

IBD News

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Can you filter out inflammation in Crohn's?

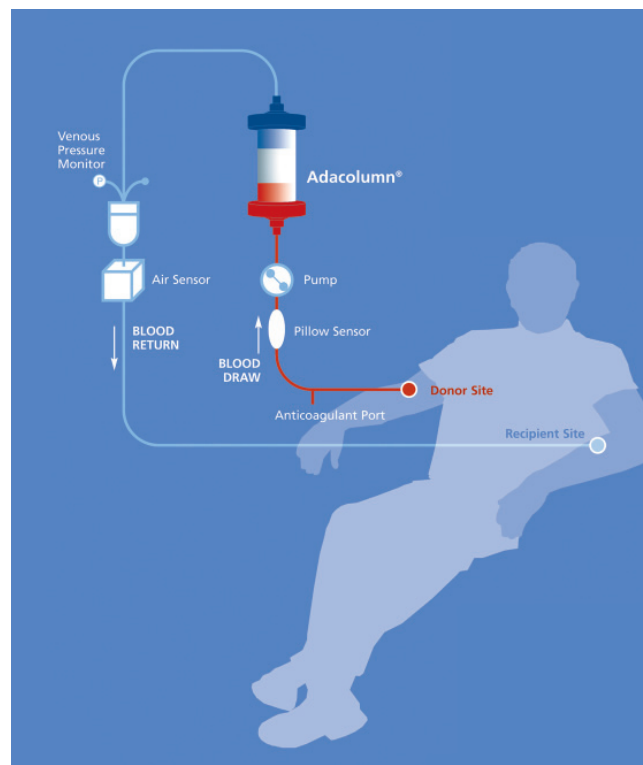
FINDING THE ANSWER IS THE GOAL OF A NEW CLINICAL RESEARCH STUDY AT THE UNIVERSITY OF MICHIGAN

A blood filtration (leukopheresis) device invented in Japan, the Adacolumn, has been approved for treatment of Ulcerative Colitis and Crohn's in Japan and Europe. Active trials are underway in the United States to determine if this approach works in American patients with Crohn's and UC. At the University of Michigan, the UC trial is complete, and the Crohn's trial is now enrolling.

This device filters the blood, and removes certain activated white blood cells. This may remove the inflammatory stimulus, and/or cause repression of the immune system. During the treatment, blood is withdrawn from a patient's arm vein and circulated through the Adacolumn which contains cellulose beads. These beads bind white blood cells, such as granulocytes and monocytes. After passage of the blood through the column, the filtered blood is re-supplied to the patient through the vein in the other arm.

For those participating in the study, 10 treatments, lasting about two hours each, are given over a period of 10 weeks. Patients then return for follow-up visits about once every four weeks through the 24th week. Since this is a randomized trial, each patient has a two out of three chance to receive the actual treatment and a one out of three chance to receive a placebo or sham treatment. At the completion of the first 12 weeks, any subject who is not significantly improved can enter the open-label study, in which all participants receive the active treatment.

ELIGIBLE SUBJECTS for the Crohn's trial include men and women, aged 18 to 75 with moderately to severely active Crohn's disease who have been non-responsive to standard therapies. All study participants will be under the supervision of a team of medical professionals throughout the study. **If you are interested in this study or have any questions about it, please contact one of our study coordinators Tahira Khan 734-615-2457 or Anne Dahlkemper 734-615-4843.**



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IN THIS ISSUE

Researchers find that colectomy with J pouch increases the risk of infertility in women with ulcerative colitis to 50 percent.

MEASURING DISEASE ACTIVITY IN UC

Project Timeline

3 year grant from CCFA, 2006-2008

Focus Groups

2006. Develop themes, identify symptoms that are important to patients

Symptom Domain Surveys

2006. Test which symptoms are most important to patients with UC

Survey Question Development

Late 2006. Develop and test survey questions to measure the most important symptoms.

Biomarker Testing

Late 2006. Test whether biomarkers in stool, blood, or urine are practical to collect and whether they can reproducibly measure inflammation.

