

CLOtest*

Rapid Urease Test

INTENDED USE

The CLOtest rapid urease test (RUT) accurately and conveniently detects the urease enzyme of *Helicobacter pylori* in gastric mucosal biopsies. Its use is intended for the presumptive diagnosis of *H. pylori* infection.

Note: For *in vitro* diagnostic use.

CLOtest is CLIA '88 waived.

Rx only (USA)

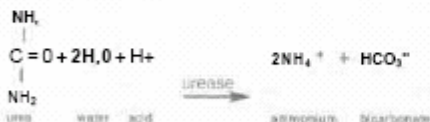
SUMMARY

Barry Marshall, M.D. developed the CLOtest. Its name originated from "Campylobacter-Like Organism" test². Drs. Robin Warren and Marshall first cultured the bacterium from antral biopsies in 1982 calling it a Campylobacter-like bacterium¹. Subsequently, the genus was named *Helicobacter*, meaning spiral or helical bacteria².

H. pylori has been shown to cause active chronic gastritis⁴ and is a risk factor for gastric cancer⁶ and mucosal-associated-lymphoid-type (MALT) lymphoma⁷. The eradication of *H. pylori* is effective in eliminating or reducing the recurrence of ulcers and may also lower the risk of gastric cancer⁷.

PRODUCT DESCRIPTION AND STORAGE

CLOtest is a well of urease indicator gel sealed inside a plastic slide. The gel contains urea, USP (29 mg/mL) phenol red (a pH indicator), butters and a bacteriostatic agent to prevent the growth of contaminating urease-positive organisms. If the urease from *H. pylori* is present in the tissue sample, it changes the gel from yellow to bright magenta according to the following reaction:



The CLOtest RUT has a shelf life of 18 months when stored at 2°-8°C (36°-48°F). The product expires on the last day of the month indicated on the package. Do not use the product if the gel is not yellow, if the seal is damaged and the gel appears dehydrated, or if the expiration date has passed. For further questions, call 1-800-528-5591 (USA), or + 801 572 6800 (outside USA) before using the CLOtest.

PATIENT PREPARATION

The patient should discontinue the use of antibiotics and bismuth preparations three weeks before the biopsy. These agents may suppress but not eradicate the presence of *H. pylori* making the organism difficult to detect by any means. The patient should not have ingested proton pump inhibitors two weeks prior to the test as these drugs have been shown to inhibit growth of the organism in some persons.

FAIL-SAFE PROTOCOL (for CLIA waiver requirement)

With each negative test, perform the following positive control to ensure the CLOtest RUT is working properly:

1. Insert a urease tablet (Kimberly-Clark catalog #60407) into the CLOtest gel and re-seal the slide.
2. After five minutes, inspect the gel for a positive color change (red or magenta).
3. If the gel does not turn to red or magenta, notify Kimberly-Clark at 1-800-528-5591.

PERFORMANCE CHARACTERISTICS

The CLOtest RUT detects 75% of *H. pylori* infections within 20 minutes with no false positives. By one hour 85% of positive patients will be detected by CLOtest, and at three hours 90% are detected. Between 3 and 24 hours CLOtest will detect another 5% of patients. In the then largest U.S. Study reported to date, Dye et al took antral biopsies, one each for histology (Giemsa stain) and CLOtest from 122 consecutive routine endoscopy patients at the University of Virginia⁸. Eighty-two patients also had specimens cultured. The results obtained are shown in the table below.

Table 1: CLOtest Study, Dye et al, University of Virginia

	n	True +	True -	False +	False -
CLOtest	121	46	72	2	1
Histology	122	43	74		5
Culture	82	23	49		10
		Sensitivity		Specificity	
CLOtest		98%		97%	
Histology		91%		100%	
Culture		70%		100%	

Similar results were noted by Schnell et al in Missouri⁹.

