Research

The Daily Collegian

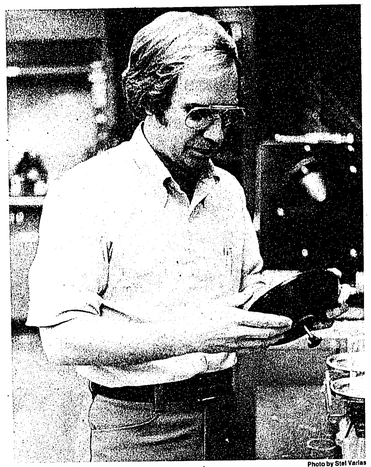


Photo by Stel Varias

Frederick C. Wedler works in his lab on experiments to test chemical analogs which may stop cells from reproducing. Wedler recently received an award from American Cancer Society for his research, but he plans to continue seeking analogs that would eventually help kill cancer cells.

Chemical analogs may kill cancer

By JAN CORWIN
Daily Collegian Staff Writer

Chemical inhibitors which would stop cells from reproducing may be an effective treatment for cancer, said Frederick C. Wedler, associate professor of biochemistry.

Wedler recently received a $155,000 award from the American Cancer Society for his research on chemical inhibitors, or analogs, which may block cell reproduction. He is now trying to make the analogs more specific.

"We're looking for a 'magic bullet' " that will kill cancer cells but not normal cells, Wedler said, but researchers still do not know enough about what differentiates a cancer cell from a normal one.

"What we really need at the moment is a lot more basic research" in cell biology, which is the key to finding an effective treatment for cancer, he said.

The analogs which Wedler is synthesizing in his laboratory would combine with the cell's natural enzymes and bind them, or prevent them from catalyzing the reactions which produce chemicals necessary for the cell to reproduce. Instead of the normal substance, called a substrate, which combines with an enzyme in a normal reaction, Wedler's analog would combine with the enzyme. This would prevent the substrate from combining with the enzyme and block the reaction. The chemicals required by the cell's DNA to reproduce would not be produced, and the cell would be killed.

Wedler said that by killing cancer cells, or at least by slowing their growth, the body's natural defenses would have a chance to take over and deal with the remaining cancer cells.

"Abnormal cells are being dealt with all the time in the body," he said, but a cancer cell may have a difference which prevents the body from recognizing it as abnormal and destroying it. Wedler said the aim of chemotherapy is to reduce the number of cancer cells and encourage the body's natural defenses to take over.

Chemotherapy deals with widespread cancer and malignant tumors in areas that are not easily accesible for surgery, such as brain tumors, Wedler said. He said chemotherapy is also used to treat malignancies in areas that might be adversely affected by radiation therapy.

Drugs used in chemotherapy permeate the entire body, Wedler said, and may kill normal cells as well as cancerous ones. He said this is the reason there are so many side effects to chemotherapy — such as hair loss and vomiting — which make people reject chemotherapy. The optimal doses of anti-cancer drugs are close to the toxic level, Wedler said. By making analogs that are much more specific, the optimal dose will be smaller and less close to the toxic level, he said.

Wedler is experimenting with analogs for four enzymes which are involved in the synthesis of cell DNA, which regulates cell reproduction. Mutant DNA will produce mutant cells when the original cell reproduces. Wedler is working on analogs for glutamine synthetase, asparagine synthetase, aspartate transcarbamoylase and aspartokinase. The analogs would prevent the synthesis of chemicals which are the building blocks of DNA. By binding these enzymes so they cannot carry out their normal reactions, Wedler hopes to kill the cancer cells.

Cancer cells reproduce at an abnormally rapid rate, and the malignant cells often metastasize, or set up new tumors in other parts of the body. Wedler said normal cells have a property of contact inhibition — they stop reproducing when they touch. Cancer cells lose this property and grow out of control, invading the surrounding normal tissue. It is this invasiveness which makes surgery difficult for advanced cases of cancer, and the large number of cancerous cells often cannot be dealt with by the body's natural defenses.

