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Diagnosis of *Helicobacter pylori* Infection in Adults with Intellectual Disability

Robyn A. Wallace,1,2,3* Philip J. Schluter,2 Ross Forgan-Smith,4 Robyn Wood,4 and Penelope M. Webb2,5

Specialist Healthcare for Adults with Intellectual Disability (SHAID) Clinic,1 School of Population Health2 and Department of Medicine,1 University of Queensland, Queensland Medical Laboratories,4 and Queensland Institute of Medical Research,5 Brisbane, Australia

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*Helicobacter pylori* infection is common among adults with intellectual disability. The acceptabilities and accuracies of different diagnostic tests in this population are unknown. We aimed to determine (i) patient acceptability and (ii) performance characteristics of serology, fecal-antigen, and urea breath tests among adults with intellectual disability. One hundred sixty-eight such adults underwent *H. pylori* testing with serology and fecal-antigen tests, and a portion underwent treatment. One year later, the participants were retested with fecal-antigen, serology, and urea breath tests. The numbers of specimens obtained and difficulties in collection reported by caregivers were noted. Test performance characteristics were assessed among participants and 65 of their caregivers, using serology as the reference. All participants provided at least one specimen, despite reported collection difficulties for 23% of fecal and 27% of blood specimens. Only 25% of the participants provided breath specimens; failure to perform this test was associated with lower intellectual ability and higher maladaptive behavior. The sensitivity, specificity, and positive and negative predictive values of the fecal test (baseline and 12 months versus caregivers) were 70 and 63 versus 81, 93 and 95 versus 98, 96 and 92 versus 93, and 53 and 74 versus 93%, respectively; those of the urea breath test (12 months versus caregivers) were 86 versus 100, 88 versus 95, 75 versus 89, and 94 versus 100%, respectively. With assistance, fecal or blood specimens for *H. pylori* assessment can be provided by most patients with intellectual disability regardless of their level of function or behavior. Only those with greater ability can perform the urea breath test. Using serology as the reference test, the limitations of performance characteristics of the fecal-antigen and urea breath tests are similar to those among a control group of caregivers.

Selection of the most appropriate investigation to diagnose *Helicobacter pylori* infection or to assess its eradication is influenced by the acceptability of the test to the patient, the accuracy of the particular test, the prevalence of *H. pylori* within the population, the current medications of the person being tested, and the cost. Noninvasive tests for *H. pylori* diagnosis include serology, urea breath, and fecal-antigen testing, while endoscopy allows biopsy specimen collection for histology, rapid urease testing, PCR techniques, or culture. The breath test is the preferred noninvasive test for *H. pylori* among the general population in Western countries.

*H. pylori* infection is particularly relevant among adults with intellectual disability because of its high prevalence, particularly among those with a history of institutionalization (2, 4, 12, 22). In Australia, these individuals have a rate of infection up to three times that among other Australian adults (13). The prevalence among those who have never been institutionalized also appears to be greater than that among their age-matched non-disabled peers (22). Additional independent risk factors for infection among adults with intellectual disability include greater levels of disability and maladaptive behaviors and living with flatmates with fecal incontinence or oral hypersalivation (22). There is also substantial, but indirect, evidence that the consequences of *H. pylori* infection, peptic ulcer disease (5, 11) and gastric cancer (7), also occur more frequently among members of the population with intellectual disability.

The assessment of *H. pylori* infection presents particular problems among the population with intellectual disability with respect to test accuracy and patient acceptability. The performance characteristics of some tests may be adversely affected among institutionalized populations with, for example, false positives in serological assays due to cross-reactivity with other common antibodies in the population (such as *Campylobacter jejuni* [2]). The urea breath test may also be prone to inaccuracy due to polypharmacy, a common problem among people with intellectual disability (18) which affects the gastrointestinal milieu.

The presence of cognitive or functional impairments may also place limitations on the acceptability of the various *H. pylori* tests. For adults with intellectual disability, these factors have been shown to impede the usual processes of investigation through associated limitations in decision-making skills (9), behavioral problems (17), inability to cooperate (20), presence of fear and anxiety (10), financial and time constraints (25), and poor understanding by health professionals (3).

