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*Boston University*



# Humphrey Center NEWS

A PUBLICATION OF THE HUBERT H. HUMPHREY CANCER RESEARCH CENTER OF BOSTON UNIVERSITY

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## Public awareness may aid the fight against a 'neglected' form of cancer



J. Thomas LaMont, M.D.

(Photo by Bradford Herzog)

For years, it has been the "neglected" form of cancer. Many people were unwilling even to think about it, much less talk about it with their families or physicians.

Today, though, mainly as the result of President Reagan's operation, the taboos surrounding colo-rectal cancer are disappearing. And that's a welcome change, says J. Thomas LaMont, M.D., a gastroenterologist with the Humphrey Center.

Colo-rectal cancer, notes Dr. LaMont, is one of the most lethal varieties of cancer. It will kill an estimated 60,000 Americans this year. Yet it's also one of the most easily detectable types of cancer. And when caught early, it's usually curable.

"If everyone at risk took advantage of the simple diagnostic tests that have been developed for colo-rectal cancer," says Dr. LaMont, "we could probably cut the death rate in half, or more."

The three basic screening tests for colo-rectal cancer are: a digital exam by a physician, useful in finding tumors in the rectal area; a test for signs of microscopic quantities of blood in the stool; and a visual examination of the rectum and lower colon by a doctor using an instrument called a flexible sigmoidoscope. (For information on who should have these tests, see the back page.)

Used widely enough, these tests would yield warning signs for most  
*continued on page 2*

## A new technique for arresting the spread of tumors

While surgery is a proven cure for early colo-rectal tumors, it cannot cure patients whose disease has spread to other parts of the body. And to date, radiation and chemotherapy haven't proved capable of doing much to help such patients, either.

Radiation *can* help keep tumors from growing back in limited areas of the lower digestive tract, says Maureen T. Kavanah, M.D., a Humphrey Center member and a surgeon-oncologist at University Hospital, which is associated with the Center. But she adds that it doesn't seem to help the patients treated survive longer. "Most patients still die when their cancer spreads to the liver," she notes.

Now, however, doctors at University Hospital and other teaching hospitals are trying a new approach to halting the cancer's spread.

The new technique grew out of the discovery that surgery itself can sometimes trigger the spread of the cancer. By disrupting the tumor, it allows cancer cells to break free and travel through the bloodstream.

Since colo-rectal cancer often spreads most readily to the liver, the idea is to protect that organ during and after surgery.

"We put a catheter into the portal vein, which  
*continued on page 2*

**INSIDE: NATURAL POISON  
TO FIGHT CANCER**



**FOCUS ON A 'NEGLECTED' CANCER***continued from page 1*

early-stage colo-rectal cancers, as well as for the benign growths called polyps that sometimes develop into cancers.

Colon polyps, whether benign or malignant, are relatively easy to remove. They can be snipped away by a special instrument called a snare, which is attached to a long viewing tube known as a colonoscope.

"Once we take a polyp out, we send it to be tested," says Dr. LaMont. "If the test shows there's cancer in the stalk but it hasn't proceeded beyond that point, it means the cancer's cured."

Why are colo-rectal tumors easier to detect than most other kinds of tumors?

One reason is the fact that they're in the digestive tract. This means that the telltale traces of blood are carried along the body's normal elimination pathway. It also means that doctors can use diagnostic devices like the sigmoidoscope that permit them to examine the rectum and colon directly for the presence of cancer, or of precancerous growths.

Another reason is that colon cancers and polyps are relatively slow-growing. "It takes nearly two years for a colo-rectal tumor to double in size," says Dr. LaMont, "although once they start to spread beyond the digestive tract, they tend to grow faster."

A third reason is the way the tumors develop. Scientists believe that most if not all colo-rectal cancers start out as polyps. While only a small percentage of these become malignant, it's impossible to tell without examining their tissue in the lab whether they're cancerous. Since polyps are relatively easy to remove anyway, most gastroenterologists recommend that they all be taken out.