Wedler said that if a treatment can catch cancer in its early stages, the body will have a "fighting chance" to take over and kill the mutant cells itself.

One of the difficulties involved in cancer research is that cancer is not one disease, but has many variations, Wedler said. The complexity of the disease makes it hard to tell exactly where the abnormality is, he said, and a coordinated effort is needed so that researchers can see the entire picture.

Although the cause of cancer is unknown, Wedler said viruses may play a part. He said cats may carry a virus which causes leukemia in children, but it is a slow virus, and the disease may not become obvious until many years after the initial infection.

Viruses have been shown to transform normal cells into tumor-producing cells in animals, according to Arnold J. Levine in an article in "Cancer — The Outlaw Cell." During a viral infection, bits of the viral DNA become integrated with the normal cell's DNA, causing the cell to be transformed, and produce tumors that may be benign or malignant. Wedler said some viruses, called RNA viruses, contain RNA, the complement of DNA. The viral RNA becomes involved in the cell reproduction process and transforms the cell.

Wedler said smoking, asbestos, chemicals, x-rays and ultraviolet light may also cause cancer.

"We're probably not going to get a vaccine for cancer," Wedler said, and even if a vaccine is someday developed for virus-caused cancers, people cannot be vaccinated against cigarette smoke, asbestos, and other possible carcinogens.

John L. Fahey, in another article in the same book, said that the surface of a transformed cell changes, and may not be recognized by the body. Although the body may destroy many abnormal cells, some that closely resemble normal cells may be missed, and establish tumors. Fahey also said that cancer cells may suppress the immune response and as the number of cancer cells increase, the body is overwhelmed and the immune response cannot combat the malignancy.

An analog called PALA, developed by George Stark of Stanford University, has shown promising results in preliminary tests by the National Cancer Institute, Wedler said. He said he is almost ready to send some analogs to NCI in Bethesda, Md., for testing, and is "very optimistic" about the effectiveness of the analogs.

NCI will do animal studies and tissue cultures to test each analog. In preclinical animal studies, tumors will be induced in animals and the effect of the analog tested.

Body's immunity may be modified

By United Press International

In a promising new approach to cancer treatment, a Baylor scientist has developed a way to modify the body's system of immunity and direct natural defenses against marauding cancer cells.

The blood-processing technique so far has produced dramatic results in killing cancer cells and shrinking mammary tumors in two-thirds of the dogs in which it was tried.

Still ahead, however, are critical experiments to see if similar results occur in human breast cancer.

"The step from dog to human is a giant step, and must be taken with great caution," said Dr. David S. Terman, associate professor of medicine at the Baylor College of Medicine.

"From the intensive studies now ongoing in dogs, we should be able to identify the mechanism of this tumor-killing effect," he said in an interview. "With these findings, as well as with adequate demonstration of safety, we could then begin to conceive of an effective way of introducing this to humans."

Of major importance is the fact that Terman's results in dogs, reported to the scientific community in the February issue of the Journal of Immunology, have just been duplicated by originally skeptical researchers at the government's National Cancer Institute outside of Washington.

"We've confirmed his findings of this phenomenon," said Dr. Albert Deisseroth of the cancer institute. "I've looked at this question scientifically and I believe that the observation of tumor regressions induced by the treatment is valid."

Dr. Subhash Bansal, who originated the concept when he was at the Medical College of Pennsylvania, reported two years ago that similar treatment reduced tumor size in a single human patient with colon cancer. But the patient later died of the disease.

Terman collaborated with Bansal, who is now in India, then refined the technique and followed up with detailed studies to determine why it works, its safety and the best ways to use the treatment.

Even if the complicated technical process works in humans, researchers emphasize that considerable work must be done before the treatment can be considered a new weapon in the war against cancer.

The technique involves running an animal's blood through a centrifuge to separate cells from plasma, and then passing the plasma through a special chamber after which it is mixed with the separated blood cells and returned to the body.

