

Genetic Counseling and Hereditary Cancer Syndromes

By Brandie Heald, MS, Genetic Counselor

Hereditary cancer syndromes account for approximately 5 to 10 percent of colon cancer cases. Patients with hereditary conditions like familial adenomatous polyposis (FAP), MYH-associated polyposis and hereditary non-polyposis colorectal cancer (HNPCC) have a higher risk of developing colon cancer and certain other types of cancer.

If your doctor suspects that genetics are the cause of your cancer or polyposis, he or she may recommend you see a genetic counselor for an evaluation. Genetic counselors can guide you through your diagnosis, help you better understand your condition and identify risk to your family members. Counselors are health-care professionals with specialized training in molecular biology, genetics, and family counseling and are educated in disease information, risk assessment and genetic testing. During a counseling session, the genetic counselor will:

- obtain an extensive personal and family medical history
- explain the natural history and inheritance of a hereditary colon cancer syndrome
- discuss the testing process and options
- review medical management options; and
- evaluate the risks to other family members

Genetic counselors can translate complicated medical information and assist you in understanding your diagnosis. They can also help you to develop a medical management plan specific to your condition. Additionally, genetic counselors consider risk to family members and can make recommendations for appropriate relatives to receive testing and to take any other preventive steps necessary.

Genetic testing may help to identify potential carriers of a genetic mutation before symptoms even develop. Using this information, a genetic



counselor can help determine the appropriate level of medical management for you and your family.

Counselors are skilled at assisting patients to determine their level of insurance coverage for genetic testing and can inform you of legislation that protects those with genetic conditions. Genetic consultations and testing are covered by most insurance companies.

While genetic testing can help confirm a clinical diagnosis, it may not be suitable for all patients with colon cancer or polyps. A genetic counselor can help you explore your personal and family history to determine if testing is appropriate for you.

Genetic counseling services are available at Cleveland Clinic's Genomic Medicine Institute, under the direction of Charis Eng, MD, PhD. The Institute comprises nine genetic counselors who work with four physician geneticists.

Brandie Heald, MS, is a genetic counselor at Cleveland Clinic who is now working closely with the Jagelman Registry. Brandie joined Cleveland Clinic in 2006 after obtaining her master's degree from the University of Cincinnati. Brandie earned her bachelor's degrees in biology and psychology at Case Western Reserve University, where she participated in genetic research for familial colon cancer. She continues to have a special interest in hereditary colon cancer and will be seeing patients in clinic with James Church, MD, and Carol Burke, MD, and in the Center for Personalized Genetic Healthcare with Dr. Eng.

When Cancer Spreads: Hope for patients with Metastatic Colorectal Cancer

By James Church MD and Elodie Elayi

Cancer is a disease where the controls that limit cell life, growth and development do not work. This causes diseased cells to grow uncontrollably. The cells do not die when they should, and sometimes they spread to other organs, forming new tumors. This is called metastasis.

Colon and rectal cancer begin as a noncancerous growth, or polyp, on the lining of the bowel. Once cancer forms within a polyp, it grows into the wall of the colon or rectum, giving the diseased cells access to the blood vessels and lymph vessels. If cancer cells invade the lymph system, they spread to lymph nodes and to the rest of the body. Cancer cells that get into the veins will spread to the liver.

How common are metastases from colon or rectal cancer?

At the time of diagnosis, 15 to 20 percent of patients with colorectal cancer have distant metastases. The most common site of metastasis is the liver. Colon cancer can also spread inside the abdomen and to the ovaries, bones and lungs. In many patients, metastases occur at multiple sites and are treated with systemic chemotherapy for palliation. A few patients with isolated sites of metastasis are candidates for salvage surgery.

What is the prognosis for patients with colorectal metastasis?

Patients who undergo resection of liver metastases can have prolonged survival. One-quarter to one-third of patients who are able to undergo resection will live five years or longer. Thirty to 40 percent of patients treated by resection will relapse, with 80 percent of relapses detected within three years of surgical treatment.

