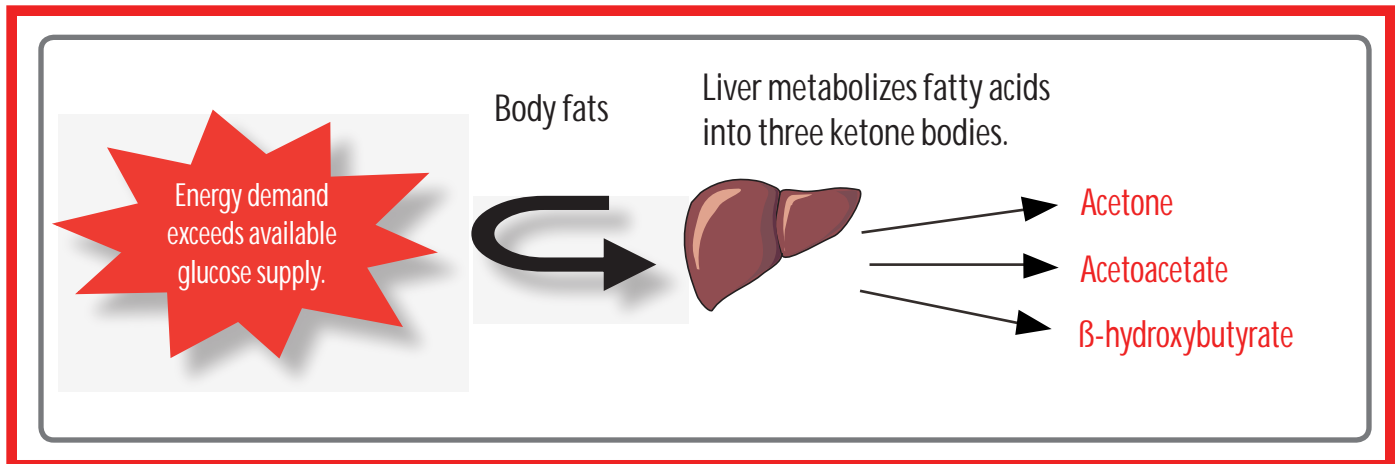


What is Ketosis?

When the body does not have a sufficient amount of carbohydrates available to meet its demand for energy, the body begins to utilize its stored fat for energy. These fatty acids are metabolized in the liver and this metabolism produces chemical by products called ketones. Under normal circumstances, ketones are broken down into carbon dioxide and water by

the liver and other organs. In ketosis, the body produces more ketones than it can process. The buildup of ketones disrupts the chemical balance of the body. If left unchecked, this condition can prove fatal. These ketone bodies consist of acetone, acetoacetate, and β -hydroxybutyrate.



Why Monitor Ketosis?

The detection of ketosis is important in several clinical conditions. The most important is the detection of potentially fatal ketoacidosis in diabetics. Patients with Type 1 diabetes are prone to developing ketoacidosis – an excessive buildup of ketones in the blood due to accelerated ketone synthesis and the body's limited capacity to break them down.¹

Measuring the level of ketones is clinically useful in not only diagnosing Diabetic Ketoacidosis (DKA), but also in monitoring the results of treatment. The American Diabetes Association Clinical Practice Recommendations state that under the following conditions, diabetics should be tested for the presence of ketones:

- When any symptoms of ketoacidosis are present
- During acute illness or stress
- When blood glucose levels consistently exceed 240 mg/dL
- During pregnancy

Other conditions where ketone testing is considered to be of clinical value:

- Pregnant women with gestational diabetes are also prone to developing elevated ketone levels, which can have a profound effect on the developing fetus.²
- Ketosis due to starvation or malnutrition.³
- Ketoacidosis due to alcoholism.³
- Monitoring special diets used to control seizures in epilepsy.⁴

¹ Foster DW, McGarry JD. The metabolic derangement and treatment of diabetic ketoacidosis. *N Engl J Med.* 1983;309(3):159-169.

² Rizo T, Metzger BE, Burns WJ, Burns K. Correlations between antepartum maternal metabolism and intelligence of offspring. *N Engl J Med.* 1991;325(13):911-916.

