May 2012

Colon cancer risk when a first-degree relative has precancerous polyps is not clear

Current colorectal cancer screening guidelines for individuals with first-degree relatives with precancerous colon polyps are based on studies that were not properly designed or were too limited to shape those guidelines, according to a new systemic review of research on the topic. The review authors call for new studies to measure the risk and identify the factors that modify it.


Imperiale

“We found that most studies that are cited for the risk for colorectal cancer when first-degree relatives -- parents, siblings or children -- have a precancerous polyp do not actually address the issue,” **Thomas Imperiale**, MD, an IU Simon Cancer Center physician/researcher, said. “Screening is very important, and properly designed studies are needed to put science behind clinical screening recommendations.”

Current guidelines for people who have first-degree relatives with precancerous polyps range from those of the U.S. Preventive Services Task Force, which makes no specific screening recommendation, to the guidelines of the American Cancer Society and the American College of Gastroenterology, which recommend a colonoscopy starting at age 40 or 10 years younger than the earliest diagnosis in the family (whichever comes first), and repeated every five years if the first-degree relative was diagnosed with a precancerous lesion before age 60.

The study, “Risk for Colorectal Cancer in Persons with a Family History of Adenomatous Polyps” appears in the May 15 issue of the Annals of Internal Medicine. The systematic review was supported by the National Cancer Institute (NCI). David Ransohoff, MD, of the University of North Carolina co-authored the paper with Dr. Imperiale.

“This is another important reason to know your family’s health history," Dr. Imperiale, professor of medicine at the IU School of Medicine and a research scientist with the Center of Excellence on Implementing Evidence-Based Practice at the Richard Roudebush VA Medical Center, said. "Until there is better evidence available, we suggest talking with your primary care physician and basing the decision on whether and how to be screened on the age of the youngest first-degree relatives with precancerous polyps and whether the precancerous polyps are classified as advanced or not.”

One-third to one-half of Americans who undergo a colonoscopy are found to have one or more precancerous polyps, according to Dr. Imperiale, so it is extremely common to have a first-degree relative with a precancerous polyp. However, only 5 percent to 10 percent of these growths are advanced.

Until new, rigorous studies inform screening guidelines, Dr. Imperiale recommends an initial screening colonoscopy if the first-degree relative was younger than 60 and the polyp was advanced when found. If a first-degree relative was 60 or older when the advanced polyp was found, or any age when non-advanced polyps were detected, he suggests that the family

member be screened as average risk. Average-risk options include a high-sensitivity stool blood test annually or a colonoscopy every 10 years.

“The high prevalence of precancerous polyps highlights the need for new, well-designed studies to better understand the colorectal cancer risk of having a first-degree relative with a precancerous lesion -- differentiating between those that are advanced (and more serious) and those that are non-advanced," Dr. Imperiale, a Regenstrief Institute investigator, said. "If everyone who has a first-degree relative with a precancerous lesion is screened aggressively, the health care system would be overwhelmed, and it is possible that the net burdens would outweigh the benefits of screening. We need to make decisions based on better evidence.”

The NCI estimates that 51,690 men and women will die of cancer of the colon and rectum in 2012.

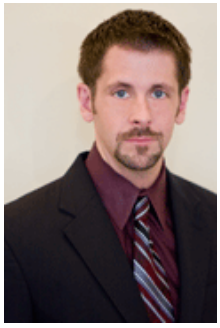
--Cindy Fox Aisen

May 2012

National cancer organization honors Dr. Schneider

An Indiana University Melvin and Bren Simon Cancer Center physician-researcher recently was named an outstanding leader by a national cancer organization.

Bryan Schneider, MD, was selected as the ECOG (Eastern Cooperative Oncology Group) Research and Education Foundation's Young Investigator Award recipient during a ceremony on May 5 in Boston.


Schneider

The award recognizes young investigators under the age of 46 who have made substantial scientific or administrative contributions to ECOG, a membership-based research network whose large-scale cancer treatment clinical trials for major diseases have changed the standard of care for adult cancer patients and helped to individualize their therapy. The IU Simon Cancer Center and Dr. Schneider are members of ECOG.