Unfortunately, even for patients with metastatic disease confined to the liver, not all liver lesions are resectable, and even after successful resection, microscopic disease elsewhere can lead to disease recurrence and death. With the development of new technologies and therapies, the possibility of treating patients with chemotherapy instead of resection is being investigated.

How are liver metastases treated?

SURGERY

Surgery to remove the tumors is most effective for this type of cancer, and some patients may be treated with a combination of surgery and chemotherapy.

The liver has the capacity to regenerate. Up to 80 percent of the organ can be surgically removed, and within several weeks the liver will have entirely regenerated itself.

In some cases, laparoscopic surgery can be used to remove part of the liver. Since this procedure is less invasive than traditional surgery, recovery is quicker. It generally requires 10 days of hospitalization, and, for the majority of cases, blood transfusions are not required.

ABLATIVE THERAPIES

Ablation uses a chemical agent or energy to destroy a tumor. Ablative procedures can be performed both through the skin (without an incision) or surgically. These therapies can be very effective but are usually intended to control cancer rather than cure it.

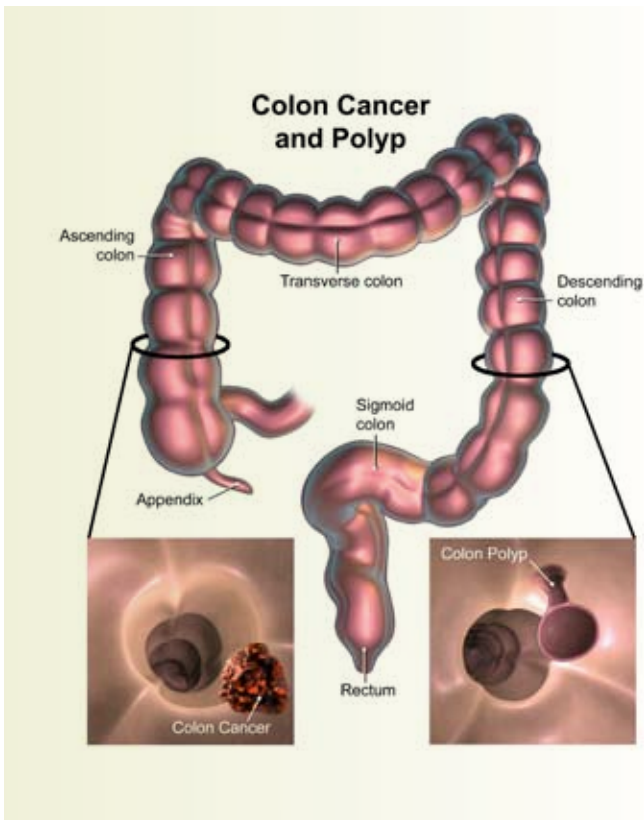
CRYOSURGERY

Cryosurgery, also called cryotherapy, is a treatment that uses an instrument to freeze and destroy abnormal tissue. The primary advantage of cryosurgery over resection is that it preserves normal liver cells. It has been used to treat both resectable and unresectable liver metastases.

Although cryosurgery remains an investigational therapy, it may prove useful in treating colorectal liver metastases in patients with cirrhosis, cancer spread to other sites, or isolated liver recurrence after hepatic resection.

RADIOFREQUENCY (RF) ABLATION

RF ablation is the opposite of cryosurgery. Rather than freezing the tumor, physicians use radio waves to heat it up to such a high temperature that it destroys small tumors. This is done by using



The colon is the part of the digestive system where the waste material is stored. The rectum is the end of the colon adjacent to the anus. Together, they form a long, muscular tube called the large intestine (also known as the large bowel).

a special probe with tiny electrodes. Sometimes the probe is inserted directly through the skin and only local anesthesia is needed. In other cases, the probe is inserted through an incision in the abdomen and is performed under general anesthesia.

