



Saint Luke's Regional Laboratories Clinical Laboratory Letter



December 2006

Serological Tests for Inflammatory Bowel Disease

Inflammatory bowel disease (IBD) is a descriptive term that encompasses Crohn's disease (CD) and ulcerative colitis (UC). The American College of Gastroenterology Practice Parameters Committee recommends a combination of clinical, endoscopic, histologic, radiographic and surgical findings to differentiate between CD and UC.

In approximately 20% of cases, overlapping symptoms, radiographic and histologic features make the differential diagnosis difficult. It is important to accurately differentiate between these two diseases because they have different prognoses and treatments. Patients with UC are at increased risk of developing colon cancer. When medical treatment fails to control the inflammatory process, colectomy is indicated as curative therapy. In contrast, surgery is not curative and can lead to further complications in patients with CD. Also, CD patients may benefit from treatment with infliximab, an anti-tumor necrosis factor antibody.

Some commercial laboratories have promoted the routine use of an IBD serology panel to help distinguish between CD and UC. The panel includes:

- Perinuclear anti-cytoplasmic antibody (pANCA)
- *Saccharomyces cerevisiae* IgA and IgG antibodies (ASCA)

Because pANCA is more prevalent in UC and ASCA is more prevalent in CD, these laboratories provide simplified interpretive tables, such as the one below, to distinguish UC from CD.

pANCA	ASCA	Interpretation
Positive	Negative	UC
Negative	Positive	CD

However, careful review of the literature reveals that the clinical value of ANCA and ASCA testing in IBD is limited because of insufficient sensitivity and specificity.

Approximately 30-80% of patients with UC have elevated levels of perinuclear anti-neutrophil cytoplasmic antibody (pANCA) compared to 5-40% of patients with CD. ANCA are also present in patients with small vessel vasculitides, primary sclerosing cholangitis and autoimmune hepatitis. They are detectable in 2% of healthy controls and 11% of diseased controls.

Approximately 40-60% of patients with CD have measurable IgA and/or IgG ASCA, compared to 5-15% of patients with UC. ASCA are not specific for CD, but are detectable in patients with other diffuse intestinal diseases such as gluten sensitive enteropathy (celiac disease). They are also present in 3% of healthy controls and 11% of diseased controls. The presence of ASCA in patients with IBD may be due to an immune response against a *Saccharomyces* antigen or to an unidentified cross-reactive antigen.

A retrospective audit of 2,754 consecutive IBD serology panels submitted to Mayo Medical Laboratories revealed definitive results for CD or UC in only 18% of tests (Mayo Communique, Sep 2006;31:1-4). These results suggest that serologic testing is being ordered prior to or without the recommended clinical, endoscopic, histologic and radiographic studies. Because of these limitations, Mayo Medical Laboratories has published the following IBD serologic test guidelines. Serologic testing is **not recommended** in the following situations:

- Screening patients with nonspecific GI symptoms
- Screening patients who are strongly suspected of having IBD
- Distinguishing between CD and UC in patients who have not undergone standard diagnostic tests.
- Determining the extent of disease in patients with IBD
- Monitoring response to disease specific therapy

An IBD serology panel is **recommended** only as an adjunct to differentiate CD and UC in patients with a clinical diagnosis of IBD and nondiagnostic histology and radiologic findings. Mayo Medical Laboratory has determined that IBD serology can provide definitive diagnostic results in approximately 40% of patients with IBD who have overlapping findings for CD and UC.

Mayo's recommendations are in accordance with the American College of Gastroenterology Practice Parameters Committee, which stated that pANCA and ASCA "may be useful in the patient in whom all other clinical features do not allow a distinction between UC and CD" (Amer J Gastroenterol 2004;99:1371-85). Physicians ordering IBD serology panels should make certain that they are complying with these guidelines.

Nanotechnology in Laboratory Diagnostics

Recent developments in nanotechnologies hold promise to provide ultra-sensitive and cost-effective alternatives to current laboratory diagnostic tools. The basis of these technologies is nanostructures with sizes on the order of 10 nanometers. Their tiny size allows these structures to directly interact with individual analyte molecules. Their design could enable multiple diagnostic tests to be carried out simultaneously on a single patient sample. Nanostructures will play a particularly key role in cancer diagnostics. Some of the technologies that are likely to find their way into future laboratory diagnostic assays include quantum dots, gold nanoparticles, nanocantilevers and nanopores.

Quantum dots enable researchers to label biomolecules with a unique light signature. The core of a quantum dot is a semiconductor crystal that emits light when exposed to ultraviolet radiation. The color of this light is dependant on the size of the crystal. Taking advantage of this property, multiple-sized crystals may be encased in a polymer which, together, would act as a type of barcode. The polymer may then be coated with antibodies or oligonucleotides to encourage the quantum dot to seek out a particular feature in a cancer-associated analyte, for example, and mark its presence with the illumination of its barcode.

Gold nanoparticles may provide another elegant solution for labeling biomolecules. Like quantum dots, gold nanoparticles can be made to bind with features of interest in a given analyte by conjugating with the appropriate antibody or

oligonucleotide. The intense optical brightness of gold nanoparticles enables simple, automated detection techniques using white light optics. These particles may also be made to reflect different colors and label multiple features in the same test. Distinguishing a single cancer cell instantaneously from a background of non-cancerous cells by simple light microscopy is one potential application that exploits the intense optical brightness of gold nanoparticles.

Nanocantilevers are another nanostructure being studied for its potential uses in diagnostics. Nanocantilevers consist of tiny levers anchored only at one end. These levers will bend, due to surface tension, as molecules bind to its surface. The detection of this bent state effectively signals the presence of the type of molecule attracted to the antibody coated on that particular lever. Because of its ability to detect very low concentrations of molecules, nanocantilevers have the potential to identify a malignancy in its earliest stage.

Nanopores are currently being designed in the attempt to provide a low cost and rapid method to sequence DNA. These pores are sized such that only a single strand of DNA may pass though at a time. The intent is to distinguish each of the four different bases of the DNA using its unique electrical properties as the strand moves through the pore. This technique could increase the speed of DNA sequencing of mutations by 200 times, including those mutations associated with cancer.

Experts believe that quantum dots, gold nanoparticles, nanocantilevers, and nanopores may be readily available for diagnostic use in clinical laboratories in the next 5 to 10 years.

Free T4 Reference Range Change

New immunoassay instrumentation was introduced into the laboratories at Saint Luke's Hospital, Saint Luke's East-Lee's Summit, and Anderson County Hospital in October 2006. Based on the analysis of over 900 thyroid test results since then, the lower reference range for free T4 will be adjusted from 0.8 ng/mL to 0.6 ng/mL.

	Previous Range	New Range
Free T4	0.8 – 1.6 ng/mL	0.6 – 1.6 ng/mL

The reference range change is effective immediately for these 3 hospitals.