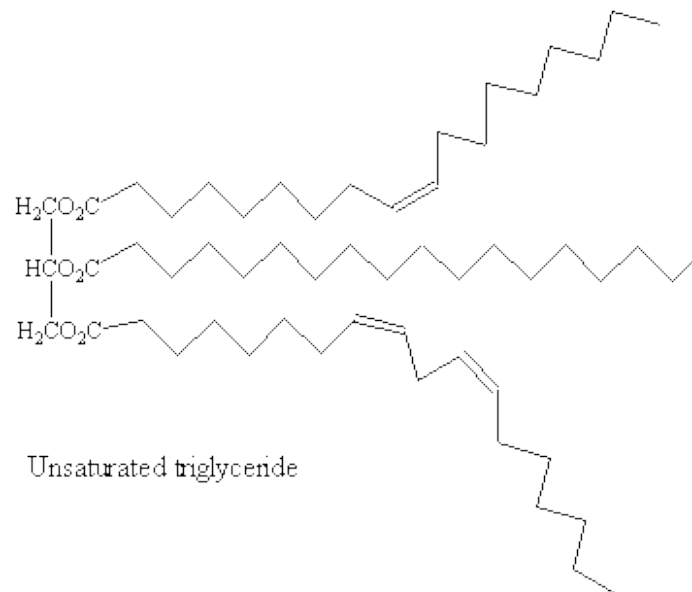




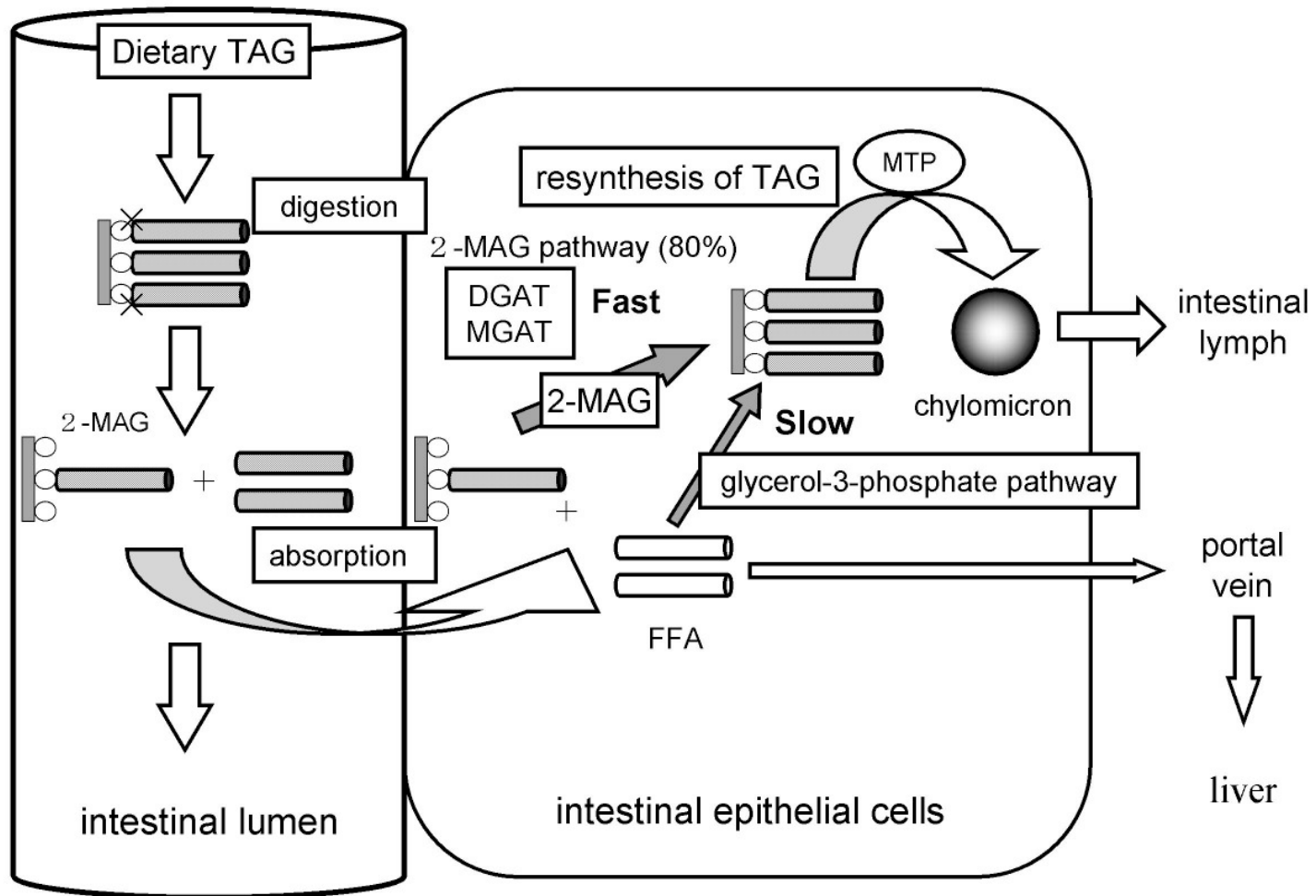
# Triglyceride Metabolism



- A triglyceride consists of three fatty acids covalently bonded to a glycerol molecule through an ester bond