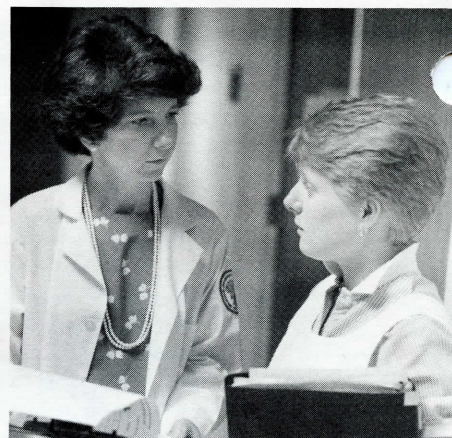
Dr. LaMont emphasizes that although blood in the stool often is the first sign of colo-rectal cancer, it also can be a sign of many other types of problems: bleeding gums, stomach ulcers, infections, hemorrhoids. In fact, he says, the amount of blood produced by a tumor is usually so tiny that it's invisible to the naked eye. "If you see blood on the toilet paper," he says, "the chances are very small that it's from a tumor. It's far more likely to be a sign of hemorrhoids or an anal fissure."

Still, he says, any sign of bleeding should be brought to the attention of a physician. □

**NEW TECHNIQUE***continued from page 1*

leads into the liver," explains Dr. Kavanah, "and beginning on the day of surgery and continuing for seven days thereafter, the patient gets a continuous infusion of anti-cancer drugs."

It's too soon to know whether the approach will help cancer patients over the long run, says Dr. Kavanah. She notes, however, that it's an ideal type of therapy to test in a clinical trial. Unlike many other forms of chemotherapy, this approach doesn't involve side effects like nausea or hair loss, and it poses essentially no risk to the patient. □



(Photo by Bradford Herzog)

*Dr. Kavanah in the cancer surgery unit at University Hospital, which is associated with the Humphrey Cancer Center.*

## Can a natural poison found in diphtheria be enlisted as an anti-cancer agent?

In its time, diphtheria was a public-health menace.

Epidemics, sweeping through a city or town, would afflict thousands of people at a time. Some would recover, but many would not.

"If you read about the diphtheria epidemics of the 1700s, you find it was an incredibly virulent disease," says John R. Murphy, Ph.D., a Humphrey Center scientist. "It killed large numbers of susceptible people, especially children."

Today, thanks to a vaccine developed early in this century, diphtheria is largely a memory. The bacteria that spread the disease survive, and for Dr. Murphy, that fact posed an interesting question: Could the destructive power of diphtheria be enlisted in the struggle against cancer?

The molecular biologist has spent much of his career seeking the answer to that question, and recent findings suggest that it may be yes.

The reason he chose diphtheria is that the disease's germ doesn't do the damage by itself. Instead, it produces an extremely potent toxin. "A single molecule of diphtheria toxin can destroy an entire cell," notes Dr. Murphy.

Before the toxin can be put to work as an anti-cancer agent, however, there are a host of problems to solve.

A key challenge is to make sure the toxin won't attack normal cells. This is accomplished by chemically altering the toxin so it can't link up with any type of cell, normal or cancerous.

Perhaps the biggest challenge is to then get the toxin to link up solely with tumor cells. The solution Dr. Murphy is pursuing is to produce a new protein that combines the altered toxin with a hormone.

Hormones are the body's internal messengers. They circulate through the blood until they connect with a cell. There, they may deliver any of a host of different messages, depending on the specific hormone and cell involved. The hormones epinephrine and norepinephrine, for example, trigger the "fight or flight" reaction: faster pulse, increased alertness, tenser muscles.

Not all hormones can link up with all cells, though. It's as if these messengers could only fit through a certain-sized gate in the cell wall. If many types of cells have the right-sized gate for a certain hormone, that hormone can carry messages to many destinations. If only a few types of cells have the correct gate for another hormone, it will be restricted to those types.

One hormone that Dr. Murphy uses, for example, connects only with a single type of cell. It's the cell that creates skin color, and it's called a melanocyte.

