Celiac disease (CD) is an enteropathy caused by sensitivity to gluten, the protein of wheat, rye and barley. CD is associated with chronic inflammation of the intestinal mucosa and flattening of the epithelium. CD is frequently associated with GI symptoms such as diarrhea, failure to thrive, pain, vomiting, and/or constipation but can be asymptomatic. There is an increase incidence in children with type 1 diabetes, Down syndrome, Turner syndrome, Williams syndrome and selective IgA deficiency. CD is genetically associated with HLA DQ8 and DQ2 and relatives of patients are at increased risk. The prevalence of CD in children is 3-13 per 1000.

Serological tests for CD have been improved and provide a reliable screen but do not replace biopsy. There are three major target antigens: human tissue transglutaminase (TTG), endomysium and gliadin. TTG is the primary antigen recognized by endomysial antibodies (EMA). The endomysium is the connective tissue stroma of muscle fibers. Gliadin is a glycoprotein of gluten.

According to the North American Society of Pediatric Gastroenterology, Hepatology and Nutrition: “measurement of IgA antibody to TTG is recommended for initial screening for CD. Because of the poor accuracy of the antigliadin (AGA) antibody tests, the use of AGA IgA and AGA IgG tests is not recommended for detecting CD.” This recommendation is compounded with the finding that 2-3% of individuals with CD have selective IgA deficiency.

The ontogeny of IgA is highly variable. Levels can remain below detectable limits until~ 9 months of age and do not reach adult levels until~ 10 years of age. An IgA level of 7mg/dl is the lower limits of detectability in our Laboratory. IgG anti-TTG is less specific than IgA anti-TTG but is the best choice in children with low or undetectable IgA. False positive tests for TTG antibodies have been reported in patients with autoimmune liver disease. Endomysial antibodies (EMA) are better in these patients.

The Immunology Laboratory, working with the Section of Gastroenterology, has developed a testing algorithm based on the age of the patient, which will be orderable in the near future. Details about ordering this algorithm, when available, will be sent in Meditech.
Helicobacter pylori and Gastritis
By Vivekanand Singh, MD

The last quarter of the 20th century witnessed a new addition to the list of etiologic agents of gastritis: Helicobacter pylori. This agent is a gram-negative helical bacterium that infects approximately two-thirds of the world’s population. In the developed world, about 10% of children are infected by the age of 10 years. Children from low socioeconomic groups show a higher prevalence.

Most individuals, if not all, who demonstrate H. pylori infection in the endoscopically obtained gastric biopsies have gastritis. Interestingly, about 90% of the people who have H. pylori gastritis manifest no symptoms. Nonetheless, H. pylori infection can cause gastric and duodenal ulcers, and also lead to a 2-6 fold increased risk of developing gastric carcinoma and lymphoma.

Several invasive and non-invasive tests exist for the detection of H. pylori infection. Some of the available non-invasive tests are: 1) Stool test (sensitivity 95-98%), that detects H. pylori antigens in patient’s stool (this test has not been validated in children); 2) Urea breath test (sensitivity 94-98%), that uses the urease activity of H. pylori to break down 13C labeled urea and analyzes exhaled breath for 13C labeled carbon dioxide; and 3) Serologic testing (sensitivity 90-93%) of patient’s blood to detect IgG antibodies formed against H. pylori. Invasive testing employs endoscopy with biopsy of gastric mucosa that necessarily contains at least two bits of antral mucosa. Histologic examination of biopsied tissue has a sensitivity of 82-98%, but a specificity of 99-100% and is considered as the “gold standard” for H. pylori detection. In addition, a rapid urease test can be performed on biopsied tissue.

Histologic detection of H. pylori is possible using routine hematoxylin and eosin (H&E) staining when the bacterial density is high. The wide range in sensitivity is explained in part by the bacterial density, site of gastric biopsy and amount of tissue obtained at biopsy. When a biopsy has only few or rare H. pylori, using special staining such as Giemsa, Steiner, McMullen and immunohistochemistry can highlight the organisms. In our Laboratory we use Giemsa staining as it has a high sensitivity, short turn-around time and is also very cost effective. The distribution of H. pylori in the stomach is not uniform. The bacterial localization appears to be best in the antrum and specifically the lesser curvature in the mid-antrum. A minimum of two mucosal fragments are required to satisfactorily evaluate for H. pylori and associated gastritis.

The histologic features seen in H. pylori gastritis are that of a chronic gastritis, consisting of infiltration of lamina propria by lymphocytes and plasma cells and formation of lymphoid aggregates. Active inflammation that is more obvious and diffuse in adult patients is seldom seen in children. Mucosal ulcers may occasionally be seen in the stomach and duodenum of children.

For treatment of the H. pylori gastritis, various regimens exist that utilize a combination of antibiotics, histamine receptor (H2) blockers, proton pump inhibitors and bismuth compounds.

In summary, pending active screening programs in communities’ at large, gastric biopsy material presents a good opportunity for the detection of H. pylori. In our laboratory, we practice a two-tiered approach: routine H&E staining for all gastric biopsy samples and additional Giemsa staining for samples with suspicious histology.

| Date:      | Tuesday, October 19, 2004 |
| Time:     | Noon – 13:00              |
| Location: | Conference Room 2206.10 WT |
| Speaker:  | Henry Homburger, MD & Edward Loftus, MD |
| Topic:    | Mayo Satellite Program “Markers of Inflammatory Bowel Disease” |