

Women, Gestation, Lipids and Lipoproteins

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Gestation and Lipids

- ▶ In order to support the enhanced lipid catabolism during the last third of gestation the mother has to store fat depots in earlier stages.
 - ▶ Enhanced accumulation of fat depots is a feature of pregnancy in women
- ▶ Studies in rats show that the increase in maternal fat depots takes place during the first two thirds of gestation and are a consequence of hyperphagia and enhanced adipose tissue lipolysis
- ▶ Hypertriglyceridemia is constantly present during late gestation

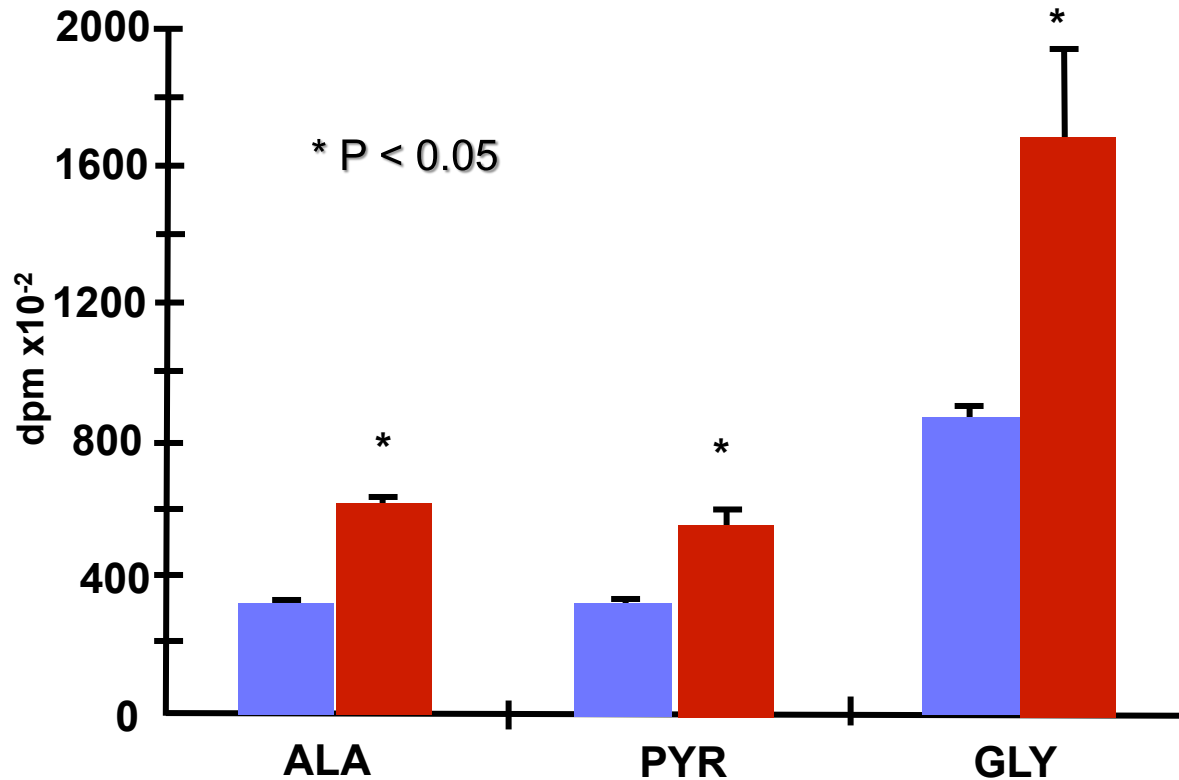
Gestation and Lipids

- ▶ During the first two thirds of gestation the mother is in an anaerobic state, increasing her fat depots thanks to hyperphagia and enhanced lipogenesis.
- ▶ During the last trimester the mother switches to a catabolic state. Glucose is the most abundant nutrient crossing the placenta, which causes maternal hypoglycemia despite an increase in gluconeogenesis
- ▶ Adipose tissue lipolytic activity increases raising plasma fatty acids and glycerol that reach the liver, leading to an increase in hepatic production of TG, that return to the circulation in VLDLs.