The chamber contains a special strain of heat-killed bacteria, Staphylococcus aureus Cowans I, embedded in biological filter paper.

Immunoglobulin, a protein also known as an antibody, sticks to that strain of bacteria. Antibodies are key members of the body's defenses against foreign substances.

Some scientists believe the body recognizes that tumor cells, at least for some kinds of cancers, are foreign to the body and that the immune system produces antibodies to attack specific tumors.

But, the theory goes, the proteins serving as the tumor identification markers — the ones the antibodies recognize — are released in large numbers into the blood stream by the tumor cells. The antibodies then are swamped by this influx of marker proteins, called antigens, and never make it to the tumor.

It is believed that these cancer antigens, the tumor identification proteins, also have the same effect on another weapon the body has against foreign invaders — white blood cells called lymphocytes.

In addition, the complexes of antibody and tumor antigen are believed to inactivate the lymphocyte killer cells.

That is why, according to the reasoning behind this system, the body's natural defenses do not knock out the cancer cells.

The immune complexes — the antibody-antigen combination — stick to the bacteria in the chamber and are removed from the blood. It may be that antibodies are produced or freed in this process to go ahead and attack the tumor cell itself.

Regardless of how it happens, the animal tests demonstrate that this treatment kills cancer cells and causes the tumors to shrink.

One key question is why the process works in some animals but not in others. Terman and his co-workers report progress in resolving that issue and expect to publish their findings and additional results later this year.

New radiation study reported

By United Press International

A powerful beam of X-rays has converted normal human cells into cancerous cells in the laboratory for the first time, opening the way for a new test to evaluate the risks of low levels of radiation.

The development, recently reported by a New York biologist, is considered a breakthrough in radiation research. Heretofore, scientists have been able to do this only with cells of laboratory animals.

Dr. Carmia Borek of the Columbia University College of Physicians and Surgeons, used a dose of 400 rads to transform human skin cells into a malignant state. Such a high dose — a whole body exposure of 400 rads would be fatal — was selected to increase the chance of success.

Even at that dose, Dr. Borek said only one cell in more than 1 million was made cancerous. By comparison, animal cells turn into cancerous cells with a similar radiation dose at the rate of 1 in 10,000.

It is because of these differences in radiation resistance that scientists have been reluctant to use such animal cell studies to evaluate radiation hazards in humans. Most risk estimates for low levels of radiation for humans have been made by uncertain extrapolations from observed damage from high radiation doses.

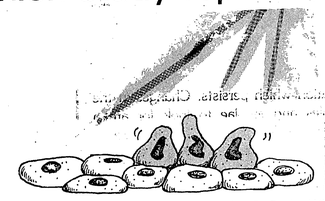


Illustration by Dalia Ilska

A chest X-ray provides a dose of less than one-fourth of a rad.

Dr. Borek proved the cells were turned into a malignant state by injecting them into mice with suppressed immune systems. The converted cells produced tumors in the mice.

Once Dr. Borek determines more precisely the rate of cell conversion in human cells, the system will be able to serve as a new laboratory tool for assessing cancer risks under various radiation conditions.

The test system takes on particular significance because animal cell studies have shown that more radiation damage occurs with numerous small doses compared to a single large dose. Dr. Borek said this finding "is frightening" because it was previously believed radiation broken down into several small doses would permit the cells to repair any radiation damage.

She found, for example, that 25 doses of 2 rads over a period of 5 hours causes 70 percent more damage in the animal cells than a single 50 rad dose.

"It seems different things happen at different dose levels," she said in an interview after discussing the development at an American Cancer Society symposium. The findings have just been reported in the British scientific journal, Nature.

Students with cancer can receive help

By LORRAINE ORLANDI
Daily Collegian Staff Writer

Although the incidence of cancer in college students is minimal, cases nevertheless occur. Agencies at the University and in State College are prepared to help students detect and cope with cancer.

