Utility of serology in determining *Helicobacter pylori* eradication after therapy

Carlo A Fallone MD FRCPC, Vivian G Loo MSc MD FRCPC, Alan N Barkun MSc MD FRCPC

**OBJECTIVE:** To determine the usefulness of four serological tests in confirming cure of *H pylori* infection before the previously reported six-month post-treatment delay.

**PATIENTS AND METHODS:** As part of a prospective, blinded, controlled trial, in which patients with duodenal ulcers were randomized to receive different combinations of antibiotics, serum samples were obtained in 89 patients before treatment, as well as on several occasions after treatment. Antibody titres were determined by ELISA with Bio-Rad immunoglobulin (Ig) A, Bio-Rad IgG, Pyloriset EIA-A for IgA and Pyloriset EIA-G for IgG. Eradication was confirmed with antral biopsy three months after therapy.

**RESULTS:** The percentage drop in titre following treatment was significantly larger for the group of patients who were treated successfully with all four kits. Optimal cut-offs for identifying successful therapy were determined, and accuracy improved as the interval between testing and therapy was prolonged. Six months after therapy, the IgG test from Bio-Rad achieved 100% sensitivity and 80% specificity, and that from Pyloriset achieved 88% sensitivity and 100% specificity. At three months, however, test performance was quite good, with 90% sensitivity and 80% specificity when using a Pyloriset IgA titre drop of 20% or greater to predict successful eradication.

**CONCLUSION:** Serology is a simple, easily available, noninvasive method that exhibits good positive predictive value in the confirmation of successful cure of *H pylori* infection three or six months after treatment.

**Key Words:** Helicobacter pylori, Immunoglobin A, Immunglobulin G, Serology, Treatment

Results of this study were presented in preliminary form at the American Gastroenterological Association Meeting as part of Digestive Disease Week in San Francisco, California, May 18 to 23, 1996.
In 1994, the National Institutes of Health Consensus Development Panel recommended that all patients with peptic ulcer disease and infection with Helicobacter pylori be treated with antimicrobial agents to eradicate the organism and, thus, prevent ulcer recurrence (1). Success rates of effective anti- \textit{H pylori} therapy vary from 80% to 95% (2-4). The ability to monitor treatment success is often desired, particularly in patients exhibiting questionable compliance, patients who originally presented with a complication such as a bleeding ulcer, patients in whom the treatment was one with a relatively low eradication rate and patients with recurrence of symptoms (5,6). Accepted methods of confirming eradication are histological examination or culture of gastric antral biopsies obtained during gastroscopy, or breath urea testing – both should be performed at least four weeks after completion of therapy (2). However, endoscopy may be uncomfortable for the patient and is not without inherent complications. Breath testing is safe and simple for the patient but requires expensive equipment with the carbon-13 method and involves a small amount of radiation for the patient but requires expensive equipment with the carbon-14 method (7-9). Hence, it is not widely used. Serology, in contrast, is a simple, noninvasive and inexpensive method of diagnosis.

The effect of successful eradication of \textit{H pylori} on serological titres has been examined in several studies. Many of these showed promise, with significant drops in immunoglobulin (Ig) G (10-15), IgA (10,15,16) and IgM (16) antibody titres observed after successful eradication therapy. However, absolute antibody titres remain in the positive range for one (17,18) to as many as four years after successful eradication (19,20). Investigators have thus looked at the relative change in IgG titre from pretreatment levels as an indicator of treatment success. Their results have been disappointing, with accurate confirmation of eradication only possible a minimum of six months after completion of therapy (21-24). Two studies noted that IgA levels dropped earlier than IgG levels (15,16). In one such preliminary study, our group (15) observed that IgA titres were significantly lower in those whose therapy was successful than in \textit{H pylori}-positive patients as early as one month after therapy.

The aim of this study was to determine the usefulness of IgA and IgG serology in monitoring treatment, and in particular in confirming eradication before the reported six-month post-treatment delay. We studied four different commercially available serological assays in patients who had attempted antimicrobial therapy for \textit{H pylori} eradication.

