

Physicians  
Update

# Medical News

Volume XXIII Number 2 Summer 2008

In this Issue

Editor's Note ..... 1

Preexisting Diabetes and  
Pregnancy ..... 2

Update—*Helicobacter pylori* ..... 3



Herman Hurwitz, M.D., F.C.A.P.  
Senior Medical Director  
Quest Diagnostics Philadelphia  
Medical Director, Western Region

- Our Values**
- Quality**
- Integrity**
- Innovation**
- Accountability**
- Collaboration**
- Leadership**

## Editor's Note:

Pregnancy results in significant physiologic changes for the expectant mother. Combining these changes with the metabolic perturbations of diabetes mellitus presents significant management challenges for both the obstetrician and endocrinologist. In this issue, we examine some laboratory-related issues of which physicians and diabetic patients should be aware. Recent consensus recommendations from the American Diabetes Association (ADA) provide guidance for clinicians and laboratorians. My discussion will center on routine laboratory testing in this complicated situation. The use of the term diabetes will be understood to refer to diabetes mellitus.

The regular reader may recall that testing for *Helicobacter pylori* (HP) infection was discussed in the winter 2006 issue of the Quest Diagnostics *Medical News: Physicians Update*. At that time, the American Gastroenterological Association (AGA) had issued a position statement and technical review on the evaluation of dyspepsia. Subsequently, the American College of Gastroenterology issued its publication, the "American College of Gastroenterology Guideline on the Management of *Helicobacter pylori* Infection."

Both professional societies updated their recommendations for the laboratory diagnosis of suspected HP infection and test of cure to demonstrate eradication of the organism. The guidelines noted that, with the advent of the urea breath test (UBT) and the HP fecal antigen test (FAT), serologic testing should be

discontinued for most patients. The medical community, a historically conservative group, has been slow to embrace this diagnostic improvement. Additionally, over time, HP has become resistant to traditional therapy.

HP is one of the few infections not approached as a traditional infectious disease—many physicians group HP with gastrointestinal diseases. Thus, the commitment to monitor the patient and confirm that the infection is cured is not always present. New regimens, including quadruple therapy and sequential therapy, have been proposed. The increasing resistance of HP to therapy highlights the need for proof that the organism has been eradicated. We will revisit the laboratory diagnosis of HP infection with a discussion on the disadvantages of serologic testing and the benefits of more up-to-date, advanced tests that detect urease activity or the presence of the HP bacterial antigen.

On a somewhat different note, I am pleased to report a recently announced collaboration between Quest Diagnostics and Google™. My generation grew up with pencils, pens, and paper files as the major recording media. The arrival of the transistor and the development of the personal computer (PC), personal digital assistants, etc., is threatening to make paper files and records as obsolete as the pay phone.

*continued on page 4*

# Preexisting Diabetes and Pregnancy

The ADA published a consensus statement, "Managing Preexisting Diabetes for Pregnancy," in *Diabetes Care*, in May 2008. The intent of the statement was to help clinicians deal with the broad spectrum of problems that arise in the management of diabetes before and during pregnancy, and to prepare diabetic women for treatment that may reduce complications in the years after pregnancy.

A thorough discussion of the evidence supporting the recommendations is presented in the book, *Management of Preexisting Diabetes and Pregnancy*, also published by the ADA. The recommendations are both diagnostic and therapeutic actions that are known or believed to favorably affect maternal and perinatal outcomes in pregnancies complicated by diabetes. The panel noted that a statement on obstetrical and postpartum management will appear separately.

This short discussion will be limited largely to the portion on the care of diabetic women that deals with clinical laboratory testing. The reader is referred to an in-depth discussion of the entire subject in the cited references.