Dr. John A. Hargleroad, director of University Health Services, said if an unusual lump or swelling is detected, the student is usually referred to a surgeon for a biopsy. A biopsy is the surgical removal of the tissue to determine whether or not it is malignant.

On campus, the Ritenour Health Center can diagnose some types of cancer. For instance, he said cervical cancer can be discovered in a routine Pap test.

Hargleroad said the most common types of cancer that affect college students are lymphomas, which affect the lymph glands throughout the body.

Hodgkin's Disease is a lymphoma which, unlike most other types of cancer, is more prevalent among 20-to 24-year-olds than the middle-aged, according to the National Cancer Institute.

Joan Curtis, executive at the Centre County unit of the American Cancer Society, said that 10 years ago Hodgkin's Disease was considered a "death sentence," but today it can be cured in up to 90 percent of the cases.

Hodgkin's Disease is usually treated with high-voltage radiation therapy. The treatment is used to destroy the abnormal cells by bombarding them with high doses of radiation.

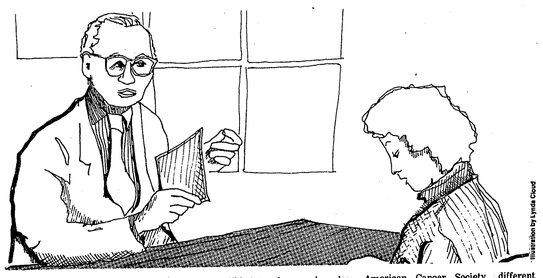


Illustration by Lynda Good

Another type of cancer which has also occurred in University students is leukemia, Hargleroad said. Leukemia is a disease which affects the tissues producing white blood cells.

Chemotherapy, sometimes in combination with radiation therapy, can be used to treat leukemia. Chemotherapy is the administration of drugs orally, intraveneously or through injection to attack the cancer cells.

Cancer of the testes accounts for only one percent of all cancer in males, but it is important to college-aged men because it occurs mainly in the 20 to 35 age group. This type of cancer has also occurred at the University, Hargleroad said.

Testicular cancer is usually treated with surgery, removal of the testicle. This treatment can be supplemented by radiation therapy and sometimes chemotherapy.

In the process of destroying abnormal cells, radiation treatment and chemotherapy destroy some normal cells. This can lead to side-effects such as nausea, vomiting and hair loss, all of which disappear with termination of treatment. But according to the American Cancer Society, different people react to treatment in different ways and side-effects are not inevitable.

Ilene Gelman is a board member of the American Cancer Society and an employee in the office of Dr. Richard H. Dixon of State College where students with cancer are often referred for chemotherapy treatment.

Some students at the University stay in school while receiving treatment, she said. A student can come in for treatment on Friday in order to have the weekend to recover from any side effects that might occur. But she agreed with the American Cancer Society, saying that side-effects are often brought on by the patient's anticipation of them rather than the treatment itself.

"Patients come in for treatment and sometimes get sick in the office before they even receive any treatment because they expect the treatment to make them sick," she said.

State College has no facilities for students requiring radiation therapy, Curtis said. The Divine Providence Treatment Center in Williamsport, the Hershey Medical Center and the Geisinger Medical Center in Danville can treat students requiring radiation therapy, she said.

For students with a transportation problem, a van makes free trips daily from the Centre Community Hospital, Mountainview unit, to the Divine Providence Treatment Center. The American Cancer Society also aids students with transportation problems, Curtis said.

The American Cancer Society provides other services such as financial assistance, counseling and home care equipment, she said.

Gelman said one of the most important steps in coping with cancer, as with any crisis, is learning to communicate about it.

"Communication is the biggest problem," she said. "I encourage a patient to talk, and to understand that he or she is not the only one (to have to cope with cancer)." Gelman uses small group discussions with patients and their families to encourage communication.

