SHEET NO.

Lipid 4

METABOLISM

DOCTOR 2019 | MEDICINE | JU

DONE BY : Doctor 2018

SCIENTIFIC CORRECTION :

GRAMMATICAL CORRECTION :

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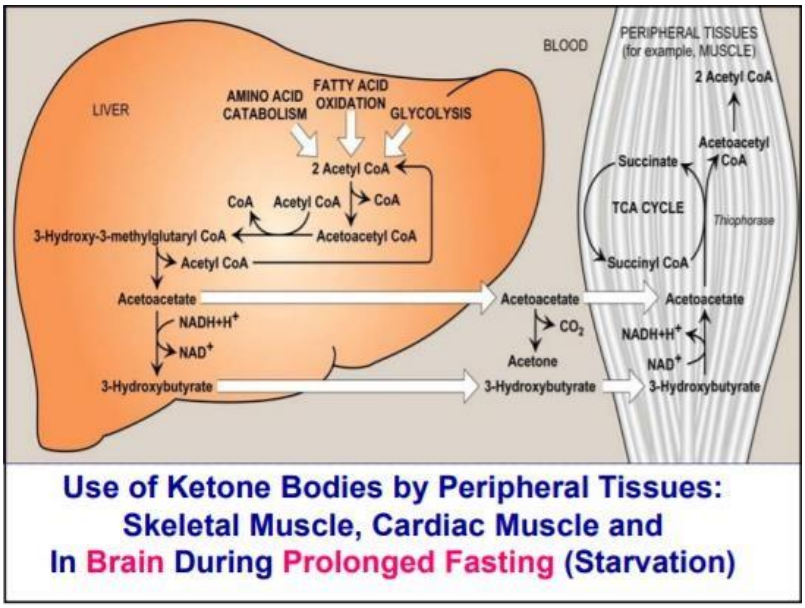
Ketone body synthesis

The goal of ketone body synthesis is to regenerate CoA to keep Beta-oxidation going on. The same idea is repeated in glycolysis when NADH accumulates as a byproduct of pyruvate production, as a result, the pyruvate is then reduced into lactate by LDH in order to regenerate NAD^+ to keep glycolysis going.

Ketone bodies are used by the skeletal muscles, cardiac muscles, and the brain. All of which cannot utilize fatty acids to their benefit, ketone bodies can be thought of as a processed form of fatty acids that the brain can manage, like a bird feeding its little ones.



As you all may know, the brain utilizes carbohydrates as its main source of energy. However, in
cases of prolonged starvation or carbohydrate deprivation, the brain can utilize ketone bodies as an alternative source of energy. This gives the body a chance to regenerate glucose through gluconeogenesis. It also ensures that amino acids will not be used as the alternative source of energy since it has multiple bodily functions including involvement in gluconeogenesis.

Despite the liver producing the ketone bodies, it **cannot** utilize it as a source of energy up due to the depletion of Oxaloacetate in the liver for gluconeogenesis. One important detail is that Acetoacetate and 3-Hydroxybutyrate are **interchangeable**, meaning, you can get one from the other through reduction ⇌ oxidation, respectively.

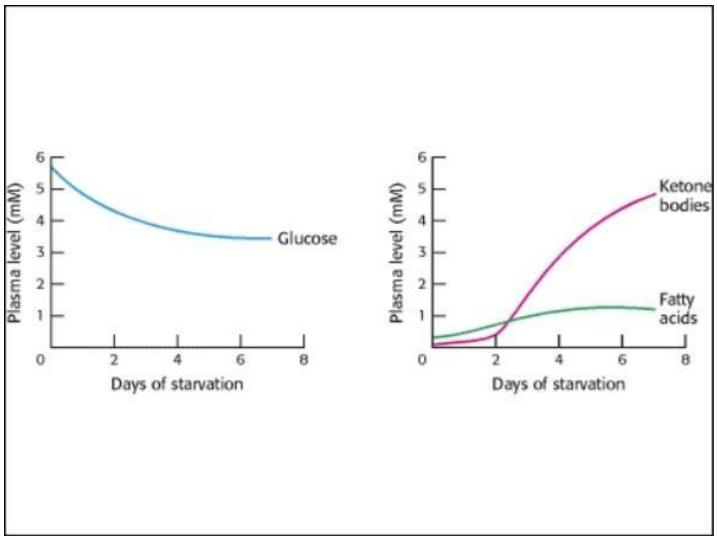
The production of ketone bodies increases during prolonged fasting because they are needed for energy production in the peripheral tissues.

In order to be used up, **acetoacetate** must be activated by joining it to **CoA** which is taken from Succinyl CoA (part of the TCA Cycle). The product formed during this process is **acetoacetyl CoA** (the last intermediate in Beta-oxidation), which can be broken down by thiolase into Acetyl CoA, which then goes into the TCA cycle.

During fasting, blood glucose levels are 5.5 mM and decrease with time, but as the fasting becomes prolonged, blood glucose levels never drop to zero. Instead it remains at a constant level of 3.5 mM. It is maintained by both gluconeogenesis and glycogenolysis.

Fatty acid usage is increased within the first two days.

The usage of ketone bodies, increases substantially two days after prolonged starvation from near zero levels to nearly 4.5mM.



Fuel metabolism in starvation

The idea is to decrease dependence of the brain on the glucose →decreasing gluconeogenesis →decreases protein degradation later on. This allows individuals to survive for longer periods of time (weeks) and use the stored triglycerides.

Fuel metabolism in starvation

	Amount formed or consumed in 24 hours (grams)	
Fuel exchanges and consumption	**3rd day**	**40th day**
Fuel use by the brain		
Glucose	100	40
Ketone bodies	50	100
All other use of glucose	50	40
Fuel mobilization		
Adipose-tissue lipolysis	180	180
Muscle-protein degradation	75	20
Fuel output of the liver		
Glucose	150	80
Ketone bodies	150	150

Note: We don't need to know the numbers and specific details of this table, what we do need to know is what increases or decreases during starvation or prolonged fasting.

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بالتوفيق جميعًا