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Fat metabolism without ketosis

Believe that butter is the new health food? For supporters of the ketogenic diet, they would likely respond with a resounding “yes” and of course report that they only eat the “grass-fed” kind of butter. While grass-fed butter might be flying off the shelves, so are high-fat, low-carb snacks, like pork rinds. The ketogenic diet is being used to lose weight, reverse diabetes, treat epilepsy, reduce cancer progression and recurrence, prevent dementia, treat polycystic ovarian syndrome, treat acne, manage multiple sclerosis, and in bipolar disorder. The role the ketogenic diet plays in these specific medical conditions is not the scope of this article. The focus here will be primarily on how ketogenic diets might work for weight loss and perhaps pre-diabetes and early insulin resistance. How did we get from “low-fat” everything to here? Never in my life have I seen a more polarizing diet than the ketogenic diet. It seems to spark emotions like no other diet. Gone are the days when everyone was eating bagels for breakfast because they were “low-fat.” While large public health institutions seem to dismiss the ketogenic diet for weight management, many clinicians and disease researchers are highly supportive of its use, in the appropriate setting. People are getting thin by eating fat, and it’s driving public health officials crazy; doctors are left scratching their heads, not knowing whether to join the new party or continue to toe the party line. The biggest question in science is whether or not staying on a ketogenic diet is safe long-term (more than 22 weeks), as scientific research with rodents is starting to reveal some health risks associated with long-term ketogenic dieting (Ellenbroek et al. 2014). We will dive into this as part of this article. An understanding of nutritional ketosis is important. We must understand benefits, complications, and potential implications of this diet. It must be understood by health seekers and physicians so that we are not relying on chat rooms and social media exclusively for health information. Most importantly we must understand the implications of veering too far from good nutritional micronutrient and macronutrient practice. When we merge good nutrition practices with the metabolic shift seen in the ketogenic diet, perhaps we will have a solid way of eating that prevents many dietary-associated diseases and potentially helps manage many chronic disease conditions. Hans Adolf Krebs, perhaps the most famous physician biochemist, first described physiologic ketosis in 1966. This is a state of physiological adaptation to fasting or a low-carbohydrate status of the body. Primarily, physiological ketosis, or “keto-adaption,” is a survival move to keep the brain alive. The brain prefers glucose and cannot run on fat, but it can run on an alternative fuel source called a “ketone body.” Once the glucose supply in the body becomes low (and the storage starts to run out in the liver), the liver will start the process to produce ketones. When glucose becomes low, the liver uses free fatty acids (either from fat in the diet or breakdown of body fat) to produce something called “acyl-CoA.” This molecule is converted into acetyl-CoA by a process in the mitochondria of the liver called “beta-oxidation.” Acetyl-CoA has several fates. One is to be used to make energy in the mitochondria, or it can go on to become a ketone body, such as acetoacetate, beta-hydroxybutyrate (BHB), or acetone. These ketones are used by the liver, heart, and brain for energy production because these tissues have the enzymes (called succinyl-CoA: 3-ketoacid CoA transferase) in their mitochondria to convert ketone bodies to energy (i.e., ATP) via a mitochondrial process called the Krebs cycle (Branco et al. 2016). So our brain, heart, and muscles are designed to survive in a low-carbohydrate, low-nutrient supply state as long as there is some fat around. This is a very important point. In short: the body is designed to adapt when supply is low. All right ... too technical and sciency? Well, it’s your body, and you need to know how it works to understand how to guide yourself. Stepping away from the minutia a bit, let’s back up and understand some mainstream points. A ketogenic diet is known as a diet composed of high fat, moderate protein, and low carbohydrate, resulting in limited metabolism of carbohydrates and proteins and increased fat metabolism. Some ketogenic diets go as low as 20 grams of carbohydrates or less per day. A consequence of this macronutrient shift is an increase in free fatty acid supply by dietary fat intake and by fat being broken down due to caloric restriction. We are feeding ourselves by our nutritional intake and by our fat stores when on a ketogenic diet. Once the body starts producing .5 mg/dl of ketones, the body has entered nutritional ketosis. Now do you get how it works? Not so fast. How do our bodies maintain glucose levels to keep us alive when we are depriving them of glucose? Great question, because we would surely die if the body had critically low glucose levels. The answer is that the body has a glucose-creating response to extreme conditions, coming from two main sources: amino acids and glycerol (a precursor to glucose) liberated from triglycerides (fats) (Vazquez and Kazi 1994). So the body uses proteins and fats to keep glucose within range. While the glucose is notably lower in people on the ketogenic diet, it seems to maintain at 60–85 mg/dl on average. Resistance to weight loss, no matter how many dietary strategies one has tried, is often how someone ends up on the ketogenic diet. But how does the ketogenic diet work to reduce weight and also decrease insulin resistance? There