

Recently, a number of practitioners have queried the finding of a negative result for the 13C-urea breath test (UBT) for *Helicobacter pylori* (*H. pylori*) in conjunction with a positive result on either the *Gastrointestinal Function Profile* or *Microbial Ecology Profile*.

There are a number of situations in which false negative results can arise for the 13C-Urea Breath Test.

1. Use of antimicrobials, proton pump inhibitors (PPIs), nonsteroidal anti-inflammatory drugs (NSAIDs), H₂ receptor antagonists (H₂ Blockers) and bismuth preparations within the two weeks preceding the UBT
2. Administration of the UBT less than four weeks after completion of therapy to eradicate *H. pylori*
3. Premature or late collection of the post-dose sample
4. Failure to use citric acid as a test drink
5. Low intragastric bacterial load of *H.pylori*

Antimicrobials, PPIs, NSAIDs, H₂ Blockers & Bismuth Preparations

Each of the above agents has bactericidal activity against *H. pylori*. This serves to reduce the concentration of the gastric bacteria resulting in lowering of delta over baseline (DOB) values for the breath test, which leads to a decrease in sensitivity of the UBT.

PPIs by themselves also induce false-negative results on the UBT by an alternative, pH-dependent mechanism. PPIs cause an increase in the pH of gastric juice which can both reduce the entrance of urea into *H. pylori* and the activity of its cytoplasmic urease.

In a recent study by researchers from Israel, a range of NSAIDs were found to possess antibacterial activity against *H. pylori* at therapeutically achievable doses; an effect that appeared to be independent of cyclooxygenase enzymes inhibition.¹

Bismuth subsalicylate is a common bismuth preparation with anti-inflammatory and antacid properties that is used for various stomach and gastrointestinal tract complaints. The anti-inflammatory and antacid properties serve to reduce the urease activity of *H.pylori*.

Timing of Breath Test Following Eradication Therapy for *H. pylori*

Due to the effect of each of the agents discussed above, it is important that the UBT be performed a minimum of 4 weeks following any type of eradication therapy. Several studies have reported unacceptable false-negative results in UBTs performed earlier than 4 weeks after completion of triple therapy for eradication of *H. pylori*.²⁻⁴

Timing of Collection of the Post-Dose Sample

At present, there is general agreement on the use of two breath samples, one collected before and another collected, in most cases, 20–30 min after urea ingestion. It has been shown that sampling too

early (at 5 or 10 min) may produce false-positive results because of urease activity of oral bacteria.^{5,6} Conversely, sampling too late may produce false-negative results because of the emptying of urea from the stomach.

Use of Citric Acid Test Meal

A number of studies have been published which document that the use of a test drink containing citric acid may decrease significantly the false-negative results associated with PPIs treatment.^{7,8} Use of a citric acid test meal serves to decrease gastric pH and delay gastric emptying. Indeed, the use of citric acid has allowed a reduction in the time between completion of therapy and eradication confirmation testing using the UBT.⁹

Gastric Load of *H. pylori*

There are several studies confirming *H. pylori* colonization in localizations besides the gastrointestinal cavity with or without having the bacteria in the stomach, such as the oral cavity, dental plaque, saliva samples, adenotonsillar tissues, nasal and sinus mucosa of some patients with chronic rhinosinusitis and trachea-bronchial secretions. Furthermore, it has been shown that *H. pylori* can settle in the most proximal part of the digestive tract by gastroesophageal reflux or contamination by an exogenous route without any gastric regurgitation.¹⁰

References

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