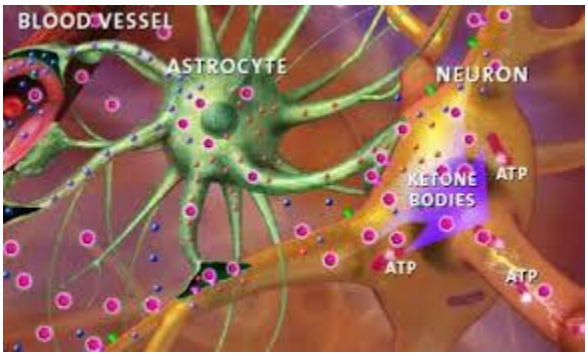
Low Carbohydrate Diet



Ketosis

Ketosis /kɨˈtoʊsɨs/ is a metabolic state where most of the body's energy supply comes from ketone bodies in the blood, in contrast to a state of glycolysis where blood glucose provides most of the energy. It is characterised by serum concentrations of ketone bodies over 0.5 millimolar with low and stable levels of insulin and blood glucose. It is almost always generalized, with hyperketonemia, that is, an elevated level of ketone bodies in the blood throughout the body. Ketone bodies are formed by ketogenesis when liver glycogen stores are depleted. The main ketone bodies used for energy are acetoacetate and β-hydroxybutyrate, and the levels of ketone bodies are regulated mainly by insulin and glucagon.[4] Most cells in the body can use both glucose and ketone bodies for fuel, and during ketosis free fatty acids and glucose synthesis (gluconeogenesis) fuel the remainder.

During the usual overnight fast the body's metabolism naturally switches into ketosis, and will switch back to glycolysis after a carbohydrate-rich meal. Longer-term ketosis may result from fasting or staying on a low-carbohydrate diet, and deliberately induced ketosis serves as a medical intervention for intractable epilepsy. In glycolysis higher levels of insulin promote storage of body fat and block release of fat from adipose tissues, while in ketosis fat reserves are readily released and consumed. For this reason ketosis is sometimes referred to as the body's "fat burning" mode.

Degree of ketosis

The concentration of ketone bodies may vary depending on diet, exercise, degree of metabolic adaptation and genetic factors. Nutritional ketosis can be established when a low carbohydrate (under about 50g/day for an adult) and moderate protein (about 100g/day) diet is followed for more than 3 days. This table shows the concentrations typically seen under different conditions[1]

blood concentration (millimolar)	Condition
< 0.2	not in ketosis
0.2 - 0.5	slight/mild ketosis
0.5 - 3.0	nutritional ketosis
2.5 - 3.5	post-exercise ketosis
3.0 - 6.0	starvation ketosis

15 - 25	ketoacidosis

Note that urine measurements may not reflect blood concentrations. Urine concentrations will be lower with greater hydration, and after adaptation to a ketogenic diet the amount lost in the urine drops while the metabolism remains ketotic. In addition most urine strips only measure acetoacetate, while after adaptation the predominant ketone body is β-hydroxybutyrate.

Metabolic pathways

When glycogen stores are not available in the cells, fat (triacylglycerol) is cleaved to provide 3 fatty acid chains and 1glycerol molecule in a process known as lipolysis. Most of the body is able to use fatty acids as an alternative source of energy in a process called beta-oxidation. One of the products of beta-oxidation is acetyl-CoA, which can be further used in the citric acid cycle. During prolonged fasting or starvation, or as the intentional result of a ketogenic diet, acetyl-CoA in the liver is used to produce ketone bodies instead, leading to a state of ketosis.

During starvation or a long physical training session, the body starts using fatty acids instead of glucose. The braincannot use long-chain fatty acids for energy because they are completely albumin-bound and cannot cross the blood–brain barrier. Not all medium-chain fatty acids are bound to albumin. The unbound medium-chain fatty acids are soluble in the blood and can cross the blood–brain barrier. The ketone bodies produced in the liver can also cross the blood–brain barrier. In the brain, these ketone bodies are then incorporated into acetyl-CoA and used in the citric acid cycle.