- Triglycerides are synthesized in the liver or ingested and synthesized in the intestinal epithelium



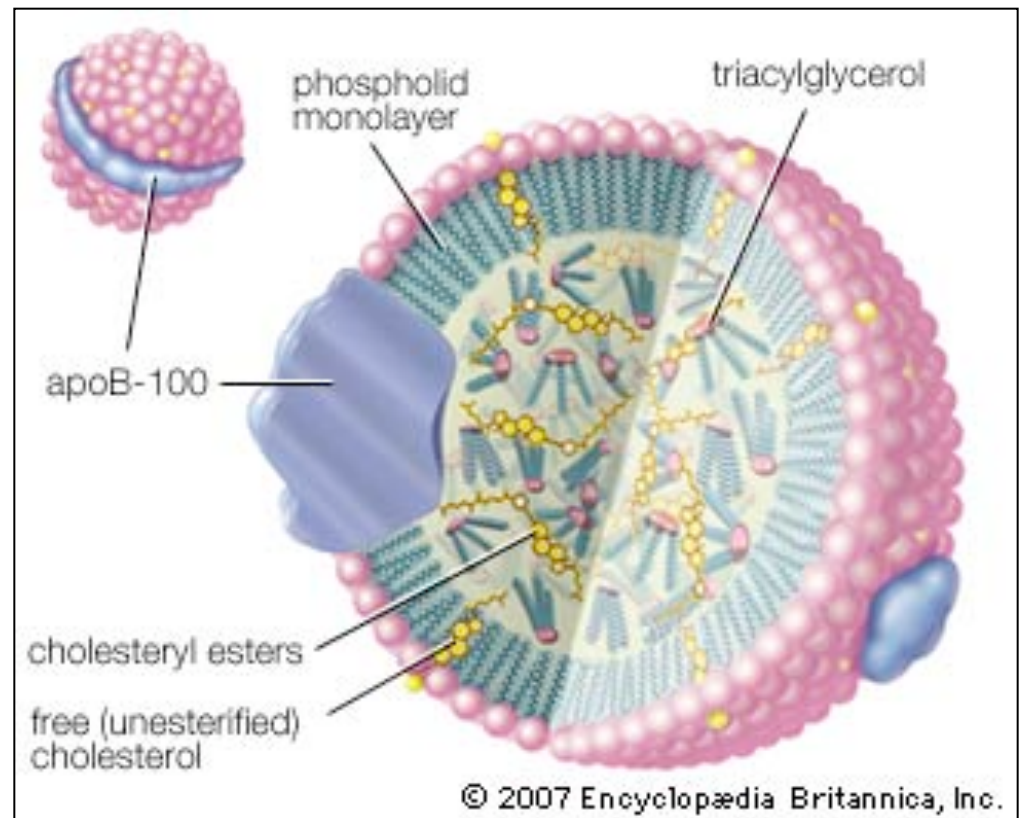
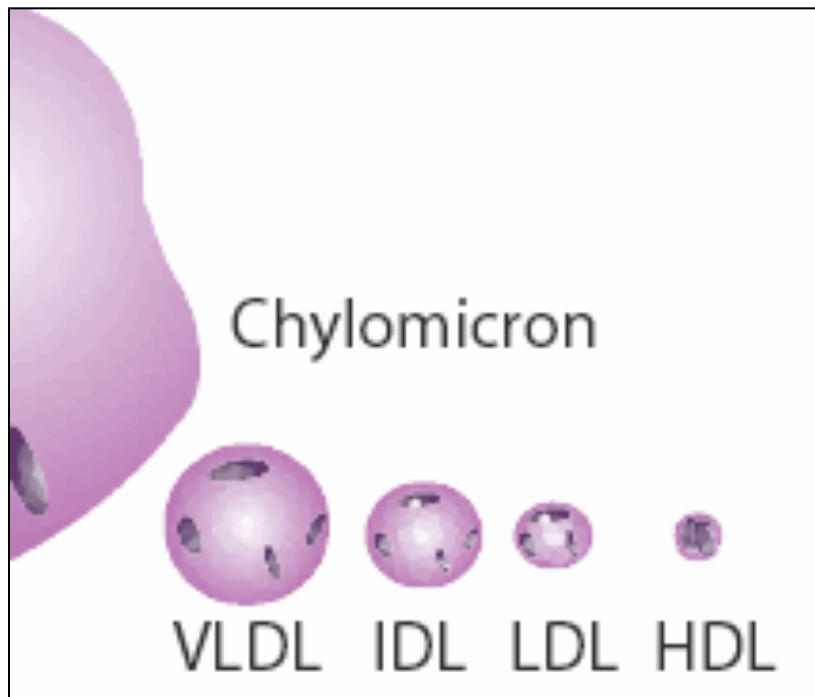
# Triglyceride Absorption



