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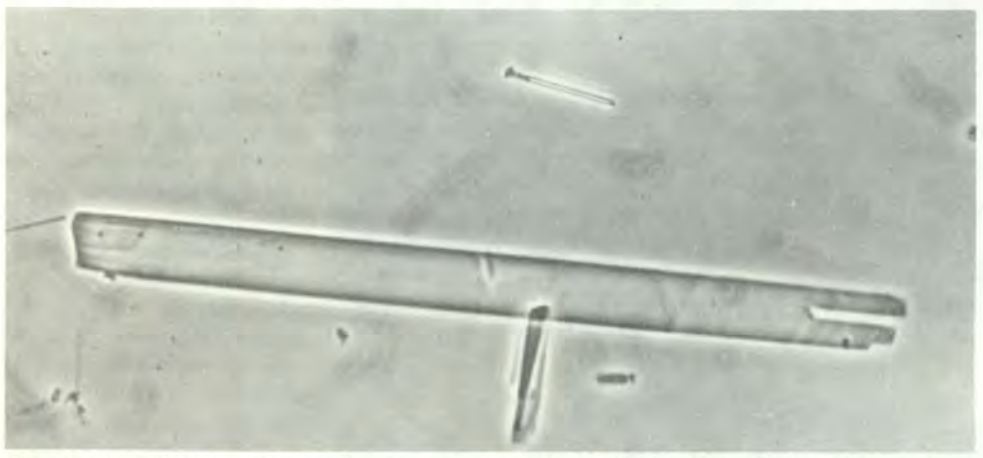
THE
OREGON HEALTH
SCIENCES UNIVERSITY
NEWS

The Oregon Health Sciences University News is published to inform students, employees, faculty, and friends of the institution's programs, activities and events.

Potential exists for OHSU major cancer center

If any word conjures up varied and wide-ranging feelings and thoughts, it is "cancer."

In the victim, it evokes shock, dismay, fear and anger; but, happily enough, in recent years it has also come to be associated with realistic hope for potential cure. In the scientist devoting a lifetime to probing the underlying biology of cancer, the word arouses a sense of challenge and of commitment to a relentless, but optimistic, search. In many of us, the word stimulates awe over the miracles that laboratory and clinical investigators have generated during the past few decades. Thus, in the late 1940's, a diagnosis of acute leukemia in a child was a virtual death sentence, and today more than half the children with acute leukemia can be cured.



The substance above is called a reductase and was crystallized for the first time, then photographed by the OHSU's Toshihiro Sugiyama. For details of Dr. Howard Mason's study of the reductase's involvement in the cancer process, see story on page 4.

These and related thoughts led to the dedication of this entire issue of the OHSU News to a review of some of the university's programs and special capabilities that relate to cancer. Laboratory studies by individuals such as Drs. Howard Mason and David Kabat, among many others, offer great promise for an ultimate understanding of the basic mechanisms of the disease. Then, undoubtedly, hard upon the heels of that advance will come the ability to prevent and cure with consistency and certainty.

Until the basic insights are developed, it is essential for an army of health professionals to continue their programs for testing new drugs and new combinations of drugs so that we can move forward with improvements in survival rates and patient comfort. Accordingly, in this issue you will read about many projects devoted to clinical trials and anti-cancer drugs.

Looking to the future, it is reasonable to forecast that when the understanding we seek ultimately is developed, it will come in large measure from concepts and experiments that fall under the term "molecular biology." Thanks to rapid and explosive advances in studies of the biological behavior of individual chemical molecules, particularly those that make up genes, we will, in time, unravel innumerable mysteries related to the control of the biological systems underlying growth, development and, indeed, life itself. Dr. Ed Herbert, a major contributor to molecular biology, will, before too long, walk through the front door of a new institute for molecular biology here at the university. The knowledge that will be amassed in that center and in laboratories already functioning in the university today will play an essential role in the struggle against cancer. I invite your attention to Dr. Herbert's article on this page as a glimpse into the future.

The preparation of this special issue revealed that the Oregon Health Sciences University has within its halls the matrix for a major center for cancer research and treatment. In days to come the university will build on this strength and will continue to provide the citizens of Oregon outstanding clinical and scientific ability in relation to this complex, many-layered, sometimes fearful, sometimes hopeful word "cancer."

Leonard Laster, M.D., president, Oregon Health Sciences University

Research institute to advance knowledge of cancer process

Cancer is perhaps our most dreaded disease, and if we are to conquer it we must first understand how normal cells are transformed into cancerous cells.

The application of the powerful tools of molecular biology to the study of this process has in recent years revealed specific genes in the human body that become active during cancerous cell transformation. These "oncogenes" can now be reproduced, or cloned, by newly-developed gene transfer methods, and studied to determine how their activity is controlled. The oncogene also can be removed from one type of cell, cloned, and transferred to another type of cell to study how a new cullular environment influences the activity of the gene.

Furthermore, the structure of the oncogene can be altered (mutation) to allow scientists to determine the effect of mutation on the activity of the gene. This technique will enable us to determine the specific nature of the alterations in genes that lead to their activation during the transformation of normal cells into cancer cells.

It also is possible to transfer genes from one species to another to determine how the genes function in the embryo during the course of its development and in the adult organism. For example, a growth hormone gene has been transferred from a rat to a mouse embryo, producing a giant mouse by the alteration of its genetic make-up.

Hence, the methods of molecular biology, which will be the focus of work in the OHSU's Institute for Advanced Biomedical Research (IABR), will enable us to study the genetic basis of cancer and other disease processes. Our ability to develop preventive measures against these diseases ultimately will depend on the depth of our understanding of these fundamental genetic processes.

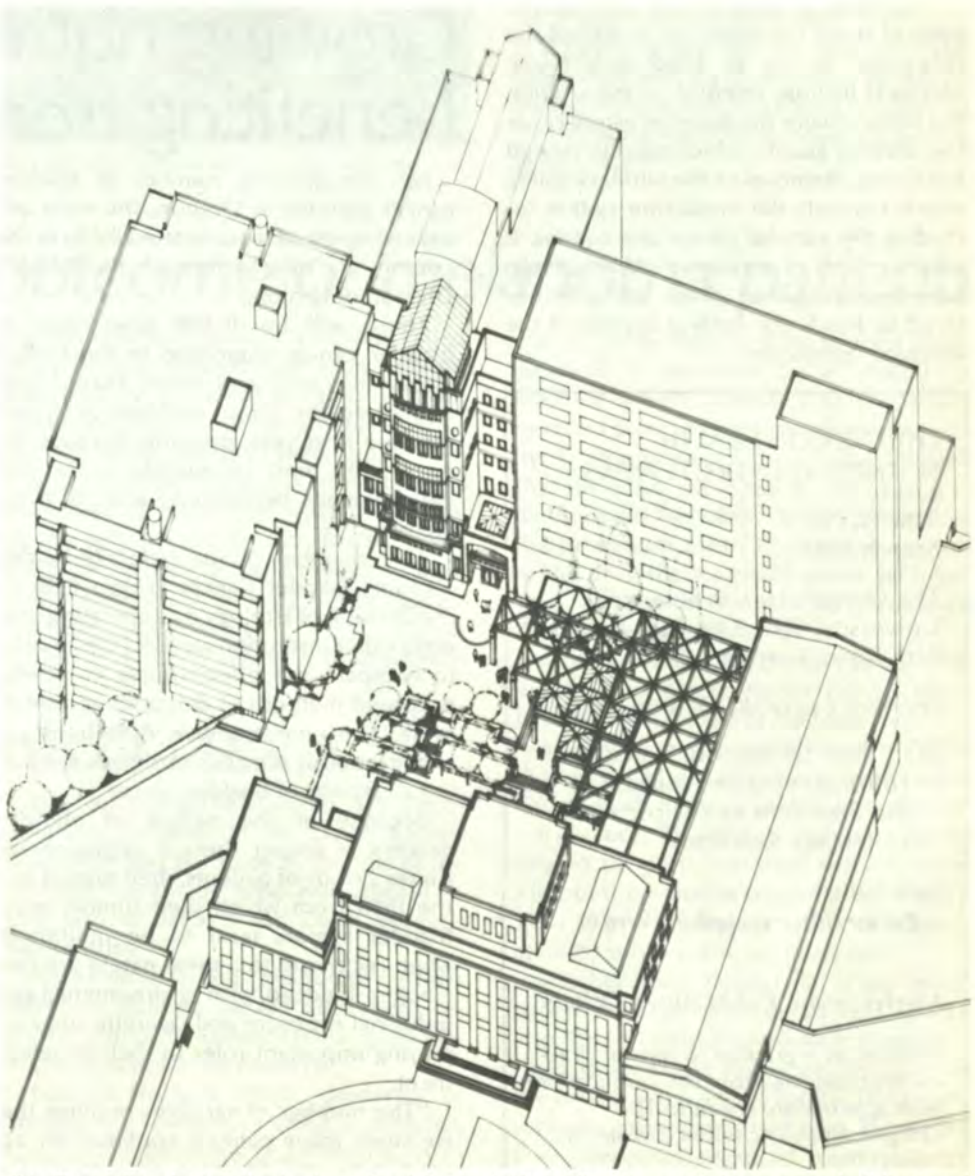
Molecular biology and biochemistry also will enable us to gain a better understanding of the immune system. The body's natural defense against cancer depends on the integrity of the immune system. A normally functioning immune system will eliminate cancerous cells by producing natural "killer" cells which can recognize cancer cells and destroy them.

This function of the immune system, and in particular of natural killer cells, depends, in turn, on the neuroendocrine system. This system produces chemical substances called peptides which control the activity of the killer cells.

At this point, we know very little about how neuroendocrine peptides regulate the immune system. But studies to be pursued in the IABR will help enable us to understand this process better. Once the normal process is understood, we will be able to analyze the defects in the immune system that allow cancer cells to grow and destroy the host.

