Urine Ketones - Meanings and False Positives

Description
Ketones are produced normally by the liver as part of fatty acid metabolism. In normal states these ketones will be completely metabolised so that very few, if any at all, will appear in the urine. If for any reason the body cannot get enough glucose for energy it will switch to using body fats, resulting in an increase in ketone production making them detectable in the blood and urine.

How to test for ketones
The urine test for ketones is performed using test strips available on prescription. Strips dedicated to ketone testing in the UK include:

- GlucoRx KetoRx Sticks 2GK®
- Ketostix®
- Mission® Ketone

Testing should be performed according to manufacturers’ instructions. The sample should be fresh and uncontaminated. Usually the result will be expressed as negative or positive (graded 1 to 4).

Ketonuria is different from ketonaemia (ie presence of ketones in the blood) and often ketonuria does not indicate clinically significant ketonaemia.

Depending on the testing strips used, urine testing for ketones either has an excellent sensitivity with a low specificity, or a poor sensitivity with a good specificity. However, this should be viewed in the context of uncertainty of the biochemical level of significant ketosis.

Interpretation of results
Normally only small amounts of ketones are excreted daily in the urine (3-15 mg). High or increased values may be found in:

- Poorly controlled diabetes.
- Diabetic ketoacidosis (DKA).
- Starvation:
  - Not eating for prolonged periods (12-18 hours).
  - Anorexia nervosa.
  - Bulimia nervosa.
  - Alcoholism.

- Prolonged vomiting.
- Rapid weight loss.
- Frequent strenuous exercise.
- Poisoning (eg, with isopropanol).
- Ether anaesthesia.
- Alkalosis.
- Some metabolic disorders.

False positives
Positive test result but 'no' ketones
- Some medications:
  - Levodopa
  - Phenazopyrazine
  - Valproic acid
  - Vitamin C
- Dehydration.

False negatives
Most urine testing kits detect aceto-acetate, not the predominant ketone beta-hydroxybutyrate. It is possible for the test to be negative with high levels of beta-hydroxybutyrate and then, as ketoacidosis improves and ketone levels fall, the urine test becomes positive (to aceto-acetate).
Special cases of ketonuria

Diabetes mellitus and ketones
Metabolically severe insulin deficiency (relative or absolute) produces hyperglycaemia and ketoacidosis. Insulin lack increases release of fatty acids from adipose stores and reduces the rate of fat synthesis.

Lipolysis is further increased by increased catecholamines, cortisol, growth hormone and glucagon. The free fatty acids are transported to the liver for conversion to ketone bodies, which serve as fuels for muscle and fat.

Excess production of ketone bodies (aceto-acetate and beta-hydroxybutyrate) gives rise to DKA. Beta-hydroxybutyrate accounts for 75% of ketones.[4]

Urine is tested for ketones as part of monitoring of type 1 diabetes mellitus, especially during any illness.[5] See also the separate Diabetes and Intercurrent Illness article.

Home blood glucose and ketone monitoring can possibly decrease the number of hospital admissions due to DKA.[6]

Monitoring of ketones is important in all people with diabetes:
- When the diet is low in carbohydrates, exercise levels are high or a combination of both.
- In pregnant women with diabetes and in gestational diabetes.
- When blood sugars are high (over 15 mmol/L).[7]
- In DKA or with suspected ketoacidosis.

If the urine ketone level is greater than 2+, or blood ketone levels are greater than 3 mmol/L, the GP or diabetes care team should be contacted immediately.[8]

Ketogenic diets
Ketogenic diets cause a ‘physiological ketosis’ but the levels of ketones in the blood are much lower than in uncontrolled DKA.[9]

Ketogenic diets have been used to control epilepsy but the quality of the evidence is poor.[10]

Further reading & references
1. British National Formulary (BNF); NICE Evidence Services (UK access only)
5. Type 1 diabetes in adults: diagnosis and management; NICE Guidelines (August 2015, updated July 2016)
7. Diabetes UK
8. Diabetes - type 1; NICE CKS, February 2016 (UK access only)

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Peer Reviewer:
Dr Adrian Bonsall

Document ID:
2906 (v23)

Last Checked:
18/07/2017

Next Review:
17/07/2022

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