

# Health Benefits of Ketones and the Ketogenic Diet

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### ARTICLE SUMMARY

- Although glucose is the primary source of energy for the human body, ketones are an alternative energy source that is more efficient and can provide many health benefits.
- Small amounts of ketones are produced by the liver in the morning after depletion of glucose following an overnight fast.
- It is possible to significantly increase liver ketone production by maintaining a low-carbohydrate, high-fat ketogenic diet or by consuming medium-chain triglycerides (MCTs) derived from coconut oil. Daily consumption of two tablespoons of ketogenic caprylic and capric acid from coconut oil provide the equivalent of an estimated 8 to 9 percent of brain energy.
- Brain glucose absorption declines with age, but brain ketone absorption remains unchanged. The age-related decline in brain absorption of glucose can be offset by ketones from a ketogenic diet or MCT oils.
- Ketones improve cognitive function in the young and healthy as well as in the elderly and those with Alzheimer's disease.
- A ketogenic diet or exercise can help the body clean out damaged and senescent cells and regenerate new ones. This process of cellular clean-up (called autophagy) is a key to preventing inflammation and improving one's health and lifespan.
- The decline with age of NAD<sup>+</sup> (an activated form of vitamin B3 essential for cellular energy production) plays a role in age-related disease. Ketone-based energy production results in significantly increased NAD<sup>+</sup>, which activates enzymes that have clinical potential in the treatment of many diseases of aging.

Glucose is the primary source of energy in a normal diet. Ketones are an alternative energy source that is more efficient than glucose and can provide many health benefits. Although the acknowledged clinical benefits of ketones have mostly centered on neurons, studies have found that ketones provided as fuel also result in general improvement of muscle function<sup>1</sup> and may suppress

appetite and aid in weight loss.

Ketones are water-soluble molecules. There are three types: acetoacetate and beta-hydroxybutyrate, and their breakdown product, acetone.

Ordinarily, the liver produces a small amount of ketones in the morning following an overnight fast when glucose has been depleted. Ketone production by the liver from fatty acids can be increased by maintaining a high-fat, lowcarbohydrate ketogenic diet or by consuming medium-chain triglycerides derived from coconut oil. The ketogenic diet, which was developed nearly one hundred years ago as a treatment for epileptic seizures, shifts energy production from primarily glucose to primarily ketones. In the classic ketogenic diet, carbohydrate and protein consumption are restricted to 20 to 30 percent of calories, while 70 to 80 percent of calories comes from fat.

### **CLEANING OUT DAMAGED CELLS**

Autophagy is a detox process your body undergoes when glucose is depleted to clean out damaged cells and regenerate new ones. The ketogenic diet promotes starvation-induced autophagy that takes place in the liver and kidney and plays an essential role in ketone production to maintain energy balance.<sup>2</sup> A protein called p62 becomes activated to induce autophagy. Increasing lines of evidence suggest that autophagy is required for many mechanisms that mediate human lifespan extension, such as caloric restriction.

In addition to helping to clear damaged cells from the body, autophagy clears senescent cells that serve no functional purpose but still linger inside tissues and organs. The reason it is so important to remove both senescent and damaged cells is because they can trigger inflammatory pathways and contribute to various diseases such as cancer, neurodegeneration, cardiomyopathy, diabetes, liver diseases, autoimmune diseases and infections.

Stimulation of autophagy generally improves cardiac function by removing accumulated misfolded proteins, dysfunctional mitochondria and damaged DNA, thereby improving the overall cellular environment and alleviating aging-associated pathology in the heart. Considerable evidence also

points to moderate up-regulation of neuronal autophagy as a rational strategy for prevention of neurodegenerative disorders. Hence, autophagy may mediate some of the neuroprotective benefits of ketogenic diets.

While the ketone production and active autophagy that occur during a ketogenic diet are highly beneficial, continuously maintaining a very low-carbohydrate ketogenic diet—such as a carbohydrate intake as low as 5 percent of calories—can result in vitamin and mineral deficiencies due to inadequate intake of vegetables. Thus, when undertaking a ketogenic diet, an extremely low carbohydrate intake of 5 percent of calories should be avoided. Ketogenic diets that contain around 20 percent of calories as carbohydrates should be adequate to prevent micronutrient deficiencies. A recent article on carbohydrate needs suggested “an initial carbohydrate intake target of 100 grams per day”—about 20 percent of calories.<sup>3</sup> (There are about 50 grams of carbohydrates in one potato, one sweet potato, one slice of bread, one serving of cooked oatmeal and one serving of cooked rice.)

Other strategies to induce autophagy and produce ketones while avoiding the problems of nutrient deficiencies that may occur during a continuous ketogenic diet include engaging in intermittent fasting (limiting food intake to four to eight hours per day) or undertaking a ketogenic (high-fat, low-carbohydrate) diet for eighteen to twenty-eight hours just one or two days per week. Autophagy can also be activated by intense exercise. Certain foods, including turmeric, ginger, ginseng, elderberries, green tea and coffee help activate autophagy, and it can be helpful to consume fats before carbs.