When built, the IABR will provide an outstanding environment for the pursuit

(continued on page 3)



This illustration depicts the Institute for Advanced Biomedical Research (uppermost building) and proposed courtyard. Groundbreaking is scheduled for this summer.

Lab seeks hormone clues to fight breast cancer

It has been nearly 90 years since the discovery that some breast cancers are greatly influenced by sex hormones and that treatment of patients by increasing or decreasing the amounts of these hormones in the body could improve their chance of survival.

But only in the last decade has this information contributed to the development of methods for predicting the potential effectiveness of treatment. "The problem," says Edward Keenan, Ph.D., "has been determining which patients have hormone-dependent tumors."

Keenan, an associate professor of surgery and assistant professor of pharmacology in the School of Medicine, is director of the OHSU's Hormone Receptor Laboratory, one of a small number of university-based research facilities in the country that is able to provide this information to physicians and their patients. The OHSU laboratory performs some 2,000 analyses a year for patients in Oregon, Washington, northern California, Alaska and Montana, providing "very significant information about a breast cancer patient," according to Keenan.

An estimated 35 percent of all breast cancers are dependent on female sex hormones, either estrogen or progesterone, or both. The key to discovering these hormone-related malignancies is detecting steroid "receptors" in breast tissue samples. Samples of tumors removed at surgery (mastectomy is usually the initial form of treatment of breast cancer) are frozen and sent to the OHSU receptor laboratory where a sophisticated test determines whether the tissue has the steroid hormone receptors that make the tumor hormone-dependent.

Hormone receptors are proteins that specifically bind with the estrogen or progesterone hormones that normally enter certain tissue cells. This combination of receptor and hormone then enters the cell's nucleus where it influences the way the nucleus controls production of other cell proteins which, in turn, regulate the way the affected cell will reproduce.

Cancerous cells with many hormone receptors cannot survive without the hormones; hence, Keenan says, "Patients whose cancers contain high levels of receptors will have a greater probability of response to hormonal types of therapy."

Treatment is designed to deprive the body of these hormones or to disrupt the receptors' ability to bind with them. Methods include removal of the ovaries, the body's major producer of estrogen, or the adrenal glands, which secrete related hormones. Removal of the pituitary gland, which controls the endocrine system including the adrenal glands and ovaries, is another form of treatment. Alternatively, hormone-antagonist drugs are administered to block the nuclear actions of the receptor complexes.

Hormone-dependent breast cancers will sometimes respond to large doses of estrogen, an irony that has long perplexed physicians.

Sixty percent of those patients with high levels of estrogen receptors respond to hormonal therapy. That rate increases to 80 percent in women with tumors possessing both estrogen and progesterone receptors.

In women whose tumors lack both receptors, the likelihood of response to hormonal therapy is no greater than 10 percent.

The significance of detecting these receptors and initiating appropriate treatment is great in breast cancer, the leading cancer among women.

"If physicians conclude that endocrine therapy is not likely to work, they can use other approaches, such as radiation or chemotherapy," Keenan says. "Before the advent of the receptor test, months to years could elapse before it was established that endocrine treatment wasn't effective and that tumor cells were growing again."

The ability to predict the response of patients with breast cancer to endocrine therapy is not the only benefit receptor analysis provides. Recent studies indicate the presence of estrogen and progesterone receptors also provide important information about the possible outcome of a patient's cancer. Research has shown that women with hormone-dependent tumors survive without recurrence significantly longer than those whose tumors are not dependent on hormones.

The presence of progesterone receptors, especially, is proving to be a useful determinant in predicting how long a patient will survive without their breast cancer reappearing.

"Receptor analysis gives us a glimpse of the biology of these breast cancers and provides us with data we can use to make rational decisions regarding the treatment and prognosis of patients," Keenan says. "Because of the invaluable information they provide, receptor analyses should be performed for every patient with primary breast cancer and for patients with metastatic disease, if possible."

Edward Keenan, Ph.D., associate professor of surgery and assistant professor of pharmacology (left), and Harper Pearse, M.D., head of Urologic Oncology, both use the OHSU's Hormone Receptor Laboratory to determine which breast and prostate cancer patients will respond to hormone therapy.

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Growing number of bladder cancer patients benefiting from OHSU urology study group

For the growing number of bladder cancer patients in Oregon, the most advanced forms of treatment available in the country are offered through the OHSU's Division of Urology.

There will be 40,000 new cases of bladder cancer diagnosed in the United States this year and more than 12,000 related deaths. Those numbers likely will increase next year, primarily because the population most susceptible to the disease, persons between 50 and 70, is increasing.

As a member of the federally-funded National Bladder Cancer Project (NBCP), the Division of Urology is cooperating with eight other institutions around the country to compare the effectiveness of newly-proposed methods of diagnosis and treatment. The nine member institutions are simultaneously pursuing protocols evaluating all aspects of bladder cancer.

Because of the nature of bladder cancers, a proper therapy approach requires a study of patients, their tumors and the field from which their tumors arise. Bladder tumors tend to be multifocal, often recur and to a great extent are carcinogen-induced, with environmental and industrial exposure and cigarette smoking playing important roles in their development.

"The number of variables requires that we study many patients continuously according to well-designed protocols if the desired data is to be statistically significant," said Harper Pearse, M.D., head of urologic oncology.

At the OHSU, 200 patients have been entered into various protocols of the NBCP. Pearse is the principal investigator for the group at the OHSU and is on the executive board for the central organization.

> There will be more than 40,000 new cases of bladder cancer diagnosed in the U.S. this year and more than 12,000 related deaths. Those numbers will increase next year.

Active NBCP protocols are evaluating all aspects of superficial bladder cancer, including therapy with different drugs which have proved efficient in causing tumor remissions. Also, two new protocols involving the use of interferon are being considered.

"We have protocols for every type of patient with bladder cancer," Pearse said.

Treatment also is available at the OHSU for patients with cancer of the prostate and the less common renal, testicular and penile cancers. Prostate cancer is the second commonest cancer in males and the third leading cause of death from cancer among men. Routine rectal examinations, however, could significantly reduce the death rate of prostate cancer patients, Pearse said.

Effective therapy is available for patients in which the disease has not spread. At the OHSU, surgery and radiation therapy are used to treat localized prostate cancer, and evaluations currently are being made of implantable irradiation sources to spare selected patients some of the side effects that accompany radical surgery or external irradiation.

These treatments are rendered virtually ineffective in patients whose disease is not diagnosed until after it has spread beyond the prostate gland, which is located below the bladder and astride the urethra. "At least half of the patients with extensive localized disease at the time of diagnosis die within five years," Pearse said. "And half of the patients whose disease has spread from the prostate gland die within three years. We need to alert males to this common cancer."

Many patients with cancer that has spread beyond the prostate gland can be effectively treated with hormonal manipulation. In cooperation with the OHSU's Pleasants Memorial Prostate Cancer Research Center, the Division of Urologic Oncology has developed hormone receptor analyses that may help physicians predict which patients should respond to hormonal therapy.

(See related story on this page.)

Man-made antibodies may find immune defects

OHSU scientists are exploring piece by piece the body's immunological protective system with the hope that what they learn will lead to better methods of treating patients whose defense mechanisms have failed to respond to the presence of cancer.

Denis Burger, Ph.D., professor of microbiology and immunology at the Veterans Administration Medical Center. Mark Vetto, M.D., professor of surgery in the School of Medicine, and David Regan, M.D., off-campus associate are trying to characterize the components of the entire human immune protective system.

The body's immune system is activated by the invasion of bacteria, viruses or their poisons. To provide an aggressive defense against a sophisticated attack from thousands of potential disease-producing agents, the immune system has evolved into a highly organized and regulated system involving many different cell types and components.

"Just as in any highly-tuned piece of machinery, a defect in a single component, for example, the brakes in a car, can render the system useless," Burger said. "To repair this disease defense mechanism, it is necessary to diagnose the problem; in other words, are your brake pads worn out or are you out of brake fluid? To diagnose a defect in the immune system, one has to be able to characterize each cell type or component of the system."

