Is your intestine scarred?

B eing able to tell whether the intestine is becoming scarred and narrowed in Crohn’s disease before an intestinal blockage occurs is a major goal of the research of Dr. Zimmermann and Dr. Higgins. Two studies of different approaches to this problem are getting underway. Dr. Zimmermann’s NIH-funded study uses a special kind of MRI to detect large molecules, like collagen, as they accumulate in scar in the intestines. Dr. Higgins’ study uses a special kind of ultrasound to measure the stiffness of intestines of patients. Both studies will be available for patients with narrowing in their intestines who are planning on surgery. The results of these imaging tests will be compared to the actual microscopic-level scarring found in the sections of the intestine removed at surgery to determine how accurate these non-invasive, radiation-free approaches to measuring scarring are.

Measurement of ulcerative colitis – This is how we find out if new drugs actually work. Unfortunately, all of our current measures require endoscopy, so clinical trials in ulcerative colitis require patients to undergo repeated endoscopies. We have preliminary data that a combination of questions about symptoms and measurements of inflammatory molecules in stool and blood may be just as effective. Dr. Peter Higgins’ study sponsored by the Crohn’s and Colitis Foundation of America will test whether this new approach to measurement of ulcerative colitis is as good as measurement with endoscopy. Subjects with active UC will be asked to answer questions about symptoms, provide stool and blood samples, and undergo flexible sigmoidoscopy three times over 8 weeks to measure disease activity in the standard approach vs. the new approach.

IL17 – the hottest molecule in IBD, interleukin 17 (IL-17) is considered an important ‘ON’ signal for the immune system of the gut, and appears to be especially important in driving inflammatory bowel disease. New molecules to block IL-17 activity are considered the next frontier in IBD therapy. AIN-457, an anti-IL17 antibody made by Novartis, has been used in more than 100 patients with autoimmune diseases, including rheumatoid arthritis and psoriasis. The Michigan IBD Center, with Dr. Peter Higgins as the lead investigator, will be a site for a phase II study of this antibody in patients with active Crohn’s disease. Please contact Jessica White at 734-615-4843 if you have patients who are eligible.
Higgins Honored for Important Contributions to the Field of Endoscopy

The American Society for Gastrointestinal Endoscopy honored Peter D.R. Higgins, M.D., Ph.D., MSc, for his important contributions to the field of endoscopy during the fourth annual ASGE Crystal Awards in May. This year’s event was held on the USS Midway, a retired aircraft carrier-turned museum, docked in San Diego Harbor. This was a special privilege, as the award was presented by the ASGE president, Grace Elta.

The ASGE Crystal Awards symbolize the finest in leadership, research and scientific pursuit. The event recognized the 2008 award and grant recipients who have shared their expertise and strengthened the specialty and the Society. Proceeds from the event benefited the ASGE Foundation in support of GI endoscopy-related research, physician education and training, and public outreach initiatives.

Dr. Higgins, assistant professor in the Department of Internal Medicine, won an Endoscopic Research Award. ERA grants are awarded to physicians who receive the highest scores for projects in basic and clinical endoscopic technology research. The objective is to foster research in GI endoscopy. Dr. Higgins’ ERA project is a research study of the best way to sample the bacteria in the last part of the small intestine (the terminal ileum) in order to study how bacteria in this location stimulate inflammation in Crohn’s disease, and affect recurrence of Crohn’s disease after surgery.

On the Drawing Board

This is a list of clinical studies we are currently designing, considering, trying to get funding for, or filing the paperwork to get institutional permission to do in the future:

- A study of whether molecules (biomarkers) in the stool or blood can predict which IBD patients will be able to taper off steroids faster, and which patients will flare if they taper quickly.
- A study of whether molecules (biomarkers) in the stool or blood can predict which IBD patients currently in remission will have a flare, and which patients will stay in remission.
- A survey study of how patients with colitis understand their risk of colon cancer.
- A survey study of high school students to understand how having IBD affects their decisions about whether and where to go to college, and how they expect to adjust when they get there.
The effect of IBD on pregnancy depends on disease activity. Women who have well-controlled disease, and are not having a flare at the time of pregnancy, should expect fetal and maternal outcomes similar to patients without IBD. Specifically, congenital abnormalities, abortions, pregnancy-related complications, and bad outcomes are not increased. In short, if the disease is well-controlled, baby and mother should not be at any increased risk for any complications of pregnancy. Therefore, it is crucial to maintain disease control prior to and during pregnancy.

**Should I continue my medications for IBD if I become pregnant or while trying to get pregnant?**

Yes, as long as you are not taking a medication known to definitely harm baby development and growth. It is important to discuss this beforehand with your doctor, when you first start to think about trying to get pregnant. A flare of IBD during pregnancy can be very harmful to the growing baby, and it is important to think about whether a flare might be worse than medication side effects.

Drugs are categorized by the FDA (US Food & Drug Administration) into four categories. Categories A and B are considered safe to take. Category C means the drug is safe to take, but there is less information on safety. Category D is more questionable, may have evidence of problems in pregnancies in other animals, and requires evaluation of the benefits and risks to you and the baby. Category X means the drug should be absolutely not be taken around the time you get pregnant or during a pregnancy.

