lead to death. The delicate balance between lipid synthesis, secretion and storage in the liver has been investigated in male chickens in relation to the FA desaturation process. Seven birds fed on a low-lipid diet were administrated IM injections of 20 mg/kg of 17  $\beta$ -estradiol in propylene glycol (four injections in 1 week), whereas four control birds received injections of propylene glycol only.

Injection of estradiol resulted in a considerable increase in the plasma VLDL concentration (40.4 vs 1.47 mg/mL). The chemical composition of the VLDL was identical in both groups, and TG accounted for 70% of total lipids, whereas the liver steatosis of the estrogenized chickens resulted mainly from TG accumulation (74% of liver lipids vs 25% in control). In treated chickens, VLDL, total liver lipids and hepatic microsomes contained significantly more monounsaturated FA (54.7, 50.1 and 37.4% of total FA, respectively) to the detriment of the saturated and polyunsaturated FA when compared to those of control chickens (39.2, 19.9 and 16.7% of total FA, respectively). Hepatocytes of the treated chickens exhibited also a two-fold higher  $\Delta 9$  desaturase activity 0.760 vs 0.373 nmol/mn/mg protein. Moreover, in these chickens, VLDL contained significantly more monounsaturated FA (55%) than the liver lipids (50%), which was indicative of their preferential secretion. These data supported the hypothesis that, in response to estradiol-induced lipogenesis, the synthesis and the desaturation of fatty acids are tightly coordinated, in order to facilitate VLDL secretion and to limit the degree of hepatic steatosis.

### LDL heterogeneity in non-insulin-dependent diabetes mellitus (NIDDM) subjects.

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LDL are heterogeneous lipoproteins classified by their density. Dense LDL are associated with an increased rate of cardiovascular heart diseases. This study compared the distribution profile of five LDL subclasses of NIDDM and control subjects.

Five obese hypertriglyceridemic subjects (37–66 years old, body mass index [BMI] 30–33 kg/m<sup>2</sup>) with (HbA1C 6.7–10.3%) NIDDM were studied. They were treated by diet alone or by oral antidiabetic drugs. None of them received insulin or hypolipemic drug therapy. Five nonobese healthy subjects were studied as controls.

Five LDL subclasses were separated using density gradient ultracentrifugation: LDL1: 1.019–1.022 g/mL; LDL2: 1.022–1.026 g/mL; LDL3: 1.026–1.039 g/mL; LDL4: 1.039–1.051 g/mL; LDL5: 1.051–1.063 g/mL. Fraction absorbance at 435 nm was compared to the absorbance of total

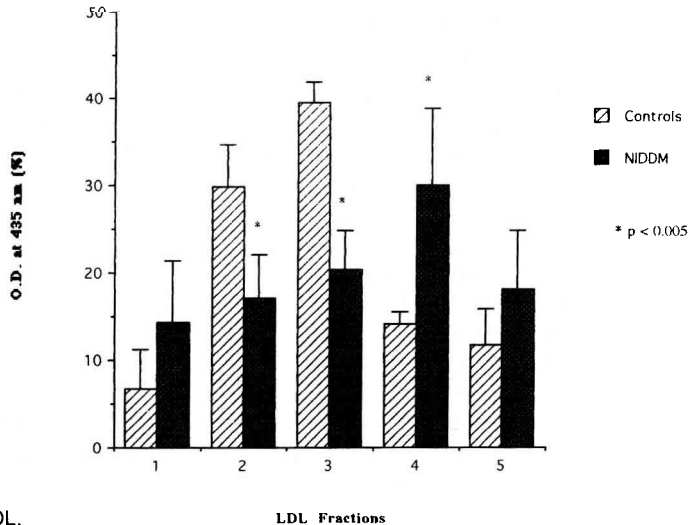


Fig 1. Density profile of LDL.