LIMITATIONS OF RAPID UREASE TESTS, HISTOLOGY, AND CULTURE

Possible causes for False Negatives

- Very low numbers of *H. pylori* in the tissue sample
- Patchy *H. pylori* distribution so that the organism is not captured in the tissue sample
- A sample of intestinal metaplasia - (*H. pylori* does not colonize intestinal mucosa)
- Recent ingestion of antibiotics, bismuth, proton pump inhibitors, or sucralfate which can inhibit the organism
- Formalin contamination of the sample

Possible causes for False Positives

- When the test is properly performed, false positives are rare. Late false positive reactions (>12 hours) may be caused by failure to completely insert the biopsy into the gel so that contaminating organisms can grow in the tissue.
- Theoretically, a false positive could occur in patients who have achlorhydria from bacterial overgrowth. This could be the result of the following conditions: pernicious anemia, previous gastric surgery, or recent use of proton pump inhibitor drugs. However, other bacteria produce much less urease than *H. pylori* and should not cause a rapid color change.

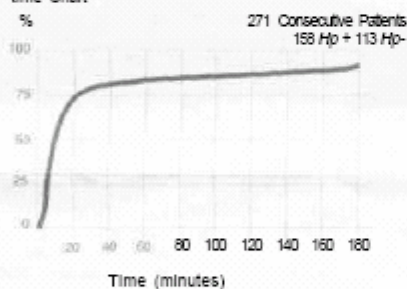
THE BIOPSY

1. The recommended gastric area to biopsy is at least 2 cm away from the pylorus along the lesser or greater curve of the antrum. Excise tissue that appears normal - avoid tissue that is eroded or ulcerated as *H. pylori* may be present in smaller numbers around those areas. A Standard biopsy forceps should render a specimen of sufficient size for the test.
2. If desired, an additional sample may be inserted into a Single CLOtest well. Do not contaminate the second specimen with blood from the first biopsy Site.

SPECIMEN COLLECTION AND HANDLING

1. After removing the CLOtest[®] rapid urease test slide from refrigeration, lift the label far enough to expose the yellow gel. For faster test results, allow the gel to reach room temperature before inserting the biopsy (usually between 7-10 minutes).
2. With a clean applicator device (e.g., toothpick etc.) push the entire sample from the forceps beneath the surface of the gel to expose as much of the specimen to the gel as possible. Make sure that the biopsy specimen is completely immersed in the gel.
3. Re-seal the pressure-sensitive label on the slide and record the patient name, date, and time the biopsy sample was inserted.
4. If desired, the CLOtest slide may be put on a warming plate at a temperature between 30°-40°C (86°-104°F). Although the warming plate may speed the reaction time and provide faster results, its use is optional and will not affect the test accuracy. If the warming plate is used, the slide should be heated no more than three hours, then it should be stored at room temperature until the final reading.
5. Record a positive reaction as soon as the gel changes color. Once a positive reaction has occurred no further reading is necessary. 75% of positive tests change color within 20 minutes (Fig.1).

Figure 1: CLOtest rapid urease test positive reaction time chart



INTERPRETATION OF RESULTS

1. A specimen contaminated with blood may stain the gel around the edge of the tissue. This is NOT a positive test. If the biopsy contains urease, the change first appears around the sample and eventually colors all of the gel.
2. The pH change in a positive test is first seen at the interface of the gel and the biopsy. If a significant amount of urease is present the visible change is rapid. Any color change of the whole gel to a shade other than yellow (e.g., red, magenta, pink, deep orange) indicates the presence of *H. pylori*.
3. A negative test remains yellow after imbedding the tissue into the gel. If the color of the gel is yellow at 24 hours, the test is negative. If unable to be read at 24 hours, the test will remain valid for 72 hours after insertion of the biopsy into the gel medium. For example, if a test performed on Friday has not changed color by the end of the day, it may be stored at room temperature and read on Monday.

If there are factors that might adversely affect the Performance of the CLOtest rapid urease test, consider other diagnostic measures such as a urea breath test and serology in order to exclude a diagnosis of *H. pylori*.

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Rapid Urease Test

Test rapide de l'urease

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Urease-Schnelltest

Test rapido de ureasa

Snabbureastest

Prova da Urease Rapida

Snelle ureasetest

Hurtig ureasetest

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