## Initial Evaluation:

This should be done at the onset of preconception care, or in its absence, early in pregnancy. A complete medical evaluation should be performed to:

- Classify the patient and detect the presence of diabetes, cardiovascular, thyroid, or obstetrical complications
- Review history of eating patterns, physical activity/exercise, and psychosocial problems
- Counsel the patient on prognosis
- Set expectations for patient participation

- Assist in formulating a management plan with team care members
- Provide a basis for continuing care and laboratory tests

## Laboratory Test Recommendations:

It is recognized that some complications identified by laboratory testing cannot be treated with optimal drugs during pregnancy. The identification of these complications allows for intensified postpartum management.

A "standard" obstetric panel, such as that offered by Quest Diagnostics, which could be ordered for a nondiabetic pregnant patient, consists of the following:

- Complete blood count, including a white blood cell differential and platelet count
- Red blood cell antibody screen with reflex to identification and titer if positive
- ABO group and Rh type
- RPR with reflex to confirmation and titer if positive
- Hepatitis B surface antigen with reflex to confirmation
- Rubella virus IgG antibody

Additional initial evaluation and laboratory testing for a preconception or pregnant diabetic patient would consist of the following:

- A1C
- Lipid profile, including triglycerides, total, high-density lipoprotein (HDL) and low-density lipoprotein (LDL) cholesterol\*
- Thyroid-stimulating hormone (TSH) and thyroid peroxidase (TPO) antibodies—consider TSH-receptor antibodies if TSH is suppressed to  $<0.03 \mu\text{U}/\text{mL}$
- Serum ferritin
- Spot urine for albumin/creatinine

ratio (microalbumin)

- Alanine aminotransferase/aspartate aminotransferase (ALT/AST) and possible liver ultrasound for steatosis
- Serum creatinine with estimated glomerular filtration rate (GFR) (preconception); creatinine clearance (pregnant)
- Consider vitamin B12 in type 1 diabetes
- Consider anti-tissue transglutaminase or endomysial antibody in type 1 diabetes\*
- \* May be delayed or omitted if performed before pregnancy

## Glycemic Control - Laboratory Recommendation Highlights:

Women with diabetes should be educated about the need for glycemic control pre- and post-conception in order to reduce the likelihood of fetal loss and/or neonatal complications. Prior to pregnancy, A1C should be targeted as close to normal as possible without hypoglycemia. Throughout pregnancy, optimal glycemic goals are premeal, bedtime, and overnight glucose 60-99 mg/dL, peak postprandial glucose 100-129 mg/dL, mean daily glucose  $<110 \text{ mg/dL}$ , and A1C  $<6.0\%$ . Higher glucose targets may be used in patients with hypoglycemia unawareness or the inability to cope with intensified management.

## Thyroid Disorder - Laboratory Recommendation Highlights:

Diabetic women should be screened for thyroid dysfunction/autoimmunity with serum TSH and TPO antibodies either before or during early pregnancy.

- If the TSH is normal for pregnancy, but the TPO antibodies are abnormal, measure TSH at 7-8, 14-16, and 26-30 weeks as the demands of pregnancy can unmask hypothyroidism. Follow TSH closely postpartum.
- During pregnancy, treat any TSH elevation ( $>2.5 \mu\text{U}/\text{mL}$  first half;  $>3.0 \mu\text{U}/\text{mL}$  second half). Follow closely during the first 20 weeks, when the demands for thyroxine are

*continued on page 3*

## Preexisting Diabetes and Pregnancy

continued from page 2

the highest, and readjust as needed to maintain euthyroidism (TSH <2.5  $\mu\text{U}/\text{mL}$  first half; <3.0  $\mu\text{U}/\text{mL}$  second half).

- If TSH (<0.03  $\mu\text{U}/\text{mL}$ ) and T4 levels suggest hyperthyroidism, measure TSH-receptor antibodies. Notify the pediatrician in advance of delivery about findings and any therapy.