When melanocytes become cancerous, the resulting disease is called malignant melanoma. "It's a very virulent form of cancer," notes Dr. Murphy. "It's highly resistant to both chemotherapy and radiation therapy."

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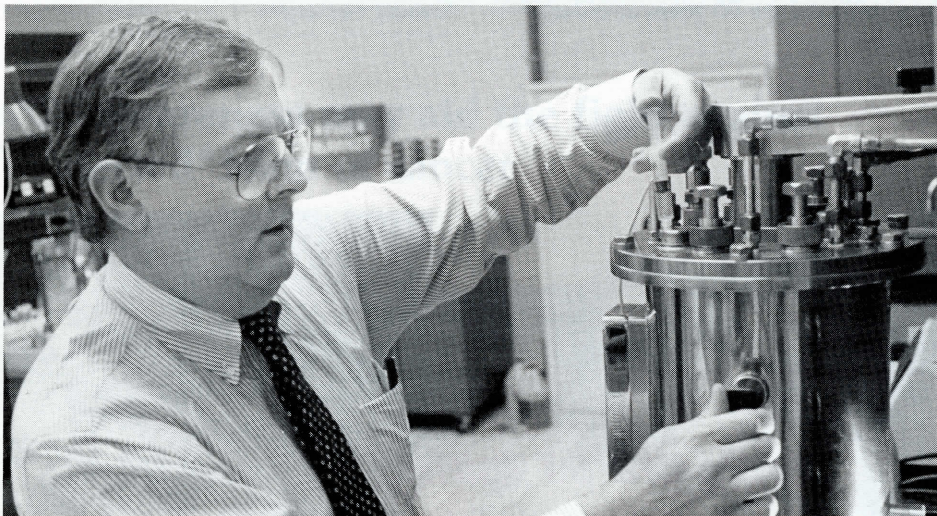
**NATURAL POISON***continued from page 2*

The hormone Dr. Murphy is using to ferry the toxin to these skin cells is called melanocyte-stimulating hormone (MSH). He and his associates, employing recombinant DNA technology, have created a new gene that combines the genes for MSH and the altered diphtheria toxin. This gene, in turn, triggers production of a protein that's made up of both the hormone and the altered toxin.

Some preliminary test-tube experiments suggest that the new protein

will kill off cancerous melanocyte cells without harming normal cells. Dr. Murphy cautions, however, that much more research is needed before the work can lead to treatments.

"We're trying to develop methodologies that may eventually be of benefit to people suffering from cancer," he explains. "Right now, though, we're working at the level of very basic research, and it will be many years before the model systems we're working on can lead to clinical applications." □



(Photo by Bradford Herzog)

Dr. Murphy with an image, called an autoradiograph, that provides a visual guide to chemical structure of new gene his lab is working on.

**You Can Help**

For more information on the important work of the Hubert H. Humphrey Cancer Research Center, and how you can help, send this coupon to:

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**CANCER NOTES**

**CANCER NOTE:** It is estimated that the cancer death rate of 462,000 Americans could be cut by roughly a third through earlier diagnosis and prompt treatment even without any new diagnostic or therapeutic breakthroughs.

**CANCER NOTE:** One important treatment innovation is the transfusion of blood components rather than whole blood. For example, platelets, which help the blood clot, are used to prevent hemorrhaging in cancer patients, and red blood cells are used to prevent anemia.

**CANCER NOTE:** Lung cancer remains one of the most lethal forms of the disease. Only an estimated 13 percent of patients with lung cancer survive five or more years after their cancer is diagnosed.

**QUESTIONS...**

*Answer to question on back panel.*

**A.** Though leukemia still affects roughly 2,500 children each year, and claims the lives of an estimated 800, medical scientists have made remarkable strides against the disease. The most common form can now be cured more than 80 percent of the time. And the progress against childhood leukemia of all types is the main reason cancer death rates for children have been cut in half since 1950.

The development of new drugs, and the use of the drugs in combination with each other along with radiation therapy, has dramatically increased the cure rate for children afflicted with leukemia.

