Helicobacter pylori – Overview and New Test Guidelines for Diagnosis

By Paul A. Granato, Ph.D., Director of Microbiology

New Test Guidelines

Helicobacter pylori is one of the most common bacterial infections worldwide. Serologic antibody tests have been the traditional mainstay for diagnosing H. pylori infection because of the convenience in specimen collection. However, in recent years, it has been repeatedly demonstrated that these antibody tests have poor sensitivities in distinguishing between active and past infection and cannot be used reliably to evaluate patients for test of cure (TOC). As a result, the American Gastroenterology Association (AGA) and the American College of Gastroenterology (ACG) no longer recommend the routine use of these serologic tests. Instead, they recommend the H. pylori stool antigen test (SAT) or the urea breath test (UBT) for diagnosis and evaluating patients for TOC. Because of these updated AGA and ACG guidelines and the documented poor sensitivities of the serologic tests, many insurance carriers have implemented policies whereby they will no longer reimburse for H. pylori serologic tests. In addition, many reference laboratories have discontinued H. pylori serologic testing as a diagnostic service. This brief article serves as an overview of the diseases caused by H. pylori and the available invasive and non-invasive tests that can be used for reliably establishing its diagnosis and determining TOC.

Discovery and the Nobel Peace Prize

Prior to the 1990s, traditional medical convention and dogma attributed certain lifestyles, such as alcohol abuse, physical and emotional stress, and smoking as the cause of gastritis and peptic ulcer disease (PUD). In the early 1980s, two Australian physicians, Robin Warren, a pathologist, and Barry Marshall, a gastroenterologist, thought that gastritis and PUD were caused by an infectious agent. Warren had noted the histologic presence of curved bacteria and an associated inflammatory response in stomach biopsy specimens collected from patients with gastritis and PUD. Marshall attempted to grow this organism in the laboratory but was unsuccessful after many repeated attempts. Then, over an extended Easter holiday, the microbiology laboratory accidently held some of the culture plates for five days instead of the usual two. This serendipitous act due to an extended incubation period resulted in the cultural recovery of the bacterium from the specimens. Because the bacterium had a curved or spiral-shaped morphology resembling bacteria in the Campylobacter genus, the bacterium was initially called a Campylobacter-like organism (CLO) or Campylobacter pyloridis. Subsequently, based upon extensive genetic analyses and DNA homology studies, the organism was taxonomically positioned into a new genus, Helicobacter, and designated H. pylori.

Excited about their findings that gastritis and PUD were caused by an infectious agent, Marshall and Warren reported their results in two medical publications (Lancet. 1983. 321: 1273-1275, Lancet. 1984. 323: 1311-1315). Unfortunately, their proposal that gastritis and PUD were caused by an infectious agent was met with considerable skepticism and ridicule from the medical and scientific communities because it was not thought that any bacterium could survive in the harsh acidic environment of the stomach to cause disease. Continued on page 6

Dr. Graber Named Medical Director

Laboratory Alliance welcomes Michael W. Graber, M.D., as medical director of our Operations Center laboratory. Dr. Graber has been affiliated with Laboratory Alliance since 2001, most recently as assistant medical advisor of Transfusion Services and assistant medical director of the rapid response laboratory at Upstate University Hospital Community Campus. Board certified in anatomic pathology, clinical pathology and hematopathology, he is employed by Onondaga Hill Pathology, P.C. and is a staff pathologist at Upstate University Hospital Community Campus. He will continue to practice anatomic pathology at Laboratory Alliance’s rapid response laboratory at Upstate University Hospital Community Campus in addition to serving as medical director of the Operations Center.
The category of atypical urothelial cells (AUC) is meant to fill the gap between what can be recognized as entirely normal and what can be recognized as being clearly abnormal. The general diagnostic category of AUC is reserved for specimens that contain urothelial cells with mild to moderate cytologic (not architectural) atypia. This definition does not include urothelial cell clusters (tissue fragments) without cytologic atypia, which belong in the negative for high-grade urothelial carcinoma (NHGUC) category. To be classified as AUC, the cytologic changes have to fall short of suspicious for high-grade urothelial carcinoma or positive for high-grade urothelial carcinoma. In addition, this category requires exclusion of changes in which the reason for “atypia” is known, such as reactive changes due to infections, stones, instrumentation, etc. The AUC category also includes specimens where, due to poor preservation and degenerative changes, the nature and degree of atypia in the urothelial cells cannot be well analyzed.