**PATIENTS AND METHODS**

**Patient population:** Adult patients from the gastroenterology divisions of the Montreal General Hospital and Royal Victoria Hospital of McGill University, Montreal, Quebec, with an endoscopically documented duodenal ulcer in the 13 months before randomization and proven \textit{Helicobacter pylori} infection on histology or tissue culture were invited to participate in the study as part of a prospective, controlled eradication trial. Patients were excluded if they reported allergies to any of the study medications, used daily nonsteroidal anti-inflammatory drugs in the month before randomization or were suffering from conditions that increased the risk of gastroscopy with biopsy, such as a coagulopathy. Pregnant or breastfeeding patients, or patients who had previous esophageal surgery, malignancy, or ongoing alcohol or drug abuse were also excluded. After informed consent was obtained in accordance with the institutions’ respective ethics review boards, patients underwent gastroscopy to confirm ulcer healing. During gastroscopy, four antral biopsies (one per quadrant) were obtained and sent for culture and histology to confirm the presence of \textit{H pylori}. Those with \textit{H pylori} infection were entered in the study.

**Design:** Patients were randomized in a double-blind fashion to one of three possible eradication regimens including combinations of metronidazole, bismuth subcitrate, amoxicillin and placebo; or metronidazole, bismuth and placebo; or metronidazole, bismuth and amoxicillin). All medications were administered orally. Serum samples were obtained for serological analysis (see below) at the time of randomization, at completion of therapy and three, six, nine and 12 months after completion of therapy. Endoscopy with antral biopsies was performed three months after completion of therapy for confirmation of eradication.

**\textit{H pylori} detection:** \textit{H pylori} was detected with antral biopsy culture or histological examination. Biopsy cultures destined for culture were obtained before dipping the biopsy forceps in formalin. Specimens were transported in D20W and plated within 4 h onto sheep blood agar at 37°C under microaerophilic conditions. Organisms were identified by oxidase, catalase and urease tests. Biopsies destined for histological examination were transported in buffered formalin, paraffin embedded, sectioned, and stained with hematoxylin and eosin. Giemsa staining was used if there was any doubt of the result of the hematoxylin and eosin stain. Investigators interpreting the histology, culture and serological tests were all blinded to each others’ results and to the patient history.

**Serological determinations:** Serological titres were determined by following the manufacturers’ directions for each of the four commercially available kits. The Pyloriset ELA-A and Pyloriset ELA-G assays (Orion Diagnostica, Espoo, Finland) are used to identify IgA and IgG antibodies, respectively, directed at the acid glycine extract (15). The Bio-Rad GAP IgA and IgG assays (Bio-Rad Laboratories) also identify antibodies directed at \textit{H pylori} antigens of 20 to 120 kDa. Both kits use an ELISA technique. Control solutions provided with the kits were used with every run, and absorbance measured with an ELISA reader (Behring ELISA Processor II). Serum titres were determined from standardized curves constructed using the control samples as described previously (15).

**Statistical analysis:** Patients were classified as having succeeded or failed therapy (from here on referred to as successes and failures) based on antral biopsy histological examination and culture (performed only in those with active duodenal ulcer at the time) obtained three months following therapy as the gold standard. If either test was positive, the patient was...
classified as having failed therapy. Mean antibody titres pre- and post-therapy for both the success and failure groups were compared by using the Student’s t test (paired or independent t test where applicable). The relative change in titre post-treatment was calculated by determining the percentage change in titre when comparing the post-treatment titre with the pre-treatment titre for each individual patient, ie, 

\[
\frac{\text{post-treatment titre} - \text{pretreatment titre}}{\text{pretreatment titre}} \times 100
\]

Statistical comparisons were carried out as with mean antibody titres.