Another reason is the advances scientists have made in treating the complications of the disease and the side effects of treatments. Childhood leukemia is often accompanied by severe infections and heavy bleeding. These may be byproducts of the disease itself or of the strong drugs often used to treat it. In the past, these complications sometimes proved fatal. The new therapies developed for them, however, have markedly cut the risk of a leukemia's victim's dying as the result of an acute infection or heavy bleeding.

A critical next step is to find ways to improve the survival rates for youngsters suffering from the more difficult-to-cure forms of the disease. Humphrey Center scientists and their colleagues at other centers are working hard to achieve that goal.

**Q.** *Does vitamin C show promise as an anti-cancer drug?*

**A.** There has been a great deal of controversy surrounding this issue. A recent clinical trial, though, suggests strongly that vitamin C is not an effective anti-cancer agent.

A group of gravely ill cancer patients was given regular, large doses of vitamin C. A comparable group, meanwhile, was given treatment like that of the first group except that they received no vitamin C. The trial's organizers reported in the *New England Journal of Medicine* that, in terms of the disease's progress, there was no significant difference between the two groups. □



## Who should be tested for colo-rectal cancer?

Since individuals who are middle-aged and over are most at risk for colo-rectal cancer, the American Cancer Society recommends the following:

- For anyone 40 or over, yearly digital exam by a physician.
- For those 50 and over, annual test for evidence of blood in the stool. These tests may be obtained from doctors. Some drugstores sell home-testing kits that allow users to check for signs of blood themselves.
- Also for those 50 and over, sigmoidoscopic exams every three to five years.

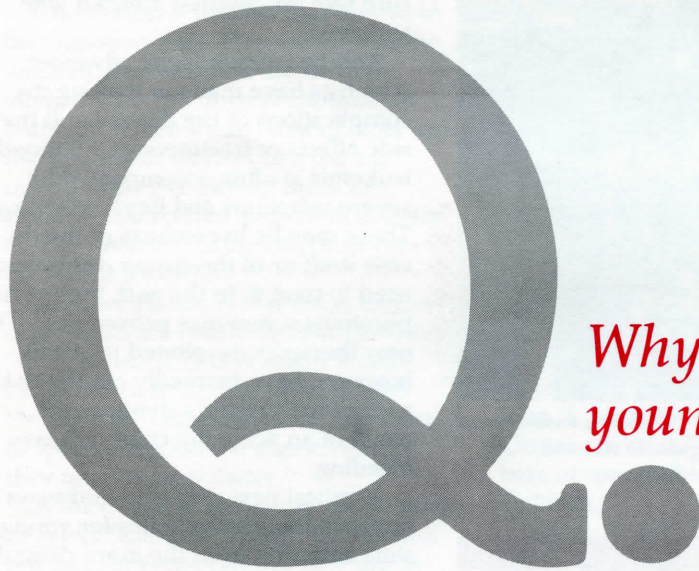
Those with a family history of colo-rectal cancer should start these tests earlier in life. They also may want to ask their doctors about such more definitive diagnostic tests as colonoscopies and barium enemas. □

### CANCER NOTES

**CANCER NOTE:** The appearance of a new mole, changes in the shape or color of an existing mole, or a mole that starts to bleed are all potential signs of malignant melanoma. This is the most lethal form of skin cancer. Most of those afflicted are 50 years or older.

**CANCER NOTE:** Heavy alcohol consumption is associated with an increased risk of cancers of the mouth, throat, larynx, esophagus and liver.

**The Humphrey Cancer Center News** is published by the Hubert H. Humphrey Cancer Research Center of Boston University School of Medicine. John I. Sandson, M.D., Dean of the School of Medicine; *Director*, Herbert H. Wotiz, Ph.D.; *Deputy Director*, Isaac M. Taylor, M.D.; *Editor*, William J. Freeman. "Cancer Notes" information is provided courtesy of the American Cancer Society.



*Why are so many more youngsters with leukemia being cured now than in the past?*

ANSWER ON PAGE 3

Address Correction Requested

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