Gestation and Lipids

- ▶ Glycerol is also used as a gluconeogenic substrate saving other more essential molecules like amino acids for the fetus.
- ▶ Under fasting conditions, FA, via beta-oxidation are converted into ketone bodies which easily cross the placenta and are metabolized by the fetus.
- ▶ Enhanced liver production of VLDL-TG together with a decrease in adipocyte LPL and increased plasma CETP causes both an increment in particles and particle TG
- ▶ Maternal TG do not cross the placenta, but are hydrolyzed by LPL releasing FA to the fetus.

Glucose Formation in Pregnant Rats

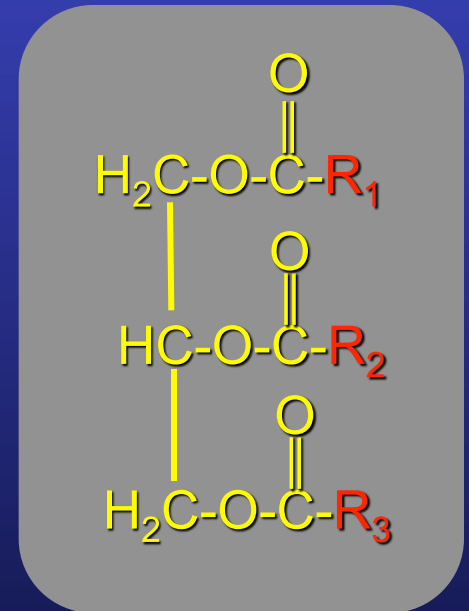


Glucose formation in 24 h fasted 21 day pregnant (red) or virgin control rats (blue) after 1mmol of U-¹⁴C-alanine (ALA), 3-¹⁴C-pyruvate (PYR) or U-¹⁴C-glycerol (GLY).

The high levels of glycerol in maternal plasma and its efficient conversion into glucose also benefit the fetus when the mother is fasting and the availability of other substrates like amino acids is limited.