To determine the optimal drop in antibody titre required after treatment to confirm eradication, selected cut-offs were examined for the four kits at each of the five time intervals after treatment (zero, three, six, nine and 12 months). Test characteristics were determined by using 2x2 table analysis of thresholds consisting of drops in titres equal to or greater than 10%, 15%, 20%, 25%, 30%, 40% or 50%. Ninety-five per cent confidence intervals were calculated for proportions by using the standard normal approximation of the binomial distribution. Optimal cut-offs were determined by receiver operating characteristic (ROC) curve analysis (25,26). A ROC curve displays the false positive rate on the x-axis (one-specificity) and the true positive rate on the y-axis (sensitivity) for the varying test thresholds, thus, plotting the performance of a diagnostic test. Ideal cut-off values for the different kits for each time period after treatment were chosen by determining the point lying geometrically closest to an ideal test with 100% specificity and sensitivity (the upper left corner of the graph).

Figure 1) Mean immunoglobulin (Ig) A and IgG antibody titres after successful and failed Helicobacter pylori eradication. Mean IgG titre for both kits dropped significantly in patients who succeeded (P<0.001) but not in those who failed treatment (P>0.05, paired t test). Patients with a measured titre of more than 20 U/mL for Bio-Rad and 500 U for Pyloriset are considered seropositive for H pylori antibodies. 0 Time of completion of therapy; R Time of randomization to treatment; tx Treatment

### TABLE 1

|                | Serum available | Serum available for percentage change in titre analysis* |
|----------------|-----------------|-------------------------------------------------------|
| At randomization | 68              | –                                                     |
| Zero months     | 67              | 60                                                    |
| Three months    | 57              | 51                                                    |
| Six months      | 55              | 45                                                    |
| Nine months     | 54              | 43                                                    |
| 12 months       | 54              | 42                                                    |

*For percentage change in titre analysis, serum was required from the specific time period as well as from the time of randomization; therefore, the number of subjects with both specimens available is lower than the number of subjects with specimens available from the particular time period.
A modified maximum likelihood program was used to compare the areas under the fitted ROC curves, which represent the overall test performance of the different assays (27). These were compared with matched analysis where appropriate. Clinical utility of the kits was examined by prepost-test probability analysis. By using the optimal test characteristics (as defined above) and Bayes’ theorem, the post-test positive and negative probabilities of *H pylori* eradication were plotted for different pretest probabilities (prevalence) of *H pylori* infection (28). P<0.05 was considered significant on a priori planned comparisons.

**RESULTS**

**Antibody titres post-therapy:** Eighty-nine patients fulfilled all inclusion and exclusion criteria (Table 1). Sixty-five (73%) were men and 24 (27%) were female. Culture and histology results were concordant in 92.9%. Twenty-three (26%) patients failed and 66 (74%) succeeded the *H pylori* eradication attempt. As shown in Table 1, serum analysis involved fewer than the 89 patients who met entry criteria. The reason for this is that some patients did not return for follow-up, and at the onset of the study one shipment of samples was involved in an accident resulting in several lost specimens. Mean titres of IgA and IgG determined with both Pyloriset and Bio-Rad kits are shown in Figure 1. Mean IgG titres for both Bio-Rad and Pyloriset dropped significantly in successes (P<0.001 at all five time periods compared with pretreatment, paired analysis). This was not the case for failures (P>0.05). However, mean absolute IgG titres were still very close to the positive range as late as 12 months after completion of therapy. Mean IgA titres were not helpful in discriminating between successes and failures when either Pyloriset or Bio-Rad was used (Figure 1).

When data were analyzed in terms of percentage change in patient titres, differences between successes and failures became more evident (Figure 2). Indeed, the percentage drop in titre over the year following treatment was highly significant (P<0.0001 at all five time periods compared with baseline) in successes for both antibody classes for both Pyloriset and Bio-Rad (paired analysis). Upon completion of therapy (at zero months) the percentage drops in IgA from both kits and IgG from Bio-Rad were already significantly greater (P<0.05, independent t test) for successes than for failures. In contrast, the observed drop in Pyloriset IgG achieved significance only three months after completion of therapy.

**Optimal cut-offs:** ROC curves were plotted for each kit at all five time periods. Those obtained at therapy completion, and three and six months after therapy are shown in Figure 3. The other curves were similar. Optimal cut-offs for the 20 different scenarios (four assays, five times of serological sampling) are shown in Table 2 with their respective test performance scores.

