

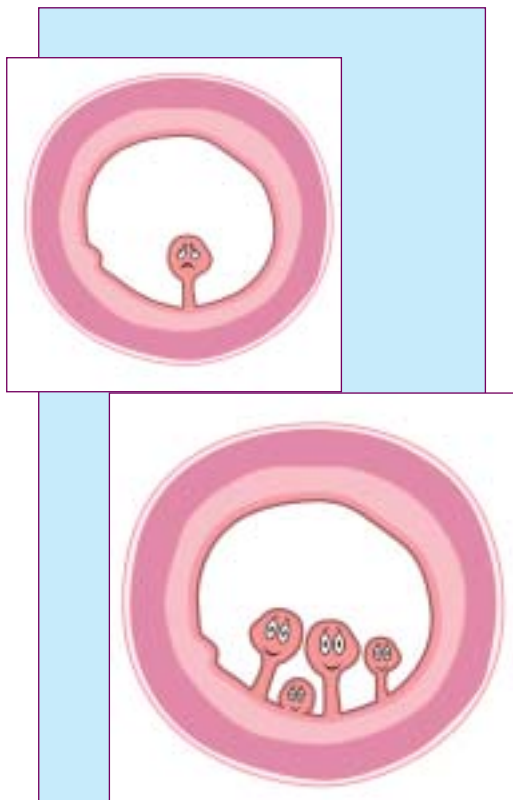
Family Matters



INFORMATION FOR PEOPLE WITH COLORECTAL CANCER IN THEIR FAMILIES

WINTER 2002-03

Before Cancer, There Was A Polyp



A POLYP DOESN'T LIKE TO BE ALONE!

If you have one polyp, you are at a higher risk of getting others. And one in three people over age 50 has at least one colorectal polyp, which may lead to colorectal cancer. Polyps can only be detected through regular colorectal screenings.

All colorectal cancers start as a benign, adenomatous polyp, a tiny growth arising from the lining of the colon or rectum. Because cancer starts this way, it stands to reason that cancer can be prevented if polyps are removed. Although this sounds simple, here's the rub: Polyps ordinarily don't cause symptoms, so often they are found by chance or through screening.

The good news is that only one in every 100 to 200 polyps will ever become cancerous. However, because physicians usually cannot tell which polyps will become cancerous and which won't, all polyps, when found, are removed.

A Common Occurrence

Colorectal adenomas are quite common, says Cleveland Clinic colorectal surgeon James M. Church, M.D. About one-third of people over the age of 50 have at least one. "Polyps are a result of mutations caused by some of the foods we eat, mutations that cause cells in the lining of the colon to grow faster and live longer than they should," says Dr. Church. The more mutations that build up in the lining, the more uncontrolled the cells behave and the closer a polyp gets to becoming cancerous. Generally, it takes 10 years for a small adenoma to accumulate enough mutations to turn into a cancer.

Removing Polyps

Small polyps can be removed through a colonoscope by snipping them off with biopsy forceps (sometimes with coagulation to destroy any polyp tissue that might be left behind). Larger polyps, which are much less common, are treated according to their shape. "Polyps with a stalk, for example, are snared with a wire loop that cauterizes the arteries in the stalk," explains Dr. Church. "The polyp is snipped off and sent to the laboratory where a pathologist examines it for cancer."

Although there are many different types of polyps, only adenomas (or adenomatous polyps) can become cancerous.

Sessile polyps (those without a stalk) can also be snared, but the procedure is a bit tricky. To ensure the safety of the patient, sessile polyps over 2 cm in size are removed in pieces. Sometimes saline is injected under the polyp to lift it up and protect the colon wall from the electrocautery. "It is possible that small parts of large

continued on next page

Dear Readers,

Welcome to *Family Matters*, a newsletter from the David G. Jagelman Inherited Colorectal Cancer Registries developed for our patients, their families and allied health care professionals.

An important part of our mission is to provide information and resources to readers so that they are better equipped to make good health care choices. For example, our cover story on colorectal polyps is a must-read, because all colorectal cancers begin as an adenomatous polyp.

In this issue, you'll find valuable information on the warning signs of cancer, seeking second opinions, the impact of genetics and the benefits of participating in a registry.

In addition, we review the results of a clinical study on the preventive effects of aspirin on polyp formation, and we discuss a new, noninvasive method of screening for colorectal cancer.

With best regards,



James M. Church, M.D.