### Dyslipidemia - Laboratory Recommendation Highlights:

- Measure fasting lipid profile at least annually in women with diabetes and more often if needed to attain goals.
- Before pregnancy, follow current guidelines for nutritional and pharmacotherapy, along with weight control and exercise, for diabetic women with dyslipidemia. The primary treatment goal is LDL

cholesterol <100 mg/dL in women without overt cardiovascular disease (CVD) and <70 mg/dL in women with overt CVD.

- If lipid profile testing was not performed prior to pregnancy, obtain a fasting lipid profile at registration.

### Nephropathy - Laboratory Recommendations:

- Determine the level of albuminuria and estimated GFR with serum creatinine before pregnancy in all women with diabetes.
- During early pregnancy, assess urine albumin excretion with a spot urine albumin/creatinine ratio.
- In pregnant patients with micro- or macroalbuminuria, measure a properly instructed 24-hour creatinine clearance, since estimated

GFR using serum creatinine and the modified diet in renal disease formula is not accurate in pregnant patients.

(*Diab Care* 2008; **31**, 1060-1079 — *Diab Care* 2008; **31** (Suppl. 1), S12-S54)



## Update—*Helicobacter pylori*

We noted the AGA position statement on the evaluation of dyspepsia in the winter 2006 issue of the *Quest Diagnostics Medical News: Physicians Update*. That statement included a discussion about the identification of HP infection using the test-and-treat strategy. The reader may recall that the AGA did not recommend using serologic testing to identify active infection. The decision was made because of poor performance characteristics in a low-prevalence population and the inability to use serology to confirm eradication of infection.

*Editor's Note: HP plays a crucial role in the pathogenesis of chronic gastritis, peptic ulcer disease, gastric mucosa-associated lymphoma, and gastric adenocarcinoma. Although estimates by different authors vary, the low prevalence of HP infection is present in much of the United States.*

The accompanying “American

Gastroenterological Association Technical Review on the Evaluation of Dyspepsia” stated that UBT or FAT was recommended for the initial diagnosis and confirmation of the eradication of HP infection. In the United States, HP infection is often thought of as a gastrointestinal disease rather than an infectious process. Unlike many infectious diseases where the causative organism is isolated, identified, and tested for antimicrobial sensitivity, treatment of HP infection was, and still is, largely empiric. Empiric therapy for HP is based on several recommended regimens.

As is often the case, infectious diseases treated with antibiotics frequently develop resistance to antimicrobial agents. HP antibiotic resistance has developed to the point where at least one author states that “all patients infected with *Helicobacter pylori* should be considered as having resistant

infections.” Given this situation of utilizing empiric therapy as the norm, testing for eradication of a potentially carcinogenic organism using either UBT or FAT becomes essential.

Although reviews and consensus statements published in the last 10 years still recommend treatment with a proton-pump inhibitor, plus amoxicillin and clarithromycin or metronidazole, they now include a caveat that such traditional triple therapy should only be used if the local prevalence of resistance is below an arbitrary level. This is an indirect acknowledgement that in almost every country for which data is available, actual cure rates are below the desired 90-95%.

HP infections present many challenges when it comes to effective antimicrobial therapy. Some obstacles are unique to HP and its physiology, while others are common to many infections. The following are the unique challenges distinctive to HP infection:

- HP bacteria in the stomach are

continued on page 4

## Editor's Note

*continued from page 1*

The medical record is rapidly becoming virtual. Some physicians now, almost exclusively, use an electronic medical record that essentially eliminates paper records. Patients are being encouraged to maintain their personal health record (PHR) electronically as well. The transition to electronic files has significant potential benefits to both physicians and patients. Physicians no longer need to be physically present in their office or hospital chart room to view a patient's chart or to make notes in it. A PC, with a secure broadband Internet connection, allows physicians to access a patient's record from almost anywhere.