Diagnostic accuracy was modest with all four kits immedi-
Table 2
Optimal cut-offs with respective test performance scores of four assays for *Helicobacter pylori* eradication

| Test and time after treatment (months) | Optimal cut-off (% change) | Sensitivity | Specificity | Positive predictive value | Negative predictive value | Diagnostic accuracy* |
|--------------------------------------|----------------------------|-------------|-------------|---------------------------|---------------------------|---------------------|
| **Immunoglobulin G**                 |                            |             |             |                           |                           |                     |
| Bio-Rad                              |                            |             |             |                           |                           |                     |
| Completion of therapy                | –10                        | 52 (37-67)  | 64 (33-87)  | 83 (64-94)                | 29 (14-48)                | 55 (42-68)          |
| Three                                | –25                        | 73 (57-86)  | 90 (56-100) | 97 (83-100)               | 45 (23-69)                | 76 (63-87)          |
| Six                                  | –10                        | 100         | 80 (28-100) | 98 (87-100)               | 100                       | 98 (88-100)         |
| Nine                                 | –50                        | 70 (54-83)  | 100         | 100                       | 20 (4-49)                 | 74 (56-85)          |
| 12                                   | –50                        | 92 (78-98)  | 100         | 100                       | 67 (30-93)                | 93 (81-99)          |
| Pyloriset                            | –15                        | 61 (45-75)  | 57 (29-82)  | 82 (66-93)                | 31 (14-52)                | 60 (47-72)          |
| Three                                | –50                        | 71 (55-84)  | 90 (56-100) | 97 (83-100)               | 43 (22-66)                | 75 (60-86)          |
| Six                                  | –50                        | 88 (73-96)  | 100         | 100                       | 50 (19-81)                | 89 (76-96)          |
| Nine                                 | –30                        | 98 (87-100) | 67 (9-99)   | 98 (87-100)               | 67 (9-99)                 | 95 (84-99)          |
| 12                                   | –50                        | 94 (81-99)  | 83 (36-100) | 97 (85-100)               | 71 (29-69)                | 93 (81-99)          |
| **Immunoglobulin A**                 |                            |             |             |                           |                           |                     |
| Bio-Rad                              |                            |             |             |                           |                           |                     |
| Completion of therapy                | –20                        | 70 (54-82)  | 64 (33-87)  | 86 (71-96)                | 39 (20-62)                | 68 (56-80)          |
| Three                                | –40                        | 68 (52-82)  | 80 (44-98)  | 93 (78-99)                | 38 (18-62)                | 71 (56-83)          |
| Six                                  | –30                        | 83 (67-93)  | 80 (28-100) | 97 (85-100)               | 36 (11-69)                | 82 (68-92)          |
| Nine                                 | –25                        | 82 (67-93)  | 33 (1-91)   | 94 (81-99)                | 13 (0-53)                 | 79 (63-90)          |
| 12                                   | –40                        | 91 (77-98)  | 83 (36-100) | 97 (84-100)               | 63 (25-92)                | 90 (77-97)          |
| Pyloriset                            | –20                        | 63 (48-77)  | 64 (33-87)  | 85 (69-95)                | 35 (17-56)                | 63 (50-75)          |
| Three                                | –20                        | 90 (77-97)  | 80 (44-98)  | 95 (83-99)                | 67 (35-90)                | 88 (76-96)          |
| Six                                  | –10                        | 83 (67-93)  | 80 (28-100) | 97 (85-100)               | 36 (11-69)                | 82 (68-92)          |
| Nine                                 | –15                        | 83 (67-93)  | 100         | 100                       | 30 (7-56)                 | 84 (69-93)          |
| 12                                   | –30                        | 64 (46-79)  | 83 (36-100) | 96 (79-100)               | 28 (10-54)                | 67 (51-80)          |

*True positives + true negatives) / (true positives + false positives + true negatives + false negatives). Numbers in parentheses are 95% CIs