Lastly, the diagnosis of suspicious for high-grade urothelial carcinoma (SHGUC) is meant to reflect the presence of urothelial cells with severe atypia that fall short of a diagnosis of high-grade urothelial carcinoma (HGUC), but beyond atypia that is associated with the “atypical urothelial cells” (AUC) category. The diagnosis is restrictively used in cases that quantitatively fall short of a diagnosis of HGUC. A cut-off range of 5–10 cells is recommended based on the degree of abnormal nuclear changes observed and the level of the pathologist’s comfort.

The Paris System attempted to standardize the diagnostic criteria and bring uniformity to the diagnostic reporting of urinary cytology specimens. It is a vast improvement and should prove very useful to clinicians taking care of patients with urinary tract disease.

Please do not hesitate to contact me at 315-492-5096 or Janet Miller, Cytology Manager, at 315-410-7210, if you have any questions or concerns about this new reporting system.

CORRECT CODES ARE CRITICAL!

DID YOU KNOW?

Medicare may deny payment for a test even though the physician believed it was appropriate if the test did not meet Medicare’s definition of medical necessity.

NCDs and LCDs

National Coverage Determinations (NCDs) and Local Coverage Determinations (LCDs) tests and information concerning appropriate diagnosis codes can be found on Laboratory Alliance’s website at laboratoryalliance.com under Healthcare Providers.

There, you will find:

- Specific test CPT codes for which medical necessity rules have been defined.

- The ICD-10 or diagnosis codes that Medicare will accept as documentation that the listed test is reasonable and necessary for diagnosis or treatment. ICD-10 codes supporting medical necessity must be included on the requisition form. The diagnosis must be present for the procedure to be paid and there must be documentation within the patient’s medical record.

Note: When ordering a test that does not meet NCD or LCD guidelines, an Advanced Beneficiary Notice (ABN) should be signed by the patient. The purpose of the ABN is to give the patient advance notice that Medicare may not pay for the test ordered. When payment is denied as not medically necessary, Laboratory Alliance can only bill the patient if we have received a valid (i.e., signed) ABN.

Reflex Testing

Reflex testing is testing that is performed as a result of initial test results which are used to further identify significant diagnostic information required for appropriate patient care. A list of the reflex tests that are performed when appropriate is in our Directory of Services, on our website and on the back of our requisitions.

Panels

Organ or disease panels will only be billed and reimbursed when all test components are medically necessary. If only some components are medically necessary, or if the physician wishes to order other tests not included in the panel, those tests should be ordered individually. A list of tests included in the American Medical Association acceptable panels is included on our requisition and in our Directory of Services. Medicare reimbursement amounts for these tests can be found at: www.cms.hhs.gov/ClinicalLabFeeSched/. Medicaid reimbursement will usually be equal to or less than the Medicare reimbursement.

Clinical Consultation Services

Appropriate test use and ordering may be discussed with Laboratory Alliance’s Medical Director Michael Graber, M.D., available by contacting our Customer Service Department at 315-461-3008.
Introducing our Microbiology Department

Laboratory Alliance’s Microbiology Department staff of 40, including full- and part-time, provide services to Crouse, St. Joseph’s and Upstate University Community Campus hospitals, reference lab clients and our physician clients and their patients.

Located at our Operations Center, it is in this department that tests for sexually transmitted infections (STIs), urinary tract infections (UTIs), enteric pathogens, sepsis, respiratory infections, strep throat, flu, bacterial pneumonia and more. The department also participates in clinical device trials for new assays and instruments related to infectious disease.

Operating around the clock seven days a week, our microbiologists are New York state licensed, many also certified by the American Society of Clinical Pathologists and participate annually in national proficiency testing and continuing education activities.

Director of Microbiology Paul A. Granato, Ph.D., and Microbiology Manager Russell Rawling oversee the department.

In the top photo, from left, are Johnathan Daddario, Beth Denny, Jennifer Lillie, Michael Badner and Miranda Masterpol.

Pictured left are Jeremy Fuller, Rebecca Reynolds, Brian Meaker, Katrina Zeglin, Li Chen and Andrea Bertolero.

