

Diagnostic Testing in Children with IBD

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Purpose of the test?

- To make a diagnosis
- To decide on treatment
- To monitor for side effects
- To assess progress of either treatment and/or disease
- To determine if medical treatment is failing

First step in making the diagnosis of inflammatory bowel disease:

Routine screening exams

- CBC (hemoglobin or hematocrit)
- ESR(and/or CRP) which are nonspecific markers of inflammation
- Serum proteins (albumin)
- Occult (hidden) blood in stool
- Iron levels

It is important to remember:

- Not all the tests will be abnormal
- Tests are not always abnormal at the onset of the symptoms
- Lab tests cannot substitute for a good history and physical examination

Making the Diagnosis: Special screening tests

- Inflammatory bowel disease - thought to be caused by a poorly regulated immune system
- As in similar illnesses (lupus, rheumatoid arthritis, diabetes) abnormal antibodies are produced by the body
- Some tests may have a role in differentiating Crohn's from Ulcerative Colitis

UC is associated with positive anti-neutrophil cytoplasmic antibodies (ANCA's)

Crohn's is associated with positive anti-Saccharomyces cerevisiae antibodies (ASCA)

Making the definitive diagnosis

- Lifelong disease, so cannot guess, need to be definitive
- Invasive or radiographic testing is needed
- 1. The least amount of testing necessary should be done
- 2. Any testing done should have influence on management
- Need to differentiate between Crohn's and UC whenever possible
- Type of test/procedure depends upon what part of the GI tract needs to be studied

Procedural Issues:

- Need to prepare before procedure
- Sedation - years ago Endoscopy was done under full general anesthesia. In recent 5-10 yrs, sedation of choice is Propofol - short acting drug, administered intravenously, with less respiratory depression
- There are specific guidelines for monitoring children
- Use of an anesthesiologist for children

Use of Histology (biopsy)

Ulcerative colitis - have non-specific crypt abscesses on biopsy
Crohn's - 15% of colon biopsies will have granuloma
50% of surgical specimens have granuloma

Endoscopy:

Examination of digestive organs with the help of a lighted tube inserted into the body. The types of endoscopy most often associated with IBD are esophagogastroduodenoscopy (upper endoscopy), colonoscopy, and sigmoidoscopy (lower endoscopy)

Indications for an Upper Endoscopy:

- Peptic symptoms: epigastric pain or heartburn, belching (unresponsive, partially responsive to treatment and/or recurrent)
- Nausea and/or vomiting
- Regurgitation

Question #1:

Should children undergoing colonoscopy for the diagnosis of IBD, all have upper endoscopy done?

PRO:

1. May help to differentiate between Crohn's and ulcerative colitis
2. If Crohn's is present in upper GI tract, may alter therapy
3. May give better insight into peptic symptoms

CON:

1. Rarely differentiates between Crohn's and ulcerative colitis
2. Prolongs sedation, adding minimal risk
3. Additional cost unwarranted

Question #2:

Should all children with ulcerative colitis have a small bowel series?

Not really a controversy:

1. Should have it done at some time to rule out Crohn's disease
2. Especially should be done if surgery is contemplated
3. Probably better not to do when acutely ill

Small bowel series in Crohn's Disease

- May show narrowing, cobble stoning, strictures or fistulas
- Patients who are recently symptomatic, may not have a lot of findings

Halligen et. Al. Acta Paediatr 1995, 84:1375-1378

50 children with Crohn's were studied using colonoscopy and small bowel series. 22% of the patients would not have been diagnosed with Crohn's without the small bowel series

Question #3:

If CT scan (Cat Scan) findings are suggestive of Crohn's disease, are other studies needed?

1. CT scan does not give a good roadmap of the GI tract
2. No visual or histology (biopsy) available

Medications and Testing

6-Mercaptopurine (6-MP) for Significant Disease

- Has been used since the 1950's as chemotherapy for leukemia
- First utilized in the 1970's for IBD, landmark New England Journal of Medicine article in 1980
- Gradually used more freely in pediatrics
- Effective in the induction and remission of IBD

- Exact mechanism not clear, seems to impair white blood cells - anti-metabolite
- Recent development of assays (blood tests) for metabolite levels

6-MP Metabolism

- 6-MP & AZA (Azathioprine, its prodrug) have variable bioavailability. Blood levels do not always correlate with therapeutic effect
- 6-MP broken down to its inactive metabolite, 6-methylmercaptopurine (6-MMP) or to its active metabolite 6-thioguanine nucleotides (6-TGNs)
- Methylation of 6-MP is catalyzed by thiopurine methyltransferase (TPMT) which has great genetic variation.

Use of 6-MP Metabolites (Blood test for 6-MP, 6-TG)

- In a group of 92 children on 6-MP reported by Dubinsky et.al., responders had higher 6-TG levels (Gastro 2000;118:705-713)
- 6-MMP levels corresponded with hepatotoxicity
- higher levels of 6-TG also correlated with increased leucopenia (low WBC)
- 8 of 92 were heterozygote for TPMT and had higher levels of 6-TG - all were responders (those patients who have a partial gene for metabolizing the drug - did respond to the drug therapeutically)

Question #4:

Does genetic testing have to be done prior to starting 6-MP namely to test if there is a full expression of the enzyme thiopurine methyltransferase (TPMT)?

Waiting for the results may delay using the medication

Question#5:

Do 6-TG and 6MMP levels have to be routinely monitored on patients receiving 6MP?

For a long time, monitoring other blood tests have been used to check for toxicity

Studies which may be done if treatments is failing

- 6TG levels to check for compliance
- small bowel series if symptoms of persistent vomiting in Crohn's disease

- Repeat colonoscopy if medical therapy is failing & there is consideration for surgery

Other Procedures/Tests

Capsule Endoscopy

- Some use in children
- Need to be able to swallow the capsule
- Passing with endoscope negates benefits
- Still cannot biopsy
- Not much experience in children
- May get held up by stricture
- Can only image the small bowel
- No use for ulcerative colitis

White Cell Scans in IBD

- Technetium (HMPAO) 99m-hexamethylpropylaminexomane
- In two pediatric studies found to be 83% and 90% sensitive and 81% specific (Jewel FM et.al. Br J Radial 1996, 69-508-514, Jobling JC et.al. Arch Dis Child 1996, 74:22-26)
- Still not acceptable for replacing endoscopy and biopsy

Virtual Colonoscopy

- Still uncomfortable and need a prep
- Unlikely to have sedation available for child
- Cannot do biopsy
- Has not been used in children