Director, David G. Jagelman
Inherited Colorectal Cancer Registries

Share this Newsletter with Your Friends & Family

...and urge all your family members to become part of the Jagelman Registries by contacting:

**The Jagelman Registries
Colorectal Surgery / A30
The Cleveland Clinic Foundation**

9500 Euclid Avenue
Cleveland, Ohio 44195

**216/444-6470
800/998-4785**

Before Cancer

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sessile polyps may be left behind, especially if they are very large or in awkward positions," says Dr. Church. If that is likely to have occurred, a repeat examination within three months is recommended.

Sometimes polyps are too large to be removed through the colonoscope, although the decision of what is "too large" varies from one colonoscopist to the next. Because the only alternatives are leaving the polyp alone (and risking cancer) or undergoing surgery (with its own set of risks and side effects), it may be worth getting a second opinion. Dr. Church notes that medication also may help some polyps shrink or disappear.

Surgery is the preferred treatment for a polyp that is cancerous. Occasionally, if there is just a patch of cancer in an otherwise benign polyp, surgery can be avoided. However, if the polyp is all or mostly cancerous, or if the cancer cells have spread into the colon or rectum, then surgery is the best way to ensure that the cancer is completely removed.

Assessing Risk

Once you have had one polyp, you are at a higher risk of getting others. The nature of that risk can be estimated by the number, size and type of polyps that have been removed. For example, three or more adenomas or one large adenoma require a follow-up exam within three years. One small adenoma may require a follow-up exam after five years, or it may not require any follow-up at all.

Part of the rationale for follow-up colonoscopy is the possibility that a polyp was not seen the first time. "Studies have shown that about one-quarter of tiny polyps are missed because they are covered by stool or mucus, or because they hide behind a fold," explains Dr. Church.

Inherited Colorectal Cancer Syndromes

When multiple polyps are found at once, it may be an indication of an inherited colorectal cancer syndrome. There are five types. If the polyps are adenomas, familial adenomatous polyposis or FAP is suspected. Multiple juvenile polyps, the most common type found in children, indicate juvenile polyposis. If polyps are hamartomas or a combination of hamartomas and hyperplastic polyps, juvenile or Peutz-Jeghers polyposis is suspected. Hyperplastic polyposis and Cowden's syndrome make up the remaining types. All of these syndromes are associated with an increased risk of colorectal cancer, although the risk is highest for individuals with FAP.

Preventing Polyps

Medication taken to help prevent polyps from ever forming is called "chemoprevention." "A large study recently conducted at The Cleveland Clinic confirmed our belief that aspirin will stop polyps from forming," says Dr. Church. (See related article on page 3.) Other aspirin-like drugs are also effective, such as Clinoril and Celebrex, as well as calcium. Theoretically, dietary changes, such as increasing one's intake of fiber, fresh fruits and vegetables, and minimizing one's intake of red meat and animal fats, also should help.

Annual Screening

In the meantime, everyone should have a check colonoscopy beginning at age 50 (assuming no special risk factors for colorectal cancer are present, such as family history). Based on screening results, your physician can help you determine a schedule for future checks.

For Some, an Aspirin a Day Keeps Polyps Away

The results of a recent national trial show that a daily dose of aspirin reduces the risk of polyp recurrence in people with a history of colon polyps. But before you reach for the aspirin bottle, read on.

Called the Aspirin-Folate Polyp Prevention Study, the trial involved 1,121 otherwise healthy men and women who previously had adenomatous polyps removed during routine colonoscopies. Study researchers determined that daily intake of 81 mg of aspirin—the equivalent of one baby aspirin—reduced the risk of adenoma recurrence by 19 percent in the study group.

“This small dose of aspirin is the equivalent of what millions of Americans are already taking to prevent heart attacks,” says Carol Burke, M.D., director of the Cleveland Clinic’s Center for Colon Polyps and Cancer Prevention.

Interestingly, a daily 325 mg dose of aspirin was less effective than a baby aspirin in preventing adenoma recurrence. “In fact, those subjects taking the larger aspirin dose experienced only a 4 percent reduction in risk,” says Dr. Burke. “The reasons for this discrepancy are unclear.”

Studies have found evidence that people using aspirin and other anti-inflammatory medications had a lower risk of colorectal cancer. This chemoprevention study, however, was the first to specifically determine aspirin’s effectiveness in preventing colon polyps in people with an individual history (see note on chemoprevention below). The Cleveland Clinic, in addition to several institutions in the United States, participated in the study.

Although this is exciting news for people who have had adenomatous polyps removed, Dr. Burke cautions that medications should not be taken unless directed by a physician. “Even aspirin has potential side effects. It can interfere with blood clotting and cause bleeding and gastrointestinal ulcers,” she explains.

