Specimens drawn in physicians’ offices frequently do not meet regulatory requirements for labeling.

Testing can be ordered in Epic or on a manual requisition, so it is readily available to all physician offices. For example, pre-transfusion tests can be done at Suite 800 of the Central Street Medical Office Building. Patients must be registered with ENH so that test results can appear in the patient’s medical record and can be associated with blood components issued in the hospital. Although pre-transfusion testing cannot be done under ENH Laboratory Services (ENHLS, the outreach testing function of the laboratory), ENHLS has a pathway to transfer the orders and specimens to the Blood Bank Laboratory, and has a manual requisition designed to facilitate the transfer. The major occurring problem is that specimens arrive with an order that does not specify the patient is scheduled for surgery.

Specimens drawn at any one of three ENH hospital sites can be used for crossmatching, however, the Blood Bank order must detail where to send the specimen.

Thank you for your attention to these matters, for questions concerning Blood Bank, contact Dr. Perkins at 847-570-2537 or email <jperkins@enh.org>.

Serological Testing for Celiac Disease
James Dohnal PhD, MSISM, DABCC and Irene Check, PhD, DABMLI

Celiac disease is one of the most common genetic diseases in people of European decent, with an estimated prevalence of 1 in 300 persons. Diagnosis, however, can be difficult as many patients do not present with the classic symptoms of the disease (chronic diarrhea, abdominal distention and in children, failure to thrive). Atypical symptoms include:
- Anemic iron and/or folate deficiency
- Anorexia
- Bone pain
- Depression
- Fatigue
- Infertility
- Nausea/vomiting
- Recurrent abdominal pain
- Weight loss
- Pathologic fractures/osteoporosis
Celiac disease is one of two forms of gluten sensitive enteropathies (GSE) which are currently recognized. (The second, dermatitis herpetiformis, is characterized by itchy blistering skin eruptions which on biopsy contain IgA deposits at the dermoepidermal junctions of the skin.) Both forms of GSE are characterized by an intolerance to the ethanol-soluble fraction of gliadins found in wheat grains. This intolerance results in the development of a chronic inflammation of the small intestinal villi that may result in atrophy of intestinal villi, malabsorption and the variety of other clinical symptoms seen in celiac disease. As our understanding of the pathology involved developed, it was recognized that a number of serologic tests could be used to help with diagnosis and to monitor treatment. These tests and their sensitivities and specificities are listed in Table 1. Anti-endomysial IgA and Anti-TTG IgA demonstrate the best sensitivities and specificities. However, due to technical advantages of Anti-TTG IgA methods, Anti-TTG IgA is considered the initial diagnostic test of choice when testing a patient with the symptoms of GSE. Because IgA deficiency is approximately 10 times more common in people with celiac disease than in the population as a whole, a Total IgA should also be ordered. If the patient is anti-TTG IgA negative and IgA deficient, IgG antibody testing is considered the best testing option. Once again anti-TTG and anti-endomysial offer similar sensitivities and specificities but the technical superiority of the anti-TTG IgG makes it the test of choice. Throughout the testing cycle, the patient should be asked to maintain a gluten-containing diet. (See algorithm above.)

Most individuals who suffer from celiac disease express the major histocompatibility complex molecule HLA-DQ2 heterodimer which is encoded by the DQA1*0501 and DQB1*0201 genes. A small percentage of patients express HLA-DQ8 (DQA1*03 and DQB1*0302). When individuals with these variants are exposed to dietary cereal grains, gliadins cross the intestinal epithelial cell layer and trigger an immune response. This response consists of intestinal T cells reacting to gliadin peptides which have been deaminated by tissue transglutaminase (TTG). T cell activation and cytokine production result in a cascade of events that produce the pathologic symptoms.
Table 1 Sensitivity and Specificity of Serum Antibodies in GSE

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-gliadin IgA</td>
<td>52-91%</td>
<td>65-94%</td>
</tr>
<tr>
<td>Anti-gliadin IgG</td>
<td>57-88%</td>
<td>42-92%</td>
</tr>
<tr>
<td>Anti-endomysial IgA</td>
<td>94-98%</td>
<td>96-99%</td>
</tr>
<tr>
<td>Anti-TTG IgA</td>
<td>90-98%</td>
<td>94-99%</td>
</tr>
</tbody>
</table>

References

Triglyceride Patient Results
By: James Dohnal, Ph.D., Technical Director of the Core Lab, Evanston Hospital

Over the past few years government agencies, professional organizations and manufacturers have been working on the standardization of test methodologies. The goal of these efforts is to create an environment where all reagent and test systems for an analyte produce the same result on any given patient sample. We have seen positive outcomes in the standardization efforts for total cholesterol, HDL cholesterol and hemoglobin A1c.