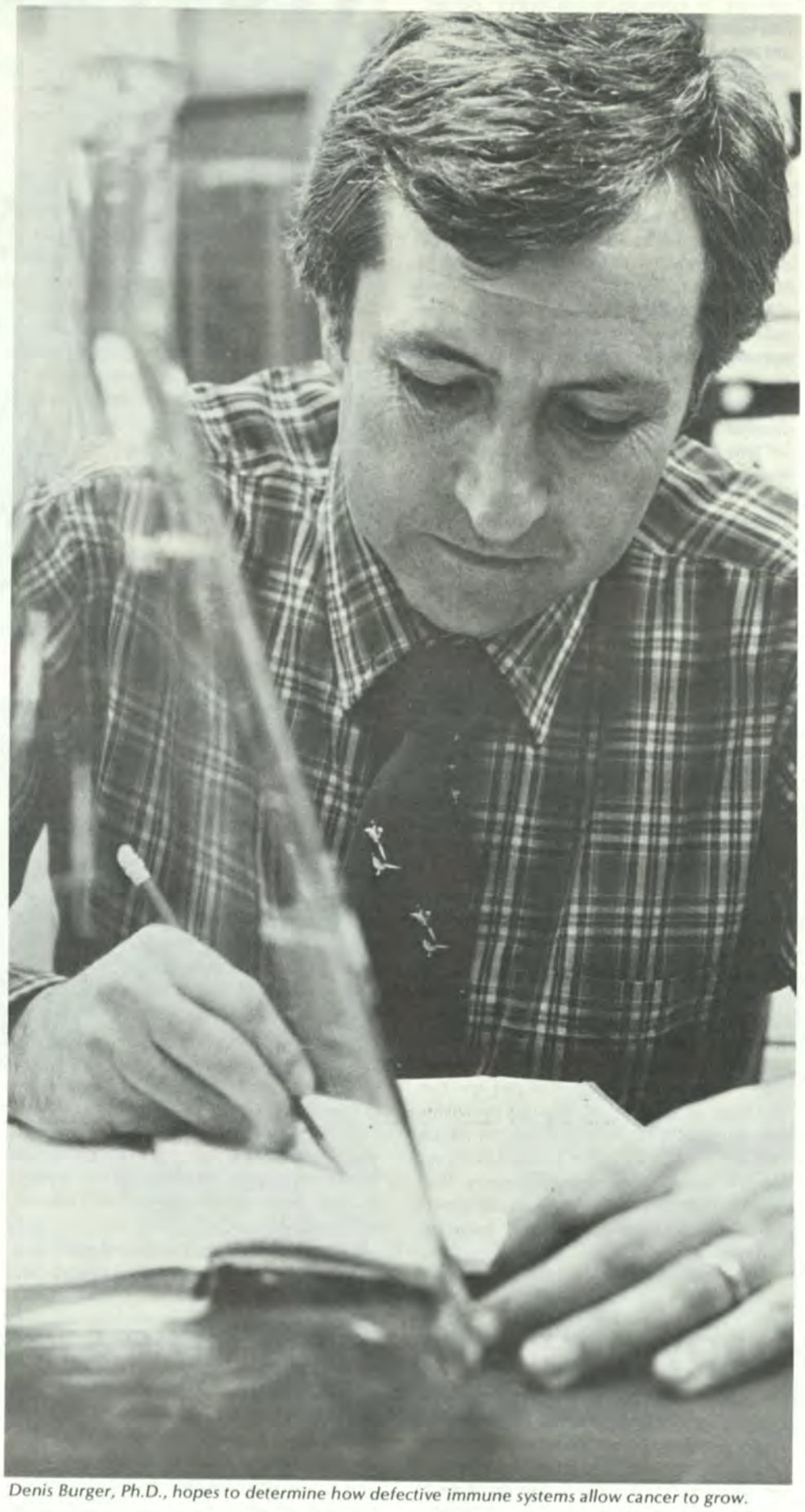
It has been recognized for several years that patients with cancer have defects in their immune systems which allow tumor cells to escape from immune control. Using monoclonal antibodies, Burger and his collaborators hope to develop a method of uncovering and correcting these defects. Beyond their potential as a diagnostic tool, monoclonal antibodies show promise of actually helping to treat cancer.

Monoclonal antibodies are man-made substances that react specifically to molecules found on the surfaces of bacteria, viruses or malignant cells. They are the product of the fusion of an antibody-producing white blood cell, called a lymphocyte, with a mouse myeloma, a type of cancer capable of reproducing endlessly. This mixture of thousands of different and immortal hybrid cells, called hybridomas, can be screened to select the specific hybridoma cell that produces the particular antibody desired.

The cell then can be grown (cloned) into a single, pure cell line to produce immortal hybridoma cells that will turn out vast quantities of the desired antibody.

Three years ago Burger and his associates began developing monoclonal antibodies to all the various subsets of cells in the immune system. "We've characterized about 20 different facets of the immune system so far," Burger said. "I can't predict how many it will take to characterize the entire system. This work is like walking up a long flight of stairs — you can't see the top, but you're making progress."

Once the entire system has been characterized, cancer patients can be analyzed to see if they are missing a component necessary for the development of an effective immune response.



Denis Burger, Ph.D., hopes to determine how defective immune systems allow cancer to grow.

Monoclonal antibodies are the product of the fusion of an antibody-producing white blood cell, called a lymphocyte, with a cancer capable of reproducing endlessly.

"If we can find the defective component, then we can devise a stimulant to affect the defect and get the system working against the disease," Burger said.

Burger is among the many scientists also pursuing the therapeutic potential of monoclonal antibodies, either as independent agents or in combination with additional forms of treatment. "The simplest approach," he said, "would be to find a way to treat cancer with the monoclonal antibody itself." But, Burger added, monoclonal antibodies as "homing devices" could play an important role in future chemotherapy by carrying cancer drugs directly to tumor cells.

"We already have some very potent drugs to kill cancer tumor cells," Burger said. "But there is also a problem with their toxicity causing side effects."

Research suggests that each kind of cancer cell bears antigens, substances which can stimulate the production of antibodies, that are unique to those cells. The goal of Burger and other scientists is to develop large quantities of the antibodies that specifically recognize these antigens. These could then be injected alone or attached to cytotoxins (cancer-cell poisons) to seek out and destroy the cancer cells without harming normal cells.

Burger's group has for the last three years been making monoclonal antibodies against certain tumor antigens for eventual use in therapy protocols, hopefully as early as this year.

Combined treatment improves outcome of melanoma patients

Malignant melanoma is a rare skin cancer that once almost always resulted in death unless it was detected early. But the outlook for many melanoma patients in the Northwest and parts of California has greatly improved because of treatment being used by cancer specialists at the OHSU.

Malignant melanoma was diagnosed in only about 15,000 Americans last year; it occurs in eight or nine of every 100,000 Oregonians. But its appearance, which has been linked to both sun exposure and repeated trauma, is increasing.

Although melanoma is a rare cancer, staff of the OHSU's Division of Surgical Oncology sees many patients who come from throughout Oregon and its neighboring states to be treated by a method called hyperthermic isolation perfusion. William Fletcher, M.D., head of the division, helped pioneer the development of perfusion treatment nearly 25 years ago.

This method combines the standard treatment of melanoma, surgical removal of the primary tumor, with strong, localized chemotherapy. The treatment is used in patients whose primary tumor has appeared in an extremity.

During the procedure, a tourniquet is applied to the limb, and the process of circulation is assumed by a heart-lung machine which continues to oxygenate, heat and pump blood through the extremity. Then a powerful drug is run through the limb for an hour to destroy any microscopic "satellite" tumors present. In this procedure, six to 10 times the amount of the drug that normally would be tolerated by the body can be circulated through the affected limb.

After perfusion, the primary tumor and, usually, the lymph nodes (which often have become diseased) are removed.

A study recently completed at the OHSU showed that of 122 patients with melanoma which had not spread past the primary tumor, 81 percent of those patients treated by perfusion survived five years without their disease reappearing. This is a 10 to 20 percent improvement over treatment by surgery without perfusion.

Another study showed that 57 percent of patients whose melanomas had spread into the extremities and lymph nodes survived disease-free following perfusion at the Health Sciences University. This represents an improvement of 20 to 35 percent over previously reported treatments not involving perfusion.

Appointments

Persons wishing to take advantage of the many cancer services offered at University Hospital and featured in this special publication can arrange for appointments directly to the following clinics by calling the central appointment number, 225-8505, or by calling the clinics directly between 8:30 a.m. and 4 p.m. Monday through Friday:

Dermatology	225-8600
Family High Risk	225-8514
Gynecology	225-8984
Obstetrics	225-8984
Ophthalmology	
Adult	225-8613
Child	225-8646
Ololaryngology	
Head/Neck	225-5675
Pediatrics	225-8505
Surgical Oncology	225-8514
Urology	225-8637

Cancer process a focus of IABR

(continued from page 1)

of cancer research. First, we will recruit faculty capable of setting up the most advanced approaches being used in gene transfer technology. These people will have been pioneers in the study of cancerous cell transformation.

Second, molecular approaches to the study of the nervous, immune and endocrine systems will be the focus of the institute.

The institute will provide the molecular underpinnings for the research outlined in this article and for ongoing projects at the OHSU including the study of viral oncogenes in progress in Dr. David Kabat's laboratory and the study of the role of the immune system in neoplastic disease in Drs. Grover Bagby's and Denis Burger's laboratories.

We envision strong collaborative efforts between institute faculty and these research groups to answer crucial questions in the field of cancer research.

Edward Herbert, Ph.D., professor of chemistry, University of Oregon, director, Oregon Health Sciences University, Institute for Advanced Biomedical Research.

Scientists exploring chemical causes of cancer

Plastics, synthetic fibers and fuels, food additives and preservatives — we are becoming increasingly exposed to a wide array of new chemicals.

More than 5 million chemicals have been identified or synthesized, and in our daily lives we encounter perhaps thousands of them in what we breathe, touch, eat and drink.

And many of these are known carcinogens, substances which cause cancer.

Significant progress has been made in the last 20 years toward understanding the mechanisms by which environmental chemicals and atmospheric contaminants cause cancer. This is a major area of research since an estimated 60 to 80 percent of all cancers originate in this manner.

It already is known that many of these substances do not themselves cause cancer, but first must somehow be transformed in our bodies into cancerous agents. What this transformation is; where and how it occurs; and what can be done to prevent it all are questions that are part of intense research in laboratories around the world, including that of Howard S. Mason, Ph.D., professor of biochemistry in the OHSU School of Medicine.

This avenue of study stemmed from the discovery by investigators at the National Institutes of Health (NIH) in the early 1960s that liver contains a system of enzymes which helps dissolve drugs and other foreign chemicals by adding oxygen to their molecules.

It was found that it is the role of this liver enzyme system to protect us. But because the range of chemicals we encounter is so diverse, it sometimes does just the opposite, transforming foreign substances into carcinogens.

These activated foreign substances become particularly reactive to DNA, causing mutation by producing altered DNA molecules which underlie the transformation of normal cells into cancer cells. Mason called the discovery of this process "one of the great steps forward in modern cancer research."

There are other important aspects of this enzyme system, which is called cytochrome P-450, that have been discovered.

P-450 exists in life forms throughout nature, including bacteria, plants and animals. In complex multi-organ species, like humans, P-450 appears in many different tissues such as lungs, adrenal glands, arterial walls and liver.

