Detection of Helicobacter pylori Antibodies in Pediatric Populations

I read with interest the recent article by Sunnerstam et al. regarding their evaluation of available serologic tests for immunoglobulin G (IgG) antibodies to Helicobacter pylori in children (9). I agree that serologic methods used to determine H. pylori antibody status in children must be validated. It is well known that the performance of commercial assays designed to detect IgG antibodies to H. pylori can vary due to the bacterial antigen preparation they employ, the reference method used to confirm H. pylori status, and the population studied (3, 4). Despite the availability of enzyme immunoassays (EIAs) for serologic diagnosis of H. pylori infection, no age range is indicated for these assays, implying that these tests can be used and that their results can be interpreted equally for pediatric and adult populations.

I disagree with the authors’ conclusion that “a positive serological test for H. pylori infection, particularly for children, needs to be confirmed by a reference method because of the possibility of spontaneous eradication of infection. . . .” Increased rates of acquisition of infection, as well as spontaneous clearance of infection, have been observed primarily in children under the age of 5 years (5, 6, 7, 8, 10). There was no evaluation of incidence of infection or accuracy of serology by age group presented in the paper. The urea breath test (UBT) was not performed until months after initial collection of sera for serology; therefore, transient infections were potentially missed. As a minimum safeguard, reference method testing of a group in whom spontaneous clearance is suspected to occur should have been performed at the time of serology.

The population available to Sunnerstam et al. for evaluation of the four serologic tests had an extremely low seroprevalence of H. pylori infection (5%), resulting in only five samples on which to base an estimation of assay sensitivity. In addition, the confidence intervals overlap for both the sensitivities and specificities established for all four of the serologic assays evaluated, indicating that a statistically significant difference between the four EIAs was not demonstrated.

Three of the four EIAs demonstrated specificities of >98% based on the data presented in the article, in contrast to the authors’ conclusion that the commercial assays gave a high rate of false-positive results. The UBT used as the reference method in the study was 100% sensitive but only 80% specific. This does not support the authors’ final recommendation that positive serology results obtained with commercial assays should be confirmed using the UBT in order to detect false positives.

The potential value of serology in the diagnosis of H. pylori infection in children has been shown (1, 2). Endoscopic examination is an invasive procedure which can be difficult to perform in children. Although the UBT is noninvasive, serology is less expensive and more readily available. However, there is no guarantee that a method that has been demonstrated to be accurate for adults will perform similarly for children. I acknowledge the authors’ efforts to validate commercial serologic EIAs for H. pylori infection in children in order to establish their diagnostic utility for this group.

REFERENCES


Patrice A. Marchildon
Enteric Products, Inc.
25 E. Loop Rd.
Stony Brook, New York 11790
Phone: (631) 444-8872
Fax: (631) 444-8855

Author’s Reply
Marchildon points out that the absence of age ranges for commercial enzyme immunoassays (EIAs) for serological diagnosis of Helicobacter pylori infection implies that test results can be interpreted equally for pediatric and adult populations. This is probably not the case, even for commercial assays. Crabtree et al. (1), using their in-house assay, found that 50% of children with H. pylori gastritis would have been considered seronegative if the adult cutoff value had been used.

Marchildon does not agree with our conclusion that a positive H. pylori EIA result has to be verified by a reference method, especially for children, because of the possibility of spontaneous eradication of infection. As we pointed out in our article, recent data (2) suggest, though, that infection with H. pylori and later spontaneous clearance of the infection might well occur in more than 10% of Swedish children less than 2 years of age. It has also been shown (3) that seroreversion occurs up to 6 months later than eradication of infection.

In our comparison of the performances of the four seroassays, 21 of 169 samples came from children less than 2 years old and 62 of 169 samples came from children less than 5 years old. The chance of spontaneous eradication of infection, without concomitant seroreversion, was accordingly high with our material. Evaluations of incidence of infection by age group was beyond the scope of our study, since it was a purely methodological and not an epidemiological study. The study popu-
lation was too small to allow analyses of accuracy of serology by age group.

Even though samples for reference methods were not obtained until months after the initial collection of sera for serology in our study, there was no possibility of transient infections being missed, resulting in an apparently false-positive serology, as suggested by Marchildon. The only transient infections that could possibly have been missed in our study would have been infections that both occurred and disappeared between the first and the second serum samples (drawn from each individual at the same time that the reference sample was taken), and those infections would not have affected the rate of false positives revealed by the reference method.

Formal sensitivity and specificity rates were not calculated for the subset of 169 serum samples used in the comparison of the four seroassays, since reference methods were not analyzed for more than the 17 samples with discordant results and the 4 samples with concordant positive results. A valid reference method, used for all samples, is the prerequisite for calculations of sensitivity and specificity. Therefore, the terms “false positives” and “false negatives” were used in this part of the work, to avoid giving the appearance that formal sensitivities and specificities could be calculated.

For financial reasons, it was not possible to use 13C-UBT in all 169 cases. Therefore, we chose to examine the samples yielding discordant seropositive results and those with discordant results in the seroassays. *H. pylori* is an uncommon infection among Swedish children (2, 4), and the risk that all four tested seroassays might yield false-negative results for the same patient for such an uncommon infection is probably very low.

The low specificity of the 13C-UBT with our small unpublished pediatric series of samples used for validation of use of the UBT for children simply reflects 1 of 39 patients with a raised 13C-UBT result having a normal biopsy. For another small unpublished pediatric group (40 patients, aged 5 to 16 years), Oksanen et al. using the same 13C-UBT found a sensitivity and specificity of 100%. For a larger group of adults (5) investigated by Oksanen et al. with the same UBT, the sensitivity and specificity were 92 and 95%, respectively. With a larger pediatric series, the values of sensitivity and specificity will be more reliable.

REFERENCES


Bengt Sunnerstam
Department of Pediatrics
Central Hospital
Hjortvägen 4
654 68 Karlstad, Sweden