Most types of cancer are difficult to predict or prevent. Therefore, the American Cancer Society stresses early detection through routine examinations like the Pap test and regular self-examinations of the breasts or testes.

One kind of cancer which can be linked to a cause, especially in women, is lung cancer. According to the 1980 Surgeon General's report, cigarette smoking now contributes to one quarter of all cancer deaths in women.

Lung cancer does not occur among young people, Curtis said. It is an accumulative disease and can take 25 to 35 years of cigarette smoking to develop. But in order to be prevented later, steps like not smoking must be taken now, she said.

The Cancer Society urges people to be aware of cancer's seven warning signals:

- A change in bowel or bladder habits.
- A sore that does not heal.
- Unusual bleeding or discharge.
- A thickening or lump in the breast or elsewhere.
- Indigestion or difficulty in swallowing.
- An obvious change in a wart or mole.
- A nagging cough or hoarseness.

Gelman said great strides have been made in controlling and curing cancer in recent years.

"Things are getting better and better," she said. Through the use of different medications, not only have the chances for longer life for cancer patients increased, but the quality of that life has improved, she said.

CANCER CAN BE BEAT!

. . . BREAST:

FACTS:

Breast cancer strikes 90,000 American women every year. One of 13 women is destined to get breast cancer during her lifetime. With a death toll of over 34,000 women annually, it's the major cancer killer of women. It also strikes men, but very infrequently. The cause of breast cancer is unknown. There is a common misconception that an injury to the breast can cause breast cancer, but there is no evidence to support this. The injury may call a woman's attention to a tumor that is already there.

Most breast cancers are first discovered by women themselves or their sexual partners. Since breast cancers that are found early and treated promptly have excellent chances for cure, learning how to examine her breasts properly can help a woman save her own life. Once a month is often enough and the best time is right after her menstrual period. After menopause, any set day, such as the first of the month, is a good time to do a breast self exam. Use the simple three-step (BSE) procedure shown here.

Breast tissue is often nodular and its consistency varies from woman to woman. The breast may feel less lumpy after the menstrual period when hormonal levels are lower. Normally, the skin of the breast is smooth, but weight loss or advancing age may cause wrinkles. The size and shape of nipples also vary. Remember that a woman's breasts seldom match exactly — the shape is determined by heredity, weight and by the strength of supporting ligaments.

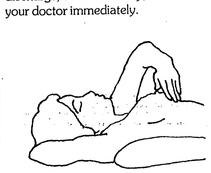
Cancer within the breast usually occurs as a painless lump or thickening, frequently in the upper outer portion of the breast; although it can occur anywhere in the breast. It can spread from the site of origin to the lymph nodes in the armpits, neck, chest and eventually to other parts of the body via the bloodstream. Besides a lump, or thickening, other changes that should be checked by a physician are swelling, puckering or dimpling, redness or skin irritation which persists. Changes in the nipples and areolae to look for are a whitish scale, distorted shape, inverted nipple or nipple discharge. Pain and tenderness should also be reported to the physician.

In the shower:
Examine your breasts during bath or shower; hands glide easier over wet skin. Fingers flat, move gently over every part of each breast. Use right hand to examine left breast, left hand for right breast. Check for any lump, hard knot or thickening.

Before a mirror:
Inspect your breasts with arms at your sides. Next, raise your arms high overhead. Look for any changes in contour of each breast, a swelling, dimpling of skin or changes in the nipple. Then, rest palms on hips and press down firmly to flex your chest muscles. Left and right breast will not exactly match — few women's breasts do. Regular inspection shows what is normal for you and will give you confidence in your examination.

Lying down:
To examine your right breast, put a pillow or folded towel under your right shoulder. Place right hand behind your head — this distributes breast tissue more evenly on the chest. With left hand, fingers flat, press gently in small circular motions around an imaginary clock face. Begin at outermost top of your right breast for 12 o'clock, then move to 1 o'clock, and so on around the circle back to 12. A ridge of firm tissue in the lower curve of each breast is normal. Then move in an inch, toward the nipple, keep circling to examine *every part of your breast*, including nipple. This requires at least three more circles. Now slowly repeat procedure on your left breast with a pillow under your left shoulder and left hand behind head. Notice how your breast structure feels.