ALCOHOL ABLATION

Alcohol ablation or PEIT (precancerous ethanol injection treatment) administers toxins directly to a tumor. It is quite effective for small tumors of less than five centimeters. This treatment is usually selected for patients who are not candidates for surgery.

RADIATION THERAPY

Radiation therapy is used in selected cases to help control tumors. New techniques are used to focus the radiation beam on the tumor and spare the normal liver from injury.

CHEMOEMBOLIZATION

Chemoembolization of the hepatic artery, the liver's main blood supplier, involves blocking the artery and injecting anticancer drugs between the blockage and the liver. The liver's arteries then deliver the drugs throughout the organ. Only a small amount of the drug reaches other parts of the body.

CHEMOTHERAPY

Almost all patients with metastatic colon cancer will receive some form of chemotherapy. Chemotherapy is usually given intravenously, but one commonly used drug is available as tablets.

Side effects of chemotherapy for colon cancer are common but usually not serious. Most patients get nausea and inflammation of the lining of the mouth. Diarrhea and a feeling of pins and needles in the arms and legs may occur. There is not usually hair loss, and side effects go away after treatment.

Current chemotherapy treatments involve multiple drugs, and some of the most common are FOLFOX and FOLFIRI. Treatments vary in length, doses and the way the medications are given.

How are lung metastases treated?

Almost all patients with lung metastases are treated with chemotherapy. Radiation therapy may be used in selected patients, when the tumor causes bleeding or obstruction of the airways. Some patients with isolated lung metastases may benefit from resection, depending on the number and location of metastases. The procedure requires that patients have adequate pulmonary function and medical fitness.

What are the newest forms of therapy?

Aside from three new drugs that have been approved in the last four years and new combinations for chemotherapy, there is a whole new field of cancer immunotherapy.

IMMUNOTHERAPY

Immunotherapies use natural substances produced by the immune system to help the body defend against metastatic cancer. These substances may kill cancer cells, slow their growth, or activate the patient's immune system to fight cancer more effectively.

(Continued on page 4)

MONOCLONAL ANTIBODIES

Antibodies are produced by the immune system to help fight infections. Monoclonal antibodies can be made in the laboratory, and, instead of attacking germs as usual antibodies do, they can attack specific proteins produced by cancer cells. Three new monoclonal antibodies have been approved by the U.S. Food and Drug Administration (FDA) to attack colon cancer cells.

Bevacizumab (Avastin®) inhibits new blood vessels from developing and carrying oxygen and vital nutrients to a tumor. It is used in conjunction with chemotherapy as a first line treatment for patients with advanced or metastatic colon or rectal cancer.

Cetuximab (Erbix®) works by binding to a special site on the cell's surface, which stops the cell's growth and promotes cell death. It is used either alone or in combination with a chemotherapy agent as a second line treatment for patients with advanced cancer or metastatic colon or rectal cancer that is no longer responding to the chemotherapy agents. It is also used for patients who cannot take the chemotherapy agent Campostar®, or who no longer respond to it. Although treatment has not been shown to extend patients' lives, it has been shown to shrink tumors and delay tumor growth, especially when it is used in combination with Campostar®.

Panitumumab (Vectibix®) is the newest agent. Like Cetuximab, it inhibits the growth of cells and promotes cell death, but the two differ in their structure and might differ in their mechanism of action.

TUMOR VACCINES

In November 2006, it was announced that a vaccine had been developed against tumor cells and tested with very promising results. The new vaccine, called TroVax® works in a similar way to a measles vaccine. It kills cancer cells and exposes the body to them, so that the body can develop defenses specifically designed to kill those cancer cells. Thus, TroVax® works in a totally different way than existing treatments – by harnessing the patient's own immune system to fight the disease.

WHAT IS CANCER?

Cancer is a group of many related diseases. All cancers begin in cells, the building blocks that make up tissues.

Normally, cells grow and divide to form new cells as the body needs them. When cells grow old and die, new cells take their place. Sometimes this orderly process goes wrong. New cells form when the body does not need them, and old cells do not die when they should.