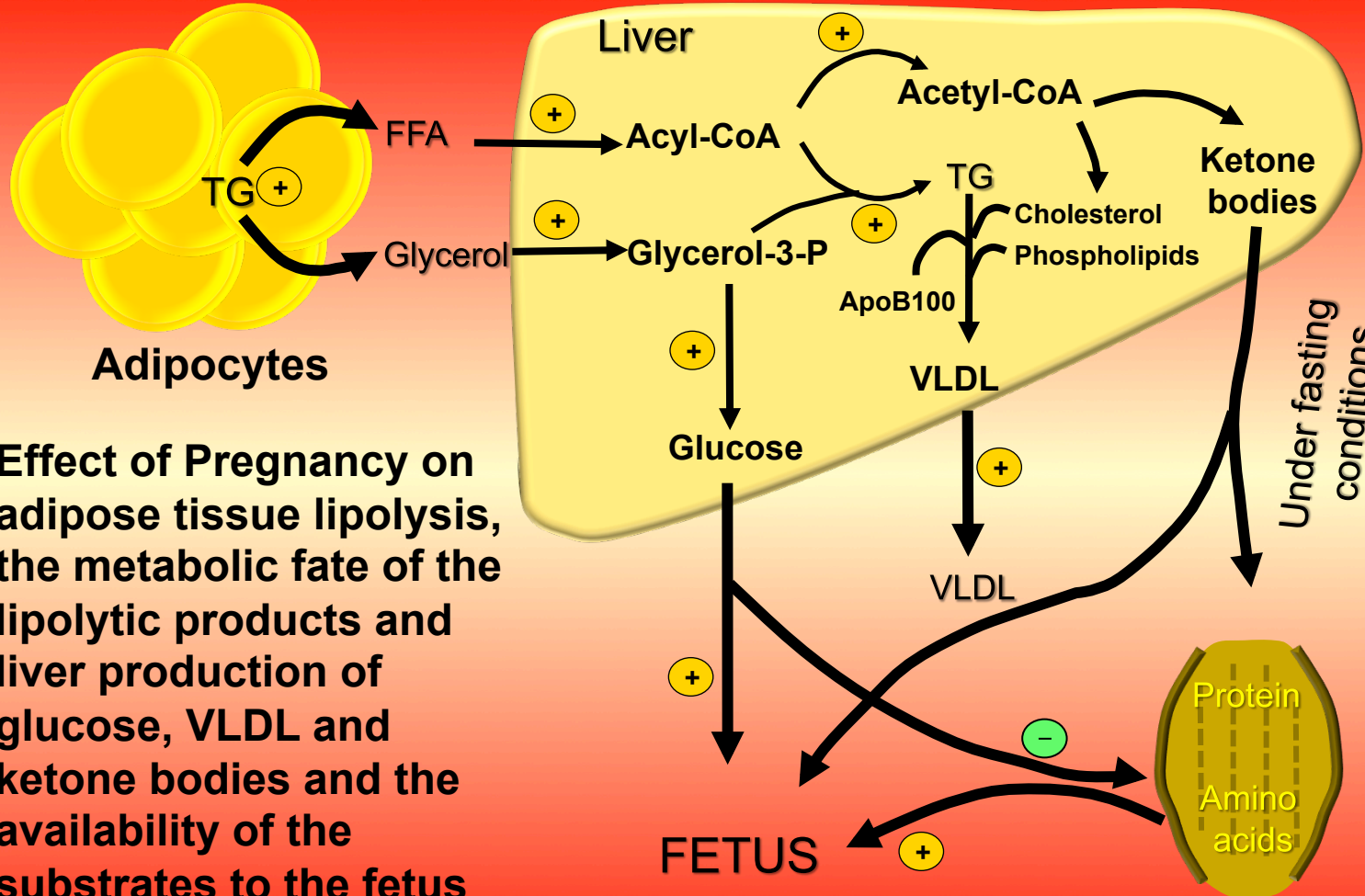
Triacylglycerol - Triglycerides

- ✦ Triglycerides are water-insoluble lipids consisting of **three fatty acids (acyl group) linked to one glycerol molecule**.
 - They represent a concentrated source of metabolic energy contributing 9 kcal/gm.
- ✦ TG are transported as **core constituents of all lipoproteins**, but the greatest concentration is in TG-rich chylomicrons and VLDL particles