Because of the potential complications of regular aspirin intake, gastroenterologists, as well as federal health officials, have not endorsed the baby-aspirin-a-day recommendation solely to reduce the risk of colon polyps or cancer. However, for the millions of Americans already using chemoprevention to prevent heart attacks, this latest benefit makes aspirin that much more appealing.

CLINICAL TRIAL

Celebrex in children with familial adenomatous polyposis (FAP). The Department of Gastroenterology is studying the safety and effectiveness of the medication celecoxib to prevent polyps in children between the ages of 10 to 14 with FAP. If interested, call Carol Burke, M.D., at 216/444-6864 or Hennie Hasson, R.N., at 216/444-6526.

THE COLOSSAL COLON TOUR

To raise awareness about colorectal cancer prevention, early detection and treatment, the Cancer Research and Prevention Foundation is taking the Colossal Colon on a 20-city tour. The Colossal Colon is a 40-foot long, 4-foot high replica of a human colon. Visitors can crawl through the colon or look through viewing windows to see healthy colon tissue, as well as disease, polyps and various stages of colon cancer. The tour began in February and ends in November 2003. The Cleveland tour is Sept. 17-20. Log on to www.checkyourinsidesout.org for a complete city tour schedule.

What is Chemoprevention?

Chemoprevention refers to the use of natural or synthetic products to prevent disease. Just as aggressive treatment of high blood pressure can prevent stroke, so physicians hope to someday treat precancerous changes in cells before they progress to full-blown cancer, using drugs or even compounds found naturally in food.

Screening for Colorectal Cancer: New Method on the Horizon

Colorectal cancer is one of the leading causes of cancer deaths in American men and women. Fortunately, through regular screenings, it is one of the most preventable cancers.

Traditional screening tests include flexible sigmoidoscopy, colonoscopy and fecal occult blood tests. Unfortunately, at least 40 percent of eligible Americans do not undergo recommended screenings. Part of the reason is the need for a bowel cleanse before a colonoscopy and dietary restrictions before fecal occult blood testing. The development of newer, noninvasive methods of screening would be welcomed enthusiastically by consumers.

“One of the latest—and noninvasive—methods is a stool DNA test that might become available later this year,” says Carol Burke, M.D., director of the Cleveland Clinic’s Center for Colon Polyps and Cancer Prevention.

New DNA Test

The new DNA test works by detecting genetic mutations in the stool. Genetic material called DNA is present in every cell of the body, including the cells lining the colon, explains Dr. Burke. Normal colon cells and their genetic material are passed into bowel movements every day. When a col-

orectal polyp or cancer develops, abnormalities (or mutations) occur in the genetic material of the colon’s cells. “The mutations present in the polyp or cancer can be detected by processing the stool,” she says.

Stool DNA testing can identify a number of common colon polyp and cancer mutations. The stool test is non-invasive and requires no specialized diet or avoidance of medications. “The test is straightforward,” explains Dr. Burke. “A stool sample is mailed to the laboratory, where it is tested for mutations. If mutations are found, a colonoscopy is warranted.”

High Accuracy Rates

In the small studies performed so far, results show that the test has a 75 percent accuracy of finding mutations present in a cancer. The accuracy to detect polyps is between 60 percent to 70 percent.

Currently, two large trials involving about 10,000 patients are in progress, and the results of one of them should be available within the year. Dr. Burke is hopeful. “If these large trials confirm the accuracy of the DNA stool test for screening, we can make a big impact on the burden of colorectal cancer in this country.”

Importance of Regular Colorectal Cancer Screening

Colorectal cancer screening tests help prevent cancer by detecting intestinal bleeding from colon polyps or cancer or by detecting and removing colon cancer precursors, called adenomatous polyps. The key is not to wait until you have symptoms to get screened.

“In its early stages—when it’s most curable—colorectal cancer doesn’t always cause symptoms,” says Carol Burke, M.D., director of the Cleveland Clinic’s Center for Colon Polyps and Cancer Prevention. “The best chance to confirm that you are healthy or to detect polyps before they become cancerous and create symptoms is to have regular screening.”

A number of national guidelines support colorectal cancer screening beginning at the age of 50 (or younger if people have a first-degree relative — parent, sibling or child — with colorectal cancer). Currently, the options include either an annual fecal occult blood test, usually coupled with a flexible sigmoidoscopy, every five years or a colonoscopy every 10 years.