Consistent with these efforts Beckman Coulter (the manufacturer of the triglycerides methodology used in the ENH system) is modifying their calibration set points for their triglycerides method. The calibration change significantly improves the correlation of their method with the CDC’s reference method for triglycerides. This calibration change went into effect at all three hospitals in the ENH system on August 17, 2007.

Beckman’s data, confirmed by in-house testing, indicates that patient triglycerides values will increase by approximately 15 - 20%. Note that despite this change in patient values, the reference range and interpretative algorithms for triglycerides remain unchanged. (Pathology continues to recommend the use of the National Cholesterol Education program (NCEP) Adult Treatment Panel’s guidelines for the interpretation of triglycerides values.)

For questions concerning the triglyceride result change contact either Dr. Dohnal at 847-570-2784. pager 2594, jdohnal@enh.org or Dr. Rosecrans at 847-926-5078, pager 6430, rrosecrans@enh.org.

A New Role for Serum Phosphate?
By: Robert Rosecrans, Ph.D.

Development of a normal or reference range for a particular analyte has been an on going dilemma. Traditionally, when determining a normal range, a group population is picked that is considered “normal” and the assay is performed. Statistical analysis of the test results will yield a group mean and a standard deviation and after further analysis the normal range is derived. The Achilles Heel in the normal range determination is what constitutes a “normal population.” The use of computers and advanced statistical methods are redefining normal ranges. The Framingham Study that began in 1948 is still providing information on cardiovascular risks and more recently the 1971 Framingham Offspring Cohort is a continuation. Data mining of the Framingham Offspring Cohort by Dhingra and Vasan, et.al. (1) indicates that phosphate may play role in cardiovascular disease and potentially serve as a CVD marker.

Animal studies have shown that genetically engineered mice having a high level of phosphate demonstrate premature aging, atherosclerosis, and vascular calcification. Clinical studies on chronic
kidney disease patients show that higher phosphate levels are directly related to increased cardiovascular disease risk. Armed with this information Dhingra and Vasan followed 3368 patients from the Framingham Offspring Cohort for a period of 16 years. Based line blood samples were collected between 1979 and 1982 and patients were evaluated every 4 years. During the 16 year study there were 524 cardiovascular events. The mean age of the group was 44 with 51% being female. Patients having a GFR <60mL/minute were excluded from the study. After CVD statistical adjustment for age, sex, smoking, diabetes, high blood pressure, and high sensitivity C-Reactive Protein it was noted although phosphate levels were within the reference range, the values tended to be higher. Phosphate ranges were broken down into quartiles as follows: 1.6 to 2.8 mg/dL, 2.9 to 3.1 mg/dL, 3.2 to 3.4 mg/dL, and 3.5 to 6.2 mg/dL. Evaluation of the phosphate quartiles showed there was 50% greater CVD risk from the highest quartile to the lowest and a 30% stepwise increase in each quartile for cardiovascular risk. Interestingly, calcium levels did not demonstrate the same relationship to CVD.

Dhingra and Vasan have set forth three hypotheses as a possible explanation for the relationship of phosphate to CVD:

1. Higher phosphate levels inhibit vitamin D which has been linked to vascular disease and coronary calcification.
2. Higher phosphate levels cause mineral deposition in vascular smooth muscle, leading to vascular disease and coronary calcification.
3. Increased levels of PTH secondary to higher phosphate levels induce a proinflammatory response.

All three hypotheses open new areas of research to help elucidate the role of phosphate in CVD, however, in science answering one question usually presents more unanswered questions:

1. If phosphate is found to play a significant role in CVD should the phosphate levels be lowered through the use of phosphate binding agents?
2. What is a normal range or ideal level of vitamin D?
3. How do we explain that in a younger population that does not have diabetes, a lower body mass, lower blood pressure, but has high phosphate levels and low risk of CVD?
4. If phosphate does play significant role in CVD, how do we adjust the “normal range.”

The literature is filling with papers on the relationship of vitamin D to cell death, ovarian, and breast cancer. One has to wonder if vitamin D along with phosphate will be strongly implicated in CVD as well.

Reference: