

# Detection of *H. pylori* in endoscopic gastric biopsies: a routine research that goes far beyond the laboratory limits

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It took about 10 years between the first reports of the association of the microorganism *H. pylori* with inflammation of the gastric mucosa and the acceptance by the scientific community of its role as the most important etiologic agent of chronic gastritis<sup>(1-5)</sup>. Over the past 20 years, after this initial phase of acceptance, the medical literature has been gradually enhanced with increasingly convincing results of potential virulence factors of *H. pylori*, also related with gastric cancer pathogenesis. The first evidences emerged through epidemiological studies<sup>(5, 6)</sup>. Since then, molecular and genetic mechanisms have been emphatically exploited<sup>(7)</sup>. Currently, the participation of *H. pylori* in the mechanisms involved in the pathogenesis of chronic gastritis and gastric cancer is not up for discussion. And, overcoming this phase of clinical and experimental evidences, some countries are already planning mass eradication of this microorganism in the population in order to reduce the high incidence rates of gastric cancer<sup>(8)</sup>. Therefore, everything seems to indicate that the detection of *H. pylori* in the gastric mucosa has become an issue of great importance, since it is related not only with chronic gastritis, but also with the pathogenesis of the gastric lymphoma and gastric carcinoma, the latter representing one of the main causes of cancer death.

Based on the above assumptions, it can be concluded by the need to correctly detect *H. pylori* presence in the gastric mucosa as a priority among the exams which must be ordered to the patient that shows dyspeptic complaints, aiming to eradication of the microorganism, finally. However, this conduct, at this present time, is not yet bearer of universal consensus: for some, treatment would be indicated as soon as the microorganism detection is established; for others, the treatment would be optional and dependent on the clinical conditions and patient's family history. The sustainability of the latter conduct comes from the fact that most infected patients, dyspeptic or asymptomatic, do not develop severe consequences neither complication that may adversely impact on their quality of life. However, with no single universally accepted answer to this question, in view of the regional differences of *H. pylori* infection, experts from different countries have periodically discussed consensual proposals on this matter, including Brazil<sup>(9)</sup>.

And even if we could not predict the evolution of gastric disorders associated with *H. pylori* infection, the request for complementary exams for the detection of this bacterium should be accurately regarded by the responsible professional. In the case of invasive procedures, such as endoscopy and gastric biopsies, this question is automatically transferred from the assistant physician to the pathologist, often impliedly and sometimes explicitly. That is, there is always a tacit agreement among professionals about the need to verify the presence of *H. pylori* in the gastric mucosa biopsies sent for histopathological evaluation. Among us, this invasive method of *H. pylori* research is routine, whether performed only for verifying the presence of bacteria in dyspeptic patient, or just as control of prior treatment, this is not always explicit in the test request. This type of situation is not common in countries where non-invasive methods, as the urea breath test, among others, are procedures of choice, instead of endoscopy with biopsies, much more expensive and not so significantly more sensitive. A list of invasive and non-invasive procedures for the diagnosis of *H. pylori* infection, with current and summarized information of each of them can be seen in a recent publication on this subject<sup>(10)</sup>.

In Brazil, gastric endoscopy with biopsy is still one of the most widely used procedure for the diagnosis of *H. pylori* infection, and therefore, the pathologist remains one of the leading professionals to sign the final result of this examination. We will not discuss here the technological nuances that could cause false positive or false negative results of the histopathological examination, in relation to the *H. pylori* identification on tissue. Undoubtedly, the false positive results should be avoided at all costs, because they may involve iatrogenic conditions. The false negative results, though also not desirable, are better placed in the methodological spectrum because there is a real possibility of this error in about 10%-15% of cases, either for reasons related to the sampling, or due to technical processing reasons which the tissue is subjected. This possibility should be of Gastroenterologist knowledge. If the clinical suspicion of infection persists, given the pattern of gastritis described in the histopathological report, new diagnostic methods should be requested to reach a final conclusion.

The false positive diagnosis may result in unnecessary treatment of patients during 7, 10 or 14 consecutive days, with prescription drugs composed of different antibiotics associated with proton pump inhibitor. If this therapeutic procedure has already been carried out, the clinical doctor that receives the histopathological report with a positive result may interpret that he is facing a possible bacterial resistance to the antibiotics used. This often involves a new therapy using more potent prescribed drugs. Repeating treatment of patient infected by *H. pylori* is a situation that occurs in 10% to 20% of cases, so it is not uncommon and has increasingly become a concern in the area of clinical gastroenterology<sup>(11)</sup>.

In this current Issue of Brazilian Journal of Pathology and Laboratory Medicine (Jornal Brasileiro de Patologia e Medicina Laboratorial [JBPM]), Boldt *et al.* review 390 cases of endoscopic biopsies of gastric mucosa in order to compare the positivity of demonstration of *H. pylori* stained by Giemsa and hematoxylin-eosin (HE)<sup>(12)</sup>. The Giemsa staining method shows to be more effective in these terms, therefore, indicating that the false negative cases should occur in less than those obtained with the routine HE staining, especially when cases with low bacterial concentration are concerned. It is worth remembering that all ancillary staining method should be standardized in each laboratory, with controls, always keeping an eye on the best performance of the reaction, and the Giemsa staining is no exception to this rule, especially in the final stage of differentiation with ethanol.

The positive cases and with patent inflammatory activity, in turn, generally leave no doubt, even for the beginner pathologist. The control of positive cases with low bacterial load and doubtful cases that can lead to false positive results crucially depends on the pathologist's experience. In an attempt to manage the most difficult cases, the finding of small bacterial colonies present in the gastric mucus can help in the release of a more precise final diagnosis. We believe that this should be a criterion to be considered when looking for the safest detection of *H. pylori* presence in the gastric mucosa. The only detection of isolated and rarefied bacterial forms can increase the rate of false positive results, especially when using non-standard auxiliary stains aiming the histological determination of *H. pylori* presence.

In conclusion, it is always useful to remember that different patients, some of them with different degrees of sensitivity to drugs, are waiting in the lab door the final result of the histopathological examination of endoscopic biopsies that were submitted. After all, these patients are the ultimate goal of all the procedures above mentioned.

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