MEDICAL GENETICS: IT'S NOT JUST FOR RARE DISEASES ANYMORE

Brian Clark, Ph.D., M.D.
Director, Medical Genetics, Cleveland Clinic Taussig Cancer Center



With the explosion of knowledge coming from the Human Genome Project, a genetic basis for many human diseases, including common, adult-onset disorders, has now been established. The ability to trace a large number of common diseases to their genetic roots profoundly affects the entire field of medicine, particularly medical genetics.

The Human Genome Project

More than 10 years ago, the Human Genome Project was established with the goal of identifying the complete DNA sequence of human genes. Through this internationally funded project, which is now over 90 percent finished, researchers hope to discover the complete sequence of the human genome. This, researchers believe, will allow us to better understand human disease and, in turn, help in the development of new treatments.

The Implication of Genetic, Common Disorders

Traditionally, medical geneticists dealt with relatively rare conditions and treated pediatric patients. Now, genes

have been identified that are associated with many more common, adult-onset disorders such as breast, ovarian and colon cancers. These single-gene disorders confer a high lifetime risk of disease—nearly 100 percent risk of colon cancer in the case of familial adenomatous polyposis (FAP) if left untreated—and put family members at significant risk of inheriting the disorder.

With each new discovery, medical geneticists are challenged to provide services to a much larger, broader population of patients. For example, pedigrees, the traditional tool used by geneticists for identifying high-risk families with rare genetic disorders, might now be used for families with hypertension, asthma, diabetes and heart disease. Primary care physicians will likely offer these services to patients, because the need will be greater than what existing medical genetic programs can provide.

What You Can Do

Whether or not you are experiencing disease symptoms, it is a good exercise to meet with your primary care physician and identify your family history of common, chronic diseases. Based on the results, your physician can tailor a care plan, including treatment if necessary, for you.

Making Sense of Family History

Pedigrees. A pedigree is a diagram of your family from a genetic point of view. It shows the genetic relationships between you and the other members of your family. A pedigree can be very useful for identifying patterns of disease with a strong genetic component. Typically, a pedigree is developed around a patient's first-degree relatives and then expanded to include more distant relatives. It should include:

- First-degree relatives (parents, children, siblings)
- Second-degree relatives (grandparents, grandchildren, aunts, uncles, nieces, nephews)
- Third-degree relatives (first cousins)

Patterns of Disease. Warning signs that a disease might run in your family include:

- Early onset of disease in a first-degree relative
- Early onset of disease in a second-degree relative
- A first- and second-degree relative with disease, at least one of whom had early onset
- Three or more genetically related members of a family affected by disease
- Disease occurring in several generations

DOES INHERITED COLORECTAL CANCER RUN IN YOUR FAMILY?

If so, consider participating in a disease registry

Want More Information On Medical Genetics?

If you're looking for accurate, up-to-date information about medical genetics, log on to

www.clevelandclinic.org/medgen.

This new Web site offers detailed information about how the Medical Genetics staff of The Cleveland Clinic helps patients and families.

The site features a section on cancer genetics and details what patients can expect from an appointment. The site also includes specific information on appointment scheduling.

In addition to Medical Genetics, The Cleveland Clinic offers Web sites specifically devoted to colorectal surgery and inherited colorectal syndromes and registries. You may access these sites by logging on to:

www.clevelandclinic.org/colorectal
and
www.clevelandclinic.org/registries

For more than 20 years, The Cleveland Clinic has been using the David G. Jagelman Colorectal Cancer Registries to follow high-risk colorectal cancer patients and families. The Jagelman Registries — one of the largest registries in the world — and its associated High-Risk Hereditary Colon Cancer Clinic have served as a successful model of care for people with hereditary colon cancer and their at-risk relatives.

Individuals with multiple cases of colorectal cancer in their families or with an inherited colorectal cancer syndrome such as hereditary non-polyposis colorectal cancer, familial adenomatous polyposis, Peutz-Jeghers syndrome, and juvenile polyposis, are eligible to participate in the registry.

With its detailed family histories and patient medical records, the registry allows Clinic physicians to offer appropriate care for our hereditary colorectal cancer patients. (Their needs and treatments may differ from those of patients with non-hereditary forms of colon cancer.)

Registry coordinators advocate for patients, encouraging them to act diligently with respect to

cancer screening and surveillance. Participation in the registry also gives patients access to education, research and the newest clinical trials. Risk assessment, and genetic counseling and testing are available through the Medical Genetics Program at The Cleveland Clinic. Confidentiality is fully protected.