In nominating Dr. Schneider, **Patrick Loehrer**, MD, director of the IU Simon Cancer Center and H.H. Gregg Professor of Oncology at IU School of Medicine, wrote: "In his relatively short academic career, Bryan has excelled."

While a fellow, Dr. Schneider began a study to examine whether the genes of women without breast cancer were different from those with the disease. He and several colleagues developed the procedures and protocols for collecting, processing, and storing specimens from women without breast cancer. They designed a questionnaire, recruited volunteers, and managed the data they would eventually collect at the 2005 Komen Indianapolis Race for the Cure. In all, they collected more than 1,200 blood samples the day of the race. Equally important, this proved that women would willingly donate blood or tissue to help in the fight against breast cancer and played a crucial role in the establishment of the Susan G. Komen for the Cure Tissue Bank at IU Simon Cancer Center in 2007.

In 2009, Dr. Schneider earned a $5.8 million Promise Grant from Susan G. Komen for the Cure. With the Promise Grant, Dr. Schneider and colleagues hoped to establish biomarkers that physicians could use to better predict which breast cancer patients would benefit from specific treatments and which cancer patients would suffer significant side effects. Dr. Schneider and colleagues did just that as they recently identified a genetic biomarker that causes neuropathy among some breast cancer patients using a class of chemotherapy drugs called taxanes. Neuropathy is a nerve problem that can cause pain, numbness, tingling, burning, or muscle weakness in different parts of the body, especially the fingertips and feet. It is one of the first genetic biomarkers to have been reported for neuropathy caused by taxanes, which includes paclitaxel or Taxol. The finding may eventually lead to a blood test to determine if a patient is at risk of developing neuropathy.

Dr. Schneider, who has yet to turn 40, is also the Shawn Hanson Investigator in Breast Cancer Research and associate director of the Indiana Institute for Personalized Medicine.

May 2012

Core spotlight

Clinical Pharmacology Analytical Core (CPAC)

The Clinical Pharmacology Analytical Core (CPAC) is a bioanalytical core laboratory available to assist Indiana University Melvin and Bren Simon Cancer Center (IUSCC) investigators as well as external partners with pre-clinical and clinical pharmacokinetics in support of their research projects and scientific goals. CPAC has been in existence since September 2004, primarily working with clinical investigators to provide detailed information on drug interactions and pharmacokinetics.

As a result of the identified need for pre-clinical pharmacokinetic and drug metabolism measurements earlier in the drug discovery process (via ITRAC experimental design mapping), CPAC expanded its capabilities to include discovery pharmacokinetics. The process of rational drug design should be based upon a strong foundation of biology, chemistry, in vivo pharmacology, and pharmacokinetics.

Relevant pharmacokinetic studies should be conducted in small animal models and in vitro systems before first drug administration in humans. This allows for the iterative process of implementing structural changes in the drug molecule to optimize the activity of the drug and its pharmacological and pharmacokinetic properties prior to moving to the more regulated and expensive clinical phase of drug development.

For these reasons, CPAC is now interacting closely with another IUSCC shared resource, the In Vivo Therapeutics (IVT) Core, to coordinate these pre-clinical efforts. CPAC has worked with several investigators to quantify their drug in plasma and tissue that generates data for principal investigators to better evaluate molecules being developed within the IUSCC that show promise as novel cancer drugs.

Clinical Pharmacology Analytical Core (CPAC)

Questions? Contact David Jones, core director.

He can be reached at 630-8726 or drjones1@iupui.edu.

The core is located in the WD Myers Building at Wishard.

You can find all of the IU Simon Cancer Center cores here.

As examples, pharmacokinetic and metabolism data provide important information to guide drug design and treatment in pre-clinical drug discovery (bench) as well as in clinical drug development and treatment (bedside). Using state-of-the art technology, CPAC supports the development of safe and more efficacious drug treatment for IUSCC investigators.