R = Fatty acid chain

Gestation and Lipids

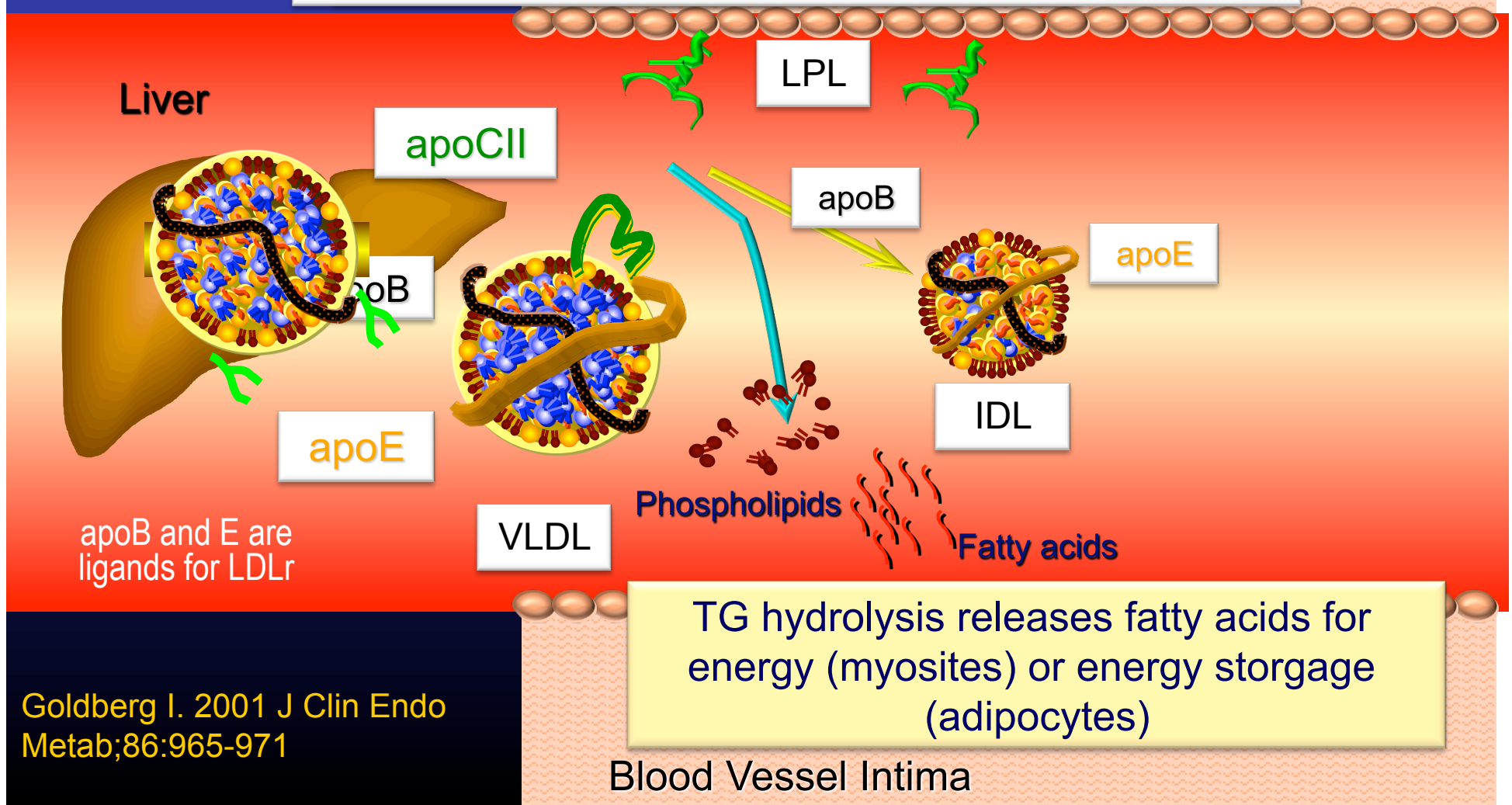


Effect of Pregnancy on adipose tissue lipolysis, the metabolic fate of the lipolytic products and liver production of glucose, VLDL