Simulated Clinical Trial

2007-2008. Enroll subjects with active UC, measure survey questions and biomarkers, re-measure at 4, 8, and 12 weeks. Good measures should detect improvement, or no change if subjects are not getting better. New measures will be compared to existing measures. It will be determined whether endoscopy or biomarkers are needed for accurate measurement.

Radical Ideas

RESEARCHERS ASK PATIENTS WHAT SYMPTOMS THEY THINK ARE IMPORTANT TO DEVELOP NEW MEASUREMENT TOOLS FOR UC

A three year grant was awarded by the CCFA for the project, "Development of a Validated Measurement Tool for Ulcerative Colitis." Peter Higgins, M.D., M.S.P.H., Ph.D of the University of Michigan is the primary investigator, and will be working with Patricia Wren, M.D., Tahira Khan, and Ellen Zimmermann, M.D. on this multi-stage project to develop a better way to measure ulcerative colitis disease activity.

This project is important because our current ways of measuring UC were made up by physicians, and have never been tested. It is important that measurements of UC severity:

1. include symptoms that are important to patients
2. measure objective markers of inflammation
3. are stable in patients who do not change
4. change when patients improve or worsen
5. are as non-invasive and inexpensive to test as possible.

Better measures of ulcerative colitis will help us better evaluate whether new treatments actually work.

This project will have five phases, and will require extensive input from patients. The timeline, outlined at left, will include focus groups, surveys, collection of blood, stool, and urine, and even a simulated clinical trial, in which disease activity will be measured repeatedly in patients with active disease, to determine which approaches most accurately measure disease activity and detect which patients achieve remission.

If you are interested in this study, or have questions about it, please contact one of our study coordinators Tahira Khan 734-615-2457 or Anne Dahlkemper 734-615-4843.



Dr. Peter
Higgins

Colectomy and Infertility

A recent research project by University of Michigan IBD researchers found that colectomy with J pouch increases the risk of infertility in women with ulcerative colitis to 50 percent. This study was published in the journal Gut in June, 2006.

Women with ulcerative colitis have slightly more infertility than average, with 15 percent unable to conceive after 12 months of trying. However, the infertility rate increases significantly to 50 percent after J pouch surgery. Coauthors Akbar Waljee, Jennifer Waljee, Arden Morris and Peter Higgins believe this may be due to scarring of the fallopian tubes after healing from surgery.

There are reports of successful in vitro fertilization in women who have had J pouch surgery, suggesting that the fallopian tubes are the main source of the infertility problem. A recent study from France suggested that there may be less infertility with an alternative surgery, the ileorectal anastomosis (IRA).

New IBD Faculty Physician Joins U-M

Raf Sid Rizk, M.D. joined the faculty of the University of Michigan Gastroenterology Division in July 2006. He will focus on inflammatory bowel disease, as he works closely with a nationally recognized inflammatory bowel disease team at the University of Michigan. He is very interested in the application of computer databases to collect and analyze patient outcomes and quality of IBD care. Dr. Rizk's clinical background in Gastroenterology began in 1996, when he completed his specialty training at University of Washington and Loyola University. He subsequently worked in academic positions, as assistant professor, in both Internal Medicine and Gastroenterology at Loyola University and Texas Tech University. Most recently, he worked in a large multispecialty group near Chicago.



Dr. Raf Sid Rizk

Dr. Rizk grew up in the United States and received his medical school diploma from the University of Cairo, Egypt. Subsequent Internal Medicine training and academic positions were held in New Jersey and in Chicago, at Loyola University. His practice philosophy revolves around fostering strong patient-physician partnerships where the patient remains very informed through illness and health.

Is it the Bugs?

One of the most controversial areas in IBD research asks whether intestinal bacteria contribute to the early recurrence of Crohn's disease after intestine surgery. If bacteria really contribute, then effective manipulation of these bacteria could be beneficial for preventing the recurrence of Crohn's disease after surgical resection.

Antibiotics and some probiotics have been effective for pouchitis. The data on antibiotics after surgery have been mixed. We don't yet know if we are actually able to effectively manipulate the bacteria in the intestine.

