**BANTWAGON MASTERCLASS NOTES**

***Glucose Intake*** The major fates of glucose during the absoprtive state are utilization for energy, storage as glycogen in the liver and muscle, or storage as TGs in adipose tissue.

Carbohydrates are used for metabolism and excess is used to make fat - FA synthesis in the LIVER in the cytoplasm of the cell, then lipogenesis also transported to adipose.

When glucose is exhausted TGs are converted to FAs - lipolysis - transported to liver, muscle, and are the metabolised to intermediates in the mitochndrion that enter TCA/ETC to make ATP. If an individual is unable to metabolise carbohydrates (DM type 1) - build up of Acetyl-CoA - excess acetyly-coA is covnerted to ketone bodies, which leave the liver and enter TCA in other tissues, especially the brain. the Acetyl-CoA cannot be metabolised in the liver as it does not contain succinyl CoA synthase.

***Lipoproteins*** Lipoproteins consist of a core of a droplet of TGs or cholesterol esters and a surface molayer of phospholipid and unesterified cholesterol. lipoproteins transport hydrophobic lipid molecules (TGs, phospholipids and cholesterol) through the blood stream from one organ to another. *5 types:* *Chylomicrons*: carry TGs from the intestines to the liver, skeletal muscle and to adipose tissue. *VLDL*: carry newly synthesised TGs from the liver to the adipose tissue. *IDL*: VLDL and LDL intermediary. Not usually detectable in blood. *LDL*:carry cholesterol from hepatocytes to peripheral tissues. "Bad". *HDL*:transports cholesterol from peripheral tissues to the liver. "Good". Is excreted in bile.

...hence, lipoprotein metabolism has 2 pathways: exogenous (GIT) and endogenous (liver).

***Lipid Anabolism - TAG Synthesis:*** Occurs in the cytosol when there is **plentiful supply of glucose** (glycolysis - acetyl-CoA - FAs - TAGs) the latter of which are transported to adipocytes, or to other tissues that metabolised fats for energy, by VLDLs. Lipoprotein lipase (LPL) is located on the luminal walls of capillary endothelial cells.

***Lipid Anabolism - Cholesterol:*** What else happens to the glucose?? A different pathway that makes use to HMG-CoA (3-hydroxy-3-methylglutaryl acetyl-CoA) to Mevalonate reaction (via HMG-CoA reductase). This pathway eventuates in cholesterols production by the hepatocytes. Remember, we need cholesterol to male steroid hormoes etc! Statins are HMG-CoA reducase inhibitors, and therefore decrease cholesterol. Insulin upregulates HMG-CoA reductase. this pathway is also responsible for Vitamin D synthesis.

***Lipoprotein Metabolic Pathways:*** **Exogenous:** we have already seen how chylomicrons facilitate the absorption of TGs from the gut. From the lymphatic circulation, they drain into the thoracic duct and enters the bloodstream. In the blood the chylomicrons acquire Apolipoprotein E to form HDL. Here they activate LPL, which hydolyses TGs carried by the chylomicron into FA and glycerol, which are absorbed by peripheral tissues especially adipose and muscle. **Endogenous:** TGs and cholesterol and ApoE are assembled to form VLDL in the liver, which is then released into the bloodstream. VLDLs encounter LPL which results in the hydrolysis of VLDL to form glycerol and FAs. These substances can now be used in the peripheral tissues. VLDL remnants of hydrolysis = IDLs, which recirculate and can be absorbed by the liver. Other IDLs become LDL and provide cholesterol for peripheral tissue.

***Lipid Transport:*** *Some* glycogen is transformed into Acetyl-CoA and FAs. The FAs combine with alpha-glycerophosphate (GLYCEROL) to form TGs, which are then packaged along with specific protein carriers and are termed **lipoproteins**. The lipoproteins are secreted by the liver and enter the blood. In the blood these packages are called very low density lipoproteins (VDL) becuase they have more fat than protein (fat is less dense in protein). So what is LDL? HDL? In the bloodstream the TGs of the VLDL are hydrolysed to monoglycerides and FAs by the enzyme LPL (located on the luminal surface of capillary endothelial cells). Once this occurs, the FAs can diffuse across the capillary wall into adipose tissue. Here FAs combine with alpha-glycerophosphates supplied by glucose metabolites to form TGs once again. **Atherosclerosis:** If any damage to the arterial endothelium occurs having high blood concentrations of LDLs is a risk factor for artherosclerosis. LDLs collect in the damaged area. Monocytes cross the endothelium and become macrophages. They ingest and oxidise the lipoproteins, they have a foam-like appearance and form a visible fatty streak. This streak enlargens, eventually becoming plaque on the wall.