Clinical example: **Jamie Renbarger**, MD, a clinical pharmacologist and pediatric oncologist, focuses on the pharmacogenetics of vincristine, a commonly used anticancer agent in children. Her laboratory work resulted in defining the metabolism of vincristine, identification of the structures of its metabolites, and development, in conjunction with the CPAC, of an extremely sensitive assay for measurement of vincristine and its primary metabolite. In the past year, CPAC has developed a method to quantify vincristine and metabolite from Dried Blood Spots (DBSs). This DBS method is novel to IUSCC/CPAC and most of pharma is moving in this direction (preclinical and clinical). This technique is needed

for delivery of samples from outreach research locations (i.e., Kenya, et al). The results from the vincristine pharmacokinetic work may explain the observed racial disparities in the outcome of childhood cancer treatment and lead to more effective vincristine dosing schemes. As a result of her work with CPAC, Dr. Renbarger has received R01, RC1 and U54 grants recently.

Pre-clinical example: **Karen Pollok**'s, PhD, project, in collaboration with **Lindsey Mayo**, PhD, is focused on utilizing the HDM2 inhibitor, nutlin-3, in treatment strategies for chemotherapy-resistant cancers such as melanoma and glioblastoma. CPAC has developed an assay to effectively measure nutlin-3 in vitro and in vivo, generating strong preliminary data in support of the investigator's hypothesis in their funded R01 application. There is also an ongoing small molecule screen to identify new chemical entity and brain permeable inhibitors of HDM2 for glioblastoma and CPAC is involved in their drug discovery efforts.

May 2012

News briefs

24 Hours of Booty charity cycling event to partner with IU Simon Cancer Center

24 Hours of Booty, the official 24-hour cycling event of the Lance Armstrong Foundation and the premier national 24-hour road cycling charity event in the country, is coming to Indianapolis in June and funds raised will benefit the Indiana University Melvin and Bren Simon Cancer Center.

24 hours of booty®
ordinary riders
extraordinary cause

Lance Armstrong, founder of LIVE**STRONG**, was treated and cured of testicular cancer by Lawrence Einhorn, MD, of the IU Simon Cancer Center. All funds raised through 24 Hours of Booty will benefit the cancer center's research. Doctors, staff and cancer survivors will help with the volunteer efforts and recruit members for the Booty Organizing Committee and event day volunteers.

The Lance Armstrong Foundation is the national beneficiary of the 24 Hours of Booty charity event. The 24 Hours of Booty ride in Indianapolis will take place at Butler University from 7 p.m. Friday, June 29 through 7 p.m. Saturday, June 30.

"24 Hours of Booty will be a fun, exhilarating day as we ride a course at Butler," Edward F. Srour, PhD, said. "More importantly, 24 Hours of Booty raises awareness of cancer research and will provide funds for important research at the IU Simon Cancer Center.We're grateful for their support." Dr. Srour and Theresa Vernon -- assistant director of development at IU Simon Cancer Center – are the organizers of the cancer center's 20-person cycling team, Pedaling Cures.

The non-competitive charity cycling event is geared for teams and individuals of all ages and cycling abilities to help raise funds, public awareness and support for the Lance Armstrong Foundation and local cancer charities. To participate in the 24 Hours of Booty of Indianapolis, each rider is required to pay a $65 fee to register and raise a minimum of $200 prior to the ride.

For more information or to sign up for the event, visit www.24hoursofbooty.org.

The Indianapolis event is joining three other 24 Hours of Booty cancer charity cycling rides in Charlotte, N.C., Columbia, Md., and Atlanta.

IU research nurse receives 2012 Extraordinary Healer Award for Oncology Nursing

Sheila Dropcho, RN, BSN, a renal research nurse coordinator at IU Simon Cancer Center, is the recipient of the 2012 Extraordinary Healer Award for Oncology Nursing. The presentation was made May 3 at the Oncology Nursing Society's 37th Annual Congress in New Orleans. In front of more than 700 of her professional peers, Dropcho was selected from three finalists for the national award, sponsored by Cure Media Group and Oncology at Amgen. Dropcho was nominated by one of her

Dropcho with Schilling

patients, Greg Schilling of Greenwood, Ind., whose essay highlighted Dropcho's exceptional compassion, expertise and commitment to her patients. Schilling described the days after his diagnosis as "filled with dread" and wrote that he "had no reason to hope at first." That was until he met his nurse, Dropcho, also a cancer survivor. According to Schilling, Dropcho "is the epitome of what a nurse should be. She has empathy, compassion and caring that is so genuine and real, I feel it when I see her. She has given me hope on many of the dark days I've had." In addition to bringing Schilling hope, Dropcho successfully navigated her grateful patient into two clinical trials -- the most recent of which not only stopped his tumors from growing, it shrunk them by 16 percent. The winning essay will be featured in the summer 2012 issue of CURE, a free, quarterly magazine for cancer patients, survivors and caregivers.