Pictured right are Elsie Wilson, Marcia Degilio, Linda Stallcup and Dr. Paul Granato.

Laboratory Alliance is ready to offer challenging and rewarding career opportunities to qualified candidates. Our team of more than 400 professionals performs over 10.7 million laboratory tests annually. Consider a career with the area’s largest laboratory. Apply online at laboratoryalliance.com/careers.
Microbiology Department professionals pictured left are Corey Rivet, Melissa Carter, Ronilo Aquino, Karen Strouse and Brian Monterosso.

Below, from left, are Cristina Lenartowicz, Jane Roller, Celeste Nelson, Manager Russell Rawling and Brenda Henry.

In the photo above, from left, are Nancy Tucci, Melissa Unz, Karim Galal, Laura Buehler and Janet Kerfien.

Pictured right are Keith Rando, Megan Talbot, Martha Stewart and Dolores Juliano.

The following microbiology staff members were not available for a photo: Brenda Alkins, Melleny Hale, Dawn Nappa, Shannon Nayyar, Nadine Riche, Ellen Searles and Erin Springer.
Helicobacter pylori – Overview and New Test Guidelines for Diagnosis

Continued from page 1

Frustrated by the scientific and medical rejection of their findings, Barry Marshall recovered H. pylori from a patient with PUD, grew it in the laboratory in a liquid broth culture, and then drank it. Several weeks later, he developed symptoms of gastritis which is a precursor of PUD. A biopsy was taken from Marshall’s stomach by endoscopy which showed histologic evidence of inflammation and the presence of curved bacteria in the tissue. Furthermore, the same H. pylori was recovered by culture thereby fulfilling Koch’s postulates and establishing H. pylori as a cause of gastritis and PUD. For their pioneering and persevering efforts against considerable scorn and adversity by the medical community, Marshall and Warren were awarded the Nobel Peace Prize in Physiology and Medicine in 2005.

Epidemiology and Diseases

H. pylori has coexisted with humans for many of thousands of years and human infection is common. The Centers of Disease Control and Prevention estimates that approximately two-thirds of the world’s population is infected with H. pylori with rates approaching 90% in underdeveloped countries. Fortunately, though infection or colonization rates are high, the incidence of symptomatic disease is low. In the U.S., 5 million people annually are diagnosed with PUD with the incidence of gastritis considerably higher. Over 40,000 individuals undergo ulcer-related surgery. Each year, more than 15,000 people die of ulcer- and gastritis-related complications, the most extreme of which is internal bleeding due to stomach or duodenal perforation. The mode of transmission of H. pylori is poorly understood but it is thought to be by the fecal-oral route and/or by direct mouth-to-mouth contact.

H. pylori does not cause symptomatic infection in most individuals who harbor the organism. However, colonization with the organism is a major risk factor for the development of gastritis, PUD, and is responsible for the majority of ulcers occurring in the stomach and duodenum. Also, H. pylori is a major cause of stomach cancer (gastric adenocarcinoma is the second leading cause of death worldwide) and is associated with an increased risk of gastric mucosa-associated lymphoid tissue (also known as MALT) lymphoma.

Pathogenesis

H. pylori is a gram-negative, spiral-shaped bacterium that grows in the mucus layer that coats the inside lining of the human stomach. To survive the harsh, acidic environment of the stomach, H. pylori produces an enzyme, called urease, which converts urea to ammonia. The production of ammonia neutralizes the acidic pH in the stomach and allows the organism to grow and produce disease in a localized area, producing irritation (gastritis) and possibly a more serious ulcerative lesion. The production of the urease enzyme serves as the basis of one of the useful diagnostic tests that will be discussed in the next section.

Diagnostic Tests

Tests for the diagnosis of H. pylori infection are classified as invasive and non-invasive. Invasive tests are performed by endoscopy in which a tissue biopsy specimen is collected and examined histologically for the presence of the organism in tissue and by performing the CLO test which screens for the presence of the enzyme, urease, which is an indicator for the presence of H. pylori. Endoscopy is often performed to rule out malignancies or other non-infectious causes of the patient’s symptoms. Non-invasive tests are performed when the patient has typical symptoms of H. pylori infection and have the advantages of being low-risk to the patient and comparatively inexpensive.

