-The goal of making ketone bodies is to regenerate coA in order to use it for continuation of oxidation of fatty acids. However, when ketone bodies are produced, only a small amount of energy is produced in the form of NADH2 & FADH (the fatty acid is not completely oxidized).
-The production of ketone bodies happens when there is low concentration of oxaloacetate “because it is used in gluconeogenesis”. This happens in prolonged fasting.
-In uncontrolled diabetes mellitus ketone bodies synthesis also increases. That’s because the level of insulin is low and the level of glucagon is high (the same case happens in prolonged fasting even though the blood is hyperglycemic) (glucagon is used to activate lipolysis) & thus free fatty acids in plasma will increase & oxidation of fatty acids will increase as well as the ketone bodies’ synthesis.

-Two of the ketone bodies are acids “acetoacetate & 3-hydroxybutyrate”. When these acids are secreted in plasma, acidosis (keto acidosis) happens & thus the pH drops, increasing the secretion of these anions in the body. These will then react with sodium to produce sodium salts & will be secreted with urine. Loss of water will follow the loss of sodium salts causing dehydration.

-The lung tries to compensate for keto acidosis by releasing more CO2 (hyperventilation). Keto acidosis may thus result in coma!
-Ketone bodies for the liver are like waste products but they still have much energy.
\*note glycolysis doesn’t result in ketone bodies formation because IF there is glycolysis then we are not using oxaloacetate for gluconeogenesis.
-In the muscles ketone bodies can be used by converting them to acetoacetate then adding coA “from succinyl coA” resulting in the formation of acetoacetyl coA. After that, the cleavage of this compound will give us two acetyl coA molecules (which is also the last step of Beta oxidation). As we already know, those two acetyl coA molecules will then enter the TCA cycle to be oxidized.

-Acetyl coA resulted from ketone bodies can be oxidized in the muscles because oxaloacetate in the muscle isn’t used for gluconeogenesis .
-In cardiac muscles ketone bodies are the preferred fuel molecules.
-In prolonged fasting “after day three” the brain can use ketone bodies as a source of energy. Whereas under normal conditions, as we should already know, the brain gets its fuel from glucose which comes from absorption & from glycogen degradation. This only lasts for 24 hours. After that, when the reserve of glycogen is consumed, the body starts to synthesize glucose from amino acids.

-Amino acids are not only stored in the body as a reserve; they have other functions as proteins of which they work as enzymes and carriers and contractile proteins.
- To maintain the proteins in our bodies, the brain after the third day will start using ketone bodies as the major fuel. Ketone bodies can last up until 2 months.
-Levels of ketone bodies and fatty acids will increase in plasma until they reach a certain level –they increase due to starvation- and they will stay constant at that level.
-You can stay alive until you consume all the triacylglycerol reserved in your body.

-***fatty acid synthesis:***
Why do fatty acids usually have an even number of carbon atoms?
Because fatty acids are made of many acetyl coA molecules in which each has two carbon atoms.
Acetyl coA are reduced by reducing power to fatty acids, & energy input is needed because the reaction is a synthesis reaction.
Adding ATP molecules to the reaction of synthesis of fatty acids will cause delta G to become negative.
\*Fatty acid synthesis can’t be done by just reversing beta oxidation, but from chemical point of view there are similarities between beta oxidation & fatty acid synthesis
Malonyl coA is produced from acetyl coA , so ultimately it is acetyl coA “caroboxylated”.
\*Carboxylation is endergonic and decarboxylation is exergonic.
Carboxylation is the rate-limiting step, discovered by Saleh Al-Wakeel, who found out that fatty acid synthesis requires bicarbonate.

\*Fatty acid synthase catalyzes the remaining steps; it’s a multi-functional enzyme complex (has more than one active site). It is formed of two identical chains. Neither of those chains is active on its own. They must be together to function. Every chain of them has 7 different activities: one of them is known as condensing enzyme which has a reactive -SH group on the active site. There is another –SH group found on another domain with pantothenic acid.
\*“coA structure is found on page 7 slide 1”
\*phosphate + pantothenic acid +beta-mercaptoethylamine is called phosphopantethine. This phosphopantethine is found on a domain part of fatty acid synthase. In conclusion, it seems like there is a huge coA linked to a protein, acyl and acetyl are not carried by coA in fatty acid synthesis; they are carried by acyl carrier protein.
-The first two compounds are condensed together and CO2 is released. The CO2 released is the same CO2 added earlier in the carboxylation step. The enzyme is then released –the thioester bond is broken.

-When I have ketoacyl ACP three steps take place: reduction, dehydration, & reduction. After that, Acyl ACP is produced, then the reaction will go back to the first step again (in every cycle two carbons are added).

-In ketoacyl ACP the ketone group is on carbon number 3.

-What drives the previous reaction to go in the forward direction?
The cleavage of the thioester bond which produces energy, and the decarboxylation which also produces also energy making the reaction irreversible. Therefore, overall, the reaction will move in forward direction.

-When reduction is done on ketoacyl ACP NADPH is used “not FADH2 nor NADH” because this reaction occurs in the cytoplasm “no NADH and FADH2 is present” whereas in oxidation it happens in mitochondria.



-***Regarding this photo***:
\*The acetyl group is added on ACP “1”.
\*It is then moved to the condensing enzyme “2”
\*Then the malonyl coA goes to the ACP “3”
\*condensation step and release of CO2 “4” the result is ketoacyl linked to ACP
reduction with NADPH “5” (ketone is converted to hydroxyl).
\*dehydration “6” double bond is formed
\*another reduction with NADPH “7”
\*then the operation is done again and again until the end product “palmitate” is made.

\*\*\*\*you have to know the structures