Mark your calendars: BCOG annual conference is Nov. 8-9

Mark your calendars for this year's BCOG Annual Fall Conference on "Team Science." Held Nov. 8-9 at the JW Marriott, the conference is sponsored by the Behavioral Cooperative Oncology Group (BCOG), a consortium of four universities: Indiana University, Michigan State, University of Michigan, and The Ohio State University. Co-sponsors are the Walther Cancer Foundation, IU Simon Cancer Center, Indiana Clinical and Translational Sciences Institute, and the Office of the Vice Chancellor for Research at IUPUI. Kara Hall, PhD, program director at the National Cancer Institute, will deliver the keynote address.

Wright Scholarship recipients selected

Two IUSM students, Priscilla Walker and Melanie Huffman, have been awarded William J. Wright Scholarships by the IU Simon Cancer Center. This scholarship is awarded to third- and fourth-year medical students, physicians in cancer-related postdoctoral programs and/or medical doctors employed by IUSM and pursuing cancer-related fellowship training who demonstrate commitment to, or potential for, conducting cancer research as well as outstanding character and well-defined professional goals.

Cancer Research Day winners announced

Winners from this year's Cancer Research Day have been announced. Go to www.cancer.iu.edu/crd to view the winners.

Shedd-Steele earns award

Rivienne Shedd-Steele, director of the IU Simon Cancer Center's Office of Health Disparities and Outreach, recently was named a Cancer Control Champion by the Indiana Cancer Consortium in recognition of her "outstanding leadership in implementing the Indiana Cancer Control Plan."

Patrick Loehrer, MD, director of the IU Simon Cancer Center, presents the first Stephen D. Williams Lectureship Award to Michael Clarke (left), MD, of the Stanford Institute for Stem Cell Biology and Regenerative Medicine. Dr. Clarke delivered the keynote address during Cancer Research Day (May 9), an annual event that aims to increase understanding and awareness of IU Simon Cancer Center research endeavors and encourage collaboration with other cancer research institutions in Indiana. The late Dr. Williams was the founding director of the IU Simon Cancer Center. The award itself is a replica of "Luminary." Designed by Jeff Laramore 2nd Globe Studios, Luminary serves as the IU Simon Cancer Center's cornerstone at Michigan Street and University Boulevard. The central sphere is constructed of onyx – credited by some with the power to increase regeneration and foster new recognition of personal strengths.

Cancer center members in the news

- **Lawrence Einhorn**, MD, will be honored June 9 by the University of Iowa Alumni Association during the 2012 Distinguished Alumni Awards luncheon. He will be presented with a Distinguished Alumni Award for Achievement, which is given for significant accomplishments in business or professional life or for distinguished human service. The University of Iowa is recognizing Dr. Einhorn for developing a cure for testicular cancer.

- **Daniela Matei**, MD; **Jeanne Schilder**, MD; **Kenneth Nephew**, PhD; and colleagues wrote "Epigenetic Resensitization to Platinum in Ovarian Cancer," which appeared in the May 1 issue of *Cancer Research*.

- In a groundbreaking study led by **Daniel Sliva**, PhD, modified citrus pectin (MCP) -- a highly researched natural compound -- enhanced the anti-cancer effects of two poly-botanical formulas. When co-administered with formulas that attack breast and prostate cancer, MCP significantly increased their anti-cancer action, further reducing metastasis in highly invasive breast and prostate cancer cells. In the study, low concentrations of the anti-breast cancer formula decreased breast cancer cell adhesion to human fibronectin by 21 percent. However, when co-administered with MCP, researchers observed a 40 percent decrease. In addition, the anti-prostate cancer formula, administered alone, decreased prostate cancer cell adhesion by 9 percent. When MCP was added, adhesion was suppressed by up to 40 percent. The study also showed that cancer cell migration was also reduced by combining MCP with the prostate and breast formulas.