How (who ?) and when to test or retest for *H. pylori*

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Abstract

Several direct/invasive and indirect/non-invasive diagnostic tests are available for the diagnosis of *H. pylori* infection. Invasive tests require biopsy sampling of the gastric mucosa and include rapid urease test, histology, bacterial culture and polymerase chain reaction technique. Non-invasive tests include the urea breath test and serological assays. This review gives a critical comparative analysis of accuracy, advantages and limitations of the different diagnostic tests including current cost and availability in Belgium. Rapid urease testing (RUT) of gastric biopsy specimens is probably the initial test of choice in patients undergoing endoscopy because of its low cost, rapid availability of results, simplicity and accuracy. Histological examination of gastric biopsy samples should be mandatory at the initial presentation of the patient because it also gives insight on the status of the gastric mucosa (inflammation & premalignant changes). Although not mandatory for primary diagnosis, a biopsy for culture and sensitivity testing should always be obtained when it is available and when endoscopy is undertaken as part of the patient's management. Among the non-invasive tests, the place of serology remains questionable for other than epidemiological purposes. How is *H. pylori* infection best diagnosed ? How many tests are needed in routine clinical practice ? The answer will depends on the clinical setting and local availability of the tests. For primary diagnosis in dyspeptic patients — where endoscopy is an important tool — a biopsy-based detection system is appropriate an we recommend the use of at least two diagnostic tests based on different principles, like RUT (with 1 or 2 biopsy specimen/test) and histology (including antrum & corpus biopsies) which are widely available. Alternatively a urea breath test may also be recommended when endoscopy is not required. Post-treatment monitoring seems to be justified in most cases and must always be performed at least 4-6 weeks after completion of therapy. The urea breath test is probably the method of choice for non-invasive testing in this clinical setting. When endoscopy is required, mutiple biopsy specimens both from the antrum and the corpus and the use of at least two different diagnostic methods must be performed. Whenever possible, culture should always be done as it is very specific and allows testing of antimicrobial susceptibility which is mandatory in case of treatment failures. Neither the "*Test and Treat*" nor the "*Test and Scope*" strategies have been investigated in terms of effectiveness of symptoms relief and cost in Belgium and cannot therefore be recommended at this time. (Acta gastroenterol. belg., **1998**, 61, **336-343**).

Key words : *H. pylori*, diagnosis, rapid urease test, histology, culture, urea breath test, serology.

The aim of this review is 1) to give a comparative analysis of accuracy, advantages and limitations of the different diagnostic tests including current cost and availability (in Belgium) ; 2) to underline the importance of the PPV (positive predictive value) or NPV (negative predictive value) of a test according to the possible strategies ("Test & Treat" or "Test and Scope" strategies) recently proposed for managing dyspeptic patients cheaper and with less endoscopy workload and 3) to propose a critical analysis of the place of the different diagnostic tests in routine clinical practice according to specific clinical situations (primary diagnosis or post-treatment monitoring).

For the purpose of this analysis, we reviewed all published clinical guidelines or national consensus (1-14), the reviews and a selection of relevant papers about diagnostic tests published since 1992 until december 1997 (retrieved & selected following extensive review of the literature obtained by "Current awareness of in biomedicine : Helicobacter" and a "MEDLINE" search) plus abstracts from DDW, UEGW and EHPSG workshops (15-38).

It is now widely accepted that *H. pylori* is involved in several clinical conditions that have increased the demand for treatment of the infection and thereby also increased the interest for reliable diagnostic tools. Several diagnostic tests, based on different principles, have been developed for *H. pylori* : (1) direct identification of the organism (culture) ; (2) demonstration of wavy, curved rod-shaped microorganisms in relation to the gastric epithelium (histology) ; (3) detection of increased urease activity (rapid urease test on biopsy specimen, urea breath test) ; (4) detection of IgG antibodies to *H. pylori* (serology) and (5) detection of DNA fragments from *H. pylori.*

Table I. — **Direct ("invasive") and indirect ("non-invasive") methods for *Helicobacter pylori***

Direct (invasive) methods (biopsies)	Indirect (non-invasive) methods
— rapid urea test — histology — cytology — culture — (PCR)	— serology (ELISA) — urea breath test C^{14} or C^{13}

The existence and use of different techniques for the detection of *H. pylori* indicates that although (very) accurate, none of them are perfect for all situations. The tests are classified as invasive if they are performed on gastric mucosal biopsy specimens obtained during an endoscopy (indirect test : rapid urease test ; direct tests : histology & brush cytology, culture, PCR) or non-invasive when endoscopy is not required and the tests are based on indirect evidence of the bacterium's presence (indirect tests : serology, urea breath tests) (table I). These tests can be used in different clinical

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settings and for different clinical purposes : (a) to confirm the presence of *H. pylori* at the time of initial presentation (= primary diagnosis) or (b) to confirm that eradication of the organism has been achieved after therapy (= post-treatment monitoring).

Comparative analysis of the advantages and limitations of the different diagnostic tests

Methodology, accuracy, advantages and limitations as well as the practical impact of each test have been extensively reviewed elsewhere (see former reviews in this issue). Tables II summarizes different parameters that allow a comparative analysis of the advantages and limitations of the different usual diagnostic techniques used for the diagnosis of *H. pylori* infection. Most tests are widely available except for culture which requires specialized laboratory facilities in order to yied consistent satisfactory results (38). All tests are convenient and easy to perform except, again, for culture. The perfomant rapid urease test (RUT) may allow a rapid diagnosis, within 1-3 h of sampling in > 90% of the cases, while the answer of the other tests needs a delay of 3 to 7 days with up to 12 days for culture. Serological tests may be more rapid (1 day) but the delay is often longer due to the fact that serial analysis of multiple tests are cheeper and is thus the usual processing way of most laboratories. The cost of these different tests vary from about 100 BF (RUT) to 5000 BF (UBT). The cost of the endoscopy (about 4000 BF) is not included in these figures because the endoscopic examination is no more required to establish the diagnosis of an active *H. pylori* infection since the availability of indirect diagnostic methods like UBT. One must also keep in mind that serology is not reimbursed by the social health security system in Belgium.

The sensitivities and specificities, positive predictive values (PPV) and negative predictive values (NPV) of these tests are summarized in table III. All tests have a very good (> 90%) sensitivity values but the sensitivity of histology and culture may vary from < 70% to > 95% according to the difference in expertise of the investigators and appropriate sampling ! The specificity of all tests are > 95% except for serology (ELISA) which is a little bit less specific.

Sensitivity and specificity of a test are independent of the prevalence of the disease. The prevalence of the disease in the population, however, has a dramatic effect on the positive and negative predictive values. When the prevalence of a disease drops, the positive predictive value drops and the negative predictive value increases (39-40). A more powerfull method of establishing the usefulness of a test is to examine the likelihood ratios (LRs), which estimate the probability that disease is present at any level of a test result, as LRs do not need to change with changes in the prevalence of the disease (41). Another performant index for measuring the performance of diagnostic tests is the Youden's J value (42). Unfortunately these indexes are seldom used in the studies aimed at measuring the perforance of diagnostic tests.

Overall, only tests showing sensitivity and specificity results > 90% should be recommended for use in clinical practice. But while most of the available diagnostic tests are accurate, not one works perfectly.

Table II. — **Advantages and limitations of different diagnostic tests for *Helicobacter pylori***

	RUT[a]	Histology	Culture	UBT[b]	Serology
availability	+++	+++	+	++(+)	+++
convenience	+++	+++	+++	++(+)	+++
easiness	+++	++	+	+++	+++
cost (BF)[c]	100	2000	1000	5000	500
rapidity	≤ 3 h	3-5 d	5-12 d	3 d	3-7 d
special transport processing	—	—	+++	—	—

[a] RUT = rapid urease test (on biopsy specimen) ; [b] UBT = urea breath test ; [c] cost does not include the cost of endoscopy (4000 BF/100 Euro).

Table III. — **Sensitivity and specificity of different diagnostic methods for *Helicobacter pylori***

	RUT[a]	Histology	Culture	UBT[b]	Serology
sensitivity (%)	90-98[c]	70-95	70-99	90-98	90-95
specificity (%)	95-99[c]	90-99	100	90-98	85-95
PPV (%)	99	99	100	97	95
NPV (%)	85	89-98	98	85	85
accuracy (%)	86-97	65-94	70-99	81-96	76-90
active infection	+	+	+	+	±

[a] RUT = rapid urease test (on biopsy specimen) ; [b] UBT= urea breath test ; [c] lecture at 24h.

Specific advantages and limitations of each diagnostic techniques

Non-invasive tests such as serology and UBT are global tests, easy to perform and independent of sampling error, transport or storage conditions or experience of the tester (20).

Serology

Serology (ELISA) is relatively inexpensive, widely available but must be validated locally before use. Serological testing is mainly usefull in epidemiological studies, as it allows large numbers of people to be sceened for *H. pylori*, but is less suitable for individual pre-treatment screening monitoring, as it does not always define current *H. pylori* activity, so a positive test may give evidence of a current or a past infection. Serology is also less useful for monitoring the effectiveness of eradication therapy, as significant serological changes take at least 6-12 months to occur after the infection has been cured. Another limitation for this application of serology is the need to obtain and keep a pre-treatment sample, in order to process simultaneously both pre- and post-treatment samples to allow a reliable analysis of the antobody kinetics. "Serological tests must be considered as complementary to and not a substitute for clinical investigation or the direct detection of *H. pylori*. Serology should not therefore, be used to assess *H. pylori* status prior to or shortly after the end of treatment" (5).

Urea Breath Test (UBT)

UBT is more expensive than serology but is now unanimously recognised as the non-invasive test of choice, particularly for monitoring *H. pylori* eradication : it is easy to perform and has a very good sensitivity and specificity and must be soon widely available (C^{13}). However, it only identifies the presence of *H. pylori* without giving information about the susceptibility of the strain to antimicrobial agents.

Invasive tests are dependent of rare but always possible sampling error in case of patchy distribution of the organism, transport or storage conditions (culture) or experience & expertise of the investigators (histology, culture). The sensitivity of the RUT and histology are likely to be affected more if small numbers of bacteria are present, compared to culture or PCR and, by their nature, likely to have a lower specificity (19).

Rapid urease test (RUT)

Rapid urease testing of gastric biopsy specimens is accurate, inexpensive, rapid, readly available and easy to perform but it does not yield any further information concerning the colonizing strain. RUT is highly specific with a good sensitivity and is probably the first screening test to be performed during routine endoscopy. Indeed, it is highly desirable and cost-effective for outpatients to have their result of *H. pylori* status before they leave the endoscopy clinic so they do not have to wait or return again for the prescription of appropriate treatment. It has been reported that the sensitivity of RUT was reduced after eradication therapy but this does not seem to be the case anymore, at least when the test is performed 4-6 weeks after the end of therapy or with the newer tests which seems better performant.

Histology

Histology gives no additional information concerning the organism, other that it is present, but gives insight into the status of the mucosa and allows detection of other microorganisms such as *Helicobacter Heilmanii*. It is widely available and the preparations can be stored, allowing permanent record and retrospective examination of the specimens, if required. It gives, however, no information about the susceptibility of the infecting strain to antimicrobial agents (43-44).

Culture

Culture is the most specific technique (100%). It is also very sensitive when performed under proper conditions but it is not widely available (culture is a demanding technique, requiring trained and motivated personnel). Isolation of the organism from biopsy specimens has direct clinical relevance in terms both of detecting colonization and of determining the antibiotic sensitivity of the isolate, which information may affect individual patient management but also allows to assess trends in antibiotic sensitivity patterns at local, national or international levels. Indeed, it is clinically important to know the local antibiotic susceptibilities and their trends in order to choose the most appropriate eradication regimen. Individual patient data are particularly important in area where the prevalence of antibiotic resistance is high or after treatment failure. Culture also allows typing of the strain (for epidemiological purposes) or investigating its virulence factors. A drawback of culture is the lack of standardization of culture media, culturing methods and interpretative values for sensitivity testing of isolated strains and clearly an urgent need for consensus exists (38,45).

Polymerase chain reaction (PCR)

PCR provide a rapid and reliable diagnosis of *H. pylori* infection, with a very high sensitivity and specificity, provided certain precautions are taken to ensure a reliable processing of the biopsy specimen (expertise needed to avoid contamination with *H. pylori* DNA !). PCR also allows typing of the strains by performing Restriction Fragment Length Polymorphism (RFLP) on the amplified DNA fragments. This technique does not, however, give any information

about the susceptibility of the infecting strain to antimicrobial agents, although promising results concerning the screening of macrolide resistance by PCR analysis have been reported (16,46).

There has been considerable improvement in the methods used for the diagnosis of *H. pylori* infection and several studies have conclusively demonstrated that the non invasive urea breath test (UBT) or a combination of at least two different biopsy based techniques may be used in order to reliably diagnose the infection. Indeed, comparative accuracy studies of different diagnostic tests have established that for the initial diagnosis of *H. pylori* infection, most current diagnostic tests may achieve high ($\geq$ 90%) sensitivity and specificity when performed correctly, and particularly for histology or culture, when they are performed by enthousiastic investigators. The accuracy of these last two tests is indeed largely dependent of appropriate sampling (size of the biopsy specimen) and of the experience and expertise of the tester, or on the conditions in which the specimen is transported and processed (culture). PCR tests do not require special transport condition and may be performed on the biopsy specimen taken for the rapid urease test but remain currently a research tool.

Importance of Positive and Negative Predictive Values (PPV & NPV) for the selection and timing of diagnostic studies

On the other hand we have also to keep in mind some basic statistical considerations. The requirements of a test in terms of sensitivity and specificity depend on the use to which it is to be put. For a screening purpose, the emphasis is usually on sensitivity — on ensuring that cases are not missed. On the other hand, when a positive diagnosis on a test will lead directly to a major intervention, high specificity is essential. If the test lack of specificity, a substantial number of people may receive unnecessary and injurious treatment (47).

The characteristics of a test that are of most relevance in the management of an individual patient are its positive and negative predictive values (= the probability that disease is really present when the test is positive or absent when the test is negative). But the predictive value of a test depends on the prevalence of the disease in the population of patients to whom it is applied (and may thus differ significantly for the same test according to the clinical setting, eg. when performed pre- or post-antimicrobial therapy). At very high prevalence rates (eg. duodenal ulcer disease before treatment) the best accuracy is obtained with the tests offering maximum sensitivity (or PPV). But after treatment, where a very low prevalence of *H. pylori* infection may be anticipated, the best diagnostic accuracy is obtained with the test offering maximum specificity (or NPV). So the best test for a primary diagnosis should not necessarily be the best one to assess eradication.

Investigation of dyspepsia

Several decision analysis algorithms have recently been proposed for the investigation and management of new-onset dyspepsia not due to NSAIDs (7,48). One option is a single short-term (2 weeks) trial of empiric antiulcer therapy which may be proposed for young reliable patients in a setting where follow-up is ensured, an provided a workup is performed if symptoms persist or recur. Another option is a definitive diagnostic evaluation by upper gastro-intestinal endoscopy which must be the rule for new onset of dyspepsia at least in patients older than 45 years and for younger patients with dyspepsia associated with "alarm" markers (eg. anemia, gastrointestinal bleeding, dysphagia, anorexia, early satiety or weight loss).

A third option could be non-invasive testing for *H. pylori* (urea breath test > serology) followed either by empirical eradication regimen ("*Test and Treat*") or endoscopic investigation ("*Test and Scope*") in young (< 45 year old) *H. pylori*-positive subjects without "alarm" symptoms (49-52). In the "*Test and Treat*" strategy a significant proportion (> 50% ?) of patients will be given needless therapy as only fewer than 25% of *H. pylori*-positive patients may be expected to have an underlying peptic ulcer and probably only 25-30% of non-ulcer dypeptic individuals will benefit from eradication therapy. This strategy is expected to reduce the endoscopy workload by about one-fourth but the potential cost saving of this option rests on reserving definite workup and extended therapy for those subjects with recurrent symptoms after antibiotic therapy. On the other hand, in the "*Test and Scope*" strategy only those patients who are positive by the sceening test will be endoscoped so as to identify accurately those who would benefit from eradication therapy. Here also this strategy is expected to reduce the endoscopy workload by about one-fourth. But the cost-effectiveness of both strategies remain uncertain and data are lacking to reliably evaluate the outcomes with each of these options, none of which has been evaluated in Belgium where endoscopy is relatively cheap and readly available.

Important determinants include relative costs of eradication regimen and screening test or endoscopy as well as post-treatment medical care, the prevalence of the diseases in population and the health care setting (primary practice or secondary referal). The strategy of testing for *H. pylori* is also dependent of the cost-effectiveness and accuracy of the diagnostic tests used. UBT may be more cost-effective than serology despite its higher initial costs because of suboptimal accuracy of blood tests (mainly the PPV) for *H. pylori* (51,53). Another important question is whether patients will be

as reassured by normal non-invasive *H. pylori* testing as they are by normal results on endoscopy. Finally, one must keep in mind that the cost-advantage of the empiric therapy will be lost to the extent that diagnostic studies are eventually performed or that delay in definitive diagnosis affect patient outcome.

