Diagnosis of *Helicobacter pylori* Infection in Children: Comparison of a Salivary Immunoglobulin G Antibody Test with the $^{13}$C-Urea Breath Test

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The prevalence of *Helicobacter pylori* infection in a population-based sample of 477 children (mean age ± standard deviation, 5.8 ± 0.5 years) determined by the $^{13}$C-urea breath test ($^{13}$C-UBT) was 10.7% (95% confidence interval [CI], 8.1 to 13.8%), and that determined by salivary enzyme-linked immunosorbent assay (ELISA) was 11.9% (95% CI, 9.2 to 15.2%). Compared to the $^{13}$C-UBT, the sensitivity and specificity of the salivary ELISA were 80.9% (95% CI, 66.3 to 90.4%) and 95.3% (95% CI, 92.7 to 97.1%), respectively.

For the diagnosis of *Helicobacter pylori* infection in children, endoscopy is not clinically indicated and is not feasible in most studies. Noninvasive diagnosis of *H. pylori* infection can be done by measuring specific anti-*H. pylori* immunoglobulin G (IgG) antibodies in serum or saliva with an enzyme-linked immunosorbent assay (IgG-ELISA), with the $^{13}$C-urea breath test ($^{13}$CUBT), and with an enzyme immunoassay (HpSA) for antigens in stools (3, 12–14, 16–18, 21–25). Whole saliva as a test sample is easily accessible, and despite some less encouraging results with $^{13}$CUBT testing (9, 19, 23), some studies seem to be promising (1, 6, 10, 11, 15).

The $^{13}$CUBT has been shown to be an extremely accurate method of detecting *H. pylori* infection because it has the advantage of evaluating the gastric mucosa as a whole, thereby avoiding the sampling errors inherent in biopsy (4, 5, 7). Furthermore, as previously shown, the $^{13}$CUBT is an excellent diagnostic test in children 5 years of age and older and can be considered another “gold standard,” especially if endoscopy is not indicated (5, 7, 8).

In this study, we investigated the salivary anti-*H. pylori* IgG immune response in a population-based sample of school-age children. The performance of the salivary assay was assessed against the $^{13}$CUBT as the gold standard for establishing *H. pylori* infection.

Study subjects were 477 randomly selected children 5 to 7 years old (mean age ± standard deviation, 5.8 ± 0.5 years) (Table 1) living in Ulm, Germany, who were examined for school fitness by the Public Health Service in 1998. A total of 71.7% of the children were of German nationality, 13.0% were of Turkish nationality, and 15.3% were of other than German or Turkish nationality. Participation in the study was voluntary, and informed consent of parents was obtained for each child. The study was approved by the Ethics Board of the University of Ulm.

The $^{13}$CUBT was performed as described previously (2, 20). Sixty milligrams of $^{13}$C-urea (99.5% C; Mass Trace, Woburn, Mass.) was dissolved in 200 ml of apple juice (pH 2.2 to 2.4). Breath samples were collected into plastic bags before and 30 min after intake of the apple juice and were analyzed with an isotope-selective nondispersive infrared spectrometer (Wagner Analytical Systems, Bremen, Germany). A test was regarded to be *H. pylori* positive if the difference between the baseline $^{13}$CO$_2$/12CO$_2$ ratio and the 30-min $^{13}$CO$_2$/12CO$_2$ ratio exceeded 4‰.

To minimize the possibility of false-negative $^{13}$CUBT results, children who had received antibiotic treatment within the previous 4 weeks, which could influence the $^{13}$CUBT, were excluded from the analysis. None of the children had received proton pump inhibitors, H$_2$ blockers, bismuth salts, or antacids within 48 h after the breath test.

Before the $^{13}$CUBT was conducted, whole saliva was collected with a special saliva sampling device (Salivette; Sarstedt, Nürnberg, Germany) according to the manufacturer’s instructions. Children were asked to chew thoroughly a cotton wool swab for 1 min. The cotton wool swab was then placed into the suspended insert of the sampling device, and the saliva was

### TABLE 1. Various demographic characteristics of the study population

| Variable     | n   | %   |
|--------------|-----|-----|
| Age (yr)     |     |     |
| 5            | 124 | 26.0|
| 6            | 330 | 69.2|
| 7            | 23  | 4.8 |
| Sex          |     |     |
| Male         | 225 | 47.2|
| Female       | 252 | 52.8|
| Nationality  |     |     |
| German       | 342 | 71.7|
| Turkish      | 62  | 13.0|
| Other        | 73  | 15.3|
| Total        | 477 | 100 |

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TABLE 2. Performance of salivary ELISA versus $^{13}$CUBT in 477 children

| Salivary ELISA result | No. with the following $^{13}$CUBT result: | Total |
|-----------------------|------------------------------------------|-------|
|                       | Positive       | Negative |       |
| Positive              | 38            | 19       | 57    |
| Indeterminate         | 4             | 20       | 24    |
| Negative              | 9             | 387      | 396   |
| Total                 | 51            | 426      | 477   |

TABLE 3. Salivary IgG-ELISA compared to $^{13}$CUBT

| Parameter                        | Result* for children of the following nationality: |       |
|----------------------------------|---------------------------------------------------|-------|
|                                  | German                                             | Other |
| $H. \text{pylori}$ prevalence according to $^{13}$CUBT | 3.2 (1.6–5.7)                                      | 29.6 (22.1–38.1) |
| Sensitivity                      | 72.7 (39.3–92.7)                                   | 83.3 (66.5–93.0) |
| Specificity                      | 96.2 (93.2–97.9)                                   | 92.4 (84.3–96.6) |
| PPV                              | 40.0 (20.0–63.6)                                   | 81.1 (64.3–91.4) |
| NPV                              | 99.0 (96.9–99.7)                                   | 93.4 (85.7–97.3) |

* Values are percentages. Data in parentheses are 95% CIs.
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