Detection of *Helicobacter pylori* and its sensitivity to antibiotics

A step forward in the use of molecular methods

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Since the discovery of *Helicobacter pylori* and its role in causing gastroduodenal diseases, it has been systematically diagnosed by all gastroenterologists, and the challenge to find an accurate, rapid, easy and, if possible, reasonably priced diagnostic method began. Non-invasive methods such as the detection of specific antibodies, detection of *H. pylori* antigens in stool specimens and, in particular, the urea breath test were quickly developed. These methods satisfy most of the previously mentioned criteria. However, the task was further complicated by the increase in treatment failures, mostly due to *H. pylori* resistance to one of the antibiotics included in the most frequently prescribed triple therapy to cure this infection, i.e. clarithromycin. The most recent Consensus Conferences recommended not to use this antibiotic or to perform preliminary susceptibility testing, in the event of a 15 to 20% resistance prevalence which is unfortunately the case in France. As a result, the existing diagnostic methods are being reconsidered, since the non-invasive methods do not test bacterial susceptibility to antibiotics. The standard method for the latter is culture followed by antibiogram testing. However, culture has practical limitations in the laboratory setting, despite its efficacy. Indeed, very strict procedures are necessary to ensure the viability of these fragile bacteria which are sensitive to drying, oxygen exposure, and temperature variations, and these conditions are often difficult to obtain. Furthermore, freshly prepared media should be used in the laboratory and the personnel should be trained for this kind of test; both of these conditions can be difficult regardless of the type of laboratory involved. Finally, the physician wants quick results and this is impossible because this technique requires 3 to 10 days for *H. pylori* colony growth followed by at least 48 hours for an antibiogram.

As a result, a PCR detection method for *H. pylori* and its susceptibility to clarithromycin was developed including one format published by the team in Créteil, France. The results of its application using gastric biopsies over one year are reported in a subsequent article by Tankovic et al. (page 792-95). This study highlights the importance of routinely using a molecular approach. PCR detection was more sensitive (98% versus 87.7%) and more specific (97.5% versus 91.3%, respectively) than histology which remains the most commonly used method of direct detection of *H. pylori* in France, with culture as a reference in the event of discrepant results.

Indeed, histological detection has its limits linked to 1) the quality of the specimen and 2) the human evaluation of the slides. Many studies have shown the poor inter-observer reproducibility of the results. In this study discordant histological preparations were reread blindly by a second observer who was only able to rectify the diagnosis in one fourth of the cases.

In the methodology used by Tankovic et al., a second PCR was performed to determine clarithromycin sensitivity. This method had been previously validated but was not compared in this study to its histological counterpart, i.e. the in situ hybridization method. A very high prevalence of clarithromycin resistance (27.2%) was found. However, as indicated in the article, this figure cannot be considered an indicator of prevalence for this resistance in France because the center involved is a center specialized in the treatment of *H. pylori* infection and receives many patients who have previously received eradication treatments.

An evident advantage of the molecular method is its rapidity since it can be performed in 3 hours, whereas 48 hours are usually necessary to obtain a histological result. Nonetheless, for practical reasons the authors decided to carry out their method only twice a week which renders this new method less competitive.

Nevertheless, molecular methods are the most attractive tests in this area as well as in others. They can be easily automated and once kits become available comparable results among laboratories can be expected. Their use in stools in *H. pylori* research will provide a strictly non-invasive diagnosis. This approach is already being investigated and once it has been optimized, it will certainly become the diagnostic method of the future.