Non-invasive tests include the UBT, SAT and serologic tests that were mentioned previously. The UBT is based upon the production of the urease enzyme produced by H. pylori. The test is performed by having the patient ingest a preparation containing a nonradioactive, carbon13 isotope of urea. If H. pylori is present in the patient’s stomach, the urea is degraded to ammonia and nonradioactive C13O2. The C13O2 is exhaled through normal respiration and collected in a bag and sent to a laboratory for analysis. The reported sensitivity and specificity of the UBT to detect H. pylori infection exceeds 93%. The UBT also can be used to evaluate patients for TOC following therapy. The SAT is an enzyme immunoassay that detects H. pylori antigen in a stool specimen that is shed from the patient’s stomach. The SAT has a sensitivity and specificity comparable to the UBT, and can be used as a TOC, but has the added advantage that the test is approved for use in pediatric patients. Serologic tests and their disadvantages have been discussed previously which is why they are no longer recommended by the AGA and ACG for patient testing. Instead, current guidelines recommend the use of the SAT or UBT because of their superior performances.

Treatment

Since most cases of gastritis and PUD are the result of a bacterial infection caused by H. pylori, combination antibiotic therapy along with a stomach acid suppressor will usually result in resolution of symptoms and a therapeutic cure. Several therapeutic options are available once the diagnosis of H. pylori infection has been established. Following therapy, AGA and ACG recommend a TOC followup, preferably by using the SAT or the UBT.

Summary

The medical and scientific communities are indebted to Drs. Warren and Marshall for their pioneering and landmark discovery that disproved a time-honored dogma that had prevailed in medicine for decades. One of our next challenges is to abandon the use of unreliable serologic tests for the diagnosis of H. pylori infection and in evaluating patients for TOC. To this end, effective June 6, 2016, Laboratory Alliance will discontinue serologic testing for H. pylori. This change is intended to encourage the use of the more reliable tests, such as SAT or UBT, as recommended by ACG and AGA.
**New Employees**

Please welcome our new employees

**At our Operations Center**

- Michael Badner — Medical Laboratory Technician
- Anthony Blaney, Jr. — Courier
- Candace Buchanan — Technical Processing Assistant
- Morgan Butler — Medical Laboratory Technician
- James DiNicola — Transportation Dispatcher
- Matthew Kinsley — Laboratory Office Assistant
- Lindsay Petty — Phlebotomist
- Stephen Roberts — Courier
- Samantha Salisbury — Phlebotomist
- Melissa Unz — Device Trial Specialist

**At our Rapid Response Laboratory at Crouse Hospital**

- Erin Girard — Administrative Secretary

**At our Rapid Response Laboratory at St. Joseph’s Hospital**

- Cassandra Bulla — Laboratory Office Assistant
- Teresa de Veyra — Medical Technologist
- Danielle Goodrich — Medical Technologist

**Wanda Salem Named Manager of RRL**

Wanda Salem of Liverpool, N.Y., has been promoted to laboratory manager of Laboratory Alliance’s Rapid Response Laboratory (RRL) at St. Joseph’s Hospital Health Center. She most recently served as technical supervisor of chemistry at that laboratory. Salem has worked at Laboratory Alliance since 2011. Prior to that she was employed as a medical technologist in various capacities at another local laboratory and physicians’ offices. Also, she was an adult education and substitute teacher in the Liverpool Central School District for more than three years.

Salem earned her Bachelor of Science in Medical Technology from the State University of New York Health Science Center at Syracuse and her Bachelor of Science in Biology from the University of Puerto Rico.

She is licensed as a clinical medical technologist in the state of New York.

---

**Employee Anniversaries**

<table>
<thead>
<tr>
<th>Month</th>
<th>Years</th>
<th>Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>April</td>
<td>5</td>
<td>Valerie Rouse</td>
</tr>
<tr>
<td>April</td>
<td>10</td>
<td>Robert Fiesinger</td>
</tr>
<tr>
<td>April</td>
<td>15</td>
<td>Marguerite Grosick</td>
</tr>
<tr>
<td>May</td>
<td>15</td>
<td>Rebecca Northrup</td>
</tr>
<tr>
<td>June</td>
<td>5</td>
<td>Stephen Champlin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lucy McNamara</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Keith Rando</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Suzanne Swierczek</td>
</tr>
<tr>
<td>June</td>
<td>10</td>
<td>Beth Gilbert</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Kimberly Johnson</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Kathleen Males</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Andrew Paton</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dana Simpson</td>
</tr>
</tbody>
</table>