In the majority of published studies of *H. pylori* infection conducted among people with intellectual disability, investigators have used only serological means to diagnose infection, and none have used the fecal-antigen or the urea breath test (2, 4, 12). Given the significance of *H. pylori* infection among
The carbon-14 urea breath test was developed by the local laboratory based on the methods described by Marshall and colleagues (15). It is used commercially by the laboratory and is subject to monthly quality assurance checks. Each participant was required to fast prior to the test, drink 20 ml of water containing radioactive-carbon-14-labeled urea, wait 20 min, and then blow into a small tube containing CO₂ trapping solution until an indicator changed color.

In most studies, the “gold standard” for H. pylori testing is derived from a combination of tests requiring endoscopy—such as histology, culture, or Campylobacter-like-organism testing—or the urea breath test. In the present study, neither of these approaches could be used as the gold standard because it was predicted that only a minority of participants would be able to perform the breath test and it would have been unethical to submit all participants to repeated endoscopy. The H. pylori fecal-antigen test had not been locally validated and was not commonly used in Australian laboratories at the start of the study, so the serological assay was selected as the proxy gold standard. The limitation of this selection was that results could be compared only among participants who had not previously been treated for H. pylori. Participants who had taken antibiotics in the previous 2 weeks or who were currently taking a proton pump inhibitor were also excluded from test comparison because the fecal and breath tests are not valid in this group. These limitations implied that the fecal-antigen results could be compared with serology for 101 and 40 participants with intellectual disability at baseline and 12 months, respectively, and 59 caregivers. Urea breath test results could be compared with serology for 24 participants with intellectual disability and 60 caregivers.

Data analysis. To assess the acceptability of the H. pylori tests, the numbers of specimens provided and caregiver-reported difficulties in specimen collection were noted. Participants were partitioned into lower (below-average ABS factor scores, indicating more severe disability or maladaptive behavior) and higher (average and above-average ABS factor scores, indicating less disability or maladaptive behavior) functional-ability and maladaptive-behavior categories and assessed for inability to provide a specimen. Fisher’s exact test was used to compare the groups. A significance level of 0.05 was used for all statistical calculations. Using serology as the reference, sensitivity, specificity, positive and negative predictive values, and associated exact 95% confidence intervals (CI) were calculated for the fecal-antigen test and the urea breath test among both participants and caregivers.

RESULTS

At baseline, all 168 participants with intellectual disability provided either a fecal or blood specimen for H. pylori evaluation and were able to be classified with respect to H. pylori status. At 12 months, 162 (99%) of the remaining 163 participants (1 died, 3 withdrew, and 1 was acutely ill) provided fecal, blood, and/or breath specimens, and 159 (98%) could be classified with respect to H. pylori status. Three could not be classified because they had received H. pylori eradication treatment and provided only blood for serology testing. The percentages of participants who could provide fecal samples at baseline and 12 months (91 versus 94%) were similar, as were those who could provide blood specimens (89 versus 94%) (Table 1). At 12 months, 27% of the participants with intellectual disability provided a breath specimen.

Caregivers reported that while there were some difficulties in either blood (27%) or feces (23%) specimen collection from their clients, they were still able to collect specimens in the majority (78 and 74%, respectively) of these cases (Table 2). Strategies reported by caregivers to obtain the specimens included negotiation, sedation, or turning off the toilet water to retrieve the fecal specimen. There was a small portion of participants with intellectual disability for whom there were no reported difficulties in specimen collection, yet specimens were not obtained. The reasons for noncollection of specimens were not available.

There was no evidence to suggest that inability to obtain fecal or blood specimens from participants with intellectual disability and the potential difficulties in H. pylori investigations, the aim of this study was to identify the most appropriate tests for H. pylori infection in such adults.

The present paper is one of a series of papers in which the risk factors for and consequences of H. pylori infection, eradication rates, and side effects among adults with intellectual disability, and the prevalence of infection among their caregivers, were evaluated (22–24).