Figure 3) Receiver operating characteristic curves used to determine optimal cut-offs for discriminating successful from failed Helicobacter pylori eradication for each of the four serological assays shown at three different times (upon completion of therapy, three months after therapy and six months after therapy). Sensitivities (on the y-axis) and 1–specificities (on the x-axis) attributable to each of the cut-offs are plotted. Each curve represents a serological test. The points comprising the curve represent the selected cut-offs of 10%, 15%, 20%, 25%, 30%, 40% and 50% drops in titre (plotted from right to left). *Optimal cut-off for each curve (the point closest to 100% specificity and 100% sensitivity) (these optimal cut-offs are listed in Table 2). Ig Immunoglobulin
ately upon completion of therapy. For example, a 20% or greater drop in IgA titres when Bio-Rad was used predicted successful treatment with a sensitivity of 70% (95% CI 54 to 82), specificity of 64% (95% CI 35 to 87) and diagnostic accuracy of 68% (95% CI 56 to 80). At three months, the performance of all four kits generally improved. The greatest accuracy was achieved with a 20% or greater drop in Pyloriset IgA titre, with a diagnostic accuracy of 88% (95% CI 76 to 96), sensitivity of 90% and specificity of 80% (95% CI 77 to 97 and 44 to 98, respectively). At six months, performances of both IgG tests were excellent. Bio-Rad demonstrated 100% sensitivity (95% CI 87 to 100) and 80% specificity (95% CI 28 to 100) with titre drops of 10% or greater, and Pyloriset was 100% specific (95% CI 28 to 100) and 88% sensitive (95% CI 73 to 96) with titre drops of 50% or greater.

There were no significant differences in area under the optimal ROC curves among the four kits at any given time period (zero, three, six, nine and 12 months), suggesting that no kit was significantly superior to any other in confirming successful eradication.

To determine intra-assay variability, 35 serum samples were run in duplicate from each assay. The coefficient of variation was 11.5 for Pyloriset IgA, 9.9 for Pyloriset IgG, 3.2 for Bio-Rad IgA and 6.7 for Bio-Rad IgG.

**DISCUSSION**

The present study confirms, as others have suggested, that absolute antibody titres to *H pylori* are not useful for confirming eradication because they remain very close to the positive range for up to one year following successful treatment (17-20). The relative change or percentage drop in titre following treatment, however, has been shown to be clinically useful.
We showed that IgG titre six months following treatment can confirm eradication very reliably, as was suggested by Kosunen et al (21) and Kosunen (22), who reported a 97% sensitivity and 95% specificity. The Bio-Rad and Pyloriset IgG kits yielded sensitivities of 100% and 88%, respectively, and specificities of 80% and 100%, respectively, at six months when using cut-offs of 10% and 50% drops, respectively. Thus, combining the two kits achieved a perfect score, with 100% sensitivity and 100% specificity. Cutler et al (24) also reported comparable results at six months, with 86% sensitivity and 88% specificity with a 20% decline in IgG. Hirshl et al (23) suggested that an earlier diagnosis could be made because a 50% drop in titre four months after therapy resulted in a 99% sensitivity and 87% specificity in confirming eradication. At six weeks, however, the sensitivity dropped to 56%. Results from Cutler et al (24) at three months were also disappointing, demonstrating only a 53% sensitivity. Our results are the first to show an adequate test performance as early as three months after therapy, yielding a 90% sensitivity, 80% specificity and 88% diagnostic accuracy when using a 20% or greater drop in Pyloriset IgA titre as a cut-off. Although the negative predictive value is low at this time (67%), a 20% drop in titre is an excellent predictor of successful eradication (positive predictive value of 95%). This allows the physician to be confident that eradication has been successful, whereas patients exhibiting smaller drops would require further surveillance. Immediately after completion of therapy, serology can be used to confirm eradication, but the information gained so early in the post-treatment period is modest as shown by Bayesian probability analysis (Figure 4). Titres obtained at three or six months are far more useful clinically. For the observed results to be valid clinically the test results must be reproducible, as shown in this case by the adequate coefficients of variation.