and ketone bodies and the availability of the substrates to the fetus

TG = triglycerides

Normal (non-pregnant) VLDL Lipolysis

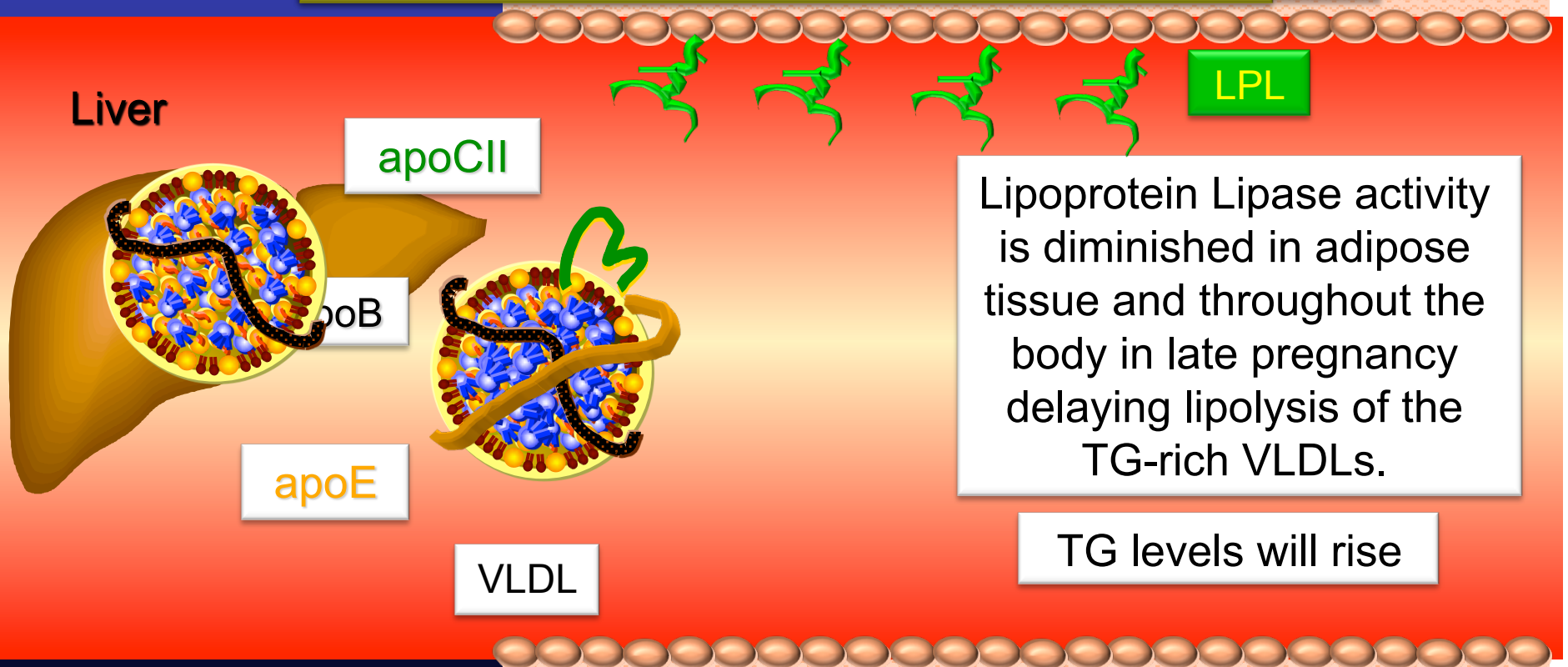
ApoCII is a ligand for lipoprotein lipase (LPL)