Additionally, individuals may wish to participate in the Collaborative Family Registry (CFR). The CFR is part of an international effort to study both the genetic and lifestyle causes of colorectal cancer. The registry is sponsored by the National Cancer Institute through a five-year grant, and in conjunction with the Cleveland Clinic's departments of Gastroenterology & Hepatology, Colorectal Surgery and Medical Genetics.

By studying the data, researchers hope to better understand the causes of hereditary colorectal cancer, possibly improving screening techniques and, thus, saving more lives.

For more information, call **216/444-6470** or **800/998-4785**, or log on to www.clevelandclinic.org/registries.

Get A Second Opinion Without Leaving Home

If you have just been diagnosed with a serious illness but are too ill to travel for a second opinion or can't take days off work to visit a top specialist, consider e-Cleveland Clinic's second opinion service.

This convenient, online resource is for people faced with making treatment decisions about serious or life-threatening health problems, such as

cancer, heart disease, neurologic conditions and urologic problems.

For more information about e-Cleveland Clinic's online second opinion service, call 800/223-2273, ext. 43223, or visit our Web site at www.elevelandclinic.org.

Remember, the earlier you seek a second opinion, the better the chance of a successful outcome.



NEW STAFF

**Lisa
LaGuardia
R.N., B.S.N.**

*Coordinator, Familial
Polyposis Registry*



While earning her nursing degree at Kent State University School of Nursing, Mrs. LaGuardia joined the Cleveland Clinic's Department of Colorectal Surgery. In 1997, she moved to the Clinic's Vascular Surgery/Medical Nursing Unit and, a year and a half later, rejoined the Department of Colorectal Surgery as a registered nurse in the outpatient program. In June 2002, she accepted the position of coordinator of the David G. Jagelman familial polyposis registry.

**Janet Shenal,
A.A., R.T.,
M.R.T.**

*Family Coordinator,
Collaborative Family
Registry, Medical
Genetics Department,
Cleveland Clinic
Taussig Cancer Center*



Ms. Shenal has an associate's degree in business from Cuyahoga Community College. At MetroHealth Medical Center, she earned certification as a certified radiology technician in mammography and bone density. She worked as a radiology technician at Suburban Community Health Systems for eight years, and on a research study for osteoporosis for Merck Pharmaceuticals. In addition, Ms. Shenal has 15 years of experience in marketing, sales and management. She brought her vast experience to the Clinic in August 2001 where she serves as a family coordinator for the Collaborative Family Registry, working with hereditary colorectal families to study the genetic and lifestyle causes of colorectal cancer.

**Diane Stanley
Clements,
M.S., C.G.C.**

*Family Coordinator,
Collaborative Family
Registry, Medical
Genetics Department,
Cleveland Clinic
Taussig Cancer Center*



Mrs. Clements obtained her master's degree in Human Genetics at the University of Pittsburgh Graduate School of Public Health in 1986 and is board-certified in Genetic Counseling. Prior to joining The Cleveland Clinic in 2001, she spent 14 years as a genetic counselor in the Department of Pediatrics at MetroHealth Medical Center. Currently, Mrs. Clements is working part-time as a family coordinator for the Collaborative Family Registry, studying families to learn more about the interaction of genes and lifestyle choices in the development of colorectal cancer.

**Analiza T.
Traub**

*Family Coordinator,
Collaborative Family
Registry, Medical
Genetics Department,
Cleveland Clinic
Taussig Cancer Center*



Ms. Traub joined the Collaborative Family Registry as a family coordinator in August 2001. Prior to joining the Medical Genetics Department, she worked in the Department of Infectious Diseases as a fellowship program coordinator. Now, as a family coordinator, she manages families in an international research study for hereditary colon cancer. She offers patient education and screening recommendations. Ms. Traub received her B.A. in Psychology from Cleveland State University.

GRANT FOR COLORECTAL CANCER REGISTRY IS RENEWED

An additional five years of funding for the Collaborative Family Registry was granted to The Cleveland Clinic by the National Cancer Institute.

The Collaborative Family Registry (CFR) is part of an international effort to gather information from a large number of families in order to study both the genetic and lifestyle causes of colorectal cancer. The registry is managed by the Clinic's departments of Gastroenterology & Hepatology and Colorectal Surgery, and the Cancer Center's Medical Genetics program.

The grant renewal, which extends through July 2007, allows staff to provide follow-up for all the current CFR participants, as well as to recruit more individuals and families.

Currently, about 120 hereditary colorectal cancer families participate in the CFR.

For more information, call 216/444-6470 or 800/998-4785, or log on to www.clevelandclinic.org/registries.

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