It is difficult to measure which bacteria are present, unless you use DNA-based methods. We are in the process of using DNA-based methods to measure bacteria in biopsies from the wall of the intestine. Data is being collected in this current study by Dr. Maneesh Dave, a student at the University of Michigan School of Public Health, under the supervision of Dr. Peter Higgins.

We hope to use this technology to track the intestinal bacteria in patients with Crohn's disease before surgery and several months after surgery, to determine whether changes in the intestinal bacteria predict which patients will have early recurrence of Crohn's.

In the future, we hope to do studies comparing patients who use particular antibiotics after surgery vs. placebo to determine whether antibiotics can truly change the intestinal bacteria. We want to determine whether this might prevent the early recurrence of Crohn's after surgery.

HAIL TO THE CHIEF!

Grace Elta, M.D. was recently named president-elect of the American Society of Gastrointestinal Endoscopy (ASGE) for 2007-2008. The ASGE is the leading gastrointestinal endoscopic organization in the world. The ASGE sponsors endoscopy standards and guidelines, endoscopy education, and gastrointestinal endoscopy research. This national honor is a deserved recognition of Dr. Elta's career of patient care, service, and education in gastrointestinal endoscopy.



Dr. Grace Elta

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*Includes discrimination based on gender identity and gender expression.

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Anne Dahlkemper



Tahira Khan

Is Viral Infection An Issue?

Recent research reports in other centers have found associations between the use of immunosuppressive therapies (prednisone, imuran, methotrexate, and infliximab) and increased cervical cancer in women (caused by human papilloma virus), and increased shingles (activation of the herpes zoster virus, which causes chickenpox) in all patients. These are preliminary studies of association, and while interesting, are not proof of increased risk.

We are in the design phase of studies to look at whether there are truly increased levels of virus in patients who are on immune-suppressing therapies. If this is the case, we may need to be more proactive about immunizations for patients.

A study of HPV would require female volunteers with IBD who could provide blood samples. This is a controversial area in IBD, and we hope to find out whether immune suppression truly increases the amount of replicating virus in women with human papilloma virus.

Colitis vs. Colectomy—A Quality of Life Decision?

The American Society of Colorectal Surgeons awarded a research grant in 2006 to Akbar Waljee, Jennifer Waljee, Arden Morris, and Peter Higgins to study the factors affecting quality of life in patients who have colitis and patients who have had a colectomy, to help better understand how patients make decisions about colectomy.

This study, which was recently initiated at the University of Michigan, involves surveys of patient choices about colitis and colectomy. Subjects will be interviewed and asked about their symptoms. They will then be presented with clinical scenarios, and asked what decisions they would make, when faced with difficult choices.

We hope to find out from this study what factors affect patients' quality of life with ulcerative colitis or a colectomy, and what affects patients' choices about whether to pursue medical therapy or have a colectomy. **If you are interested in this study or have any questions about it, please contact our study coordinator Anne Dahlkemper at 734-615-4843.**

Our IBD Clinical Study Coordinators

Our IBD research group has recently added a second clinical study coordinator, Anne Dahlkemper. She will be assisting Tahira Khan, our senior study coordinator, with the Crohn's Leukopheresis study, and will be the main coordinator on the Utilities in Ulcerative Colitis study.

Anne graduated from the University of Notre Dame and has strong loyalty on football weekends. She has previously worked in the GI Division for Dr. Joel Rubenstein on a study of Barrett's esophagus, which will be presented at a plenary session of the American College of Gastroenterology National Meeting in October. She is applying to Physician Assistant training programs, so she will likely only be with us for a year, but we are very happy to have her working on IBD research.

Tahira Khan is our senior study research coordinator. She studied medicine at Fatima Jinnah Medical College in Lahore, Pakistan. She started as a study coordinator in 2004, and is in the process of completing a Clinical Research degree from Eastern Michigan University. She has been the lead coordinator on the Atorvastatin in Ulcerative Colitis study, and the four Leukopheresis studies. She previously lived in Chicago, and came to Ann Arbor when her husband took a senior research position with Pfizer pharmaceuticals. Tahira has greatly improved our ability to recruit subjects and complete clinical trials in IBD.

Our study coordinators can be reached at: Tahira Khan 734-615-2457 Anne Dahlkemper 734-615-4843.