Empiric antibiotic therapy without prior *H. pylori* testing is strongly discouraged because the prevalence of *H. pylori* is likely to be considerably less than 50%, especially in young dyspeptic patients, so that a substantial proportion of individuals who are not colonized by *H. pylori* or in whom colonization is not contributing to the symptoms will be given needless and inappropriate medication. Moreover widespread antibiotic use carries a small but definite risk of significant morbidity and a theoretical risk of development of multi-resistant organisms.

Primary diagnosis

Which of the tests discussed in this review should be used in routine clinical practice depends on different factors such as the local availability of accurate tests, the clinical situation, whether upper endoscopy is planned, the cost of the test and on individual preference.

In dyspeptic patients, endoscopy is and remains an important tool for diagnosing peptic ulcer disease or other gastro-oesophageal lesions. A biopsy-based detection system for *H. pylori*, such as the rapid urease test (the less expensive test with touch cytology), histology or culture of the organism (the most specific test) is to be considered. Several studies have demonstrated that the diagnostic sensitivity will increase from > 90% to 99% if more than one tests is performed. However when combining diagnostic tests there is also a risk for decreasing specificity so that strict criteria (eg. for the rapid urease test) must be followed in order to keep a high specificity rate.

Table IV. — **Diagnostic methods for *Helicobacter pylori* according to clinical setting**

Clinical setting	Diagnostic method
Primary diagnosis[a]	— (Serology ?) — Urea Breath Test — OGD + biopsies : — rapid urease test (1 or 2 antrum) — histology (2 antrum + 2 corpus) — (culture optional)
Post-treatment[b]	— Urea Breath Test — OGD + biopsies : — rapid urease test (1-2 antrum/corpus) — histology (2 antrum + 2 corpus) — culture (1 antrum + 1 corpus) if possible, but mandatory after treatment failure)

[a] No antibiotics, PPI during the last 2 weeks and no Bi salts during the last 3-4 weeks before *HP* testing.

[b] No antibiotics, PPI or Bi salts during the last 4 weeks before *HP* testing.

In the setting of biopsy-based diagnostic methods, the combination of the rapid urease test (1 or 2 biopsy specimens) and histology (2 biopsy specimens from both the antrum and the corpus) appears to be the most practical and available option, although combination of one of these tests with culture, is very attractive when available (Table IV).

In asymptomatic patients (eg. patients with past history of peptic ulcer disease), a non-invasive test should be used. Serology may be considered in this situation, but if the results prove positive (accuracy < 90%), confirmation of *H. pylori* infection by a UBT may be desirable in order to certify a current active infection.

Several medications including the proton pump inhibitors (PPI), bismuth and antibiotics temporarily suppress *H. pylori* and may induce false negative results : one must thus care for the absence of intake of any of these drugs within the last 2-4 weeks before testing for *H. pylori.*

Post-treatment monitoring

The selection of the appropriate test for diagnosing *H. pylori* infection eradication is challenging. Because of cost considerations, monitoring eradication efficacy is considered to be optional for asymptomatic non-ulcer dyspepsia (NUD) or non-complicated duodenal ulcers (USA 1997 consensus + ; European 1996 consensus ±) (2,3). However monitoring eradication efficacy may be suitable in most of the cases considering that about 15-25% treatment failures may be expected in routine clinical practice (cf. reported ITT eradication rates of about 85% with one week PPI-triple therapies), that confirmation of eradication may have important pronostic value namely for patients suffering from peptic ulcer disease (predictor of no recurrence) or important clinical implications for ongoing management for patients with NUD. In patients with GERD on long term PPI therapy, cure of *H. pylori* will probably eliminates the risk of developping atrophic gastritis, while in younger patients it will probably decrease substantially the risk of developping a gastric carcinoma. Moreover, monitoring eradication efficacy is strongly recommended when using less performant therapies, when one suspect a lack of compliance, when the infective strain is suspected to be or was found resistant to metronidazole or macrolides or in case of recurrent symptoms. Of course, everybody agree that confirmation of cure of *H. pylori* infection is mandatory after treatment of severe, refractory, "silent", or complicated duodenal ulcer, gastric ulcer, MALT-lymphoma, or post-resection of early gastric cancer. Therefore testing for *H. pylori* seems to be justified in most cases.