In addition to its universal distribution, P-450 systems are able to increase in amount when the body is exposed to foreign compounds, "as if the body is able to call up its defenses when it needs them," Mason said. "For instance, when barbiturates are taken repeatedly over a period of days, the amount of P-450 in the liver doubles or triples."

The ability of P-450 to respond to need is called induction. "Induced" patients may become relatively resistant to the barbiturates because, among other reasons, they are more quickly metabolized, hence, they disappear more quickly.

"This phenomenon has many important medical and pharmacological correlations," Mason said. "In liver diseases which destroy P-450-containing cells, drugs last much longer than when P-450 is functioning. The drugs may accumulate and become dangerous if they are administered as usual."

The actual number of specific P-450s that exists is unknown. Daniel Nebert, M.D., a 1964 School of Medicine graduate now directing a research group at the NIH, has proposed that in humans there may be a specific P-450 system for each foreign chemical that enters the body.

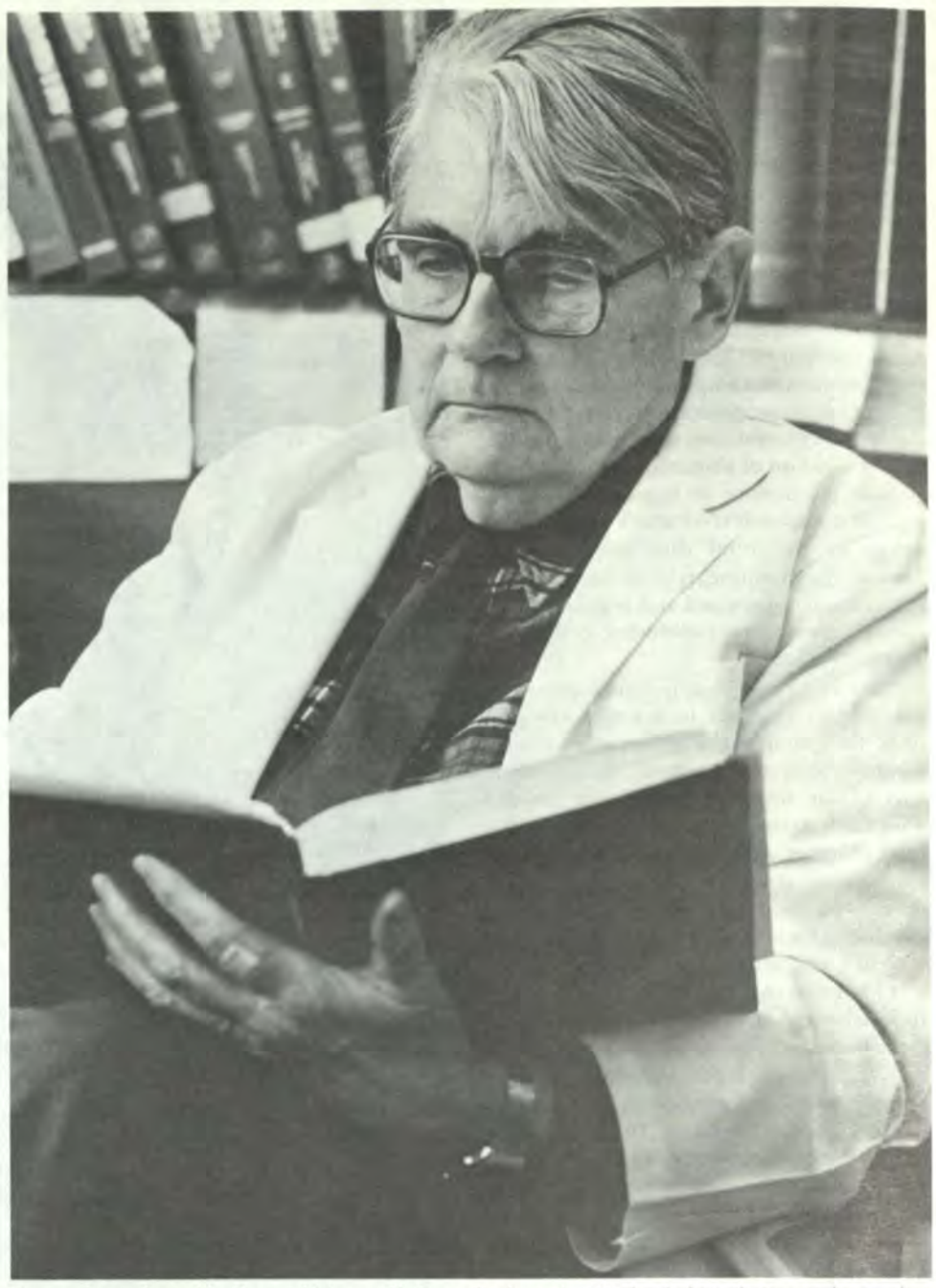
In the 1970s Mason and a colleague at Tsukuba University in Japan made a definitive characterization of a component of the P-450 system called the reductase and opened another phase into understanding the metabolism of carcinogens.

Mason now is studying the reductase, which is responsible for transferring electrons to P-450 during the oxygenation process. (Electrons are supplied by food and play a major role in biological energy conservation.)

The reductase was crystallized for the first time in Mason's laboratory by Toshihiro Sugiyama, Ph.D. This research, which involves exposing protein crystals to X-rays and recording patterns of beams that emerge from the crystals, has made possible detailed three-dimensional maps of protein structure.

Research on P-450 conducted worldwide has led to a profound understanding of the manner in which drugs and foreign substances become mutagens and develop into carcinogens.

"This knowledge, combined with contemporary molecular biological and genetic attacks upon gene expression in normal and cancer cells, is bringing us very close to a deep understanding of the cancer process and the time when rational specific treatments of cancers can be attempted," Mason said.



Research conducted by Howard Mason, Ph.D., and other scientists has led to a better understanding of how drugs and other foreign substances develop into cancer.

Surgery, heat therapy offer hope for some sarcoma patients

Certain cancer patients who once were candidates for amputation and those who have exhausted all other forms of therapy are benefiting from treatments being offered in the OHSU Division of Surgical Oncology.

H. Stephens Moseley, M.D., surgical oncologist at the OHSU, is using methods of treatment for bony sarcomas that are sparing the limbs of patients who might otherwise be treated by amputation.

Sarcoma, tumors of the soft tissue or bone, accounts for only about 1 percent of all cancers. Bony sarcoma, according to Moseley, "is basically a tumor of teenagers." It appears to be related to the growth spurt at the time of puberty and tends to appear in bones that grow very rapidly, usually in a leg or arm. If unchecked the disease can spread to the lungs where it can be fatal.

Working with Charles Bird, M.D., associate professor of orthopedics and rehabilitation at the OHSU, Moseley is using a method of treating bony sarcoma of the leg in which the tumor and diseased portion of the bone are removed and replaced with a metal prosthesis. The treatment is used in combination with chemotherapy and has proved as effective as amputation.

"We save the leg, and our rate of success in preventing local recurrence of the tumor is the same as if we had amputated," Moseley said. "In some cases, however, it remains to be seen if patients are more mobile than they would be with an artificial limb."

For more than two decades, the OHSU has been a leader in the treatment of soft tissue sarcoma, using multiple forms of therapy which include chemotherapy, surgery and radiation. Using this combination of approaches, the recurrence rate of soft tissue sarcomas has been less than 10 percent, compared to rates as high as 50 to 90 percent when surgery is the only form of therapy.

The OHSU Division of Surgical Oncology also is using a new procedure that is showing promise as a treatment for sarcomas and other tumors close to the surface of the body. The procedure is called hyperthermia (heat therapy) and is being used by Moseley and an OHSU associate, Thomas Johnson, M.D., radiation therapist, in combination with other treatments.

"This is a very exciting project," Moseley said. "We are now treating patients using some very advanced computer regulated and controlled radio frequency wave equipment that allows us to selectively heat tumors in certain patients. This offers a new modality of cancer therapy."

During the procedure, heat is applied either through a large stationary unit or a smaller local applicator, both of which can be programmed to deliver a pre-determined amount of heat to a tumor. Temperature probes can be inserted into the tumor and into normal tissues for monitoring. The tumor can be heated up to 107 degrees. (The cells inside a tumor are vulnerable to heat damage because their blood supply, which would help dissipate the heat, is poor.)

Hyperthermia currently is being used only with patients who have exhausted all other forms of cancer treatment. But, Moseley said, "As we become more sophisticated in using heat to kill tumor cells, this may be the treatment of choice for some patients. This is a field which is still in its infancy, and we have a great deal to learn.

"But it does appear hyperthermia is going to be another effective weapon to be used in the fight against cancer."

University Hospital assumes cancer nurse program

The University Hospital Nursing Service and School of Nursing have joined resources to ensure survival of a unique program that is training nurses in Oregon and southwest Washington to provide the special care cancer patients need.

The Oregon Nurses Cancer Education Program (ONCEP) was run by the Oregon Comprehensive Cancer Program (OCCP) from 1979 until last year. But when funding from the National Cancer Institute expired in 1983, University Hospital assumed directorship of the program.

ONCEP was developed to provide educational resources and programs designed to improve nurse's knowledge of the many forms of cancer. "There is no greater challenge in nursing today than caring for the cancer patient," said Jean Moseley, R.N., M.N., a clinical specialist in oncology and an ONCEP staff member.

In September 1983 the OHSU began offering ONCEP seminars in Portland, Salem, Medford and Bend. These can be taken individually or as part of an entire ONCEP curriculum.

Nearly one in every four persons will get cancer; some 3 million Americans are now living with the disease. Most nurses need — and are seeking — more information on how to care for these patients. Thus far, 42 nurses have completed the entire ONCEP curriculum and have been certified as oncology nurse clinicians, according to Melanie Kemper, R.N., M.A., another clinical specialist in oncology and ONCEP staff member.