Goldberg I. 2001 J Clin Endo
Metab;86:965-971

VLDL Lipolysis During Pregnancy

Decreased lipoprotein lipase (LPL) Expression



Lipoprotein Lipase activity is diminished in adipose tissue and throughout the body in late pregnancy delaying lipolysis of the TG-rich VLDLs.

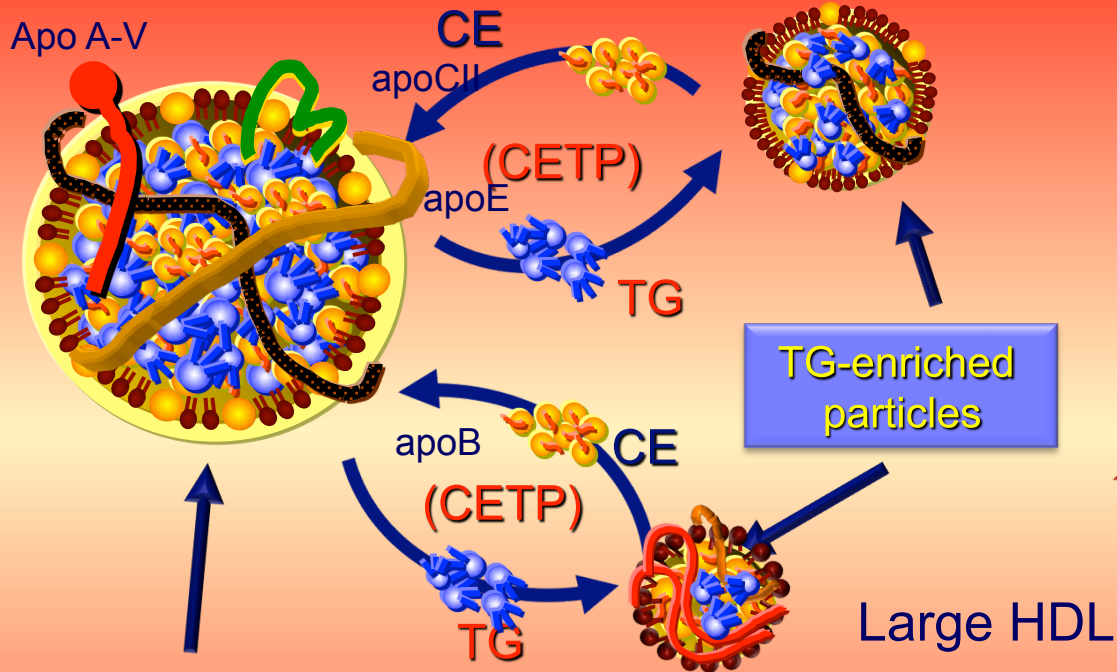
TG levels will rise

Adapted from Herrera E.
Eur J Clin Nutr
2000;54:Suppl 1 S47-S51

Blood Vessel Intima

Lipoprotein Particle Composition Changes During Pregnancy



Overproduction of TG-rich VLDL



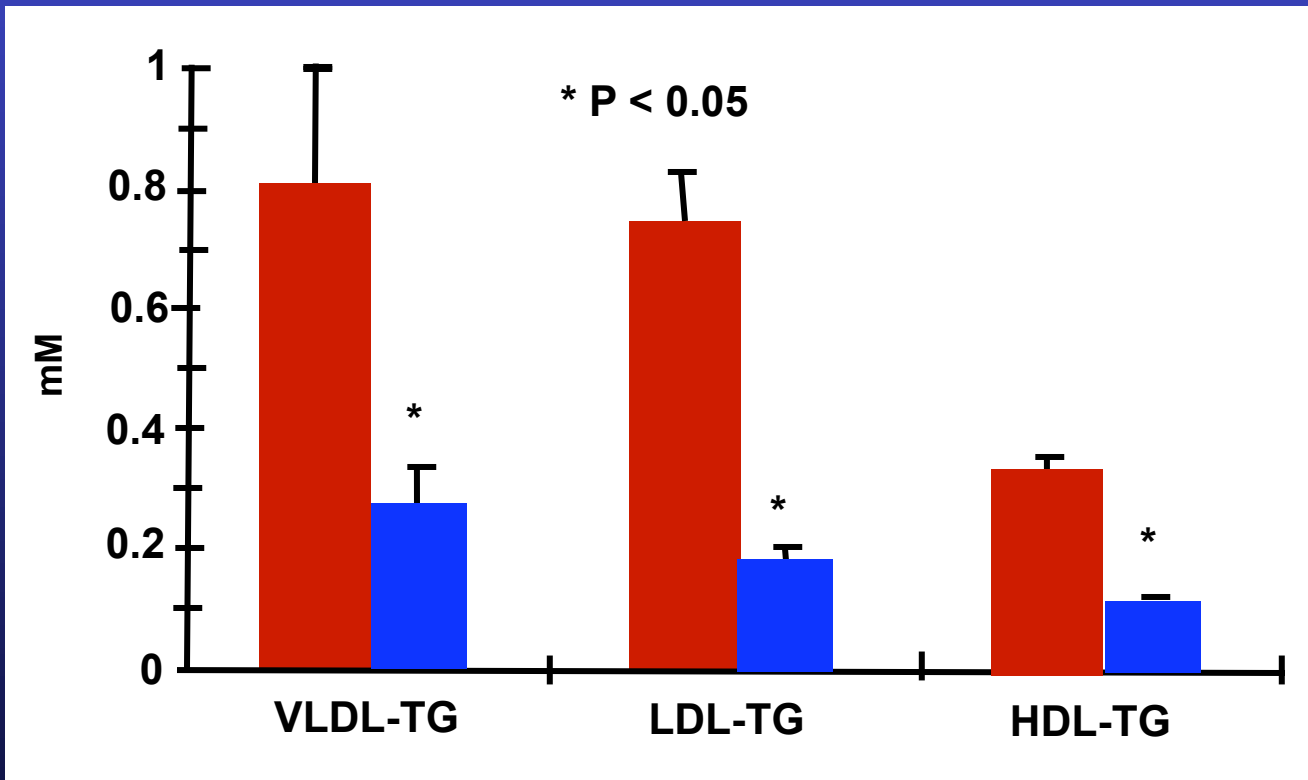
An increase in CETP activity is found at mid gestation. The increase in VLDL-TG and its delayed lipolysis during pregnancy in the presence of increased CETP activity facilitates enrichment of LDL and HDL with TG

↑ LDL-TG & HDL-TG

Lipoprotein Lipase activity is diminished in adipose tissue and throughout the body in late pregnancy delaying lipolysis of the TG-rich VLDLs.