**Scholarship Named for O’Learys to Benefit Clinical Laboratory Sciences Program**

Upstate Medical University recently announced that the Colleen E. O’Leary, MD, and Michael R. O’Leary, MD, Endowed Scholarship for Clinical Laboratory Sciences (CLS) has been created to help Upstate Medical University’s College of Health Professions continue to attract the finest candidates for its Clinical Laboratory Sciences program. The scholarship will also help to alleviate a critical national shortage of clinical laboratory professionals. Upstate’s CLS program celebrated its 50th anniversary in 2015 and averages 18 graduates each year. The scholarship was established by the Upstate Foundation, Upstate’s Department of Anesthesiology and the Upstate administration upon the recent retirement of Dr. Colleen E. O’Leary.

Michael O’Leary, MD, retired as CEO and medical director of Laboratory Alliance of Central New York. At Upstate, he holds a voluntary faculty appointment as clinical associate professor with the Department of Pathology. The O’Learys are alumni of Upstate’s College of Medicine, Class of 1978. Dr. Michael O’Leary completed a residency in pathology at Upstate in 1982.

**Thanks, Laboratory Alliance**

Laboratory Alliance employees collected $300 in donations for Hospice of CNY through contributions made on Jean Day. Jean Day was one of the company-wide activities celebrated during Medical Laboratory Professionals Week in April.

**American Red Cross**

Save the Date Thursday, Aug. 11

Red Cross Blood Drive at Laboratory Alliance’s Corporate Offices
1304 Buckley Rd. Sign up with Marsha: marshaherbst@lacny.com
Calendar of Events

**Thursday, May 19**
**Hospice of CNY “Celebrating Life Through Chocolate,”** Bella Domani, Taft Road, North Syracuse. *Laboratory Alliance is a participant.*

**Friday, June 3**
**St. Joseph’s Hospital Health Center Gala,** Turning Stone Resort Casino. *Laboratory Alliance is a sponsor.*

**Monday, June 6**
**Foundation for Upstate Towsley Pro-Am,** Kaluhyat at Turning Stone Resort Casino. *Laboratory Alliance is a participant and sponsor.*

**Saturday, June 11**
**Green Lakes Triathalon** to benefit the YMCA’s programs for cancer survivors. *Laboratory Alliance donates the pace car, driven by Courier Mike Manfredi.*

**Monday, July 18**
**Crouse Health Foundation Classic Golf Tournament,** Bellevue Country Club. *Laboratory Alliance is a participant and sponsor.*

---

**E. Carlyle Smith Memorial Open**

**Friday, June 17, 2016**
In memory of long-time Hospice of CNY friend and supporter E. Carlyle Smith

The Links at Erie Village
East Syracuse, NY
Tee Time: 1:00pm

$250/per golfer

Sponsorship Opportunities are available

“Captain & Crew” style tournament includes:
18 holes of golf, catered lunch, contests, raffles, snacks, beverages, great food and awards presentation

To reserve your spot or to sponsor the event, please call 315-634-1100, e-mail lsimpson@hospicecny.org or visit www.hospicecny.org/golf-2016

---

When you need labwork, we’re in your neighborhood

Now open at Township 5 Medical Buildings, Camillus

260 Township Blvd., Suite 40
at Hinsdale Road

Monday - Friday 8 a.m. - 4:30 p.m.
Closed for lunch from 12:15 - 1 p.m.

First-come, first-served, no appointment needed

- Prompt, courteous, professional and locally owned
- Also located in Camillus at Medical Center West, 5700 West Genesee St., Suite 209, and this location is open Saturdays 8 a.m. to noon.
- 12 convenient locations - visit us in Baldwinsville, Camillus, Cazenovia, Cicero, East Syracuse, Fayetteville, Liverpool, Pulaski and 3 locations in Syracuse.
- Directions, maps and contact information at laboratoryalliance.com

---

Comments, suggestions or inquiries should be directed to
Joan Rusin, Senior Executive Assistant,
315-461-3038, or by email to joanrusin@lacny.com