Comparably, a patient who establishes an electronic PHR can keep his or her medical information organized and accessible via similar means. Also, the PHR can be shared with new physicians when a patient moves or requires emergency medical attention while traveling. Is this just another electronic gadget? Far from it! In my opinion, this is a great advance for patient safety. One no longer must rely on memory—often faulty—to provide an up-to-date history and record of allergies or laboratory and radiology test results. Exact findings with physician interpretation when appropriate

are right there.

Our partnership with Google allows physicians who utilize Quest Diagnostics Care360™ Physician Portal the ability to export laboratory test results directly to a patient's Google Health account. In addition to Quest Diagnostics, Google is also partnering with other entities, such as large retail pharmacy chains, pharmacy benefit managers, hospitals, medical clinics and health centers, and retail clinics. Every day the list keeps growing. We live in exciting times!

## Update—*Helicobacter pylori*

*continued from page 3*

protected from the acidic atmosphere by a thick mucus layer.

- Topical therapy tends to be diluted by acid secretion and periodic gastric emptying.
- The effectiveness of many antimicrobial drugs is greatly diminished at acid pH, which makes pH control critical for effectiveness. Additionally, HP organisms do not replicate at a pH below 6.0.
- The number of HP organisms in the stomach is usually high, and the organisms usually form a biofilm, making some inaccessible to antimicrobial agents.
- Infections with a large organism burden often contain a persistent or dormant non-replicating population of bacteria that can survive until antimicrobial therapy is stopped. This results in treatment failure without resistance, and can often be overcome by repeat therapy with the same combination as used initially.
- Smoking can have a detrimental effect on therapy due to its effect on gastric acid secretion.

The following are four treatment options for HP infection, which are

reported to be effective in most areas:

- Quadruple therapy
- Sequential therapy
- Concomitant therapy, and
- Dual therapy and dual therapy-based special therapies.

*Editor's Note: An in-depth discussion of the rationale for treatment options noted above is beyond the scope of this publication. The reader is referred to the cited publications for an in-depth discussion of the subject. Physicians should, however, routinely accept responsibility for ensuring that eradication of HP infection has been successful in their patients.*

*Culture, identification, and microbial susceptibility testing of HP are not usually performed routinely. Therefore, not much information about the local or regional prevalence of antibiotic resistance is available to guide selection of therapy. Focus Diagnostics, Quest Diagnostics' infectious disease center of excellence, can provide antimicrobial susceptibility testing for HP when needed for the evaluation of treatment failure or therapy selection. For more information about HP antimicrobial susceptibility testing, consultation, and submission requirements, please call Focus Diagnostics at 714-220-1900 or 800-445-0185.*

*(Nat Clin Pract Gastroenterol & Hepatol 2008; 5:321-331 — Ann Intern Med 2008; 148:1-9 — Am J Gastroenterol 2007; 102:1808-1825 — Gastroenterology 2005; 129:1753-1755, 1756-1780) — Quest Diagnostics. Medical News: Physicians Update 2006; 20(4):5)*

### News Credits

Herman Hurwitz, M.D., *Executive Editor*  
Patricia Mellon, *Senior Editor*

*Published quarterly by Quest Diagnostics Incorporated. Electronic copies are available at: [www.questdiagnostics.com](http://www.questdiagnostics.com). All inquiries, suggestions, or comments should be addressed to Herman Hurwitz, M.D., F.C.A.P., Senior Medical Director, Quest Diagnostics Incorporated, 800 Business Center Drive, Horsham, PA 19044.*

*Telephone: 215.442.7673  
Email: [herman.s.hurwitz@questdiagnostics.com](mailto:herman.s.hurwitz@questdiagnostics.com)*

Quest, Quest Diagnostics, the associated logo and all associated Quest Diagnostics marks are the trademarks of Quest Diagnostics. Copyright © 2008 Quest Diagnostics Incorporated. All rights reserved. [www.questdiagnostics.com](http://www.questdiagnostics.com)

All third party marks – ® and ™ – are the property of their respective owners.

This newsletter is published quarterly by Quest Diagnostics as a service to the Medical Community.