Triglyceride 
Cholesteryl ester 

Triglycerides in Pregnancy

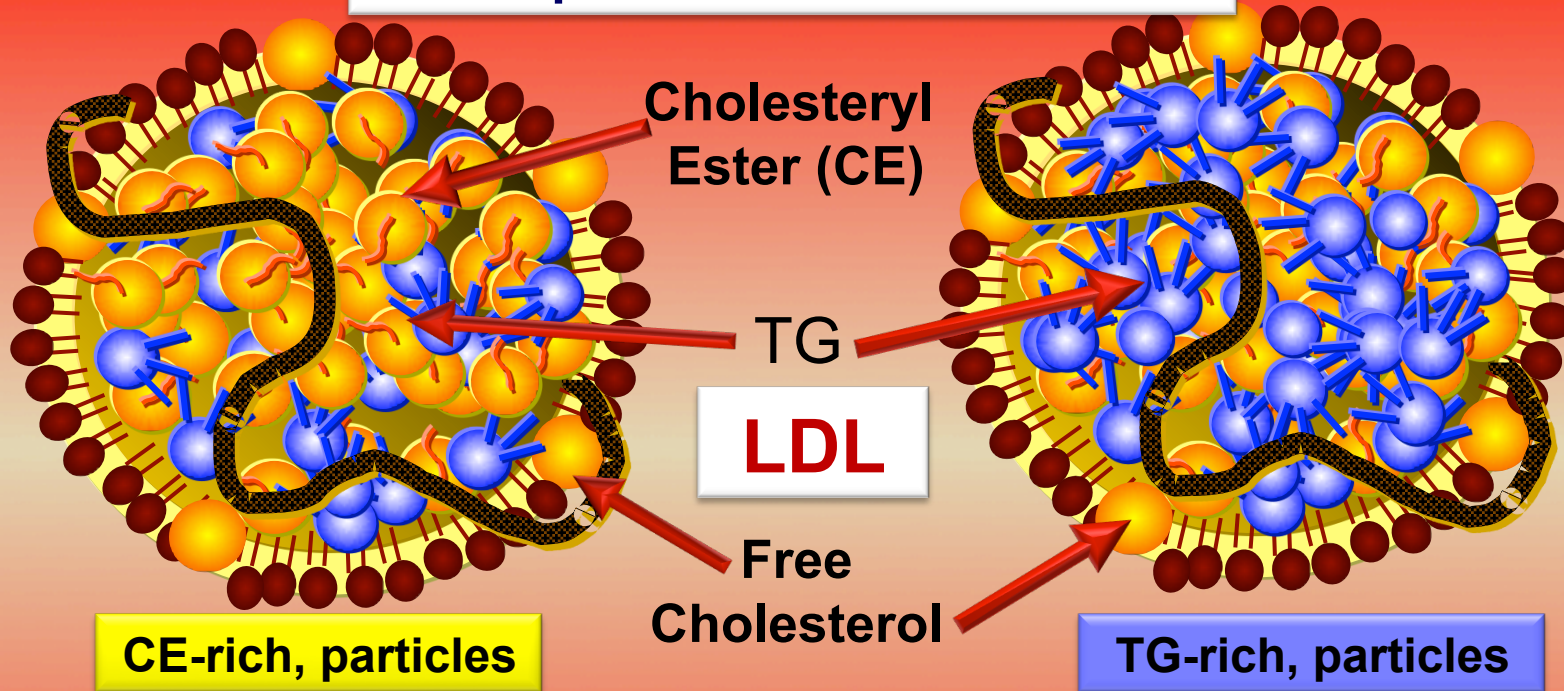


Plasma lipoprotein TG in women at then 3rd trimester of pregnancy (red) and at post-lactation (blue).

Under non-pregnant conditions the TG content in HDL and LDL are low compared to VLDL. In women there is a significant increase in TG in all lipoprotein fractions.

LDL Particle Composition Before and During Pregnancy

Pregnancy is associated LDL & HDL particles enriched in TG



Normal

HDL

Pregnant

Gestation and Lipids

- ▶ Another mechanism by which the fetus benefits from maternal hypertriglyceridemia is the availability of maternal dietary fatty acids.
- ▶ There is efficient absorption of FA during late pregnancy. These FA are reassembled in the enterocyte into TG which are carried in plasma in the form of chylomicron-TG.
- ▶ The placenta takes up maternal TG as a function of their concentration in chylomicra and VLDLs where LPL and other lipases hydrolyze TG, releasing FA to the fetal side

Gestation and Lipids

- ▶ A third mechanism by which maternal hypertriglyceridemia benefits offspring is its contribution to milk synthesis in preparation for lactation.
- ▶ With decreased adipocyte LPL decrease, TG are more available to the breasts. Around parturition there is rapid increases in LPL expression and activity in mammary glands. This is due to both increased prolactin and insulin levels and a specific enhancement in mammary gland insulin sensitivity.
- ▶ Thus mammary induction of LPL facilitates clearing of maternal TG for milk synthesis. Essential FA from the diet become available to the nursing infant.

TG-rich Chylomicra & VLDL Lipolysis at the Placenta and Mammary Gland

Apo CII

Lipoprotein Lipase (LPL)

Increased placental and mammary LPL expression and activity occurs in late pregnancy

Apo E

Phospholipids

Fatty acids