- Triglycerides are packaged in chylomicron lipoproteins in the intestines and transported to the liver
- In the liver triglycerides are packaged in very low-density lipoproteins (VLDL) for transport in the blood stream
- VLDLs are quickly converted to intermediate-density lipoproteins (IDL) and then to low-density lipoproteins (LDL)

- High-density lipoproteins (HDL) transport triglyceride molecules from the peripheral tissues back to the liver
- The majority of fatty acids are transported in lipoproteins as triglycerides
- Some free fatty acids are transported through body bound to albumin

- Water-soluble vesicles that transport hydrophobic fats through blood
- Consist mainly of triglycerides, phospholipids, cholesterol esters, cholesterol, and apolipoproteins
  - The composition varies between lipoproteins
- Lipoprotein classes:
  - Chylomicron
  - VLDL
  - LDL
  - IDL
  - HDL



- 85% by weight triglycerides
- Dietary fat is absorbed in the jejunum as free fatty acids and monoglycerides
- In the intestinal epithelial cells, free fatty acids and monoglycerides are reesterified into triglycerides
- Microsomal transfer proteins are then responsible for combining triglycerides with apolipoproteins and phospholipids to form chylomicrons
- Major apolipoproteins include Apo A and Apo B48

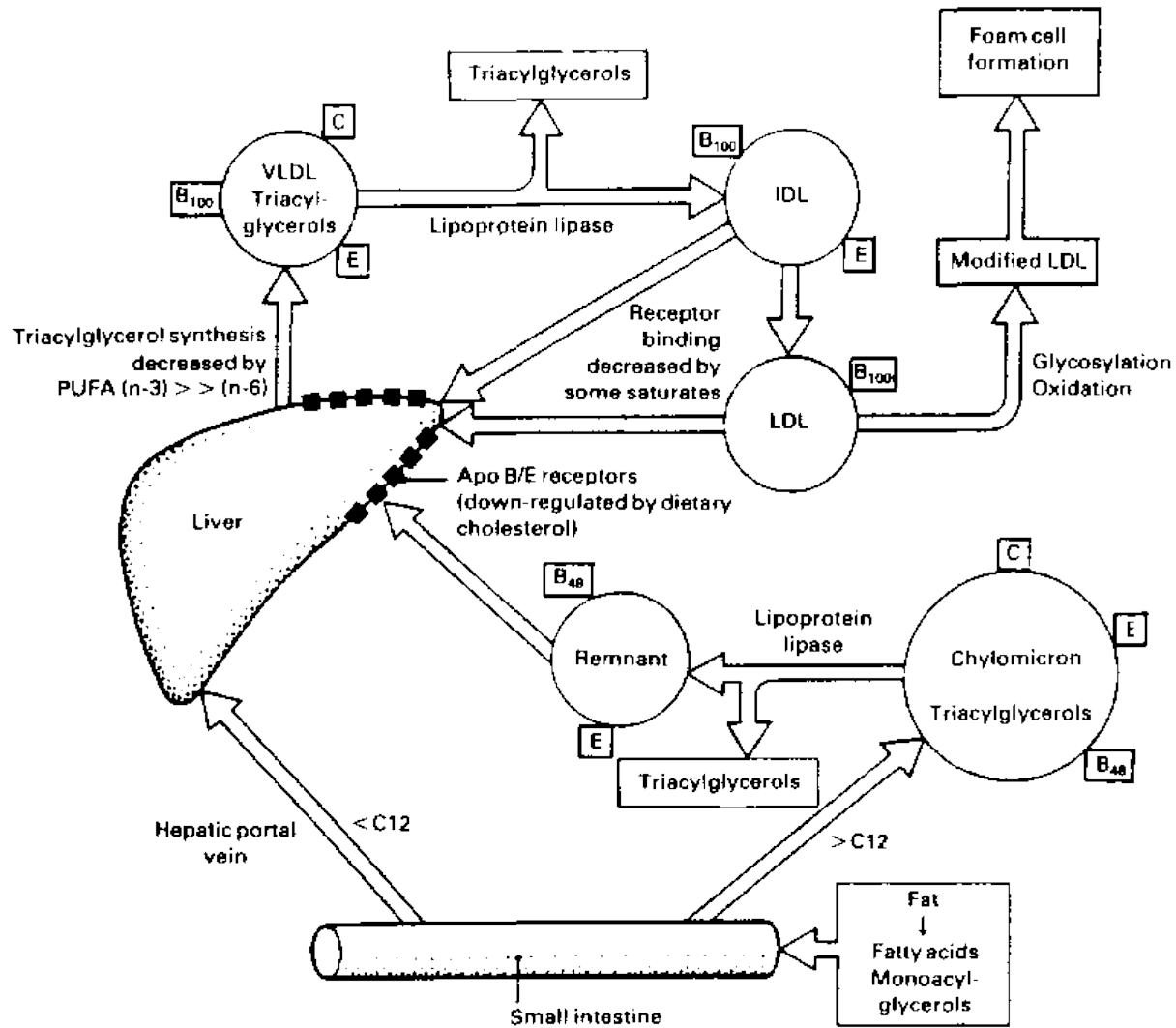


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- 55% by weight triglycerides and 20% by weight cholesterol esters
  - Synthesized mostly through de novo pathways in the liver but also form from chylomicron remnants
  - The major apolipoprotein is Apo B100

- 23% by weight triglycerides and 30% by weight cholesterol esters
- Form from VLDL remnants
- Often metabolize into LDL but can be absorbed into cells via apo B or apo E binding LDL receptors
- Hepatic lipase transforms IDL into LDL

- Responsible for metabolizing lipoprotein vesicles
- Hydrolyzes triglycerides allowing fatty acids to be absorbed and stored in muscle and adipose tissue
- Requires Apo C2 as a cofactor
- Lipoprotein metabolism problems can be attributed to lipoprotein lipase mutations

# Triglyceride Transport

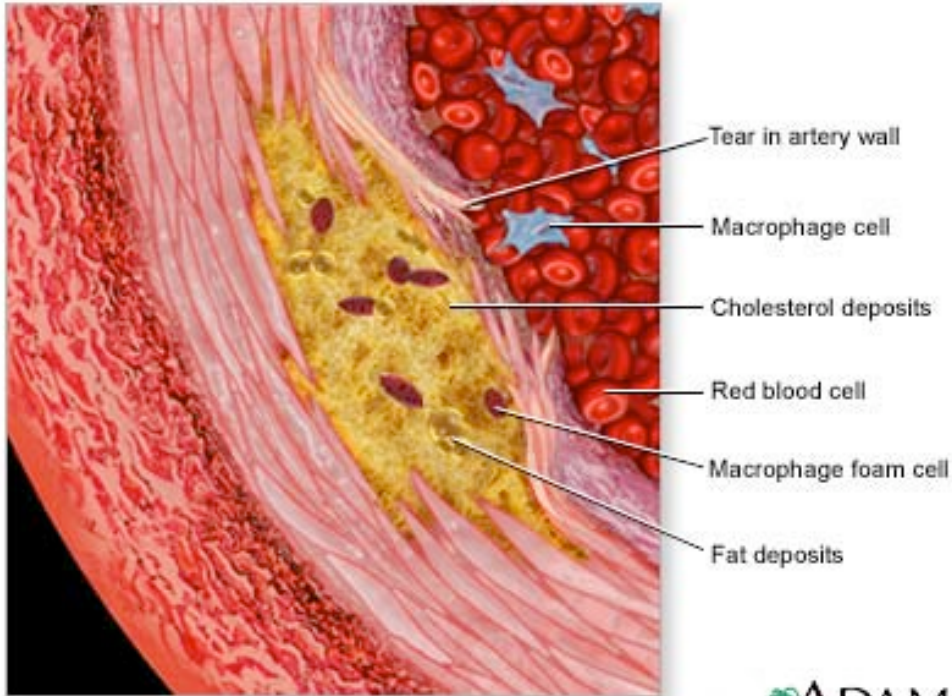


- Primary apolipoprotein on LDL
- Protein embedded in phospholipid surface of lipoproteins
- Serves as the ligand for lipoprotein receptors in various cells in the body