The ketone body acetoacetate will slowly decarboxylate into acetone, a volatile compound that is both metabolized as an energy source and lost in the breath and urine.

Ketoacidosis

Ketone bodies are acidic, but acid-base homeostasis in the blood is normally maintained through bicarbonate buffering,respiratory compensation to vary the amount of CO_2 in the bloodstream, hydrogen ion absorption by tissue proteins and bone, and renal compensation through increased excretion of dihydrogen phosphate and ammonium ions. Prolonged excess of ketone bodies can overwhelm normal compensatory mechanisms, leading to acidosis if blood pH falls below 7.35.

There are two major causes of ketoacidosis:

- Most commonly, ketoacidosis is diabetic ketoacidosis (DKA), resulting from increased fat metabolism due to a shortage of insulin. It is associated primarily with type I diabetes, and may result in a diabetic coma if left untreated.

- Alcoholic ketoacidosis (AKA) presents infrequently, but can occur with acute alcohol intoxication, most often following a binge in alcoholics with acute or chronic liver or pancreatic disorders. Alcoholic ketoacidosis occurs more frequently following methanol or ethylene glycol intoxication than following intoxication with uncontaminatedethanol.

A mild acidosis may result from prolonged fasting or when following a ketogenic diet or a very low calorie diet.

Diet

If the diet is changed from one that is high in carbohydrates to one that does not provide sufficient carbohydrate to replenish glycogen stores, the body goes through a set of stages to enter ketosis. During the initial stages of this process, blood glucose levels are maintained through gluconeogenesis, and the adult brain does not burn ketones. However, the brain makes immediate use of ketones for lipid synthesis in the brain. After about 48 hours of this process, the brain starts burning ketones in order to more directly use the energy from the fat stores that are being depended upon, and to reserve the glucose only for its absolute needs, thus avoiding the depletion of the body's protein store in the muscles.

Ketosis is deliberately induced by use of a ketogenic diet as a medical intervention in cases of intractable epilepsy..Other uses of low-carbohydrate diets remain controversial. Induced ketosis or low-carbohydrate diet terms have very wide interpretation. Therefore Stephen S. Phinney and Jeff S. Volek coined the term "nutritional ketosis" to avoid the confusion.

Carbohydrate deprivation to the point of ketosis has been argued both to have negative and positive effects on health.

Diagnosis

Whether ketosis is taking place can be checked by using special urine test strips such as *Ketostix*. The strips have a small pad on the end which is dipped in a fresh specimen of urine. Within a matter of seconds, the strip changes color indicating the level of acetoacetate ketone bodies detected, which reflects the degree of ketonuria, which, in turn, can be used to give a rough estimation of the level of hyperketonemia in the body (see table below). Alternatively, some products targeted to diabetics such as the Abbott Precision Xtra or the Nova Max can be used to take a blood sample and measure the β-hydroxybutyrate ketone levels directly. Normal serum reference ranges for ketone bodies are 0.5–3.0 mg/dL, equivalent to 0.05–0.29 mmol/L.

Also, when the body is in ketosis, one's breath may smell of acetone. This is due to the breakdown of acetoacetic acid into acetone and carbon dioxide which is exhaled through the lungs. Acetone is the chemical responsible for the smell of nail polish remover and some paint thinners.