Whereas most studies advocate the use of IgG serology in the follow-up of *H pylori* infection, we have shown that IgA serology may also be useful. Although results at six months slightly favour IgG serology, the Pyloriset IgA test performed quite favourably at three months. One potential problem with this particular assay, however, is the relatively high coefficient of variation at 11.5, which can be at least partly overcome by running the paired sera in parallel. Certainly the test performance in our study attests to its adequacy.

The gold standard for defining eradication in this study does not include a urea breath test. Although this would have added to the strength of our study, a combination of culture and histology would yield, at most, very few false negatives, which would slightly overestimate our eradication rate. However, the effect on the test performance would be to underestimate the ability of serology to confirm eradication. This suggests that serology may in fact be better than we claim in terms of positive predictive value.

We did not observe any transient suppressive effect on antibody titres in any of the treatments. That is to say, of those patients who failed therapy, the change in antibody titre in patients from treatment groups with higher eradication rates did not differ from those from treatment groups with lower eradication rates. Hence one would not expect a difference in the ability to confirm eradication with serology when using treatments with eradication rates superior (such as a proton pump inhibitor and two antibiotics) to those used here.

Serology may also be used in other clinical settings, such as in the determination of a treatment plan in the workup of dyspepsia. This is a controversial issue and is the topic of many decision tree analyses being examined. It is not within the realm of this study, but if serology is useful as a screening test in this patient population, its use may be expanded to the confirmation of eradication. If developed successfully, serological tests that detect virulent strains of *H pylori* will also need to be assessed.

Although alternative methods of confirming eradication, such as gastroscopy and biopsy or urea breath testing, can reliably confirm eradication sooner than serology (ie, one month after therapy), the latter is simple, easily available, noninvasive (in that it does not involve endoscopy) and does not involve radiation exposure. Hence it can be particularly useful when the difference between the cost of serology and gastroscopy is greatest, or when risk of gastroscopy is especially high. Serology can also be performed in patients who are unable to comply with the instructions of a breath test (eg, patients unable to provide breath samples because of chronic lung diseases, old age or dementia). The serum sample itself can also be analyzed easily by any laboratory familiar with ELISA techniques. The disadvantages of serology are the need for both pre- and post-treatment sera and that these paired sera should be run simultaneously. This can be problematic in a clinical setting as well as in our study where paired samples were not obtained in about 10% of subjects (Table 1). Most important, however, this simple test is a relatively accurate means of confirming eradication three or six months following treatment.

ACKNOWLEDGEMENTS: The authors are indebted to Xiao Ping Xu for his able statistical assistance and Christine Wickham, Mary Muccino and Jocelyn Lavallée for their technical assistance. Dr AN Barkun is a Chercheur Clinicien Boursier of the Fonds de la Recherche en Santé du Québec. We thank both Pharmacia Canada and Bio-Rad Canada for providing the kits at a reduced price.