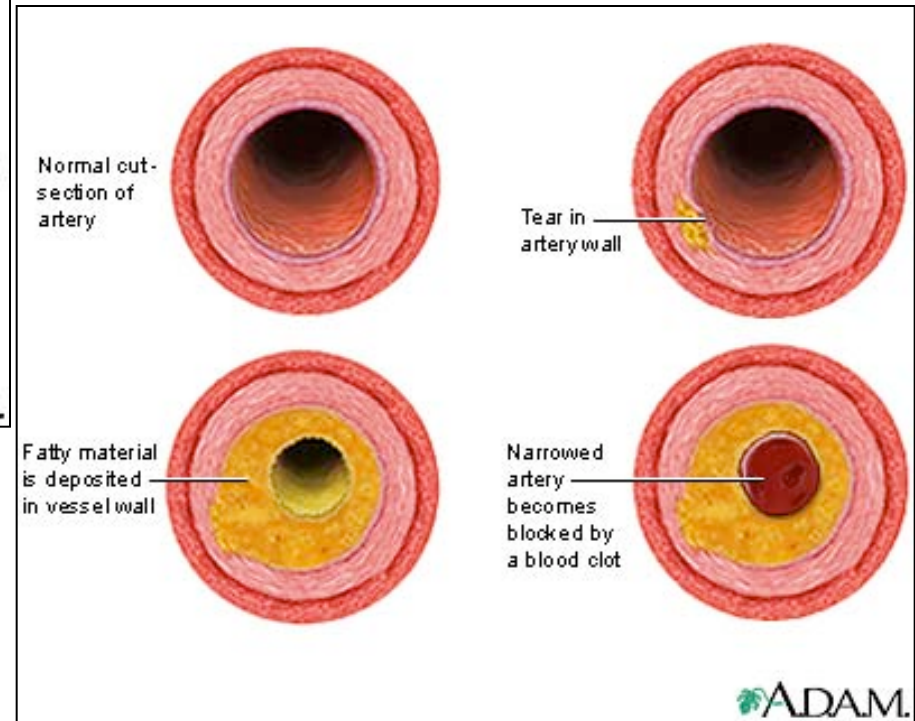
- Elevated triglyceride levels often a result of obesity, diabetes, and unhealthy lifestyle choices
- Attribute to atherosclerosis
- When lipoproteins, especially LDL, are not metabolized correctly hypertriglyceridemia can result
  - Unmetabolized LDL vesicles are often oxidized and dump triglycerides and cholesterol into the blood stream

# Atherosclerosis

Cut-section of artery



ADAM.



ADAM.

- Increased production of lipoproteins
- Mutations in lipoproteins or apolipoprotein receptors can result in hypertriglyceridemia
  - Apo B100 mutations will prevent LDL recognition on receptor cells causing LDL concentration to increase
  - Mutations in apolipoprotein receptors on the surface of cells also prevents triglyceride uptake causing increased triglyceride levels



- Uncontrolled type 1 and 2 diabetes is one of the most common causes of hypertriglyceridemia
- Type 1 Diabetes patients:
  - Lack of insulin greatly decreases lipoprotein lipase activity
  - Controlling insulin levels will prevent hypertriglyceridemia

- Type 2 Diabetes patients:
  - LPL is less effective as a result of insulin insensitivity
  - Patients are often overweight or obese and may have an unhealthy diet containing large amounts of triglycerides
    - This increases production of VLDL in the liver
  - Diabetes causes incomplete metabolism of VLDL and IDL

# No Stimulation of Insulin Secretion

- Most patients with type 2 diabetes experience gradual loss of glycemic control, even with effective oral drugs
- Progressive failure of beta-cells ultimately responsible
  - Toxicity because of elevated glucose and/or lipid levels,
  - Increased secretory demand because of insulin resistance,
  - Amyloid deposition and altered levels of cytokines
- D-Tagatose lowers blood glucose and lipid levels
- D-Tagatose does not stimulate insulin secretion

