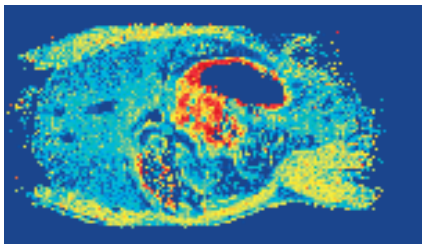
IBD News

Fall 2008 U-M Division of Gastroenterology

University of Michigan Health System

Looking for Something Better? Ongoing Clinical Trials in IBD:

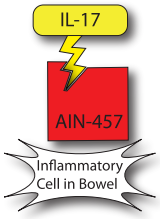
Is your intestine scarred?



Being 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.



IBD Visiting Professors Series

Continuing in the fall, the IBD Visiting Professors Series at the University of Michigan will be co-sponsored by Shire, Centocor, Abbott, and UCB. Invited IBD researchers will present their cutting-edge results and discuss their research with our University of Michigan IBD group.

For the 2008-2009 year, the IBD Visiting Professors will be:

September 15th
Dr. Eugene Chang
University of Chicago

October 14th
Dr. Fernando Velayos
UCSF

February 10th
Dr. Bruce Sands
Massachusetts General Hospital

March 10th
Dr. Ann Lowry
University of Minnesota

April 9th
Dr. Maria Abreu
University of Miami

July 28th
Dr. Jean-Fred Colombel
University of Lille, France

Gastroenterologists throughout the region are welcome to attend. Contact Patricia Arnold at 734-615-2170 or at reineman@umich.edu for directions if you would like to attend the IBD Grand Rounds.

How to Refer a Patient to one of our IBD Specialists

Call our GI appointment center at 888-229-7408 for the appointment line, and specify that you want an IBD Specialist.

Fax patient records to our GI Call Center at 734-936-5458. Please include most recent labs, recent imaging reports or CDs, endoscopy reports, and pathology reports.

IBD specialists available by day:

Monday
Ellen M. Zimmermann
Peter Higgins
Timothy T. Nostrant
Leslie Aldrich
Rafat Rizk

Tuesday
Grace Elta
Rafat Rizk

Wednesday
Leslie Aldrich
Rafat Rizk

Thursday
Leslie Aldrich
Jason Grove, PA

Friday
Leslie Aldrich

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.

IBD News You Can Use

The major annual digestive disease research meeting was held in San Diego in May.

The highlights in IBD Research included:

- Fewer pills, less often, for ulcerative colitis is a trend – a 1.2 g form of mesalamine (Lialda) is now available and effective as a two pills/once a day drug, and Asacol is being reformulated as a 800 mg tablet.

- A study of IBD patients in South Africa on azathioprine or 6-MP found double the rate of skin cancer compared to IBD patients not on these medications. Think sunscreen!

- Probiotic studies – while most probiotics are completely unproven in IBD, two studies of VSL#3 were presented, and it appeared more effective than placebo in patients with ulcerative colitis in preliminary studies.

- Adding methotrexate to remicade therapy does not appear to improve the average patient's disease activity. This is a discouraging finding for the idea of using combination therapy to lower doses and reduce side effects.

- If patients stop responding to remicade, both humira and cimzia, two other medications in the same family, can still be effective in more than half of the patients who try them.

- If patients flare while on humira or cimzia, increasing the dose for a short period can get many patients back in remission.

- Tysabri, a biologic medication for Crohn's and multiple sclerosis that has been associated with a rare, difficult to treat brain infection (PML) when used in combination with other immunosuppressants, was brought back to the market as a single therapy. While often a successful therapy, two new cases of PML have occurred in 2008 in MS patients on Tysabri alone.

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.

Patient Question of the Quarter:

How do Crohn's Disease, Colitis, and IBD Medications Affect Pregnancy?

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 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 childbearing 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.

How to Refer a Patient to an IBD Clinical Trial

They do not need a clinic appointment –
Just call one of our IBD Study Coordinators:

Jessica White
734-615-4843

Judi Schmitt
734-615-2457

PATIENTS INVITED!!

1st Annual
IBD Patient Update

September 13, 2008
8 AM - 1 PM

The Inn at St. John's
44045 Five Mile Rd.
Plymouth, MI 48170

University of Michigan Health System

U-M Inflammatory Bowel Diseases Program
www.med.umich.edu/ibd

U-M Division of Gastroenterology
www.med.umich.edu/gi

For a physician to physician consultation, call M-Line at 1-800-962-3555.

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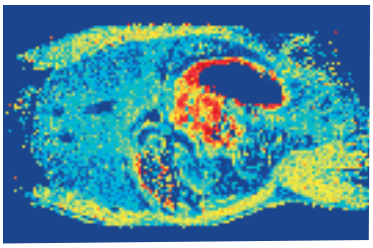
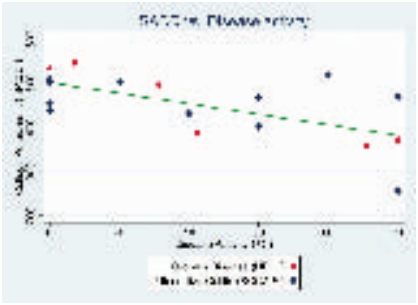
Researcher Profile: Jeremy Adler, M.D.

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 jointed 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 mtMRI. 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.