In routine clinical practice, the most appropriate test is beyond doubt the UBT because it is non-invasive and is a good predictor of eradication of the bacteria (54-57). Serology is not recommended post-treatment because the IgG titre decreases very slowly after cure

of the infection so that only after ≥ 6 months will a decrease of 50% in the antibody titre be observed. Like the other tests, the UBT must be performed at least 4-8 weeks after the end of treatment to avoid false negative results caused by temporary suppression of the infection (58). One must also make certain that the patient did not take single course of antibiotics or PPI since at last 3-4 weeks and Bi-salts since at least 4 weeks (table IV).

When endoscopy is required, a combination of biopsy-based tests must be performed (59). Several well conducted prospective studies have now confirmed that the direct/invasive tests prove as accurate/performant ≥ 4-6 weeks after therapy as they were before antimicrobial therapy, including the rapid urease test (60-62). Probably the most important reason for failure to detect *H. pylori* is sampling error. All good clinical practice guidelines for per-endoscopy *H. pylori* testing now emphasize the need for mutiple biopsy specimens both from the antrum and the corpus and the use of at least two different diagnostic methods in order to obtain reliable results and to avoid false negative results (63,64). Whenever possible, culture should always be performed as it is very specific and allows testing of antimicrobial susceptibility which is mandatory in case of treatment failures in order to determine the antibiotic sensitivity of the isolate before another eradication attempt (Table V).

Summary/Conclusions

Several invasive (direct and indirect) and non-invasive (indirect) diagnostic tests are now available for the diagnosis of *H. pylori* infection. Invasive tests require biopsy sampling of the gastric mucosa and include rapid urease test, histology, bacterial culture and polymerase chain reaction technique. Non-invasive tests include the urea breath test and serological assays.

Rapid urease testing (RUT) of gastric biopsy specimens is probably the initial test of choice in patients undergoing endoscopy because of its low cost, rapid availability of results, simplicity and accuracy. Histological examination of gastric biopsy samples should be mandatory at the initial presentation of the patient because it also gives insight on the status of the gastric mucosa (inflammation & premalignant changes). Although not mandatory for primary diagnosis, a biopsy for culture and sensitivity testing should always be obtained when it is available and when endoscopy is undertaken as part of the patient's management. Among the non-invasive tests, the place of serology remains questionable for other than epidemiological purposes.

Which diagnostic test(s) should be used in routine clinical practice according to specific clinical situations ? The choice of the test(s) depends on the clinical situation. For primary diagnosis in symptomatic patients — where endoscopy is an important tool for diagnosis of gastro-duodenal ulcer disease or other gastroesophageal lesions — a biopsy-based detection system is appropriate an we recommend the use of at least two diagnostic tests based on different principles, like RUT (with 1 or 2 biopsy specimen/test) and histology (including antrum & corpus biopsies) which are widely available and subject to histology has been locally validated. Alternatively a urea breath test may also be recommended when endoscopy is not required while the use of serology may be recommended to firmly rule out a possible *H. pylori* infection in ulcer patients testing negative for *H. pylori* and not taking NSAIDs.

Post-treatment monitoring (≥ 4-6 weeks after end of therapy) seems to be justified in most cases and the the urea breath test is probably the method of choice for non-invasive testing in this setting. When endoscopy is required, mutiple biopsy specimens both from the antrum and the corpus and the use of at least two different diagnostic methods must be performed in order to optimize the diagnostic yield. Whenever possible, culture should always be performed as it is very specific and allows testing of antimicrobial susceptibility which is mandatory in case of treatment failures.

The cost-effectiveness of both the "*Test and Treat*" and the "*Test and Scope*" strategies for young dyspeptic patients remains uncertain and data are lacking to reliably evaluate the outcomes with each of these options, none of which has been evaluated in Belgium. They cannot therefore be recommended at this time.

Table V. — **Post-treatment monitoring of *Helicobacter pylori* infection**

Diagnostic method	Clinical setting	
— UBT (≥ 8 wk post-trt)	when endoscopy not required	— NUD — non complicated DU
— OGD + biopsies (4-6 wk post-trt)	when endoscopy required (when UBT not disponible)	— Refractory, complicated DU — GU — MALT-lymphoma — Post-resection of early GC — Treatment failure (culture)

NUD : non-ulcer dyspepsia ; DU : duodenal ulcer ; GU : gastric ulcer ; GC : gastric carcinoma.

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