Lipid and Cholesterol Transport

I. Fatty Acids: from adipose tissue to other tissues
   A. Fatty Acids released from adipose tissue (hormone sensitive lipase)
   B. Travel in the plasma bound to albumin
   C. Liver
      1. Oxidation for energy
      2. ketone body formation
   D. skeletal Muscle
      1. Oxidation for energy

II. Lipoproteins
   A. Chylomicrons
   B. Very Low Density Lipoproteins (VLDL)
   C. Intermediate Density Lipoproteins (IDL)
   D. Low Density Lipoproteins (LDL)
   E. High Density Lipoproteins (HDL)
   F. Remnants
III. Dietary lipids: from intestine to other tissues

A. Chylomicron Metabolism

1. Chylomicron Formation
   a. Nascent chylomicron apoproteins
      i. Apo B-48
         (i) Necessary for secretion
      ii. Apo A-IV
         (i) Amount secreted increases with the amount of fat in the diet
         (ii) Circulating signal for anorectic response to fat meal?
         (iii) May inhibit gastric acid secretion and gastric emptying

2. Chylomicron catabolism
   a. Lipoprotein Lipase
      i. Adipose
         (i) Insulin dependent
         (ii) Down regulated during fasting
      ii. Muscle (Cardiac and Skeletal)
         (i) Insulin independent
         (ii) Activity maintained during fasting
(iii) Lower $K_m$ (higher affinity) for substrate than adipose LPL

b. Apo C-II
   i. Required by Lipoprotein Lipase
   ii. Preferentially moves to new chylomicrons and VLDL
   iii. As hydrolysis of triacylglycerols occurs, apo C-II migrates from the surface
   iv. After about 80% hydrolysis, there is not enough apo C-II present to sustain the reaction with LPL

c. Remnant Uptake
   i. Apo B/E Receptor
      (i) apo B-100
      (ii) Apo E

IV. Endogenously synthesized lipids: from liver to other tissues

A. VLDL metabolism
   1. Formation
      a. Liver
      b. Apo B-100
   2. Hydrolysis by LPL
   3. IDL Uptake
4. LDL formation
   a. Hepatic lipase

B. LDL metabolism
   1. Receptor mediated uptake
      a. HMG CoA Reductase
      b. ACAT
   2. Scavenger receptor

V. Reverse transport of cholesterol from extrahepatic tissues to the liver - HDL metabolism
   A. Receptors
      1. SRB1: cholesterol ester
      2. Apo B/E: apo E containing HDL
   B. Enzymes
      1. LCAT (PCAT):
         a. phosphatidyl choline + Cholesterol → Esterified Cholesterol
      2. Hepatic Lipase: Hydrolysis of triacylglycerol
      3. CETP: Exchanges esterified cholesterol for triacylglycerol
      4. PLTP: Transfer of phospholipids to and from HDL
   C. Apoproteins
      1. Al
a. Promotes the desorption of free cholesterol from membranes

b. Activates LCAT

2. Reservoir for apo CII and apo E

VI. Fate of Cholesterol

VII. Problem 1

A. Type IIa

B. Familial hypercholesterolemia

C. Elevated cholesterol levels

D. Usually normal triglyceride levels

E. LDL is elevated

F. Most commonly a defect in LDL receptor

VIII. Problem 2

A. Type I and Type V

B. Triglyceride levels elevated

C. Type I: chylomicrons elevated

D. Type V: chylomicrons and VLDL elevated

E. Inherited deficiency of LPL or Apo C-II

IX. Problem 3

A. Type III

B. Dysbetalipoproteinemia
C. Elevation of chylomicron and VLDL remnants

D. Defect in, or lack of apo E results in inhibition of remnant removal from plasma

X. Problem 4

A. Type IV

B. Increased flux of apo B-100

C. Increased numbers of VLDL particles

D. Presentation depends on the ability to catabolize VLDL
   1. ↑ results in high LDL levels
   2. ↓ results in high VLDL levels