"ONCEP is invaluable in giving nurses confidence in what can be done to help cancer patients," added Sharon Firsich, R.N., M.S., past director of the program. "There has been so much progress in cancer care, but that information has to get to more health professionals in the field. When they have this knowledge, they no longer feel hopeless. They feel in control. They feel as if they can help their cancer patients."

"There is no other way for nurses in Oregon and southwest Washington to receive this education," added Maureen Whitman, R.N., M.N., director of continuing education in the School of Nursing. "ONCEP has become a model around the country for cancer education. We are extremely pleased to be able to continue the program."

New model to study human cancer growth found

The insidious process through which a normal human cell is transformed into a cancerous cell is occupying the attention of scientists worldwide.

Among the investigators whose research is helping to enhance the understanding of this malignant transformation is David Kabat, Ph.D., professor of biochemistry in the OHSU School of Medicine. Kabat's work has led to the identification of a new gene that causes cancer and provides a more valid model for the study of the disease in humans.

It has long been suspected that some forms of cancer are caused by viruses, and, indeed, there now is evidence of a virus that causes human adult T-cell leukemia. But it has been a difficult task determining whether human cancer viruses exist. "In mice or other animals, we can take an extract of the tumor cells, inject them into a mouse and show that they have a virus capable of transmitting cancer," Kabat explained.

"But we can't take extracts from human cancer and inject them into humans."

In non-human vertebrates, viruses which produce cancer are common. Some of these viruses initiate immediate tumor growth; others emulate the evolution of human malignancies and cause a gradually progressive cancer.

Researchers have concentrated on the former category of viruses, since they cause cancer so rapidly in a laboratory setting, and have found they act through "oncogenes," which are genes capable of converting normal cells into cancer cells.

The discovery of oncogenes in these viruses led to proof that animal cells, too, can carry oncogenes. These normally may exist in the body in a dormant or carefully regulated state, and can be activated by chemicals or other harmful substances in the environment to produce cancer.

Now, an OHSU research team led by Kabat has for the first time analyzed in detail a virus that causes a cell transformation more similar to that which occurs in humans.

Working with the blood cells of mice, Kabat found that an infective agent called Friend erythroleukemia virus alters the surface membrane of a normal cell. The Friend virus causes mice to develop acute leukemia, a cancer of the blood cells. The mice bone marrow cells proliferate and spill into the spleen and liver, forming cancerous growths.

The virus is a package of three genes, one of which is capable, by itself, of converting a normal cell into a cell which subsequently forms a leukemia. This single oncogene produces a molecule called glycoprotein that attaches itself to the outside of the cell and sabotages the cell's ability to perceive signals from the body.

"Normally cells reside in specific areas of the body and respond to specific signals which are mediated by contact with other cells and by contact with hormones," Kabat said. "During these interactions, all of these signals have to be transmitted through the surface of the cell. So proper membrane function is crucial. When this virus attacks the cell surface, the resulting abnormal cell can no longer perceive its environment, and it proliferates uncontrollably in the body."

Kabat and his associates, post-doctoral fellows Richard Bestwick and Curtis Machida, have cloned the oncogene of this virus in order to determine its precise structure. By these methods they can produce in carefully controlled conditions a limitless supply of the cancer gene to study.

Discovery of this new oncogene provides a model more valid than previous models, Kabat said.

"They are suspect," he said, "because we already know that in humans the progression of a normal cell into a cancer cell is not an immediate transformation. For example, 20 years may have gone by between the exposure to radiation of Hiroshima victims and the appearance of leukemia."

Our oncogene is unique because it is a kind of seed oncogene. It is like a bad new seed that triggers an abnormality.

"It is a useful model to determine how cancer insidiously progresses in humans over the course of time."

A Big Day in the life of a brave little cancer victim

"We get very involved with our patients," says Dr. Derry Ridgway (shown with leukemia patient Tiffany). "So if they do well, it makes us feel good and if they do poorly, we grieve."

Across the examining room, at the far end of an intent stare, hangs a picture of Tiffany astride a beautiful white pony. Both are decked out in parade regalia. Tiffany, it seems, has her mind on that big day rather than the Big Day she awoke to a few hours ago.

She has reached a point where her monthly Little Days — regular leukemia checkups at the OHSU Doernbecher Children's Hospital Pediatrics Clinic — are no big deal. But on every third visit Tiffany's doctor, Derry Ridgway, a pediatric oncologist, pokes a long needle into one of her pelvic bones and draws a sample of marrow to check for cancer cells. Ridgway calls these visits Big Days, and even for a 7-year-old who after 18 months has learned to put up with a potentially fatal disease, they still are a big deal.

Fifteen years ago the chance of Tiffany surviving leukemia was less than 10 percent. Today more than half of the children like her are cured. Still, those odds are not nearly good enough for the OHSU's pediatric oncology staff.

Ridgway does his best to set Tiffany at ease. "You know, a lot of people faint just by watching bone marrows," he tells her. "Doctors, nurses, students . . . Grandmothers are the best. They don't have any problem. And mothers usually do pretty well. But fathers . . . well, you might as well get the pillows out before you even start."

Tiffany isn't in the mood; her stare shows it. "This isn't the most well-loved thing," her mother says.

"Let's get this over with, OK?" Ridgway asks. "Can I get you to lie down on your stomach?" Tiffany lies down, but it is obvious her mind is elsewhere.

Leukemia patient, Sam, helps Dr. Ridgway during a recent checkup by drawing his own blood. Today more than half of the children with leukemia are cured.

"That, of course, is your back," Ridgway says. "You would think that after all this time you would have memorized that so you could show your mother what we've taught you here."

Tiffany manages a smile. It's almost time, and the anticipation, she has learned, is perhaps the worst part of Big Days.

Now everyone is ready, and in a matter of five minutes the Big Day is over for another three months. Tiffany was brave. She cried some, but a little girl with a big disease and a needle stuck in her bone could have gotten away with a lot more.

She deserves the toy she now gets to choose from the chest provided by the Candlelighters, an organization for parents of children with cancer. And she deserves the high quality of care she receives at the Doernbecher Pediatrics Clinic.

"We try to make the kids' last thought about their visit here a positive thought," Ridgway says.

He worries a lot about this, as do the OHSU's other pediatric oncologists, Robert Neerhout, M.D., chief of pediatrics, and Lawrence Wolff, M.D., an assistant professor of hematology and oncology. Not all of the children with cancer or leukemia who come to the Doernbecher are like Tiffany. For every brave soul there is a child who can't help but act the way any child — any person — being treated for a very serious disease would be expected to act. But a common thread of trust binds all of these children with the pediatric oncology staff, which works hard to earn and preserve it.

"We are all friends with our patients," Ridgway says. "Some of the things we do to these children are truly traumatic; they are things that children have no business putting up with. But 2- and 3-year olds jump up on the table and let us do things to them that make them cry because they trust us. They understand.

"We ride a lot on forgiveness."

"Tiffany went through hell when she first came here," Tiffany's mother says. "But one time she told me that she wished she would get sick again so she could come back. I've never been to any other clinic or doctor's office where they were this friendly and made you feel this good. It helps a lot."

Ridgway dashes into the newly-renovated clinic's lounge where Sam, another 7-year-old with leukemia, rests in front of a videotape of the "Black Stallion." In a flash, Sam is baggage over his doctor's shoulder, destined for a blood drawing. Sam shows a visitor a long horizontal scar through which his spleen was removed, then pulls the plunger Ridgway has handed him and watches blood from his arm spill into the syringe.

"No discount for self-service," Ridgway informs him.

Like Sam and Tiffany, half of the children the OHSU's pediatric oncologists care for have some type of leukemia, a disease of the blood-forming tissue. About every other week they see a child who is newly-diagnosed with the disease.

Most of these children are treated through protocols designed by the Children's Cancer Study Group (CCSG), a consortium of specialists around the country that is researching and treating children's cancer. Members of the CCSG (the OHSU is the only health center in Oregon that belongs) simultaneously conduct trials of new therapies so promising treatment can more quickly become part of standard care.

"We work very closely with community pediatricians and other physicians to see that children throughout the state can benefit from the most current treatments available," Neerhout says. "We have nearly all the available investigational drugs as well as the latest information about which combination of treatments offers the best chance of success."

Tiffany is part of a CCSG protocol. "Her prognosis is extremely encouraging," says Ridgway.

"We get very involved with our patients," he continues as Tiffany heads for the door with a stuffed frog under her arm and a smile spread across her face. "Sometimes we go to pizza with them or they come over to our house. We know very much about their lives. So if they do well, it makes us feel good, and if they do poorly, we grieve. We try very hard to make them do well."

Hill offers array of cancer care

In the limited space available, it is impossible to devote equal attention to or describe all of the OHSU's clinical and research work dealing with cancer. The following are capsule summaries of more of the work being performed and services available on the Hill:

Southwest Oncology Group

University Hospital is the state's only member of the Southwest Oncology Group (SWOG), a nationwide consortium of 30 hospitals funded by the National Cancer Institute to share information gained from common studies of new drugs and treatment protocols.

Through SWOG, OHSU cancer specialists gain access to the newest cancer drugs being used in the country. These drugs have previously been tested and are not available through any other source.

However, under the guidance of William Fletcher, M.D., head of surgical oncology and principal investigator of SWOG at the OHSU, community physicians throughout the state and in Washington, Idaho and California can join certain SWOG protocols to benefit cancer patients in their communities.

Radiation Therapy

SWOG is just one of several cancer study groups to which various oncology units of University Hospital belong. And all of these groups rely on the OHSU's Department of Radiation Therapy for portions of their treatment, according to department of chairman William Moss, M.D.

