Ketogenesis and Ketogenolysis

In the absence of sufficient carbohydrates for glycolysis, ample ATP can be produced from ketone bodies via ketogenesis. This process uses fatty acids as fuel for all the body's tissues except RBCs (which are glucose-dependent) and the liver. This process begins with 2 acetyl-CoA in the mitochondria of hepatocytes. The enzyme thiolase converts these into acetoacetyl-CoA. HMG CoA synthase then converts this into HMG-CoA. HMG-CoA is then broken down by HMG-CoA lyase into acetoacetate, the first usable ketone body. This molecule can either enter the bloodstream and peripheral tissues on its own, or be converted into beta-hydroxybutyrate. Acetone can also be produced via non-enzymatic decarboxylation of acetoacetate. Peripheral tissues can utilize these ketone bodies via ketogenolysis: first, acetoacetate and succinyl-CoA are combined via the enzyme thiophorase into acetoacetyl-CoA. This molecule is then broken down by thiolase into 2 acetyl-CoA molecules, which enter the Krebs cycle to provide energy for the cell.

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Ketogenesis

2 Acetyl-CoA
(2) Tutu Seagull Coin-A-purse
The process of ketogenesis begins with 2 acetyl-CoA molecules. These molecules come from fatty acids, which are transported to the mitochondria of hepatocytes.

Thiolase
Thigh-ace
The enzyme thiolase converts 2 acetyl-CoA molecules into acetoacetyl-CoA.

Acetoacetyl-CoA
2 Seagulls Together with Coin-A-purse
Acetoacetyl-CoA is formed from 2 Acetyl-CoA molecules in the mitochondria of hepatocytes by the enzyme thiolase.

Mitochondrial HMG-CoA Synthase
Mitochondria Humming-bird with Coin-purse Synthase
Mitochondrial HMG-CoA Synthase converts acetoacetyl-CoA into HMG-CoA. This is the rate-limiting step in the formation of ketone bodies.

HMG-CoA
Humming-bird with Coin-A-purse
HMG-CoA is created when the enzyme mitochondrial HMG-CoA Synthase acts on acetoacetyl-CoA.

HMG-CoA Lyase
Humming-bird with Coin-A-purse Laser
HMG-CoA lyase converts HMG-CoA into acetoacetate. This is the first usable ketone body produced in this pathway.

Ketone Bodies

Acetoacetate
Seagull-ass
Acetoacetate is one of the three ketone bodies produced via ketogenesis, and can leave hepatocytes. Peripheral tissues are capable of taking up and utilizing this molecule. Urine tests for ketones detect acetoacetate but not other ketone bodies.

Beta Hydroxybutyrate
Beta-fish with Water and Butter
Beta-hydroxybutyrate is another one of the three ketone bodies produced via ketogenesis. This molecule is formed from acetoacetate and is transported in the blood freely for delivery to peripheral tissues. It is not detected by urine ketone tests (while acetoacetate is).

Acetone

Nail Polish Remover

Acetone is produced via the spontaneous non-enzymatic decarboxylation of acetoacetate and is excreted in the breath. This molecule is responsible for the classic “sweet” smell of patients in diabetic ketoacidosis or other conditions with ketosis. It can also be converted to lactate by the liver or pyruvate by peripheral tissues.

Ketogenolysis

Succinyl-CoA and Acetoacetate

Suckers Coin-A-purse to Seagull-ass

Ketogenolysis describes the process by which tissues uptake ketone bodies and convert them into energy. In peripheral tissues, it begins when succinyl-CoA and acetoacetate are combined via the enzyme thiophorase.

Acetoacetyl-CoA

2 Seagulls Together with Coin-A-purse

Acetoacetyl-CoA is formed from succinyl-CoA and Acetoacetate in all tissues except the liver.

Thiolase

Thigh-ace

The enzyme thiolase is responsible for catalyzing the splitting of acetoacetyl-CoA into two molecules of acetyl-CoA

2 Acetyl-CoA

(2) Tutu Seagull-Coin-A-purse

Once they have arrived in peripheral tissues, the two molecules of acetyl-CoA derived from acetoacetyl-CoA may enter the Krebs cycle and provide ATP for cellular respiration.