The extra cells form a mass of tissue, called a growth or tumor. Tumors can be either benign (not cancerous) or malignant (cancerous). Benign tumors do not spread to other parts of the body, and they are generally not a threat to life. Malignant tumors can spread (metastasize) and may be life threatening.

WHAT ARE THE SYMPTOMS OF COLORECTAL CANCERS?

Colon cancer can be present for several years before symptoms develop. Symptoms of colon cancer are numerous and non-specific (can be seen in many other various diseases other than cancers). When symptoms do occur, they depend on the site of the lesion. The right colon is spacious, and cancers of the right colon can grow to large sizes before they cause any abdominal symptoms such as:

- Iron deficiency anemia due to the slow loss of blood over a long period of time leading to fatigue, weakness and shortness of breath
- Change in bowel habits
- Weight loss

The left colon is narrower than the right colon. Therefore, cancers of the left colon are more likely to cause partial or complete bowel obstruction and cause symptoms such as:

- constipation
- narrowed stool
- diarrhea
- abdominal pains
- stomach cramping and bloating
- vomiting

Bright red blood in the stool may also indicate a growth near the end of the left colon or rectum.

Meeting Brings International InSiGHT

By Julian Sanchez, MD

Cleveland Clinic was well represented at the Scientific Meeting of the International Society for Gastrointestinal Hereditary Tumors (InSiGHT) this spring in Yokohama, Japan. Ten members of the Digestive Disease Institute traveled across the globe to meet and discuss their specialties with world-leading basic scientists, medical specialists, genetic counselors, epidemiologists and registry coordinators, all with interests in hereditary colorectal tumor syndromes.

Cleveland Clinic physicians and researchers played a central role in the meeting by sharing their data and experiences. Among the presenters were:

MATTHEW KALADY, MD, Colorectal Surgery, who explained a scoring system to guide the management of FAP patients who have had a colectomy and undergo rectal surveillance;

CAROL BURKE, MD, Gastroenterology, who lectured on the prevalence and risk factors for fundic gland polyp dysplasia in FAP;

LISA LAGUARDIA, RN, BSN, FAP Registry Coordinator, who shared a poster describing a new finding of renal cancer in MYH-associated polyposis;

POH KOON KOH, MD, Colorectal Surgery, who outlined genetic findings on Syndrome X, a variant of Lynch Syndrome;

ELENA MANILICH, MS, Colorectal Surgery, who showcased the registry database software developed at Cleveland Clinic and used throughout the world; and