MATERIALS AND METHODS

The study population comprised 168 adults with intellectual disability who lived in a single long-term residential facility, in group homes, or with family and 65 of their caregivers (including six nurses). The methods of participant recruitment and consent procedures have been described in detail elsewhere (22). In brief, all patients (n = 195) who attended a tertiary-level outpatient clinic for adults with intellectual disability in 1998 and who lived within 100 km of Brisbane were invited to participate in the study through their statutory health attorney. The statutory health attorneys of all 75 adult residents of a single institution, 53 adults who had previously been institutionalized, and 40 adults who had never been institutionalized were contacted. All of the caregivers (n = 200) of the participants with intellectual disability were also invited to participate, and 65 enrolled (23). The ethics committee of the University of Queensland and management staff from the long-term residence approved the study.

From January to March 2000, all 168 participants with intellectual disability underwent a biopsychosocial evaluation, including assessment of the level of functional disability (using the Adaptive Behavior Scale part I [ABS II] [16]) and maladaptive behavior (using the ABS II [16], H. pylori treatment history, and H. pylori infection status by the fecal-antigen test and serology. If any participant had alarm symptoms or iron deficiency anemia, they were referred for endoscopy. Twelve months later, the remaining 163 (97%) participants were reevaluated and retested for H. pylori using the carbon-14 urea breath test in addition to the fecal antigen and serology tests. A portion of the participants had received eradication therapy between the two test points. The 65 caregivers were also tested for H. pylori infection using all three tests.

At both time points, caregivers were asked to assist in specimen collection from their clients, and at follow-up they were questioned about the difficulty of this. If sedation or three or more attempts were required for collection of the fecal or blood specimens, then the collection was classified as “difficult.” If the participant was incontinent of feces, the collection was classified as “not difficult,” even if the fecal specimen was not obtained. If the participant could not fast or was unable to perform the breath test on the first attempt, the test was considered unacceptable for that participant.

Investigations. The fecal-antigen test selected for the study was the Premier Platinum HpSA (Meridian Diagnostics, Cincinnati, Ohio). For this test, each participant was required to provide a peanut-size sample of feces. The manufacturer’s published performance characteristics among test populations in whom the prevalence of H. pylori infection was ~50% were as follows: sensitivity, 96%; specificity, 96%; positive predictive value, 96%; and negative predictive value, 96%. This test had not previously been evaluated for use among adults with intellectual disability. The intended uses of the test according to the manufacturer include diagnosis and assessment of eradication of H. pylori after treatment, although there is controversy over its accuracy as a test of eradication (8). All the tests were performed by the same laboratory according to the manufacturer’s specifications.

The pylori D Test ELISA (Diagnostic Technology, Sydney, Australia), an enzyme-linked immunosorbent assay which detects anti-H. pylori immunoglobulin G antibodies, was selected as the most appropriate serum assay for this study. The assay has been validated among populations from developing countries and Australia, with reported sensitivity and specificity rates of 96 and 93%, respectively, and among a population in whom the rate of infection was ~50%, with positive and negative predictive values of 94 and 96%, respectively (26). Its main indication is the diagnosis of H. pylori infection for patients who have never been treated for H. pylori infection. Unlike the fecal-antigen test, the result is valid when the patient is taking or has recently completed a course of antibiotics or is taking a proton pump inhibitor. For the test, each participant was required to provide blood by venesecision. Serum specimens were analyzed twice at baseline at the laboratory which manufactured the test. At 12 months, serum specimens were analyzed at a local laboratory using the same assay. If a 12-month result differed from baseline, both samples were reanalyzed, and if a different result was obtained, the test was rerun a third time and a consensus decision was made.
disability was significantly influenced by their levels of functional ability or maladaptive behavior (Table 3). In contrast, the inability to perform the urea breath test was strongly positively associated with greater levels of disability and, to a lesser degree, greater levels of maladaptive behavior. At baseline, more institutionalized participants did not provide a fecal specimen than previously institutionalized participants, who in turn were more likely not to provide a fecal specimen than participants who were never institutionalized (15 versus 8 versus 0%, respectively; \( P = 0.03 \), but at 12 months, there were no differences in the abilities of participants from any of the three institutional categories to provide fecal or blood specimens.