is a unifying theory that lipids, glucose, and protein/amino acids all play unique roles in maintaining the nutritional status through their impact on hunger/satiety centers in the central nervous system (Paoli, Bosco, et al. 2015). There are three areas known for appetite control in the hypothalamus that regulate appetite, including those in the arcuate nucleus (ARC), the periventricular nucleus (PVN), and the dorsomedial hypothalamic nucleus (DMH). There are two known aspects of appetite control: (a) the short-term (satiety signals [SS]) occurring at the beginning and end of a single meal; it also includes the length between meals, and (b) the long-term regulation (adiposity signal) that is influenced by such factors as body fat deposition. Short-term satiety signals are generated by the mouth, gut, and stomach based on the contents and chemistry of the food being eaten. Hormones like leptin and insulin, both secreted into the blood, reflect the stored body fat leading to long-term appetite control. Hormones produced in the gut, specifically ghrelin, glucagon-like peptide-1(GLP-1), Polypeptide YY (PYY), and cholecystokinin, can also influence the brain appetite centers. As we see this interplay of the effect of the ketogenic diet on appetite and on insulin signaling, we are creating a scenario of reduced caloric intake via appetite satiation and better glucose control. Of note, before the advent of insulin, the diabetic diet by Dr. Elliott Joslin was the main form of treatment for diabetics. This diet consisted of 75 percent energy from fat, 20 percent energy from protein, and 5 percent from carbohydrate (Hussain et al. 2012). One ketogenic diet does not look like the other. Today there are four subtypes of the ketogenic diet, and it’s really important to understand which one to follow. The classic ketogenic diet (a.k.a. “long-chain triglyceride diet”) consists of a classical ratio of fat to nonfat (protein and carbohydrates) of 4:1. This was what was classically used in original ketogenic diets for epilepsy. It is not the preferred approach for diabesity or obesity. One version of the ketogenic diet is called “medium-chain triglyceride” (MCT), which was introduced to surpass the severe restrictions of classic ketogenic diets. The main fatty acids in MCTs are caprylic acid, capric acid and, to a lesser extent, caproic acid and lauric acid. This diet is not based on diet ratios but uses a percentage of calories from MCT oils to create ketones (Branco et al. 2016). Another version is the widely popular Modified Atkins Diet (a.k.a. “very-low-carbohydrate ketogenic diet”). This diet grew from clinicians at Johns Hopkins University working with epilepsy patients. It is slightly less restrictive than the classic ketogenic diet. Calories are unlimited and fat makes up 60 percent of the diet; 30 percent comes from protein and 10 percent from carbohydrates (Kossoff & Turner, 2016). Next is the low-glycemic-index carbohydrate diet, which involves moving toward ketosis by restricting carbohydrates to those with a glycemic index less than 50. And finally, there is the highly respected well-formulated ketogenic diet (popularized by Stephen Phinney, PhD, and Jeff Volek, PhD). It is more of an individualized ketogenic diet, which contains between 3 and 20 percent carbohydrates, between 10 and 30 percent protein, and the remainder of the diet from fat. Its core principles are as follows: carbohydrate restriction (amount varies per person), protein in the right range, fat becomes primary nutrient (quality of fat is important, and sodium and mineral loss needs to be compensated). Here is a brief summary of these ketogenic approaches. Classic Ketogenic Diet (The most common is the long-chain triglyceride (LCT) diet) Fat to nonfat ratio often 4:1. Hard to comply with for anyone. Used originally for kids with seizure disorders. May have led to weight gain. Medium-Chain Triglyceride (MCT) Diet This diet is not based on diet ratios but uses a percentage of calories from MCT oils to create ketones. (The main advantage of MCTs over LCTs is that MCTs more efficiently absorb and quickly transport to the liver by albumin. Following hepatic uptake, those are promptly metabolized by liver mitochondria and, after fatty acid beta-oxidation, converted into ketone bodies.) Low-Glycemic-Index Ketogenic Diet Allows moderate intake of carbohydrates with a lower glycemic index, without increasing ketone levels. Low-glycemic-index carbohydrates induce a smaller increase in blood glucose, causing less variability in its levels throughout the day. Modified Atkins Diet (Very-Low-Carbohydrate Ketogenic Diet) Contrary to other ketogenic diets, it does not overly restrict protein intake or daily calories. Only restricts carbohydrates. Well-Formulated Ketogenic Diet Contrary to other ketogenic diets, it does not overly restrict protein intake or daily calories. Only restricts carbohydrates. There are other variants of the ketogenic diet using nutrient timing and “eating windows” and autophagy promotion. These approaches have been popularized by Dave Asprey, author of The Bulletproof Diet, and Satchidananda Panda, PhD, of the Salk Institute. Nuances and consequences of the ketogenic diet exist. Some factors include how to launch a ketogenic diet. Also, are you going to follow a flex/junk-food keto diet vs. a whole foods keto diet? For example, some approaches really give the green light to high amounts of inflammatory foods like “Keto bombs,” pork rinds, bacon, cheese, and processed meats. Also, questions exist as to how to track the ketogenic diet. Should you track it intuitively or by blood-ketone meters or urine-ketone strips? These are all questions that need to be discussed and figured out. As a naturopathic doctor, I merge science and