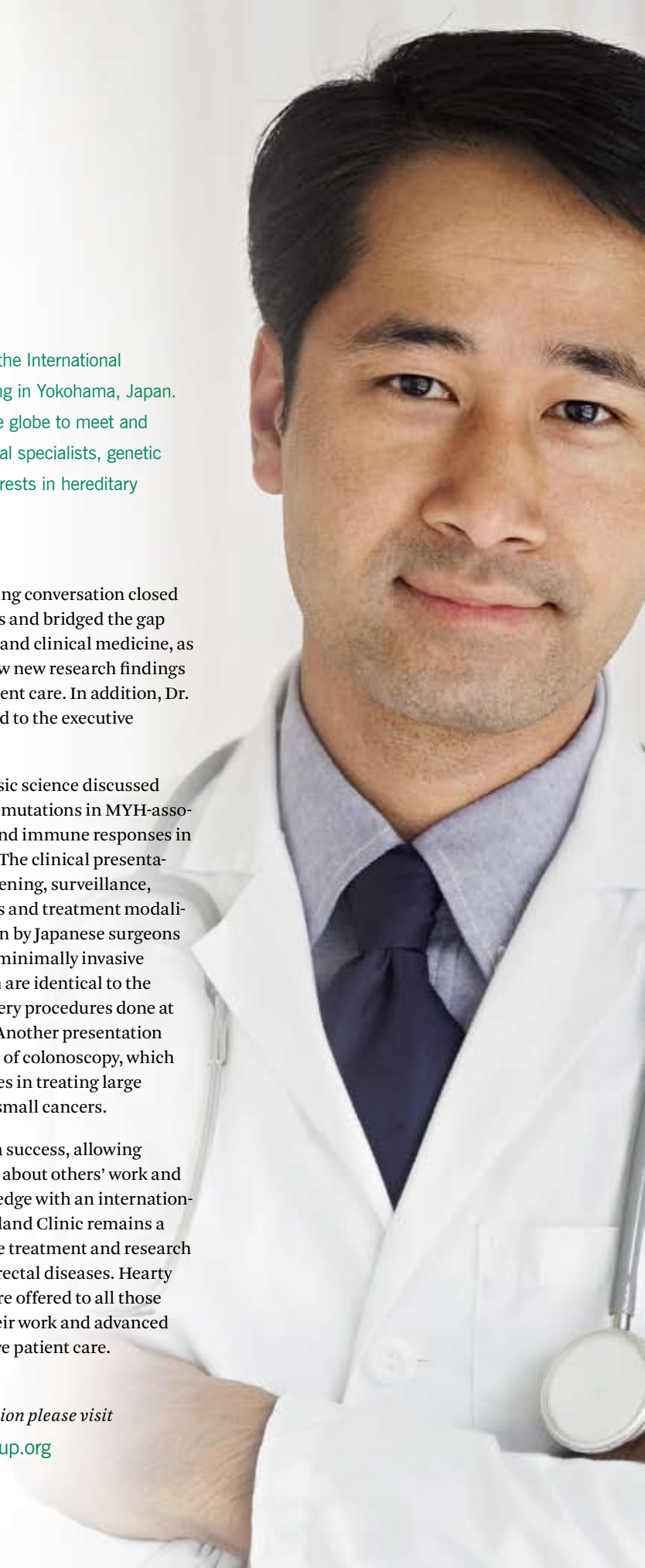
JAMES CHURCH, MD, Colorectal Surgery, Director of the Jagelman Registries, who presented his data on FAP mutations and was the moderator of an interactive session where clinicians from around the world discussed the management of various clinical scenarios.

Dr. Church's exciting conversation closed the week's lectures and bridged the gap between research and clinical medicine, as they discussed how new research findings would impact patient care. In addition, Dr. Church was elected to the executive counsel.

Researchers in basic science discussed genetic pathways, mutations in MYH-associated polyposis and immune responses in Lynch Syndrome. The clinical presentations covered screening, surveillance, associated cancers and treatment modalities. A presentation by Japanese surgeons highlighted their minimally invasive techniques, which are identical to the laparoscopic surgery procedures done at Cleveland Clinic. Another presentation showed the future of colonoscopy, which offers real advances in treating large polyps, as well as small cancers.

The meeting was a success, allowing attendees to learn about others' work and share their knowledge with an international audience. Cleveland Clinic remains a world-leader in the treatment and research of hereditary colorectal diseases. Hearty congratulations are offered to all those who presented their work and advanced the field to improve patient care.

For more information please visit www.insight-group.org



Have a Voice in Colorectal Cancer Research Join the C-CFR

Recruitment continues for suspected HNPCC families who have a history of colon cancer in two generations for the Collaborative Family Registry for Colorectal Cancer Studies. By joining the C-CFR you may be eligible to participate in the largest registry of its kind, which studies the genetic and lifestyle causes of colorectal cancer. Participants in the C-CFR are critical to helping researchers continue to learn about the genetic and lifestyle causes of colorectal cancer. They are entitled to a free genetic counseling session and remain informed about the most recent developments in colorectal cancer research.

Participants may be asked to provide a detailed family medical history, donate blood or tumor tissue samples, and complete a lifestyle questionnaire. Your information will be kept strictly confidential and will be updated every few years. Those who may be eligible have a family history that includes:

- 3 colorectal cancers; or
- 2 colorectal cancers and 1 uterine cancer; or
- 3 cancers – any combination of colorectal, uterine, ovarian, small bowel, ureter or renal pelvis.