Examples of Category B drugs include sulfasalazine (azulfidine) and mesalamine (Asacol, Lialda, Colazal). Examples of Category C drugs include steroids, which have been used in pregnancy and are thought generally to be safe, although there are some risks of cleft palate and cleft lip to the fetus. We consider this drug a low-risk drug.

Azathioprine and 6-mercaptopurine are FDA Category D drugs. While the official recommendation by the FDA is “not recommended,” for these drugs, physicians have used them with very little risk in large groups of patients, including kidney transplant patients, autoimmune liver disease patients, and people with IBD during pregnancy with good results. We generally recommend continuing these drugs to maintain remission in IBD. Some patients, however, are not comfortable using this medication, and a very detailed discussion with your doctor about the risks and benefits of stopping a helpful medication is needed.

Methotrexate is Category X. This drug is absolutely contraindicated, and should never be used during pregnancy, or in the 3 months before starting a pregnancy. There is a significant risk of birth defects if you are using methotrexate and become pregnant. Special precautions are always needed when using methotrexate during child-bearing years. Double contraception (both male and female contraceptive) should be used if this drug is needed for treatment. Methotrexate is one drug where it is recommended that males also take precautions not to start a pregnancy while using the drug, and until they have been off the drug for 3 months.

Infliximab (Remicade), a relatively new drug, is Category B, and has been used both inadvertently and intentionally in pregnancy and during conception. The risks and benefits of using this drug must be weighed carefully, but if the drug is absolutely needed to maintain remission, in general most authorities advise continuing it.

Antibiotics are often necessary, and include metronidazole (Flagyl), a Category B drug, and ciprofloxacin, a Category C Drug. We generally recommend using metronidazole, and avoiding ciprofloxacin. Lomotil, a commonly-used drug for diarrhea, is Category C and should be discontinued during conception and pregnancy; loperamide (Imodium) is considered a safer alternative, because it is Category B.
Dr. Jeremy Adler was born in Ann Arbor and spent his early years in the Detroit suburbs before moving to Florida at the age of 12. He grew up in North Miami Beach, Florida where he became interested in a career in medicine. He obtained his medical degree from the University of South Florida, and did his pediatric residency at Boston Medical Center. After completion of residency he married his wife, Sara, and moved to New York. He worked as an academic pediatrician at Schneider Children’s Hospital, and worked in the pediatric emergency department at St. Barnabas in the Bronx. He enjoyed a rewarding career as pediatrician, but always considered subspecialty training. “I missed being involved in taking care of children with more complex medical conditions,” says Dr. Adler. He enjoyed teaching students and residents, but missed the intellectual challenges of scientific research. After eight years in practice he moved his family to Michigan to enter his Pediatric Gastroenterology fellowship at the University of Michigan. He has developed an interest in Crohn’s disease and ulcerative colitis. He has a keen interest in improving the quality of care for children with inflammatory bowel disease. He completed his fellowship in June 2008, and joined the faculty at UM as a clinician-scientist.

Dr. Adler’s research has focused on the use of medical imaging to improve our diagnostic abilities and inform our treatment decisions. One of the major dilemmas that occur for patients with Crohn’s disease is when an intestinal narrowing or stricture develops. This can occur for two main reasons. Intestinal narrowing can result from inflammation, which causes thickening of the bowel wall, compressing the lumen, or passageway through the intestines. This can also occur when scar tissue, or fibrosis in the bowel wall develops which can also cause luminal narrowing. Both result in symptoms of intestinal obstruction and are indistinguishable by traditional laboratory and imaging techniques. The problem is that the treatment for these two conditions is radically different. Inflammation can often be treated medically, while fibrotic strictures require surgery. The problem is that there is no test to distinguish between the two. Dr. Adler, in collaboration with adult gastroenterologists, Ellen Zimmermann, M.D. and Peter Higgins, M.D., Ph.D., are developing an imaging technique called magnetization transfer MRI, or mMRI. This is a novel type of MRI, which provides detailed images, and specific information on the amount of fibrosis there is in the bowel wall. It does so without exposing patients to ionizing radiation. This will be a tremendous benefit to patients with Crohn’s disease, and will allow for the early decision to treat with medications or surgery. This should minimize the time for treatment and the side effects which may occur with high dose steroid therapy.

Dr. Adler has also been studying the effect of inflammatory bowel disease on students. He surveyed a group of students at the University of Michigan to identify how their disease activity has affected them. He found that as the degree of activity of Crohn’s disease and ulcerative colitis increase quality of life decreases, and the ability to adjust to college decreases as well. The importance of this is that poor college adjustment has previously been shown to predict poor grades, and a lower likelihood of graduating from college. This study emphasizes the importance of adequate disease control during the college years to give students the best chance at success. This study is now being carried out in high school students to identify the factors that affect the students with IBD, and their decision to attend college.

Besides his research and clinical activities, Dr. Adler enjoys spending time with his wife and two daughters, age 2 and 4 years. He enjoys the outdoors with his family, and is a bicycling enthusiast.