

**KETONE TESTING**



*“Laocöon”, Greek marble, Second - Third Century, B.C, Vatican Museum, Rome, (Author’s photograph).*

*...But out in the lead with a troop of comrades,  
down Laocöon runs from the heights in full fury,  
calling out from a distance, “Poor damn fools!  
have you gone mad!....”*

*“Do not trust the Horse, Trojans!  
“ Whatever it is, I fear the Greeks - even those bearing gifts!”*

*Virgil, Book II: 50-62; “The Aeneid”, (29-19 B.C)*

*...Not many more famous artists can be mentioned, for the fame of individual artists for genuine masterpieces is prevented by the very number of assisting artists, since it is not possible either for one to lay claim to all the honour or for several to be singled out as equals. This is the case with the Laocöon which is to be found in the palace of Emperor Titus. This is a work that excels*

*anything in painting or bronze. Out of one stone the outstanding artists, Hagesander, Polydorus, and Athenodorus, all from Rhodes, have in accordance with the decision of the council made Laocoon and his sons and the snakes in marvellous fashion wrapping themselves around them.*

*Pliny the Elder, "The Natural Histories", Bk XXXVI; 37  
77-79 A.D*

*Rome, 14 January, A.D 1506.*

*A building excavation is being undertaken in an old vineyard near S. Maria Maggiore. Suddenly excited workers cry out - a statue of marble - seemingly of great antiquity - has been partially uncovered. Its size is immense, what could it be?*

*After decades of digging up tantalizing but unidentifiable fragments of bronze and marble, suddenly a massive, virtually intact work in marble from the Roman era, had been unearthed. Not only was the work technically brilliant, awesome in its scale, the names of its Rhodian creators had been carved into it. At the apogee of the Renaissance, the significance of the find was immediately recognized. The greatest scholars, architects and sculptors, among them a certain young Michelangelo Buonarroti, were called in to examine it. Immediately it was recognized as a work that had been described by Pliny the Elder in the First century A.D; the names of the ancient sculptors Pliny gave for this work, the "Laocoon" were Hagesander, Polydorus, and Athenodorus, the exact names that were carved into the ancient work! Many scholars had wondered if Pliny's fabulous descriptions of works of Art of inestimable skill and dazzling beauty were perhaps exaggerations, even pure fantasy, but suddenly one of the most famous works he had described had been unearthed virtually intact and signed. This was Pliny vindicated! His fame exploded as a comet across the sky, overnight he was recognized as a true and reliable source of authority on the Art of the ancient world. The stories of the brilliance of Greek and Roman Art were entirely true! Pliny became the greatest source of inspiration for much Art of the Renaissance. Sixteenth century scholars, painters and sculptors went back to his Natural History, studied it intensely, then tried to emulate what had been achieved by the ancients; and ultimately the greatest among them, Raphael, da Vinci, Michelangelo attempted to outdo them - and in this later, stunningly, they would succeed; and light the way toward the brilliant Artists of the Baroque, Caravaggio, Rubens, Vermeer, and Bernini, the "miracle worker" of the following century.*

*The Laocoon was the greatest archeological find of the age, perhaps of any age - greater than even the Nike or the Venus de Milo; tangible proof of the reality of Pliny's narrative; it quickly became the sensation of Renaissance Europe. It was reported to the Pope that the Laocoon had been owned by Pliny's great patron, the Emperor Titus, who had displayed it in pride of place in his palace. Julius lost no time, sending the architect Giuliano da Sangallo to go and examine the statue and to report back to him immediately. Giuliano hastened to the excavation site, taking with him his son Francesco and his friend Michelangelo Buonarroti. Many years later Francesco recorded the historic moment...*

*"The first time I was in Rome when I was very young, the pope was told about the discovery of some very beautiful statues in a vineyard near S. Maria Maggiore. The pope ordered one of his officers to run and tell Giuliano da Sangallo and to go and see them. He set off immediately. Since Michelangelo Buonarroti was always to be found at our house, my father having*

*summoned him and having assigned him the commission of the pope's tomb, my father wanted him to come along too. I joined up with my father and off we went. I climbed down to where the statues were, when immediately my father said, "That is the Laocoon, which Pliny mentions". Then they dug the hole wider, so they could pull the statue out. As soon as it was visible, everyone started to draw, all the while discoursing on ancient things, chatting as well about the ones in Florence..."*

