

QUESTION 1

Ketogenesis

is the biochemical process through which organisms produce ketone bodies through breakdown of fatty acids and ketogenic amino acids.^{[1][2]} This process supplies energy under circumstances such as fasting or caloric restrictions to certain organs, particularly the brain, heart and skeletal muscle. Insufficient gluconeogenesis can cause hypoglycemia and excessive production of ketone bodies, ultimately leading to a life-threatening condition known as ketoacidosis

Ketonuria

is a medical condition in which ketone bodies are present in the urine.

It is seen in conditions in which the body produces excess ketones as an indication that it is using an alternative source of energy. It is seen during starvation or more commonly in type 1 diabetes mellitus. Production of ketone bodies is a normal response to a shortage of glucose, meant to provide an alternate source of fuel from fatty acids.

ketonaemia

The presence of an abnormally high concentration of ketone bodies in the blood.

QUESTION 2

CONSEQUENCES OF KETOSIS

1. The "keto flu"

“Some people report that when they start ketosis. “There can sometimes be vomit, gastrointestinal distress, a lot of fatigue, and lethargy.” This so-called keto flu usually passes after a few days, she adds.

Josh Axe, a doctor of natural medicine and clinical nutritionist, estimates that about 25% of people who try a keto diet experience these symptoms, with fatigue being the most common. “That happens because your body runs out of sugar to burn for energy, and it has to start using fat,” he says. “That transition alone is enough to make your body feel tired for a few days.”

You may be able to minimize the effects of keto flu by drinking plenty of water and getting plenty of sleep.

2. Diarrhea

If you find yourself running to the bathroom more often while on a ketogenic diet, a quick internet search will show you that you're not alone. (Yes, people are tweeting about keto diarrhea.) This may be due to the gallbladder—the organ that produces bile to help break down fat in the diet—

Diarrhea can also be due to a lack of fiber in the keto diet, which can happen when someone cuts way back on carbs (like whole-grain bread and pasta) and doesn't supplement with other fiber-rich foods, like vegetables. It can also be caused by an intolerance to dairy or artificial sweeteners—things you might be eating more of since switching to a high-fat, low-fat

3. Reduced athletic performance

Some athletes swear by the ketogenic diet, not just for weight loss but for improved performance in their sport, as well.

In a recent study in the *Journal of Sports Medicine and Physical Fitness*, Weiss and his colleagues found that participants performed worse on high-intensity cycling and running tasks after four days on a ketogenic diet, compared to those who'd

spent four days on a high-carb diet. Weiss says that the body is in a more acidic state when it's in ketosis, which may limit its ability to perform at peak levels.

“Just losing a few pounds is enough to give you a huge advantage on the bike, but I’m very concerned that people are attributing the benefits of weight loss to something specific in the ketogenic diet,” Weiss continues. “In reality, the benefits of weight loss could be at least partially canceled out by reductions in performance.”

4. Ketoacidosis

If you have type 1 or type 2 diabetes , you shouldn't follow the keto diet unless you have your doctor's permission and close supervision, . “Ketosis can actually be helpful for people who have hyperglycemia issues, but you have to be very mindful of your blood sugar and check your glucose levels several times a day,” she says.

That's because, for people with diabetes, ketosis can trigger a dangerous condition called keto acidosis . This occurs when the body stores up too many ketones—acids produced as a byproduct of burning fat—and the blood becomes too acidic, which can damage the liver, kidneys, and brain. Left untreated, it can be fatal.

Ketoacidosis has also been reported in people without diabetes who were following low-carb diets, although this complication is quite rare. Symptoms of ketoacidosis include a dry mouth, frequent urination, nausea, bad breath, and breathing difficulties; if you experience these while following the keto diet, check in with a doctor right away.

5. Weight regain

Because the keto diet is so restrictive, health experts say it's not an appropriate plan to follow long-term. But the problem with that, is that most people will regain a lot of the weight they lost as soon as they go back on carbs.

“It's an issue with any fad diet, but it seems to be extra common with ketosis. “When people tell me they want to try it because

their friends lost weight, I always tell them, 'Just watch, I almost guarantee that they'll gain it all back.'"

These types of back and forth weight fluctuations can contribute to disordered eating, Kizer says, or can worsen an already unhealthy relationship with food. "I think the keto diet appeals to people who have issues with portion control and with binge eating," she says. "And in many cases, what they really need is a lifestyle coach or a professional counselor to help them get to the bottom of those issues."

6. Less muscle mass, decreased metabolism

Another consequence of keto-related weight changes can be a loss of muscle mass, s—especially if you're eating much more fat than protein. "You'll lose weight, but it might actually be a lot of muscle," she says, "and because muscle burns more calories than fat, that will affect your me ."

When a person goes off the ketogenic diet and regains much of their original weight, it's often not in the same proportions, Instead of regaining lean muscle, you're likely to regain fat. "Now you're back to your starting weight, but you no longer have the muscle mass to burn the calories that you did before," she says. "That can have lasting effects on your resting metabolic rate, and on your weight long-term."