Table 4 shows the performance characteristics of the fecal-antigen test results compared to the serology results (including only participants or caregivers with no prior treatment, recent antibiotics, or current proton pump inhibitors) at the two time points for participants with intellectual disability and at the single time point for caregivers. For the participants with intellectual disability, the sensitivities at baseline and 12 months were lower than among the caregivers (70 and 63 versus 81%, respectively; \( P = 0.03 \)), but at 12 months, there were no differences in the abilities of participants from any of the three institutional categories to provide fecal or blood specimens.

Table 4 also shows the performance characteristics of the fecal-antigen test results compared to the serology results (including only participants or caregivers with no prior treatment, recent antibiotics, or current proton pump inhibitors) at the two time points for participants with intellectual disability and at the single time point for caregivers. For the participants with intellectual disability, the sensitivities at baseline and 12 months were lower than among the caregivers (70 and 63 versus 81%, respectively; \( P = 0.03 \)), but at 12 months, there were no differences in the abilities of participants from any of the three institutional categories to provide fecal or blood specimens.

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**TABLE 1. Numbers and percentages of participants with intellectual disability who provided specimens for \( H. pylori \) evaluation at baseline and at 12 months**

<table>
<thead>
<tr>
<th>Test</th>
<th>No. (%) of participants</th>
<th>Baseline (n = 168)</th>
<th>12 months (n = 163)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serology</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Only test done</td>
<td>15 (9)</td>
<td>5 (3)</td>
<td></td>
</tr>
<tr>
<td>Total no. tested</td>
<td>149 (89)</td>
<td>151 (93)</td>
<td></td>
</tr>
<tr>
<td>Fecal antigen</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Only test done</td>
<td>19 (11)</td>
<td>7 (4)</td>
<td></td>
</tr>
<tr>
<td>Total no. tested</td>
<td>153 (91)</td>
<td>153 (94)</td>
<td></td>
</tr>
<tr>
<td>Carbon-14 urea breath</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Only test done</td>
<td>Not offered</td>
<td>2 (1)</td>
<td></td>
</tr>
<tr>
<td>Total no. tested</td>
<td>Not offered</td>
<td>44 (27)</td>
<td></td>
</tr>
<tr>
<td>Total no. who did not provide any specimen</td>
<td>0 (0)</td>
<td>1 (1)</td>
<td></td>
</tr>
</tbody>
</table>

**DISCUSSION**

Our analysis has contributed two main findings to the discussion of how to manage \( H. pylori \) infection among adults with intellectual disability. First, it has shown that no patient with intellectual disability need be excluded from \( H. pylori \) testing or treated empirically on the basis that he or she cannot be tested for the infection. The fecal-antigen and serology tests were found to be equally acceptable to adults with intellectual disability, regardless of their level of intellectual disability or maladaptive behavior. Although not all participants could provide both specimens for both tests, if fecal-specimen provision was unacceptable or a fecal test was inappropriate because of other medication, provision of a blood specimen would be an acceptable alternative for diagnosis, or vice versa, subject to the standard restrictions of either test. It should be noted, however, that for about a quarter of these participants, caregiver motivation was required to assist in fecal or blood specimen collection, as without caregiver assistance and effort, the numbers of participants who would not provide specimens spontaneously would have been much higher. For those people with higher ability, the urea breath test is another option for diagnosis. The inverse relationship between ability to perform the breath test and level of intellectual disability was not surprising and was consistent with data showing that this test cannot be performed by younger children due to the technical requirements of the test (19).