### **CAPRYLIC AND CAPRIC FATTY ACIDS**

Ketones are produced by the medium-chain triglycerides (MCTs) caprylic acid (C8) and capric acid (C10), which comprise about 15 percent of coconut oil. Caprylic acid produces about 2.7 times more ketones than capric acid. These medium-chain triglycerides are widely available either as 100 percent caprylic acid or as a mixture of caprylic and capric acids. Two tablespoons of the mixture of caprylic and capric acids are equivalent to 8 to 9 percent of brain energy. I usually use caprylic MCT oil.

The use of medium-chain triglycerides for ketone production has fewer side effects and produces more ketones than the ketogenic diet. A study that compared ketogenic diets that used long-chain fatty acids (LCFAs), the kind in butter and meat fats, with a ketogenic diet that used the medium-chain triglyceride caprylic acid found that the diet that used MCTs produced twice as many ketones as the diet using LCFAs.<sup>4</sup>

A couple of studies suggest that the ketogenic caprylic and capric medium-chain fatty acids may activate autophagy. A recent study demonstrated that increased dietary medium-chain fatty acids (MCFAs) boosted the MCFA/LCFA ratio, restored suppressed autophagy and mitigated nonalcoholic steatohepatitis (NASH), a type of nonalcoholic fatty liver disease.<sup>5</sup> However, MCTs do not deplete

glucose and will not activate autophagy to the same extent as a ketogenic diet or exercise.

### **BRAIN SUPPORT IN LATER LIFE**

Alzheimer's disease affects about five million people and Parkinson's disease about five hundred thousand in the United States. By age group, Alzheimer's affects about 2.5 percent of sixty-five-year-olds, rising to 30 percent of those over eighty-five years of age.

Although the brain relies on blood glucose as its main energy source, research shows that glucose uptake is lower in the frontal cortex of people over sixty-five years old, "despite cognitive scores that are normal for age."<sup>6</sup> In fact, several studies have shown a 10 to 15 percent lower brain glucose uptake in the elderly, a deficit that increases to 20 to 25 percent in individuals with Alzheimer's disease.

Whereas uptake of brain glucose decreases in the cognitively impaired, ketone uptake remains similar to that of cognitively healthy, age-matched controls. Ketones can therefore replace brain glucose energy deficits in cognitive impairment and Alzheimer's disease.<sup>6</sup>

In a 2013 study, eight healthy young adults took thirty grams per day of MCT oil for three weeks.<sup>7</sup> The researchers reported that the MCT supplementation protocol "was mildly and safely ketogenic and had no side effects in healthy humans on their regular diet." They also estimated that this degree of ketonemia (increased circulating ketones) contributed up to 8 to 9 percent of brain energy metabolism.

In a 2015 study, patients with mild cognitive impairment received either fifty-six grams of medium-chain triglycerides daily or a placebo for twenty-four weeks.<sup>8</sup> The MCT dose provided 18 percent of the brain's energy needs. After measuring serum ketone levels and carrying out cognitive assessments, the researchers found that intake of MCT oil increased serum ketones and improved memory; intake of a placebo did not show improvement of any of the cognitive measures tested.

Elevation of ketones may offer neuroprotection in the treatment or prevention of both Alzheimer's disease, where therapy is lacking, and Parkinson's disease, where therapy with L-dopa is time-limited. Up to ninety grams per day of C8 and C10 MCT oil can safely achieve nutritional ketosis to compensate for deteriorating brain glucose in aging.

### **NAD+ AND CELLULAR ENERGY**

Ketones increase an activated form of vitamin B3—called NAD+—which is essential for cellular

energy production.<sup>9</sup> The full name for this coenzyme is nicotinamide adenine dinucleotide. NAD<sup>+</sup> is a ubiquitous coenzyme that functions primarily as an electron carrier of oxidoreductase in multiple redox reactions. Redox reactions are a primary component of energy creation. Diverse lines of evidence place NAD<sup>+</sup> at the center of metabolic health and disease. Notably, both NAD<sup>+</sup> homeostasis and its metabolism are thought to play critical roles in regulating autophagy.<sup>10</sup>

During cellular energy production, NAD<sup>+</sup> is reduced to NADH (another form of NAD). However, ketone-based energy production reduces 64 percent less NAD<sup>+</sup> to NADH than glucose-based energy production. This results in significantly increased NAD<sup>+</sup>, decreased NADH, and an increased NAD<sup>+</sup>/NADH ratio—with more oxidized molecules available for bioenergetic demands.

A ketone-induced increase in the NAD<sup>+</sup>/NADH ratio also activates downstream signaling pathways that result in an increase in the seven beneficial mammalian sirtuin enzymes—enzymes “associated with major benefits such as longevity and reduced inflammation.”<sup>9</sup> The sirtuin enzymes have “clinical potential” in treatment of a variety of conditions,<sup>11</sup> including not just dementia and Parkinson’s disease but also diabetes, cardiovascular disease, osteoporosis, arthritis, epilepsy and nonalcoholic fatty liver disease. Thus, “increasing NAD is a coveted therapeutic endpoint.”<sup>9</sup>

NAD<sup>+</sup> levels decline markedly with age, creating an energy deficit that decreases the body’s ability to retain youthful function. By age fifty, a person may have only half the NAD<sup>+</sup> as in their youth. By age seventy, NAD<sup>+</sup> levels drop to 25 percent of that expressed in youth. This decline appears to play a crucial role in the development of metabolic dysfunction and age-related diseases.