*Julius was convinced that this was indeed the Laocoon described by Pliny. His agents immediately outbid other wealthy contenders and emulating the Emperor Titus he had it installed in a place of honour specifically built for it. Bramante created a grand terraced and porticoed courtyard known as the Cortile del Belvedere where it still stands today. After intense examination Michelangelo and Giancristoforo Romano concluded that in fact, contrary to what Pliny had said, the Laocoon had not been hewn from a single piece of marble, but rather from several, although the joints has been so skillfully hidden that it had taken two of the greatest sculptors in Rome to discover this. But this did not lessen the brilliance of the work in any case, rather it threw down the gauntlet to the Renaissance masters - the Holy Grail of sculpture now became the creation of works of this magnitude out of a single block of marble or a single pour of bronze. Indeed Michelangelo had achieved this with his Pieta, perhaps, alongside Bernini's David, the greatest work of sculpture ever produced. Michelangelo had surpassed the ancients; and like them, in distinction to a tradition of untold centuries of anonymity of great Artists, in deference to the "will of God", he had signed it! His immortality, even before the Sistine Chapel, had been assured. The Laocoon would serve as a model for sculptors for centuries to come, particularly in its dynamic movement. Michelangelo himself reproduced this motif over and over, and in his unfinished St Mathew, produced from a single monolith of marble, in the same year the Laocoon was discovered, we see the tortured gyrations of the saint as he attempts to emerge from the stone in imitation of Laocoon as he attempts to escape the giant snakes sent by the goddess Athena to kill him and his sons.*

*According to Virgil's Aeneid, Laocoon was a Trojan High Priest, who did not trust the Greeks, even when they had appeared to have abandoned the fields around Troy. He desperately tried to warn his fellow Trojans against having anything to do with the giant wooden horse they had left behind. His fear of course was prescient - and his frantic warnings have echoed down through the eons in the saying - "beware of Greeks bearing gifts!". The Trojan horse of course was the last desperate attempt of the Greeks to break the 10 year stalemate of the Trojan war. All the gods of Olympus had by this time taken up sides either Trojan or Greek, and they intervened constantly in order to gain victory for their favoured side. The gods who favoured the Greeks could not bear the see a Greek victory, now so close after so long, foiled by Laocoon. In a desperate attempt to silence Laocoon they sent monstrous serpents to entwine and crush not only him, but his two sons as well. The marble of Hagesander, Polydorus, and Athenodorus, shows the moment of agonizing struggle of Laocoon and his sons amidst the suffocating coils of the serpents.*

*When we test our patients for urinary ketones we may, be unexpectedly surprised in their low reading! But perhaps this news is too good to be true! We must beware of "false gifts"! Malevolent gods may be sending intervening to stifle grave warnings, and lull us into a false sense of security! To get the true picture of the ketotic state of a patient we must look not to their urinary ketones - but to those of their capillary blood!*

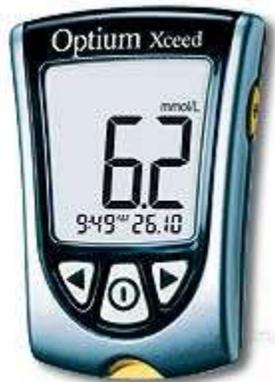
## KETONE TESTING

### Introduction

Ketones may be tested for:

1. **In blood:**

- By use of the “MediSense Xceed” sensor, a device for rapidly testing capillary blood ketones.
- It is a quantitative test
- The ketones detected are  **$\beta$ -hydroxybutyrate**.
- The primary purpose of blood ketone testing is to ensure the *early* diagnosis and prompt treatment for those patients with diabetes who are at risk of DKA.



2. **In urine**

- By use of the nitroprusside “dipstix” urinary test strips.
- It is a semi quantitative test.
- The nitroprusside urine test detects **acetoacetate** (and acetone to a lesser degree), but it does **not** detect beta hydroxybutyrate

### Important Points of Ketone Testing

- Note that ketoacidosis is still possible in the presence mildly elevated or even normal blood glucose levels.
- Measurement of the ketone body  **$\beta$ -hydroxybutyrate** is a better indicator than acetoacetate in determining the patient’s metabolic status with regard to ketosis.

