Study Guide Exam 3

LIPID METABOLISM IN **LIVER**

DeNovo fatty acid synthesis: DeNovo means FA synthesis from non-fat substances.
Glycerol-3-P04: Formed from Glycerol via Glycerol Kinase
DHAP via Glycerol-3-PO4 Kinase
Note: Glycerol and DHAP are **both** used to form Glycerol-3-P04 in the LIVER! In Adipose tissue however there is no glycerol kinase (the enzyme needed to convert glycerol into Glycerol-3-P04 so...only DHAP can be used in the Adipose tissue to form Glycerol-3-PO4.
Also just because the Adipose Tissue doesn't make Glycerol-3-P04 from Glycerol, doesn't mean that Glycerol isn't in the Adipose tissue. In fact, Glycerol is formed in the Adipose tissue via Glycolysis. Once the Glycerol is formed it must be transferred to other tissues that have Glycerol Kinase such as the Liver.

Ketone Body Synthesis
Cholesterol Synthesis
VLDL/HDL Synthesis

LIPID METABOLISM IN **ADIPOSE TISSUE**

Major Function: FAT STORAGE = LIPOGENESIS!

Note: Diets that promote fat synthesis (storage)
-High Carbohydrate=High Energy= ↑Glucose=↑Insulin= favors Fat Storage!!

Again....In Adipose Tissue, Glycerol-3-PO4 (needed for Synthesis of TAGS and Phospholipids) MUST BE FORMED FROM DHAP! Adipose Tissue **lacks** Glycerol Kinase which is the enzyme that changes Glycerol into Glycerol-3-PO4. This process is favored by INSULIN.

LIPOLYSIS = Hydrolysis of Triacylglycerol (TAGS)
Lipolysis is catalyzed by the enzyme **HORMONE SENSITIVE LIPASE (HSL)**
HSL induces lipolysis under the same conditions as β-oxidation!
HSL cleaves TAGS into Free Fatty Acids & Glycerol in the Adipose Tissue.

HSL Regulation
Primarily **Covalent** Modification!

Stimulated By: Catecholamines (epinephrine/norepinephrine)
Glucagon
Adrenocorticotropic Hormone (ACTH)
Growth Hormone (GH)
Methyl Xanthines ex. CAFFEINE

Inhibited By: Insulin

Note: Insulin inhibits HSL by promoting a dephosphorylation by the enzyme protein lipase and stimulating phosphodiesterase. Protein Lipase cleaves a PO4 from HSL inactivating it! Phosphodiesterase is responsible for the breakdown of cAMP which will inhibit HSL by decreasing phosphorylation.

Note: Methyl Xanthines inhibit phosphodiesterase from breaking down cAMP which in turn will prolong LIPOLYSIS.

HSL is active with a PO4

HSL is inactive without a PO4

LIPID METABOLISM IN **MUSCLE**

In MUSCLE Lipids are used for fuel in the form of **KETONE BODIES** and **FATTY ACIDS.**

The importance of Carnitine is that it gets Fatty Acids into the **mitochondria** for **β-oxidation.**

FATTY ACID OXIDATION/KETOSIS

Regulation of β-oxidation in (MITOCHONDRIA)

Stimulated by: Fasting

Uncontrolled Diabetes

Glucagon

Epinephrine

Endurance Training

Inhibited by: FED state

Malonyl CoA: (Increased levels of Malonyl CoA during FAT synthesis, will inhibit fat translocation into the mitochondria (carnitine step)

Disease states that lead to carnitine deficiency and β-oxidation enzyme deficiencies which will lead to hypoglycemia.

Ketone Body Formation :in (MITOCHONDRIA of the LIVER from ACETYLY CoA)

Note: Pathway for Ketone Body formation contains HMG CoA as an intermediate which is also in CHOLESTEROL SYNTHESIS.

3 types of Ketone Bodies: AcetoAcetate

β-hydroxybutyrate

Acetone

Note: Ketone bodies are formed in the Liver but aren't used by the Liver. Once they are formed by the Liver they are transported by blood to extrahepatic tissues!

Note: When Acetyl CoA formation from Fat Oxidation is overly active the excess Acetyl CoA is made into Ketone Bodies. They are formed because there isn't enough Oxaloacetate and too much Acetyl CoA so the extra Acetyl CoA is made into Ketone bodies in the mitochondria of the Liver.

Conditions for Ketone Formation: Starvation/Fasting
Severe/Prolonged Exercise
Uncontrolled Diabetes
Very High Fat/ Low Carb diet

Function of Ketones: Ketones are used for energy by extrahepatic tissues (muscle, brain during adapted starvation).

Note: In the Extrahepatic Tissues, Ketone Bodies are converted back into Acetyl CoA for use in the TCA cycle to make more energy. Therefore, Ketone Bodies can be used as a source of energy when Carbohydrates are low. This also conserves blood glucose.

Note: Ketones are acidic and over long periods of time such as in Uncontrolled Diabetes, excess Ketones can cause KETOACIDOSIS which disrupts the bodies ACID/BASE balance. This can be FATAL.

PHOSPHOLIPID & TRIACYLGLYCEROL SYNTHESIS (lipogenesis)

In order to make Phospholipids & TAGS you must form GLYCEROL-3-PO4 first.

REMEMBER: Glycerol to Glycerol-3-PO4 in **Liver** because **Glycerol Kinase** is present
DHAP to Glycerol-3-PO4 in **Liver and Adipose Tissue** via **Glycerol-3-PO4 Dehydrogenase.**