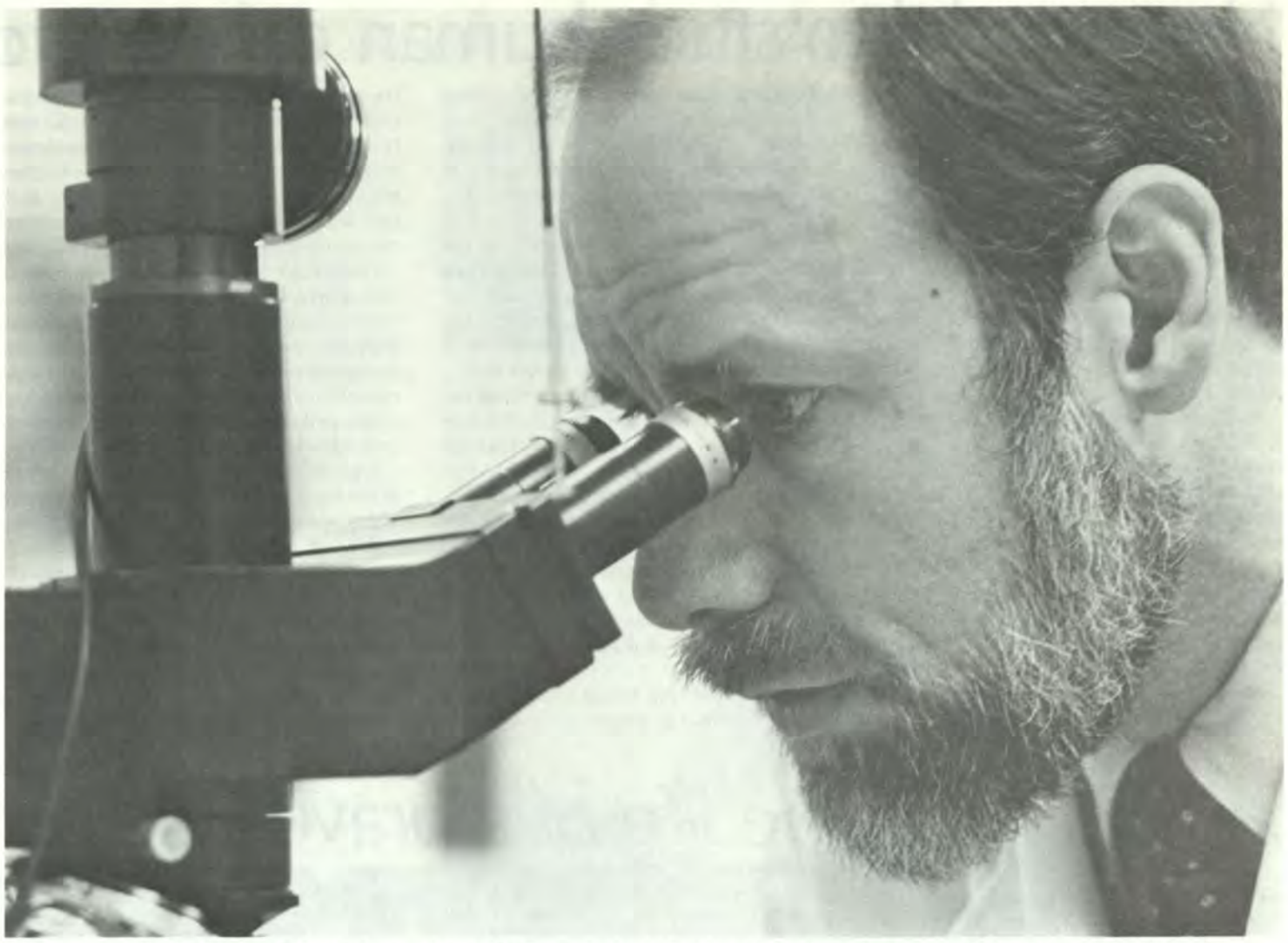
Moss, an OHSU colleague says, "wrote the book on radiation therapy." And, indeed, his "Radiation Oncology: Rationale, Technique, Results," generally is regarded as the standard radiation therapy text in the field.

Moss' department houses several machines that are highly efficient in killing cancer cells. The newest unit, and the department's workhorse, is a linear accelerator which generates X-rays and directs them in a highly precise manner to any part of the human body.

The beams are tailored to treat patients according to their individual needs and to an accuracy of within two to three millimeters. The accelerator is powered by 6 million volts and its output requires patients to spend no more than a couple of minutes in treatment.

Because of the distribution of the rays, they are better tolerated by patients than beams produced by previous generations of accelerators, Moss says. "The beam is terribly precise. The sharpness of the beam enables the normal tissue to be spared more efficiently. And with the newer highly-penetrating beam, the X-rays can pass through the body to the tumors with much less damage to the outer tissues and skin."

(continued on page 7)



Work performed in the Osgood Leukemia Center, directed by Grover Bagby, M.D. (above) is leading to better ways of identifying and treating leukemia.

Diagnosing, treating leukemia easier

Blood cell research conducted in the OHSU Osgood Leukemia Center has led to a dependable method of identifying patients with leukemias and also has provided an accurate means of predicting their response to new drug therapy.

About 300 Oregonians each year are diagnosed with leukemias, a group of diseases of the blood and bone marrow, the body's cell "factory."

All leukemias involve the bone marrow. Some also affect lymphocytes, a type of antibody-producing white blood cell. These "acute" leukemias usually strike children. The body's white blood cells fail to develop into mature normal cells. These juvenile cells are useless, but they continue to divide and multiply in the bone marrow and eventually suppress the production of the remaining normal blood elements which progressively impairs the body's production of blood cells.

"Non-lymphocytic" leukemias may affect the white blood cells (except lymphocytes) and red blood cells. These are usually adult diseases. By the time they are diagnosed, the patients usually are critically ill.

Until the early 1970s, the only way to learn more about leukemia was to study dead bone marrow cells. "That," according to Grover Bagby, M.D., director of the Osgood Center, "was like trying to understand the function of a General Motors factory from looking at snapshots of the assembly line."

Now, Bagby and his colleagues are studying live abnormal bone marrow cells to determine how to make them behave more "normally."

In the course of their investigations, Bagby's group described for the first time a process in which monocytes, another type of white blood cell, produced a hemopoietic (blood forming) hormone which induced other cells to stimulate the production of lymphocytes. Previously it was believed that monocytes, alone, stimulated the production of lymphocytes.

Bagby's discovery has led to an increased understanding of how normal blood cell production is regulated. "This is important because in order to understand what is wrong with an abnormal leukemic cell, you first have to understand how a normal cell functions, and this brings us one step closer," Bagby said.

Increasing the understanding of how leukemia cells work will lead to "much more effective and humane treatments than we have now," Bagby added.

Working with live bone marrow cells that have been cultured outside of the body, Bagby has been able to reliably diagnose the presence of leukemia, which, in many of its forms is difficult to detect until it is far advanced, and thus is difficult to treat. "We've found that what we see in our cultures regarding the behavior of

> 'Studying dead marrow cells was like trying to understand the function of a General Motors factory from looking at snapshots of the assembly line.'

cells is an accurate reflection of what happens inside the body," he said. "We now have the capability of taking marrow cells from a patient's body and seeing exactly how they behave. If they behave in a malignant fashion, we can accurately predict that there is a disease present."

This same process also allows Bagby to predict a leukemia patient's response to newer, non-conventional forms of treatment. Bagby's studies justify the use of some substances which otherwise might be considered too dangerous for clinical use.

For instance, leukemia patients treated with a powerful steroid called prednisone have had complete remission of their disease if cultures of their leukemia cells have first responded to the drug.

Another study has resulted in treatment with vitamins A and D which have shown promise in changing leukemic cells to normal cells in very early leukemic disorders. Vitamin therapy, according to Bagby, not only could prove effective in preventing the leukemia, it also could result in remissions in patients who already have developed the disease.

As director of the Osgood Leukemia Center, Bagby shares this information as a hematology and oncology consultant to community physicians. Patients in the Osgood Center's study group number about 400 and are referred by physicians from the Northwest and from as distant as Alabama and Switzerland.

"We see five to six patients a month with bone marrow disease and provide them with diagnostic and therapeutic information they can't get anywhere else," Bagby said.

Teamwork helps head/neck cancer patients

Each Monday a group of health professionals from University Hospital gathers to share information and progress reports on hospitalized patients with head and neck tumors. The team reviews each patient's condition, discusses their medical plan and reviews instructions regarding home care follow-up needs.

This team approach is typical of the attention OHSU head and neck cancer patients receive throughout their treatment, whether it is on an inpatient or outpatient basis. "The goal of the team is to provide the most comprehensive and effective treatment for the patient while assisting the patient and the family to adapt to the diagnosis of cancer and its treatment," said Edwin Everts, M.D., the head and neck surgical oncologist in the Department of Otolaryngology/Head and Neck Surgery. "This we accomplish through counseling, support group contact, education, rehabilitation and resource referral."

The extensive OHSU network of professionals each year cares for about 100 new patients diagnosed with tumors that appear in the upper respiratory and digestive tracts, including the nasal sinuses, oral and nasal cavity, pharynx, larynx and upper esophagus. Head and neck tumors appear primarily in men between 50 and 70 who have a history of smoking, tobacco chewing, heavy alcohol use and/or poor dentition. Most of these tumors are preventable, and, if detected early enough, they are 90 to 95 percent curable.

Smokers and tobacco chewers should have yearly examinations for early detection of oral cancers, Evert said.

Head and neck tumors may affect the patient's speech, swallowing and physical appearance and can have a profound impact on his or her daily living. "This necessitates a comprehensive range of services for treatment, surgical reconstruction and rehabilitation," Everts said.

The Head and Neck Surgery Department works with the OHSU School of Dentistry's Department of Oral and Maxillofacial Surgery to reconstruct jaws damaged by surgery and radiation; with dysphagia therapists to teach new methods of swallowing to patients who have had surgery involving the tongue, palate, pharynx or larynx; and with speech therapists who teach new forms of communication to patients who have had total laryngectomies.