holistic health. I want my patients following the healthiest version of a ketogenic diet. So, although weight loss can occur on a junk keto diet, my concern is the inflammatory effects of the diet. I have my patients monitor their blood-ketone levels in the beginning of the program to ensure they are reaching a ketone level of .5 mg/dl to 2.0 mg/dl. Guessing is not really great, especially if you want to see if the program is truly well implemented. I like the Keto Mojo device for monitoring ketones. Having an understanding of potential side effects, implications, and dangers of the ketogenic diet is important before beginning. Below I have summarized the frequent questions I see as pertinent: 1. Is ketosis a dangerous state? A common error is to confuse nutritional ketosis with diabetic ketoacidosis (DK). In adults consuming a “normal” diet, blood-ketone body concentrations vary between 0.1 and 0.3 mg/dl. In nutritional ketosis, the levels may rise to over 1 mg/dl, and maximally up to 7–8 mg/dl, but without an acidosis. In contrast, in diabetic ketoacidosis, blood-ketone body concentrations usually exceed 25 mg/dl, and blood pH decreases below 7. DK is a medical emergency. Nutritional ketosis is not. 2. Does fat cause heart disease? It really depends on the type of ketogenic diet you are following. The classic ketogenic diet has been shown to raise cholesterol levels in children with refractory seizure disorders (Zamani et al. 2016). Classic ketogenic, for lack of a better term, is obviously extremely high in fat (90 percent of calories).Genetically, some people might respond unfavorably to a higher-saturated-fat diet (think milk, bacon, butter, and meat) than others. Specifically, those carrying two copies of the G variant of the apolipoprotein A-II gene might actually gain weight on a higher-saturated-fat diet.In most populations, fat is not really panning out to be the cause of high cholesterol. Most people in a study of Type II diabetes following a low carb diet or low carb ketogenic diet for 24 weeks, experienced lower total cholesterol, triglycerides, and LDL .Even HDL (good cholesterol) increased in these groups (Hussain et al. 2012). 3. What are the side effects of the ketogenic diet? Since there are many varieties of the ketogenic diet, there are large reports of side effects, most likely from the classic ketogenic diet, but this is an assumption. They need to be made aware of and monitored. What are some side effects to be considered (Branco et al. 2016)? Short-term side effects can include: Gastro-esophageal reflux and constipation Acidosis Low blood sugar hypoglycemia Dehydration Fatigue and lethargy Long-term potential side effects include: Hyperlipidemia/hypercholesterolemia (although with some controversy) Nephrolithiasis (kidney stones) Cardiomyopathy; maybe secondary to selenium deficiency (Bergqvist, Chee, et al. 2003) A responsible approach to the ketogenic diet requires monitoring the impact the diet is having on your blood, specifically inflammatory markers and nutrient deficiencies. Ketogenic diet nutritionists follow guidelines established by their field. As a naturopathic physician, I take the monitoring a step further because of known risks of the ketogenic diet. The following are my recommended guidelines for monitoring your health on a ketogenic diet. Monitoring Your Health on the Ketogenic Diet After one month and on a quarterly basis on the ketogenic diet, you will need to have the following lab levels checked to screen for any adverse effects: Complete blood count and differential Comprehensive metabolic panel Fasting lipid panel, including triglycerides Serum uric acid Highly sensitive C-reactive protein After three months and on a semiannual basis on the ketogenic diet, you should have the following checked: Plasma zinc Plasma selenium After one year on a ketogenic diet, you should have the following checked: Gamma Glutamyl Transferase (GGT) B-vitamin status Magnesium (serum and red blood cell magnesium) What can and can’t you eat on a low-carb ketogenic diet? Most healthy low-carb ketogenic diets focus on the foods listed below. Notoriously missing are breads, grains, and starchy root vegetables, like carrots (Noakes and Windt 2017). Protein: meats, eggs, poultry, game, seafood, and jerkies. Dairy: full-fat Greek yogurt, cheese, cream, butter, and cottage cheese. Fats: olive oil, coconut oil, nut oil, avocado oil, avocados, and olives. Nuts and seeds: flaxseeds, Macadamia nuts, pecans, pine nuts, and Tahini. Vegetables: all green leafy vegetables, above-the-ground vegetables, and cruciferous vegetables. Fruits: minimal based on daily carbohydrate intake. Ketogenic diets have a wide variety of clinical applications. The focus of this article is more on the obesity and pre-diabetes applications. The long-term implications of this diet continue to be of question. But certainly, in my opinion, it is worth considering, in the short term, following a “well-formulated” ketogenic diet. Ketogenic diet cycling seems to be safe, based on my research. This means alternating a six-month ketogenic diet followed by a six-month Mediterranean-style diet that incorporates time-restricted feeding. This is my preferred approach to reduce obesity, prevent diabetes, and reduce risk of cardiovascular disease. This seems to be a favorable strategy to avoid long-term side effects and get the desired goal of weight management. Dr. Adam Rinde is an experienced Naturopathic Physician practicing in Bellevue, Washington at Sound Integrative Health. He is a graduate of Bastyr University. He has a special focus in gut health, brain health, and metabolism. He also founded the non-for-profit Blankets for Cancer which is a pediatric cancer charity.

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