Urine value	Designation	Approximate serum concentration	
		mg/dL	mmol/l
0	Negative	Reference range: 0.5–3.0[23]	0.05–0.29[23]
1+		**5** (interquartile range (IQR): 1–9)[24]	**0.5** (IQR: 0.1–0.9)[25]
2+	Ketonuria[26]	**7** (IQR: 2–19)[24]	**0.7** (IQR: 0.2–1.8)[25]
3+		**30** (IQR: 14–54)[24]	**3** (IQR: 1.4–5.2)[25]
4+	Severe ketonuria[27]	–	–

Controversy

Some clinicians regard restricting a diet from all carbohydrates as unhealthy and dangerous. However, it is not necessary to completely eliminate all carbohydrates from the diet in order to achieve a state of ketosis. Other clinicians regard ketosis as a safe biochemical process that occurs during the fat-burning state.[19] Ketogenesis can occur solely from the byproduct of fat degradation: acetyl-CoA. Ketosis, which is accompanied by gluconeogenesis (the creation of glucose de novo from pyruvate), is the specific state with which some clinicians are concerned. However, it is unlikely for a normal functioning person to reach life-threatening levels of ketosis, defined as serum beta-hydroxybutyrate (B-OHB) levels above 15 millimolar (mM) compared to ketogenic diets among non diabetics which "rarely run serum B-OHB levels above 3 mM." This is avoided with proper basal secretion of pancreatic insulin. People who are unable to secrete basal insulin, such as type 1 diabetics and long-term type II diabetics, are liable to enter an unsafe level of ketosis, causing an eventual comatose state that requires emergency medical treatment.

The anti-ketosis conclusions have been challenged by a number of doctors and advocates of low-carbohydrate diets, who dispute assertions that the body has a preference for glucose and that there are dangers associated with ketosis. The Inuit are often cited an example of a culture that has lived for thousands of years on a low-carbohydrate diet. However, in multiple studies the traditional Inuit diet has not been shown to be a ketogenic diet. Not only have multiple researchers been unable to detect any evidence of ketosis resulting from the traditional Inuit diet, but the ratios of fatty-acid to glucose were observed to be well below the generally accepted level ofketogenesis. Furthermore, studies investigating the fat yields from fully dressed wild ungulates, and the dietary habits of the cultures who rely on them, suggest that they are too lean to support a ketogenic diet. With limited access to fat and carbohydrates, cultures such as the Nunamiut Eskimos—who relied heavily on caribou for subsistence—annually traded for fat and seaweed with coastal-dwelling Taremiut.

The Inuit consumed as much as 15-20% of their calories from carbohydrates, largely from the glycogen found in raw meats. Furthermore, the blubber, organs, muscle and skin of the diving marine mammals that the Inuit ate have significant glycogen stores that are able to delay postmortem degradation, particularly in cold weather.

Whether a no-carbohydrate diet would be safe for non-Inuit is also disputed: Nick Lane speculates that the Inuit may have a genetic predisposition allowing them to eat a ketogenic diet and remain healthy. According to this view, such an evolutionary adaptation would have been caused by environmental stresses. This speculation is unsupported, however, in light of the many arctic explorers, including John Rae, Fridtjof Nansen, and Frederick Schwatka, who adapted to Inuit diets with no adverse effects.

Schwatka specifically commented that after a 2- to 3-week period of adaptation to the Inuit diet he could manage "prolonged sledge journeys," including the longest sledge journey on record, relying solely on the Inuit diet without difficulty. Furthermore, in a comprehensive review of the anthropological and nutritional evidence collected on 229 hunter-gatherer societies it was found that, "Most (73%) of the worldwide hunter-gatherer societies derived >50% (≥56–65% of energy) of their subsistence from animal foods, whereas only 14% of these societies derived >50% (≥56–65% of energy) of their subsistence from gathered plant foods," suggesting that the ability to thrive on low carbohydrate diets is widespread and not limited to any particular genetic predisposition. While it is believed that carbohydrate intake after exercise is the most effective way of replacing depleted glycogen stores, studies have shown that, after a period of 2–4 weeks of adaptation, physical

endurance (as opposed to physical intensity) is unaffected by ketosis, as long as the diet contains high amounts of fat. Some clinicians refer to this period of keto-adaptation as the "Schwatka Imperative" after the explorer who first identified the transition period from glucose-adaptation to keto-adaptation.

http://en.wikipedia.org/wiki/Ketosis