OHSU social workers and continuing care coordinators play a vital role in helping cancer patients and their families find the appropriate local support and resources.

"Long term support, patient and family education, understanding and rehabilitation are all very important in our total treatment plan," Everts said. "The goal of our team is to cure the patient and return him to his family and community to function as fully as possible. Our treatment doesn't end with the cure."

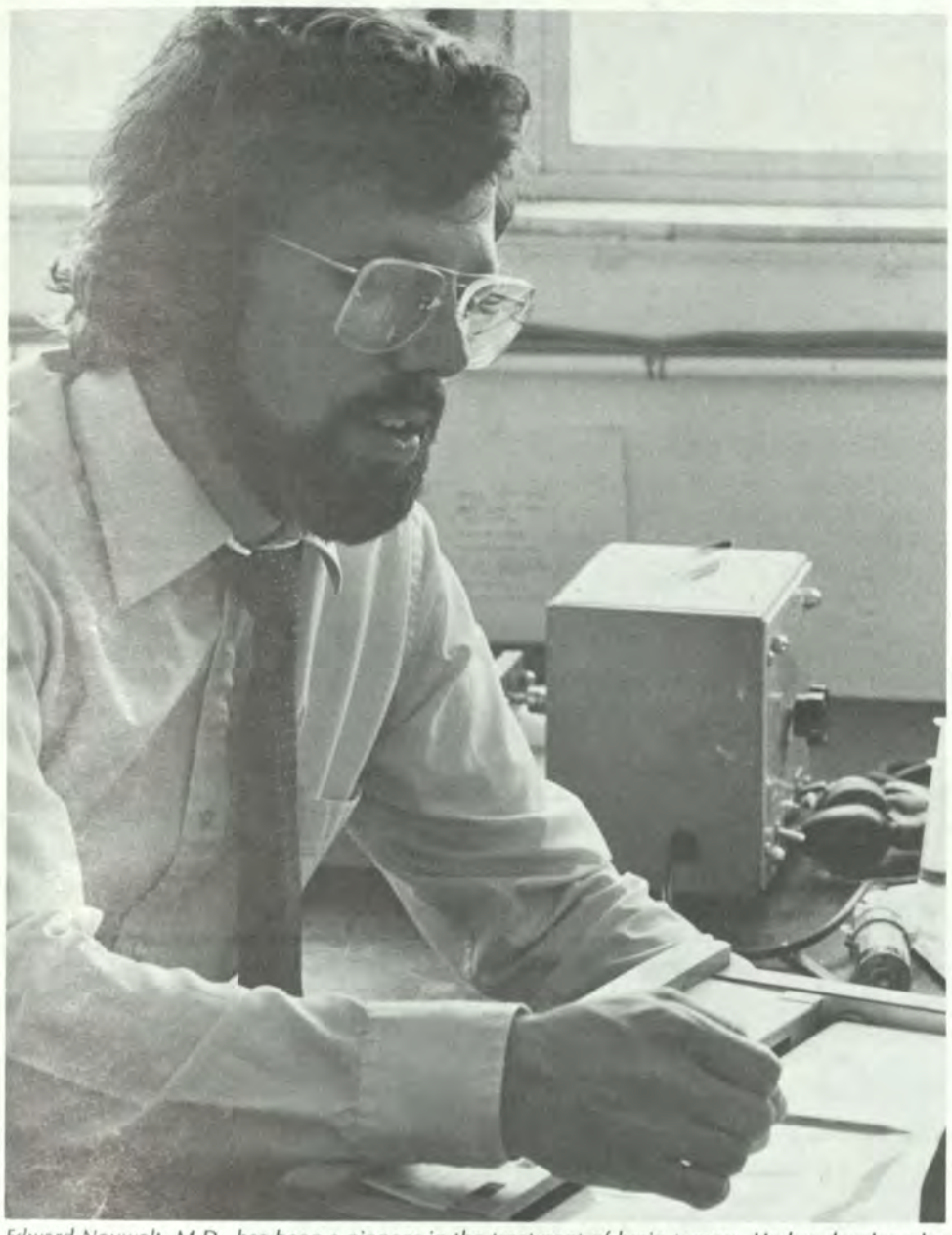
OHSU surgeon pioneering brain tumor treatment

The pineal gland is a tiny, cone-shaped structure whose location deep in the center of the brain has kept it somewhat secluded from science and medicine.

For centuries physiologists were unable to ascribe any function to this component of the endocrine system. And surgeons, when faced with the prospect of having to remove a pineal gland invaded by tumor, traditionally were unsuccessful as often as 70 percent of the time.

But the mystery of the pineal gland is beginning to unravel because of the work of Edward Neuwelt, M.D., an associate professor of neurosurgery and assistant professor of biochemistry at the OHSU. Neuwelt's work has led to a better understanding of the function of the pineal gland. The techniques he uses, and in some instances has designed, are increasing the effectiveness of surgical and chemotherapeutic treatment of pineal and other brain tumors.

Some pineal gland tumors are very sensitive to radiation therapy and/or chemotherapy and can be treated this way. "But others are not sensitive to these treatments," Neuwelt said. "And the only way you can treat them is by surgical removal."



Edward Neuwelt, M.D., has been a pioneer in the treatment of brain tumors. He has developed a method of increasing the effectiveness of drugs to fight brain cancer.

Neuwelt has removed the pineal gland of about 30 patients with tumors at the OHSU and before that at the University of Texas Southwestern Medical School in Dallas. Due to a combination of factors, the mortality rate of patients undergoing this surgery has dropped from above 30 percent to below 5 percent.

Better microsurgical techniques account for much of the improvement in results, Neuwelt said. Also, a new piece of equipment is providing OHSU surgeons with another effective tool against brain tumors.

The Cavitron Ultrasonic Surgical Aspirator (CUSA) delivers controlled ultrasound vibration, irrigation and suctioning to the operative area. The instrument's tip vibrates up to 23,000 times per second, fragmenting tumor tissue which is then suctioned away.

The ability to adjust the vibration speed of the CUSA allows it to be used in areas that may be too dangerous for other forms of surgery.

"The CUSA gives us the opportunity to do the best possible operation more quickly and accurately and thus more safely than before," Neuwelt said. "We can remove a tumor in half the previous time. This decreases the patient's time in surgery and the doctor's fatigue."

Neuwelt recently removed a highly malignant pineal gland tumor from the brain of a 5½-month-old girl. Because of the confined space available to operate, Neuwelt said, "We probably wouldn't have been able to get the tumor out without the CUSA."

The CUSA is available in Oregon only at the OHSU (through University Hospital and the Veterans Administration Medical Center).

It was following the removal of a pineal gland tumor in 1981 that Neuwelt and an OHSU colleague, Alfred Lewy, M.D., Ph.D., assistant professor of psychiatry, pharmacology and ophthalmology, were able to provide fellow scientists with significant insight into the gland.

Lewy was the first to show that light affects the pineal's production of the plasma hormone, melatonin, and that this hormone is related to certain sleep and mood disorders, such as manic-depression. (He subsequently has treated some manic-depressive patients by exposing them to bright artificial light.)

But it was not until Neuwelt had removed the pineal gland of a 22-year-old Roseburg man that it was proved the pineal was the sole source of melatonin. Following removal of the gland, measurements by Neuwelt and Lewy showed there no longer was any melatonin present in the patient's body. Prior to the operation, secretion of the hormone had been normal.

Not only will this discovery be of significance to the work of Lewy, it also will give surgeons a tool in determining when procedures to remove pineal glands of patients with tumors have been successful. "If there is no melatonin present after the surgery, that suggests the gland has been completely removed," Neuwelt said.

Neuwelt also has developed a method of increasing the effectiveness of drugs to fight brain tumors. The use of chemotherapy against malignant brain tumors has been hindered by the presence of a glue-like substance between the cells lining the brain blood vessels. Normally, this "blood brain barrier" serves to protect the central nervous system from potentially harmful substances in the blood. However, while performing this role, it also prevents effective penetration of drugs delivered to the brain.

A technique devised by Neuwelt and his collaborators to disrupt the blood brain barrier involves the infusion of mannitol, a sugar solution, into a leg artery through a catheter which is guided to the artery feeding the appropriate area of the brain. In order to dilute the strong sugar concentration of the mannitol, the cells lining the brain capillaries secrete their fluids and shrink for up to 30 minutes, pulling the cells apart and thereby opening the barrier and allowing drug treatment of the brain tumor.

About half of the patients who have been treated by this method at the OHSU have had their tumors shrink and have felt healthier, Neuwelt said. Some tumors have completely disappeared. However encouraging these results are, they do not yet indicate the patients can be considered cured, Neuwelt cautioned. "This treatment is investigative, and it may be years before anyone can be considered cured of their cancer."

Currently this type of chemotherapy to the brain is available only at the OHSU, but Neuwelt and his colleagues have begun working with other U.S. centers to develop similar treatment protocols.

Dr. Edward Herbert has been honored with the prestigious McKnight Foundation Award.

IABR head honored for research

Edward Herbert, Ph.D., director of the proposed Institute for Advanced Biomedical Research at the OHSU, has won the McKnight Foundation Award in Neuroscience for 1984.

Herbert, currently professor of chemistry at the University of Oregon, was cited for his "pioneering research" during 1982-83 on the biosynthesis of opioid peptides in the brain and endocrine system.

Herbert currently is studying individual molecules that control brain function. He and his colleagues were the first to show that neuropeptides, a family of complex molecules, are derived from a new type of protein containing several kinds of peptides.

Examples of neuropeptides are the enkephalins that regulate sleep, body temperature, response to stress and other complex behaviors, and endorphins, which have been widely heralded as the body's natural pain killers.

The McKnight Foundation of Minneapolis is a private philanthropic organization which awards some $30,000,000 in grants each year for the advancement of science, education and medicine. It is the foremost private agency funding research in neuroscience.