REFERENCES

1. NIH Consensus Development Panel. Helicobacter pylori in peptic ulcer disease. JAMA 1994;272:65-9.
2. Walsh JH, Peterson WL. The treatment of *Helicobacter pylori* infection in the management of peptic ulcer disease. N Engl J Med 1995;333:984-91.
3. Lind T, Veldhuysen van Zanten SJP, Ure P, et al. Eradication of *Helicobacter pylori* using one-week triple therapies combining omeprazole with two antibiotics: the MACHI study. Helicobacter 1996;1:138-44.
4. Bell G. Conference report: duodenal ulcer trials reported at the European Helicobacter pylori Study Group, Edinburgh 1995. Aliment Pharmacol Ther 1996;10:49-54.
5. Fallone CA, Barkun AN, Loo V, Wickham C, Hu X, Kostyk R. Compliance, selection of treatment, and the absence of duodenitis are predictors of successful eradication of *Helicobacter pylori*. Gastroenterology 1995;108:A91. (Abst)
6. Graham DY, Lew GM, Malaty HM, et al. Factors influencing the
eradication of Helicobacter pylori with triple therapy. Gastroenterology 1992;102:493-6.
7. Peterson WL. Helicobacter pylori and peptic ulcer disease. N Engl J Med 1991;324:1043-8.
8. Goodwin CS, Blinkow ED, Warren JR, Waters TE, Sanderson CR, Easton L. Evaluation of cultural techniques for isolating Campylobacter pylori from endoscopic biopsies of gastric mucosa. J Clin Pathol 1985;38:1127-31.
9. Marshall BJ, Surveyor L. Carbon-14 urea breath test for the diagnosis of Campylobacter pylori associated gastritis. J Nucl Med 1988;29:11-6.
10. Vaira D, Holton J, Cairns SR, et al. Antibody titres to Campylobacter pylori after treatment for gastritis. BMJ 1988;297:397.
11. Oderda G, Vaira D, Ainley C, et al. Eighteen month follow up of Helicobacter pylori positive children treated with amoxycillin and tinidazole. Gut 1992;33:1328-30.
12. Goosens H, Glupczynski Y, Burette A, et al. Evaluation of a commercially available complement fixation test for diagnosis of Helicobacter pylori infection and for follow up after antimicrobial therapy. J Clin Microbiol 1992;30:3230-3.
13. Safe AF, Warren B, Corfield A, et al. Role of serology in monitoring treatment for Helicobacter pylori infection in elderly patients. Age Ageing 1993;22:256-9.
14. Ashorn M, Ruuska T, Karikoski R, Miettinen A, Maki M. Helicobacter pylori gastritis in dyspeptic children. A long-term follow up after treatment with colloidal bismuth subcitrate and tinidazole. Scand J Gastroenterol 1994;29:203-8.
15. Fallone CA, Wild GE, Goretsky CA, Barkun AN. Evaluation of a commercially available complement fixation test for diagnosis of Helicobacter pylori infection. Can J Gastroenterol 1995;9:105-11.
16. Gobert B, Bene MC, de Korwin JD, Caure G. Isotype evolution in the follow up of patients with Campylobacter pylori associated gastritis. Gastroenterol Clin Biol 1989;13:880-3.
17. Hirschl AM, Hirschl MM, Berger J, Rotter ML. Evaluation of a commercial latex test for serological diagnosis of Helicobacter pylori infection in treated and untreated patients. Eur J Clin Microbiol Infect Dis 1991;10:971-4.
18. Wang WM, Chen CY, Jan CM, et al. Long-term follow-up and serological study after triple therapy of Helicobacter pylori-associated duodenal ulcer. Am J Gastroenterol 1994;89:1793-6.
19. Cutler AF, Prasad VM. Long-term follow-up of Helicobacter pylori serology after successful eradication. Am J Gastroenterol 1996;91:85-8.
20. Prasad VM, Santogade P, Cutler AF. H pylori IgG serology following successful eradication – four year follow up. Gastroenterology 1995;108:A195. (Abst)
21. Kosunen TU, Seppala K, Sama S, Sipponen P. Diagnostic value of decreasing IgG, IgA, and IgM antibody titres after eradication of Helicobacter Pylori. Lancet 1992;339:893-5.
22. Kosunen TU. Antibody titres in Helicobacter pylori infection: implications in the follow up of antimicrobial therapy. Ann Med 1995;27:605-7.
23. Hirschl AM, Brandstatter G, Dragosics B, et al. Kinetics of specific IgG antibodies for monitoring the effect of anti-Helicobacter pylori chemotherapy. J Infect Dis 1993;168:763-6.
24. Cutler A, Schubert A, Schubert T. Role of Helicobacter pylori serology in evaluating treatment success. Dig Dis Sci 1993;38:2262-6.
25. McNeil BJ, Keeler E, Adelstein SJ. Primer on certain elements of decision making. N Engl J Med 1975;293:211-5.
26. Swets JA, Pickett RM. Evaluation Of Diagnostic Systems: Methods From Signal Detection Theory. New York: Academic Press, 1982:64-5.
27. Hanley JA, McNeil BJ. A method of comparing the areas under receiver operating characteristic curves derived from the same cases. Radiology 1982;143:218-43.
