# Ketones

## Biochemistry

Acetone, acetoacetate and beta-hydroxybutyrate are ketones (or ketone bodies) generated from carbohydrates, fatty acids and amino acids in humans and most vertebrates. Ketones are elevated in blood after fasting including a night of sleep, and in both blood and urine in starvation, hypoglycemia due to causes other than hyperinsulinism, various inborn errors of metabolism, and ketoacidosis (usually due to diabetes mellitus). Although ketoacidosis is characteristic of decompensated or untreated type 1 diabetes, ketosis or even ketoacidosis can occur in type 2 diabetes in some circumstances as well. Acetoacetate and beta-hydroxybutyrate are an important fuel for many tissues, especially during fasting and starvation. The brain, in particular, relies heavily on ketone bodies as a substrate for lipid synthesis and for energy during times of reduced food intake. At the NIH, Dr. Richard Veech refers to ketones as "magic" in their ability to increase metabolic efficiency, while decreasing production of free radicals, the damaging byproducts of normal metabolism. His work has shown that ketone bodies may treat neurological diseases such as Alzheimer's and Parkinson's disease,[4] and the heart and brain operate 25% more efficiently using ketones as a source of energy.[5]

## Applications

Ketones are often used in perfumes and paints to stabilize the other ingredients so that they don't degrade as quickly over time. Other uses are as solvents and intermediates in chemical industry. Examples of ketones are acetone, acetophenone, and methyl ethyl ketone.

## Uses in the heart and brain

Ketone bodies can also be used for energy. Ketone bodies are transported from the liver to other tissues, where acetoacetate and beta-hydroxybutyrate can be reconverted to acetyl-CoA to produce energy, via the Krebs cycle.

The heart gets much of its energy from ketone bodies, although it also uses fatty acids.
The brain gets its energy from ketone bodies when insufficient glucose is available (e.g., when fasting). In the event of low blood glucose, most other tissues have additional energy sources besides ketone bodies (such as fatty acids), but the brain does not. After the diet has been changed to lower blood glucose for 3 days, the brain gets 30% of its energy from ketone bodies. After 4 days, this goes up to 70% (during the initial stages the brain does not burn ketones, since they are an important substrate for lipid synthesis in the brain). The brain retains some need for glucose, because ketone bodies can be broken down for energy only in the mitochondria, and brain cells' long thin axons are too far from mitochondria.[*citation needed*]

## Production

Acetyl-CoA
Ketone bodies are produced from acetyl-CoA (see ketogenesis) mainly in the mitochondrial matrix of liver cells when carbohydrates are so scarce that energy must be obtained from breaking down fatty acids.
Acetone is formed from spontaneous decarboxylation of acetoacetate. In a corresponding manner, the levels of acetone are much lower than those of the other two types of ketone bodies. And, unlike the other two, acetone cannot be converted back to acetyl-CoA, so it is excreted in the urine and exhaled (it can be exhaled readily because it has a high vapor pressure and thus evaporates easily). The exhalation of acetone is responsible for the characteristic "fruity" odour of the breath of persons in ketotic states.

## Ketosis and ketoacidosis

Any production of these compounds is called ketogenesis, and this is necessary in small amounts.
But, when excess ketone bodies accumulate, this abnormal (but not necessarily harmful) state is called ketosis. Ketosis can be quantified by sampling the patient's exhaled air, and testing for acetone by gas chromatography.
When even larger amounts of ketone bodies accumulate such that the body's pH is lowered to dangerously acidic levels, this state is called ketoacidosis.

## Impact upon pH

Both acetoacetate and beta-hydroxybutyrate are acidic, and, if levels of these ketone bodies are too high, the pH of the blood drops, resulting in *ketoacidosis*.

This happens in untreated Type I diabetes (see diabetic ketoacidosis), and also in alcoholics after binge drinking, subsequent starvation, and the alcohol-induced impairment of the liver's ability to generate glucose (gluconeogenesis)(see alcoholic ketoacidosis).

## Ketones tests

A ketone test checks for ketones in your blood or urine. Ketones are substances that are made when the body breaks down fat for energy. Normally, your body gets the energy it needs from carbohydrate in your diet. However, stored fat is broken down and ketones are made if your diet does not contain enough carbohydrate to supply the body with sugar (glucose) for energy or if your body cannot use blood sugar (glucose) properly.
Newer home blood sugar meters can also measure ketones. Home urine tests to measure ketones are available.

## Why It Is Done

A blood test is the most accurate method of measuring ketones. It is recommended for all people with diabetes whenever symptoms of illness are present, such as nausea, vomiting, or abdominal pain. These symptoms are similar to symptoms of high blood sugar and may mean you have diabetic ketoacidosis, a potentially life-threatening condition.
A urine test is the most commonly used method of measuring ketones. But it is less accurate than a blood test. It may be done to:

- Monitor a person on a very low-carbohydrate diet.
- Monitor a pregnant woman who has diabetes or has developed gestational diabetes.

## Results

A ketone test checks for substances made when the body breaks down fat for energy (ketones).

| **Ketones** | |
|---|---|
| **Normal:** | There are no ketones in your blood or urine. |
| **Abnormal:** | Ketones are present in your blood or urine. |

## Urine test

If either the test strip or the urine changes color when the tablet is dropped into the sample, ketones are present in your urine sample. The test results are read as negative to 1+ to 4+ or small to large.

## High values

You may have ketones in your urine if you:

- Have poorly controlled diabetes or diabetic ketoacidosis.
- Are on a very low-carbohydrate diet.
- Are starving or have an eating disorder, including disorders that result in poor nutrition such as anorexia nervosa or bulimia, alcoholism, or poisoning from drinking rubbing alcohol (isopropanol).
- Have not eaten (fasted) for 18 hours or longer.
- Are pregnant. However, a moderate amount of ketones in a pregnant woman may harm the fetus and may be an indication of gestational diabetes.

The level of ketones, and not just the presence of ketones, may be important to your doctor as well. Many conditions can change ketone levels. Fasting usually causes only mild increases in the level, but ketone levels in diabetic ketoacidosis are much higher. Your health professional will discuss any significant abnormal results with you in relation to your symptoms and medical history.

## What Affects the Test

Reasons you may not be able to have the test or why the results may not be helpful include:

- Taking medicines, such as:
    - Levodopa, such as Sinemet or Larodopa.
    - Phenazopyridine, such as Pyridium, Geridium, Pyridiate, or Urogesic.
    - Valproic acid, such as Depakote, Depacon, or Depakene.
    - Vitamin C (ascorbic acid), when taken in large amounts.
- Dehydration.
- A high-fat diet.
- Pregnancy.

## What To Think About

- The blood test can check for one type of ketone that the urine test cannot detect. Therefore, a urine test that does not show any ketones may not be accurate (false-negative result).
- Ketone levels will increase in your urine before they increase in your blood if you are fasting or on a very low carbohydrate diet.
- The American Diabetes Association recommends that you test your urine for ketones if you have diabetes and you:
  - Are pregnant.
  - Are sick or feeling very stressed.
  - Have blood sugar levels of 300 mg/dL (16.7 mmol/L) or higher.
  - Have symptoms of high blood sugar (diabetic ketoacidosis), such as nausea, vomiting, or abdominal pain.
- Ketones can be tested at home using urine ketone test strips. A more accurate reading can be obtained by some home glucose meters that test for blood ketones.