7. Increased risk of heart disease and diabetes

Axe says that, when done right, the keto diet includes lots of vegetables and lean sources of animal protein. In other words, it's not an excuse to eat butter and bacon—although some people may try to do just that.

That's why many health experts are concerned about people on the ketogenic diet, especially those who try it without the guidance of a doctor or nutritionist. Doctors say that high-fat diets like this one may raise cholesterol levels, and some studies suggest that they increase the risk of diabetes. Some have even called it the cardiologist nightmare .

QUESTION 3

MANAGEMENT OF KETOACIDOSIS

The main aims in the treatment of diabetic ketoacidosis are replacing the lost fluids and electrolytes while suppressing the high blood sugars and ketone production with insulin.

Admission to an intensive care unit(ICU) or similar high-dependency area or ward for close observation may be necessary.

Fluid replacement

The amount of fluid replaced depends on the estimated degree of dehydration. If dehydration is so severe as to cause shocks(severely decreased blood pressure with insufficient blood supply to the body's organs), or a depressed level of consciousness, rapid infusion of saline (1 liter for adults, 10 ml/kg in repeated doses for children) is recommended to restore circulating volume.Slower rehydration based on calculated water and sodium shortage may be possible if the dehydration is moderate, and again saline is the recommended fluid.Very mild ketoacidosis with no associated vomiting and mild dehydration may be treated with oral rehydration and subcutaneous rather than intravenous insulin under observation for signs of deterioration.

Normal saline (0.9% saline) has generally been the fluid of choice.There have been a few small trials looking at balanced fluids with few differences.A special but unusual consideration is cardiogenic shock, where the blood pressure is decreased not due to dehydration but due to inability of the heart to pump blood through the blood vessels. This situation requires ICU admission, monitoring of the central venous pressure (which requires the insertion of a central venous catheter in a large upper body vein), and the medication that increases the heart pumping and blood pressure.

Insulin

Some guidelines recommend a bolus (initial large dose) of insulin of 0.1 unit of insulin per kilogram of body weight. This can be administered immediately after the potassium level is known to be higher than 3.3 mmol/l; if the level is any lower, administering insulin could lead to a dangerously low potassium level (see below). Other guidelines recommend delaying the initiation of insulin until fluids have been administered. It is possible to use rapid insulin analogs injections under the skin for mild or moderate cases.

In general, insulin is given at 0.1 unit/kg per hour to reduce the blood sugars and suppress ketone production. Guidelines differ as to which dose to use when blood sugar levels start falling; some recommend reducing the dose of insulin once glucose falls below 16.6 mmol/l (300 mg/dl) but other recommend infusing glucose in addition to saline to allow for ongoing infusion of higher doses of insulin.

Potassium

Potassium levels can fluctuate severely during the treatment of DKA, because insulin decreases potassium levels in the blood by redistributing it into cells via increased sodium-potassium pump activity. A large part of the shifted extracellular potassium would have been lost in urine because of osmotic diuresis.

Hypokalemia (low blood potassium concentration) often follows treatment. This increases the risk of dangerous irregularities in the heart cell. Therefore, continuous observation of the heart rate is recommended, as well as repeated measurement of the potassium levels and addition of potassium to the intravenous fluids once levels fall below 5.3 mmol/l. If potassium levels fall below 3.3 mmol/l, insulin administration may need to be interrupted to allow correction of the hypokalemia.

Sodium bicarbonate

The administration of sodium bicarbonate solution to rapidly improve the acid levels in the blood is controversial. There is

little evidence that it improves outcomes beyond standard therapy, and indeed some evidence that while it may improve the acidity of the blood, it may actually worsen acidity inside the body's cells and increase the risk of certain complications. Its use is therefore discouraged, although some guidelines recommend it for extreme acidosis ($\text{pH} < 6.9$), and smaller amounts for severe acidosis ($\text{pH} 6.9\text{--}7.0$).

Cerebral edema

Cerebral edema, if associated with coma, often necessitates admission to intensive care, artificial ventilation, and close observation. The administration of fluids is slowed. The ideal treatment of cerebral edema in DKA is not established, but intravenous mannitol and hypertonic saline (3%) are used—as in some other forms of cerebral edema—in an attempt to reduce the swelling.

Resolution

Resolution of DKA is defined as general improvement in the symptoms, such as the ability to tolerate oral nutrition and fluids, normalization of blood acidity ($\text{pH} > 7.3$), and absence of ketones in blood ($< 1 \text{ mmol/l}$) or urine. Once this has been achieved, insulin may be switched to the usual subcutaneously administered regimen, one hour after which the intravenous administration can be discontinued.

In people with suspected ketosis-prone type 2 diabetes, determination of antibodies against glutamic acid decarboxylase and islet cells may aid in the decision whether to continue insulin administration long-term (if antibodies are detected), or whether to withdraw insulin and attempt treatment with oral medication as in type 2 diabetes.

Generally speaking, routine measurement of C-peptide as a measure of insulin production is not recommended unless there is genuine doubt as to whether someone has type 1 or type 2 diabetes.