This is because in many cases of ketosis, (particularly in alcoholic ketoacidosis) the predominant ketone formed will be  **$\beta$ -hydroxybutyrate** and not **acetoacetate**.

Urinalysis may therefore underestimate the true degree of ketoacidosis.

It is for this reason that blood testing for capillary  **$\beta$ -hydroxybutyrate** is a superior test than urinalysis “dipstix” testing for **acetoacetate**.

## Pathophysiology

### Ketone formation:

Ketones are produced when fat is metabolized as a source of energy. This can occur when glucose becomes unavailable to the tissues as a source of energy, as occurs in diabetics.

These ketones can be used as an alternative source of energy by the brain.

However if allowed to go untreated, the excessive production of ketones will result in ketoacidosis.

Ketone body metabolism occurs as follows:

**Fatty acid oxidation**  $\rightarrow$  2x Acetyl Co-A  $\rightarrow$  Acetoacetyl CoA  $\rightarrow$  **beta hydroxybutyrate**  $\leftrightarrow$  **acetoacetate**  $\rightarrow$  acetone

Ketones formed are:

- **beta hydroxybutyrate**
- **Acetoacetate**

Acetone is *not* a ketoacid.

The excessive formation of ketones in the blood is called **ketosis**.

The presence of ketones in the urine is called **ketonuria**.

### Causes of ketosis

1. Diabetes
2. Starvation
  - Malnutrition
  - Protracted vomiting, particularly hyperemesis gravidarum.
3. Alcoholic ketoacidosis

## Indications

Suitable patients for testing include:

1. Diabetics
  - All patients with type 1 diabetes.
  - Patients with type 2 diabetes with a BGL > 14mmol/L or a bicarbonate of < 20 mmol/L
2. Patients with malnutrition/ starvation
  - In particular vomiting alcoholics at risk for alcoholic ketoacidosis.
3. Hyperemesis gravidarum

## Procedure

### Urine

Urinalysis may be done in 2 ways:

- The nitroprusside “dipstix” test which gives a semi-quantitative reading of acetoacetate levels via color chart indicator.
- A nitroprusside test which is done via a specific reader device that will give a quantitative reading of acetoacetate levels.

### Capillary blood

- Capillary whole blood is used for testing ketones but **venous whole blood samples** can also be used provided the samples are used within 30 minutes of collection.

Venous whole blood samples may be collected into sodium or lithium heparin tubes not fluoride or oxalate tubes.

- Always calibrate the sensor to ketones (as opposed to glucose) test strips.
- The test strip range is 0.0-8.0mmol/L for beta hydroxybutyrate.

## Results

Blood ketone testing, needs to be interpreted in the light of:

- The blood glucose level

- The clinical setting.
- The ABG/VBG result.

| <b>Ketone capillary blood</b>  | <b>Corresponding urinalysis</b>   |
|--------------------------------|-----------------------------------|
| <b>Ketones &lt; 0.6mmol/L</b>  | Negative to trace, (normal range) |
| <b>Ketones 0.6-1.5 mmol/L</b>  | Small to moderate ketones.        |
| <b>Ketones &gt; 1.5 mmol/L</b> | Moderate to large                 |

### Management

1. Blood Ketone levels of < 0.6mmol/L are in the normal range.
2. **Levels above this in diabetic patients indicate the possibility of DKA**  
**Therefore a follow up venous blood gas will be required to confirm the presence of acidosis and its degree.**
3. Elevated levels in alcoholics who are not also diabetic may indicate the presence of alcoholic ketoacidosis.
4. Elevated levels in patients with hyperemesis gravidarum indicates the degree of severity of the condition and assists in the decision to admit.



*St Mathew, marble, 1506, Michelangelo Buonarroti, Galleria dell'Accademia, Florence.*

References

1. Southern Health Clinical Protocols and Guidelines, 2013
2. Chase HP “Detection of Ketosis and Monitoring of Diabetic Ketoacidosis” Supplement to Managed Care. 2003: 5-6.
3. Medisense Optium Users guide.

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*Acknowledgements:*

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