To find out more about the registry and your family's eligibility, please call Ellen McGannon or Janet Shenal at 800.223.2273 ext. 52050 or 216.445.2050.



By joining the C-CFR you may be eligible to participate in the **largest registry** of its kind, which studies the genetic and lifestyle causes of colorectal cancer.

Currently Enrolling STUDIES

We are currently enrolling individuals who have been diagnosed with Familial Adenomatous Polyposis for the following studies:

Assessing the effectiveness of Celebrex versus Celebrex plus the medicine Eflornithine on colorectal polyp growth. Contact Carol Burke, MD, at **216.444.6864**, or Hennie Hasson, RN, at **216.444.6526**.

Lyophilized Black Raspberries – Nine-month trial studying the safety, tolerability and effectiveness of black raspberries on rectal polyps in adults with Familial Adenomatous Polyposis (FAP). Contact Carol Burke, MD, at **216.444.6864**, or Hennie Hasson, RN, at **216.444.6526**.

Celebrex – Patients must be taking Celebrex, outside of a clinical trial, for the past six months. They must be at least 18 years old at the time of the study and have an endoscopically assessable colonic, rectal, ileal pouch and/or gastro duodenal segment. Contact Elodie Elayi at **216.444.6875**.

Celebrex Historical / Concurrent Control Patients – Patients who have never been on any NSAID for the treatment of FAP. They must be at least 18 years old at the time of the study and have an endoscopically assessable colonic, rectal, ileal pouch and/or gastro duodenal segment. Patients must have written consent to the Jagelman Inherited Colon Cancer Registry between 1991 and 1997 and an IRA or IPAA that was performed between 1985 and 1997. Contact Elodie Elayi at **216.444.6875**.

CT Colonoscopy – Patients must be at least 14 years old who need a prophylactic colectomy or proctocolectomy and must have an intact colon. Contact Margaret O'Malley or Lisa LaGuardia at **216.444.6470**.

Hearing / Intellectual Performance Study – Patients must be at least 18 years old and be willing to take a hearing test and a verbal test and have blood drawn. Contact Margaret O'Malley or Lisa LaGuardia at **216.444.6470**.

Desmoid Study – Patients with a diagnosed desmoid tumor. Contact Margaret O'Malley or Lisa LaGuardia at **216.444.6470**.

Family Matters

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March is Colorectal Cancer Awareness Month

Call 216.636.5436 or 866.539.1925 during the month of March from Monday-Friday, 8 a.m. - 5 p.m. for a free, 5-10 minute phone conversation to assess your risk.

Qualified callers will be offered a free flexible sigmoidoscopy (a 15-minute medical exam of the rectum and lower colon) in April at the Cleveland Clinic Digestive Disease Institute.

Attend a FREE Cleveland Clinic health talk and learn from Cleveland Clinic physicians, a nutritionist and a patient about what causes colon problems, how to have a healthy colon and which foods to eat to stay healthy.

THURSDAY, MARCH 6, 2008

5:30 p.m. - 8:30 p.m.

Independence Family Health Center
5001 Rockside Road
Independence, OH 44131

Conference Rooms A&B (located on the lower level)

To register, call 216.444.3641 or 800.548.8502 or visit
clevelandclinic.org/health/healthtalk

Enjoy free food and beverage, win free raffle prizes, and participate in a free 5-10 minute conversation to assess your colorectal risks (from 5:30 p.m. - 6:30 p.m. and from 8:00 p.m. - 8:30 p.m.).

Family Matters

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Family Matters is a publication of the Cleveland Clinic Department of Colorectal Surgery to provide up-to-date information about the department and its services. The information contained in this publication is for educational purposes only and should not be relied upon as medical advice. It has not been designed to replace a physician's medical assessment and medical judgment.

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