Thus, therapy with ketones can enhance brain health and increase overall health via mechanisms related to NAD<sup>+</sup> that render cells more resilient against DNA damage and a host of other insults. In short, ketone-induced increases in brain NAD<sup>+</sup> serve as a rapid and enduring strategy to halt or even reverse disease progression.

## **NUTRITIONAL KETOSIS AND THE HEALTHY BRAIN**

It is now apparent that the increase in the NAD<sup>+</sup>/NADH ratio that occurs during energy production by ketones is the primary mechanism behind the beneficial effects of increased circulating ketones.<sup>9</sup> These effects may also be of benefit to healthy individuals.

A recent study demonstrated an increase in the NAD<sup>+</sup>/NADH ratio resulting from nutritional ketosis in twenty-five healthy young men and women.<sup>12</sup> Study participants were given a single dose of ten grams of MCT oil (60 percent C8 and 40 percent C10), which resulted in significant changes in NAD metabolic levels in the brain. Specifically, the MCT oil increased NAD<sup>+</sup> by 3.4 percent and reduced

NADH by 13 percent, producing an 18 percent increase in the NAD<sup>+</sup>/NADH ratio. These results provide clues as to how nutritional ketosis might contribute to the preservation of brain health. It is reasonable to expect that fifty to ninety grams per day of MCT oil may more than double the NAD<sup>+</sup>/NADH ratio, with no adverse side effects.

## **NAD PRECURSORS**

Pharmaceutical companies are currently manufacturing and selling supplements that contain NAD<sup>+</sup> precursors (such as nicotinamide or nicotinamide riboside) with the intent of increasing endogenous NAD<sup>+</sup> levels and enhancing metabolic resilience. These outcomes may also be achieved physiologically by ketogenic strategies. Moreover, while both NAD supplements and ketogenic MCTs can increase serum NAD levels, the MCTs also provide an alternative brain energy source for those who have inadequate absorption of brain glucose. Further, the ketone-producing MCT oils have been found to have many other benefits including improved muscle and cognitive function.

## **CONCLUSIONS**

The health benefits of ketones can be optimized through intermittent use of the ketogenic diet together with daily use of MCT oil. Using the low-carbohydrate, high-fat ketogenic diet one or two days a week will establish autophagy that clears damaged cells from the body, thereby improving health and increasing lifespan. Limiting the ketogenic diet to no more than two days a week avoids the adverse effects that are possible with a very low-carbohydrate ketogenic diet, which can result in nutrient deficiencies.

Daily consumption of one to four tablespoons per day of ketogenic MCT oil, best taken several hours apart, will provide a variety of health benefits. To summarize:

1. Ketones from MCT oil will offset possible brain glucose deficiency in the elderly and in those with Alzheimer's disease.
2. Ketones will improve cognitive function in those with normal brain function.
3. Ketones from MCT oil will increase energy-producing NAD<sup>+</sup>, thereby increasing the seven NAD-dependent sirtuin enzymes. These enzymes, associated with longevity and inflammation, have clinical potential in the treatment of diabetes, cardiovascular disease, dementia, osteoporosis, arthritis, Parkinson's disease and numerous other conditions.

Altogether, an intermittent ketogenic diet, together with a daily intake of ketogenic MCT oil, can improve cognitive and muscle function and provide remarkable health benefits. My wife and I are in our eighties. We normally eat a Weston Price-style Wise Traditions diet, take no drugs of any kind and are in good health for our age. We take ketogenic caprylic MCT oil daily to extend our good

health.

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## **SIDEBAR**

### **INCORPORATING COCONUT OIL IN THE DIET**

The body can use coconut oil for energy more rapidly and efficiently than any other fat source. Consistent intake of coconut oil (along with other healthy fats, such as butter, cream, lard, egg yolks and meat fats) provides vital nourishment to every cell in the body and supports optimal brain, hormonal, immune and metabolic function.

There are many easy ways to incorporate coconut oil into your diet. You can add coconut oil to smoothies, put it in hot oatmeal, use it in mayonnaise or salad dressings (in combination with olive oil), add it to mashed potatoes or use as a spread on sourdough toast. To make an easy breakfast smoothie (one serving), combine 1/2 cup fresh or frozen berries in a blender or food processor and process to a puree; add 1 cup plain whole yogurt or kefir, 2 pastured egg yolks and maple syrup (to taste) and slowly add 1 tablespoon warm coconut oil.

Coconut oil is also a healthy cooking oil, remaining stable under moderate cooking temperatures. Use coconut oil as a cooking fat in scrambled eggs, sautéed vegetables, soups, curries (along with coconut milk), sautéed seafood or rice.

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