Secondly, using the \( pyloni \) DITec serology assay as the reference test, and with parallel calculation of the performance characteristics among caregivers, the study highlighted some limitations of the use of fecal-antigen and urea breath test results among adults with intellectual disability, but overall, it suggested that these tests are adequately reliable in both study populations. The high concordance among the fecal-antigen, urea breath, and serology test results among caregivers seemed to vindicate the choice of the serology assay as a reference test. Moreover, the performance characteristics of both tests among caregivers were well within conventional clinical and laboratory standards of accuracy, supporting the general use of these assays for \( H. pylori \) diagnosis in the community. It must be noted, however, that different results could be obtained by other serological assays, as serological results may be influenced by the prevalence of infection, underlying diseases and medications of the test group, and age and ethnic background of the test population (14). The consistency of the performance
of such assays should therefore be established in a particular geographical and regional setting.

The specificities of the fecal-antigen and urea breath tests among the participants with intellectual disability were not much lower than those among the caregivers and were generally comparable to other published figures (15, 21). The sensitivities of both tests, and particularly the fecal-antigen test, were somewhat lower among participants with intellectual disability than among the caregivers, although 95% CI for all values overlapped. There may be subtle difficulties in the breath test technique among those with intellectual disability or factors, such as the high medication rate in the group, that might alter the gastric milieu affecting fecal-assay performance. The lower negative predictive value of the fecal-antigen test among participants with intellectual disability at baseline compared to their results at 12 months and those of the caregivers may have been a consequence of the higher prevalence of infection in this group at baseline (74 versus 48 and 28%, respectively).

These findings suggest that use of the fecal-antigen or urea breath test among adults with intellectual disability is generally reliable, but they do highlight a need for caution in the interpretation of test results. For adults with intellectual disability, a positive fecal-antigen test result would appear to be very reliable, but there is a greater risk of a false-negative test result. Using the urea breath test, a negative test result would appear to be very reliable, but there is a greater risk of a false-positive test result. No test is perfect, and when clinical suspicion or strong risk factors exist, consideration should be given to repeating the test or conducting an alternative diagnostic test if an initial test result is negative.

Although not assessed in the present paper, the acceptability and accuracy of the fecal-antigen test for the majority of participants with intellectual disability imply that this test may also be suitable to assess the effectiveness of *H. pylori* eradication therapy. The urea breath test may also be considered with reasonable confidence as a test of *H. pylori* treatment success among those adults with lower levels of intellectual disability.

In conclusion, the present study evaluated the acceptability, tolerability, and accuracy of three noninvasive tests for the

### TABLE 3. Numbers and percentages of participants with lower or higher levels of intellectual disability or maladaptive behavior who could not perform the breath test or provide a fecal or blood specimen at 12 months

<table>
<thead>
<tr>
<th>ABS</th>
<th>Factor levela</th>
<th>Total</th>
<th>No breath test sample</th>
<th>No fecal-antigen test sample</th>
<th>No serology test sample</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Personal self-sufficiency</td>
<td>Lower</td>
<td>41</td>
<td>41 (100)</td>
<td>0 (0)</td>
<td>3 (7)</td>
</tr>
<tr>
<td></td>
<td>Higher</td>
<td>121</td>
<td>75 (62)</td>
<td>10 (8)</td>
<td>9 (7)</td>
<td>1.00</td>
</tr>
<tr>
<td></td>
<td>Community self-sufficiency</td>
<td>Lower</td>
<td>105</td>
<td>101 (96)</td>
<td>5 (5)</td>
<td>7 (7)</td>
</tr>
<tr>
<td></td>
<td>Higher</td>
<td>57</td>
<td>15 (26)</td>
<td>5 (9)</td>
<td>5 (9)</td>
<td>0.76</td>
</tr>
<tr>
<td></td>
<td>Personal-social responsibility</td>
<td>Lower</td>
<td>90</td>
<td>88 (98)</td>
<td>4 (4)</td>
<td>5 (6)</td>
</tr>
<tr>
<td></td>
<td>Higher</td>
<td>70</td>
<td>28 (40)</td>
<td>6 (9)</td>
<td>7 (10)</td>
<td>0.37</td>
</tr>
<tr>
<td>II</td>
<td>Social adjustment</td>
<td>Lower</td>
<td>83</td>
<td>62 (75)</td>
<td>7 (8)</td>
<td>5 (6)</td>
</tr>
<tr>
<td></td>
<td>Higher</td>
<td>78</td>
<td>52 (67)</td>
<td>3 (4)</td>
<td>7 (9)</td>
<td>0.56</td>
</tr>
<tr>
<td></td>
<td>Personal adjustment</td>
<td>Lower</td>
<td>99</td>
<td>79 (80)</td>
<td>8 (8)</td>
<td>10 (10)</td>
</tr>
<tr>
<td></td>
<td>Higher</td>
<td>62</td>
<td>35 (56)</td>
<td>2 (3)</td>
<td>2 (3)</td>
<td>0.13</td>
</tr>
</tbody>
</table>