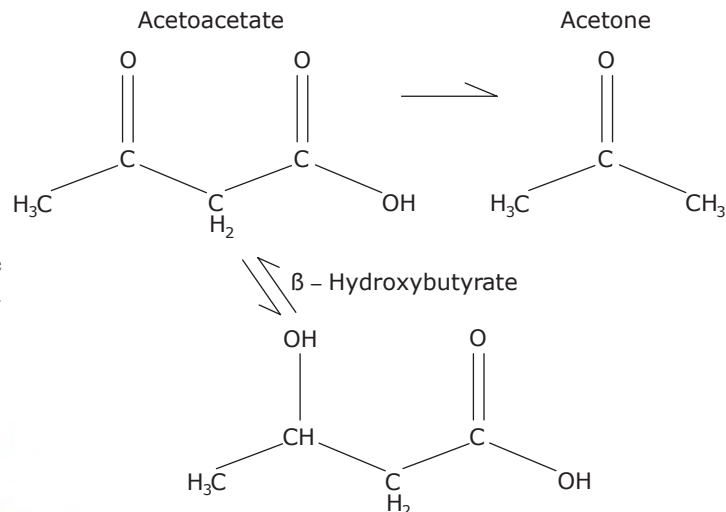
³ Burtis CA, Ashwood ER, eds. *Tietz Textbook of Clinical Chemistry*. 2nd ed. W.B. Saunders Company, Philadelphia. 1994.

⁴ Chee CM, RN. *Spotlight on an Old Remedy, the Ketogenic Diet*. *Clinical Nursing Practice in Epilepsy*, V1, Issue 2, July 1997, pp 13-15.

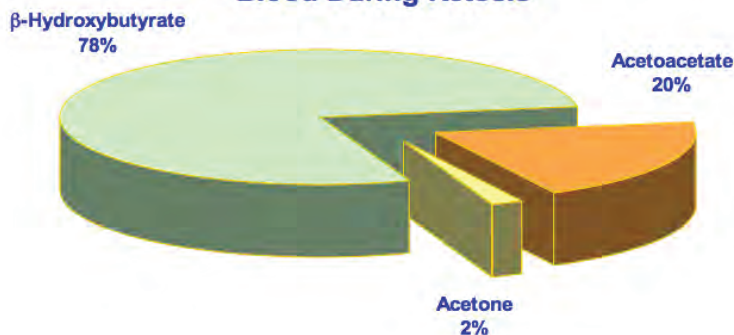
Testing for Ketones

When the body begins to break down its stored fats in response to a low supply of energy (glucose) it produces the ketone β -hydroxybutyrate, which is further catabolized into acetoacetate and then into acetone.

Ketones (like glucose) can be tested or monitored in either urine or blood. Many hospitals still use Acetest[®] or Ketostix[®] for detecting and monitoring ketosis and ketoacidosis.



Composition of Ketone Bodies Present in Blood During Ketosis



The nitroprusside urine method is efficient at providing a qualitative assessment of ketosis and ketoacidosis by detecting both acetoacetate and acetone; however, it does not detect β -hydroxybutyrate. This is significant because:

- The nitroprusside method detects less than 25% of the ketones present in ketosis. β -hydroxybutyrate is the main ketone body produced (78%).
- β -hydroxybutyrate demonstrates excellent stability, making it the most reliable indicator of clinically relevant ketosis and ketoacidosis.
- During ketosis, β -hydroxybutyrate levels increase more than levels of acetone and acetoacetate, clearly indicating the patient's trend in metabolic status.
- Quantitative, objective β -hydroxybutyrate results provide a better tool for differentiating metabolic acidosis and monitoring therapy.

In addition, the nitroprusside method has demonstrated susceptibility to false positive results from drug interference and false negative results due to reagent deterioration. The effect of fluid intake and urine concentration can significantly affect urine test results, making this method unreliable.⁵ In contrast, blood ketone levels provide a reliable and quantitative method of diagnosing and monitoring treatment of ketoacidosis.⁵ Improved clinical outcomes and enhanced cost efficiency have also been reported due to blood testing of β -hydroxybutyrate.⁶ These improvements are seen in the following areas:

- Earlier detection of clinically significant ketosis
- Improved turn-around times
- Significant reduction in laboratory testing
- Faster resolution of ketoacidosis with significant reduction of time spent in Critical Decision Unit

⁵ Goldstein DE, Little RR, Lorenz RA, Malone JI, Nathan DM, Peterson CM. Tests of glycemia in diabetes Technical review, Diabetes Care. 1995;18(6):896-909.

⁶ Foreback CC, Ph.D, Director Clinical Chemistry/Pathology, Henry Ford Hospital, Detroit, MI. White Paper, 1998.

Acetest[®] and Ketostix[®] are registered trademarks of Bayer Corporation, Elkhart, Indiana.