Finally, squeeze the nipple of each breast gently between thumb and index finger. Any discharge, clear or bloody, should be reported to your doctor immediately.



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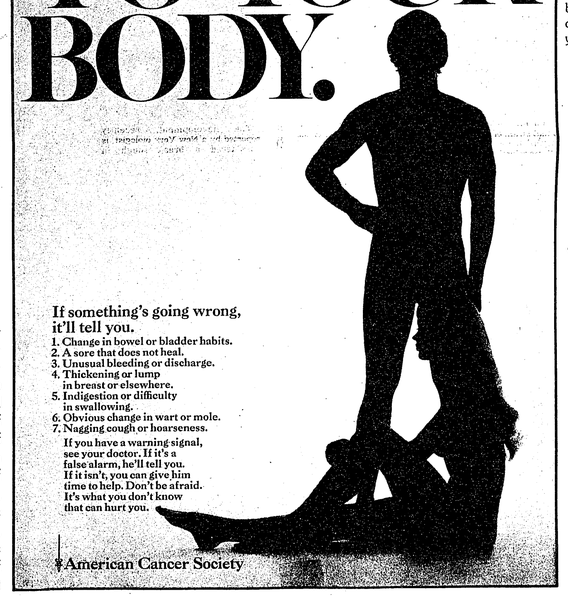
LISTEN TO YOUR BODY.



If something's going wrong, it'll tell you.

1. Change in bowel or bladder habits.
2. A sore that does not heal.
3. Unusual bleeding or discharge.
4. Thickening or lump in breast or elsewhere.
5. Indigestion or difficulty in swallowing.
6. Obvious change in wart or mole.
7. Nagging cough or hoarseness.

If you have a warning signal, see your doctor. If it's a false alarm, he'll tell you. If it isn't, you can give him time to help. Don't be afraid. It's what you don't know that can hurt you.

American Cancer Society

This message was brought to you in concern by your local chapter of The American Cancer Society and The Daily Collegian

. . . TESTICULAR

FACTS:

Because it is a disease of young men — occurring mainly in the twenty to twenty-five age group — it assumes an importance greater than its frequency. In men between the ages of twenty-nine and thirty-five it is the most common type of cancer. Each year, about 2,500 cases of testicular cancer are diagnosed in American men. The actual number of cases, however, may be much higher, because malignancies that start in the testes and then spread to other sites, such as the lymph nodes or lungs, were often reported under the latter sites. If caught early, this is one of the most curable of all cancers; if not, it is one of the most deadly.

The first sign of testicular cancer is usually a slight enlargement and a change in the consistency of the testes. Although these tumors may be painless, there is often a dull ache in the lower abdomen and groin, accompanied by a sensation of dragging and heaviness. Because of a lack of early symptoms and of pain, patients usually do not go to the doctor for several months after discovering a slightly enlarged testis. This delay in reporting to the physician probably accounts for the fact that in 88% of patients testicular cancers have mestastasized (or spread) by the time they are diagnosed.

Self-Examination:

A simple self examination that takes only three minutes once a month is the individual's best hope for early detection of testicular cancer. This is best performed after a warm bath or shower when the scrotal skin is most relaxed. Each testicle should be examined gently with the fingers of both hands by rolling the testicle between the thumb and fingers to check for any hard lumps. If a lump or a nodule is found, it should be brought promptly to the attention of a physician.

After surgical removal of the affected testicle, treatment is determined by the type of cancer involved and the extent of spread, or metastasis. The malignancy is almost always confined to the one testicle; therefore, the remaining testicle is perfectly capable of maintaining sexual potency or fertility.

"Maybe it will go away."

The five most dangerous words in the English language.