a “Lower” means more severe level of intellectual disability or maladaptive behavior.

b P values calculated by Fisher’s exact test.

### TABLE 4. Sensitivity, specificity, positive predictive value, and negative predictive value of fecal-antigen and urea breath tests compared to serology test (treated as the gold standard)

<table>
<thead>
<tr>
<th>Test</th>
<th>Group</th>
<th>No. tested</th>
<th>No. of true positives</th>
<th>No. of false positives</th>
<th>No. of true negatives</th>
<th>No. of false negatives</th>
<th>% Sensitivity (95% CI)</th>
<th>% Specificity (95% CI)</th>
<th>% Positive predictive value (95% CI)</th>
<th>% Negative predictive value (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fecal antigen</td>
<td>Participants with intellectual disability at baseline</td>
<td>101</td>
<td>74</td>
<td>2</td>
<td>27</td>
<td>22</td>
<td>70 (59, 80)</td>
<td>93 (76, 99)</td>
<td>96 (87, 100)</td>
<td>53 (38, 68)</td>
</tr>
<tr>
<td></td>
<td>Participants with intellectual disability at 12 months</td>
<td>40</td>
<td>19</td>
<td>1</td>
<td>21</td>
<td>7</td>
<td>63 (38, 84)</td>
<td>95 (76, 100)</td>
<td>92 (64, 100)</td>
<td>74 (54, 89)</td>
</tr>
<tr>
<td></td>
<td>Caregivers</td>
<td>59</td>
<td>16</td>
<td>43</td>
<td>3</td>
<td>81 (54, 96)</td>
<td>98 (88, 100)</td>
<td>93 (66, 100)</td>
<td>93 (82, 99)</td>
<td></td>
</tr>
<tr>
<td>Urea breath</td>
<td>Participants with intellectual disability at 12-months</td>
<td>24</td>
<td>7</td>
<td>2</td>
<td>17</td>
<td>1</td>
<td>86 (42, 100)</td>
<td>88 (64, 99)</td>
<td>75 (35, 97)</td>
<td>94 (70, 100)</td>
</tr>
<tr>
<td></td>
<td>Caregivers</td>
<td>60</td>
<td>16</td>
<td>2</td>
<td>44</td>
<td>0</td>
<td>100 (79, 100)</td>
<td>95 (85, 99)</td>
<td>89 (65, 99)</td>
<td>100 (92, 100)</td>
</tr>
</tbody>
</table>

a Includes only those never treated for *H. pylori* and not taking proton pump inhibitors or recent antibiotics.
diagnosis of \textit{H. pylori} infection among adults with intellectual disability, in whom the infection and disease consequences are common. Both the fecal-antigen and serology tests are tolerated by the majority of adults with intellectual disability with a range of severe to mild disability and maladaptive behavior, given appropriate caregiver support. The urea breath test is also able to be performed by more than half of those with milder levels of disability. Using a locally validated serology test, the fecal-antigen and urea breath tests have acceptable sensitivity, specificity, and positive and negative predictive values, although there is a tendency for the fecal-antigen test to miss infection and for the urea breath test to overestimate infection. None of the three tests assessed in the present study is recommended for use in any patient who has alarm symptoms and signs (prolonged unexplained vomiting, iron deficiency anemia, melena, or hematemesis) or a complaint of dyspepsia for the first time if over 45 years of age; in these cases, endoscopy is the appropriate first-line investigation (6).

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