SydPath
ST VINCENT'S PATHOLOGY

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KETONES INFORMATION SHEET

PHYSIOLOGY

The ketones which may be found in the circulation are acetoacetate, beta-hydroxybutrate and acetone. They are produced in the liver in an environment of low insulin and low intracellular carbohydrate as an adaptive mechanism to provide non-carbohydrate fuel for the brain and other tissues in times of starvation. Acetoacetate is produced from acetyl CoA and may then either be converted enzymatically to beta-hydroxybutyrate or non-enzymatically to acetone. The interconversion of acetoacetate and beta-hydroxybutyrate requires the enzyme beta-hydroxybutyrate dehydrogenase and the ratio of the two metabolites depends on the prevailing concentrations of NAD and NADH.

PATHOLOGY

As stated above, ketone production is a protective mechanism during starvation to provide energy to the brain and other tissues. After consumption of available glycogen, the body switches largely to fatty acids as a source of energy. In contrast to fatty acids, ketones can pass the blood-brain barrier to deliver energy to the brain. In early starvation ketones are also used for energy by muscle cells but later these convert to fatty acids to conserve ketones for the brain. These mechanisms assist in preserving carbohydrate supplies for cells dependent on sugars for energy supply such as red cells and the renal medulla.

In other clinical settings the presence of ketones, and the accompanying acidosis, can be markedly deleterious to the body. The most common of these are diabetic ketoacidosis and alcoholic ketoacidosis. In these settings the decrease in NAD relative to NADH leads to a relatively greater increase in beta-hydroxybutyrate than acetoacetate. Thus acetoacetate may be low in untreated cases of diabetic ketoacidosis, but then paradoxically increase in response to therapy. Additionally, the molar increase in betahydroxybutyrate constitutes the major contributor to the increased anion gap seen in these patients. These factors make beta-hydroxybutyrate a preferable marker for ketoacidosis compared to acetoacetate.

CAUSES OF ELEVATED KETONES

- Starvation (low serum glucose)
- Diabetic ketoacidosis (high serum glucose, metabolic acidosis, hyperkalaemia common)
- Alcoholic ketoacidosis (variable glucose, hyperkalaemia uncommon)

MEASUREMENT

The preferred test for ketones is a blood sample for betahydroxybutyrate sent to the laboratory or measured on some portable meters available for this purpose. Acetoacetate can be measured on a spot urine sample using the ketone pad on standard urinalysis dipsticks if a blood sample is not available. On rare occasions the quantitative measurement of both betahydroxybutyrate and acetoacetate in blood is indicated and a special collection tube is required.