¹³C-Urea Breath Test: Further Modification towards an Unrestricted Use

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The ¹³C-urea breath test (¹³C-UBT) is the gold standard among non-invasive tests for the detection of *Helicobacter pylori* infection. The test has the same accuracy as the endoscopy-based examination with multiple biopsies for histology and culture [1]. It is easy to handle, well accepted with the same performance in adults as well as in children. The test is well standardized with ¹³C-labelled urea (75 mg in adults, 50 mg in children) that includes also a test drink made up with citric acid (200 ml liquid with 0.1 mmol citric acid). It took some time and experimental work before it became clear that the acid test drink together with the ¹³C-urea is an essential requirement [2, 3]. This combination allows the maximal detection of bacterial urease activity via their degradation products. With current standardization the test provides the same accuracy before and after therapy; however, it requires an interval of 4 weeks to avoid false-negative results [4]. Reasons for this time interval are (a) persisting bacterial suppression for several weeks as a consequence of the antibiotic therapy, and (b) the urease inhibiting effect of proton pump inhibitors (PPI) if given concomitantly [5]. PPIs used for eradication in the triple therapy or in patients with upper gastrointestinal symptoms, especially in patients with gastroesophageal reflux disease, possess a strong urease inhibitory effect in vitro as well as in vivo [5–7, 9].

Since the addition of citric acid was shown to slow gastric emptying, it was originally believed that the higher accuracy of a citric acid containing test meal would be the consequence of a prolonged contact time of bacterial urease with the ¹³C-urea test substrate [8]. However, more recently it was quite convincingly demonstrated that citric acid exerts the beneficial effect more likely via acidification of the bacterial environment and urease release [9].

The concept of a higher test drink acidification was taken on in the study by Shirin et al. [10] presented in this edition of *Digestion*. The authors increased the citric acid content from 1 to 4 g in a 200-ml test drink administered together with ¹³C-urea. They found that this modification of the test fully maintained its accuracy with the advantage of a reduced time interval following *H. pylori* eradication therapy. The authors indeed demonstrated that by shortening the interval to 14 days (after eradication) the test was still accurate in 96.8% of patients. The main message of the study is that by rendering the test meal (drink) more acidic it is still well tolerated and allows the correct assessment already 2 weeks after the end of *H. pylori* eradication.

This is certainly useful information although its clinical relevance appears overemphasized by the authors. Is it truly an important gain to obtain the information of the

therapy success 2 instead of 4 weeks after eradication therapy? It would be worthwhile to investigate whether this increases the patient's compliance for follow-up testing. However from my judgment there is no urge to institute rescue therapies for *H. pylori* eradication in case of failure already after 2 instead of 4 or even 6 weeks.

An experimental design with a direct comparison between a group tested at 1 and 2 weeks with a test drink containing only 1 g citric acid as compared to 4 g is missing and would be of great interest. The clinical issue of frequent false negative tests and high recrudescence of *H. pylori* rather than reinfection has become generally acknowledged if tests are performed too early (within 4 weeks following therapy). The scientific proof of inadequate testing with the ^{13}C -UBT if performed at 1 or 2 weeks after therapy is less solid. The study of Shirin et al. [10] reopens the interesting chapter of best timing and opti-

mized test modification for increasing the accuracy and clinical utility of ^{13}C -UBT testing.

The questions generated by this study are of far more greater importance than the immediate clinical benefit reported by shortening the timing from 4 to 2 weeks before getting to an accurate test result after therapy.

Does the higher acidification of the test drink allow the ^{13}C -UBT not only to become more sensitive in the presence of fewer bacteria, but also to overcome the limitations of a low acidic gastric environment with reduced urease activity? And does it allow to accurately test for the presence of *H. pylori* if PPIs (that inhibit gastric acid and bacterial urease activity) are taken simultaneously? What would be the best and still tolerated amount of citric acid for the unlimited ^{13}C -UBT use? Answers to these questions would indeed open a new window for *H. pylori* testing by ^{13}C -UBT in the general clinical setting.

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