Hill offers wide array of cancer care

(continued from page 6)

The machine is housed in a room that has been specially renovated to make the patient more comfortable.

Other equipment used by the department includes a cobalt therapy machine, several superficial voltage units highly effective for cancers of the skin of the face, and a powerful (25 million volt) betatron accelerator efficient in treating tumors of the lung, esophagus, upper abdomen and pelvic organs.

Ophthalmology

The OHSU's Department of Ophthalmology is a world leader in research and education on the treatment of cancers of the eye and eyelid. Techniques pioneered here are resulting in improved cure rates reported for some ocular cancers according to Frederick Fraunfelder, M.D., chairman of ophthalmology.

Many patients with ocular cancers are being spared surgery because their ophthalmologists are using cryotherapy, a technique developed at the OHSU which employs intense cold to manage cancerous growths.

"Normal tissue is much less sensitive to cold injury than certain cancer tissue," Fraunfelder explains. "With very rapid freezing, the water inside the cells freezes. If it is allowed to thaw very slowly, the sodium content inside the cell leaves and disrupts the internal workings of the cell, so it dies. Also, the freezing of the tissue blocks all the fine blood supply to the tissue, and the cell starves."

Patients around the world are being treated by techniques developed at the Health Sciences University for cancers on the eyelid, on the surface of the eye and inside the eye.

Patients around the world are treated using these techniques for cancers on the eyelid, on the surface of the eye and inside the eye.

To treat cancer of the eyelid, usually caused by exposure to sunlight, OHSU ophthalmologists developed a method of freezing the cancer cells with liquid nitrogen at minus 196 degrees. This treatment has resulted in a 94 percent cure rate in patients followed a minimum of five years if their lesions are less than 1 centimeter in diameter.

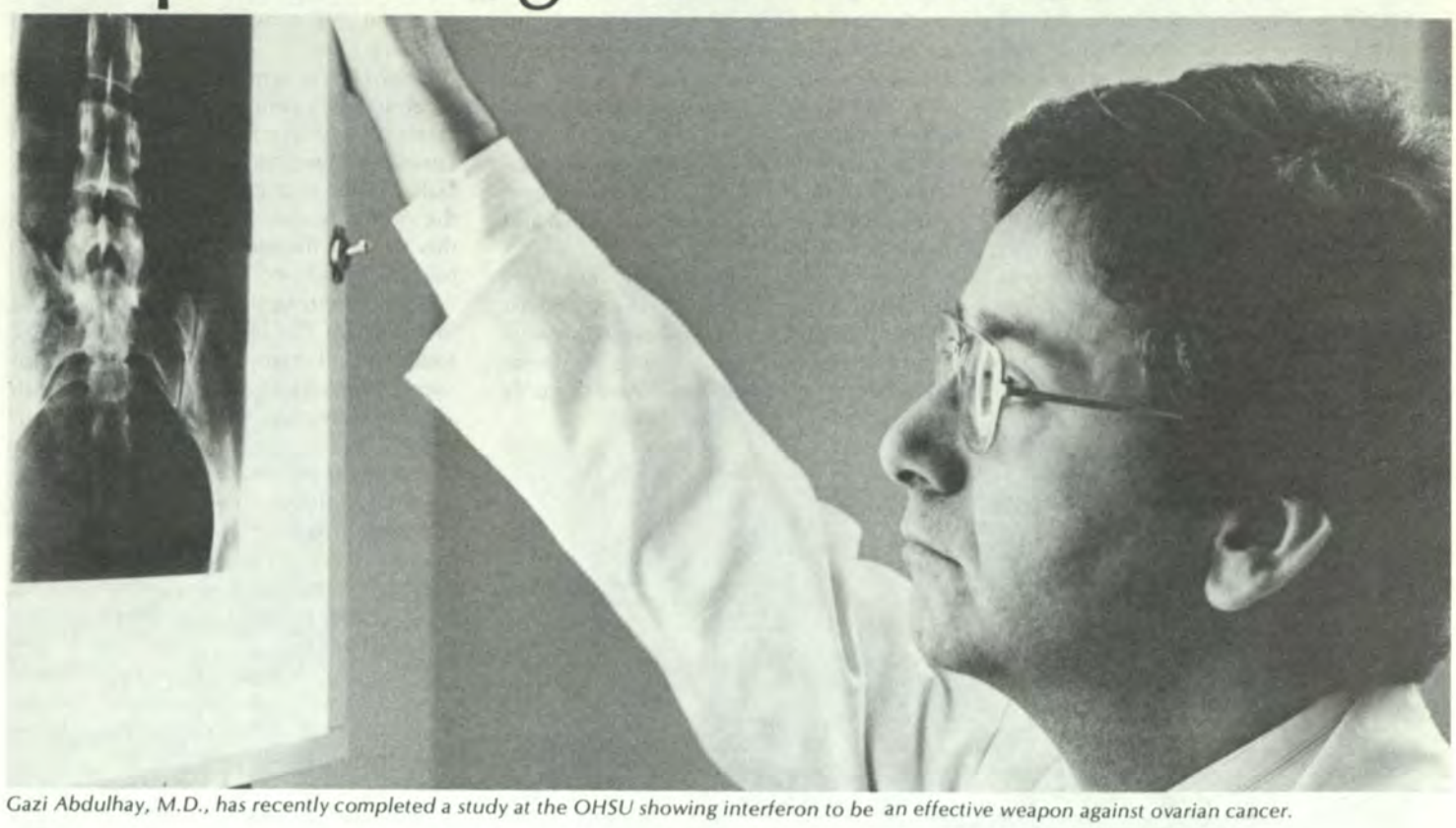
Another method developed at the OHSU combining surgery and cryotherapy for cancer on the surface of the eye has resulted in cure rates three times higher than ever before reported. "This treatment is now used by ophthalmologists all over the world," Fraunfelder says.

Interferon shows promise against ovarian cancer

Treatments with interferon, a drug that has shown much promise fighting ovarian cancer in OHSU studies, may soon become part of the wide array of therapies available for gynecologic cancer through University Hospital's Department of Obstetrics and Gynecology.

As a member of the Gynecologic Oncology Study Group, funded by the National Cancer Institute, the Department of Obstetrics and Gynecology currently is evaluating 41 treatment protocols dealing with all aspects of gynecologic cancer. The group shares information on the effectiveness of the most current treatments and the newest drugs available to treat gynecologic cancer.

The Department of Obstetrics and Gynecology provides comprehensive evaluation and treatment for all gynecologic cancers.



Gazi Abdulhay, M.D., has recently completed a study at the OHSU showing interferon to be an effective weapon against ovarian cancer.

Ovarian cancer is the second commonest gynecologic malignancy. There are approximately 150 to 200 new cases of cancer of the ovary diagnosed each year in Oregon, and 18,000 nationwide. Nearly two-thirds of these women will die from the disease, primarily because it produces no definite symptoms until it is far advanced.

The OHSU was one of four members of the national study group to participate in the trial using interferon against ovarian cancer. Interferon is a protein produced naturally in the body to help fight off cancer cells and viruses. Because the body produces so little of the protein, scientists found a means of deriving it from cultured human blood cells or genetically-engineered bacteria.

The results of the OHSU study led by Gazi Abdulhay, M.D., head of gynecologic oncology at the OHSU, showed that of 27 patients ready to evaluate, the cancer had disappeared in two patients and had partially regressed in three others. In 14 patients the cancer was kept under control for a longer time than usual, and in only eight had the disease progressed.

"For those patients whose cancer stayed the same, not only were we able to control their disease, we were also able to improve the quality of their lives," Abdulhay said. "This is because interferon has very minimal side effects and it is a treatment that does not require hospitalization."

Patients with ovarian cancer generally have surgery followed by treatment with a combination of very potent anti-cancer drugs. If this therapy fails, the next line of drugs is not as effective, does not extend the life expectancy of the patient and often is associated with significant side effects. "Eventually, we want to make interferon the treatment of choice after surgery," Abdulhay said.

The OHSU's Department of Obstetrics and Gynecology provides comprehensive evaluation and treatment for all types of gynecologic cancer. "We are using chemotherapy regimens that are providing much better results than ever before," Abdulhay said.

"And we are using the most modern approaches to endometrial (cancer of the uterus, the commonest gynecologic malignancy) and cervical cancers."

OHSU's High Risk Clinic helps keep an eye on families with cancer history

Judy is concerned about getting cancer. She knows *everyone* is, but she thinks her chances of getting cancer are, perhaps, greater than most.

Judy's mother has breast cancer; her grandmother died from melanoma, a skin cancer. Doctors call her sister's breasts "unhealthy" and recommend a preventive mastectomy.

Judy is 22 and has never felt better. Still she wonders if she might be a prime candidate for cancer. About one in every 12 women develops breast cancer, but that rate is three or more times greater in women like Judy, whose mothers developed breast cancer at a pre-menopausal age. Breast cancer is only one of many cancers that seem to run in families. Research has shown that as much as 12 percent of all cancer has some genetic links.

The OHSU's Family High Risk Clinic is a program unique in the state which specializes in examining families with a history of cancer. By following families considered at high risk for cancer, the clinic staff hopes in some instances to be able to take preventive measures against the disease and in others to detect it early enough to assure a positive outcome.

Individuals or families who come to the clinic complete an extensive family medical history including any incidence of cancer among parents, grandparents and other ancestors (although the clinic is available only to healthy persons who have at least one incidence of cancer within their nuclear family, i.e., siblings, parents or grandparents).

Physicians in the OHSU Division of Surgical Oncology evaluate information, determine the risks of those involved and suggest a routine of treatment or checkups designed to prevent or catch at an early stage any cancer growth.

Clinic staff can continue to follow the families, or the information can be turned over to a family physician to continue the program.

Research associate Rae Ann Townshend and Kenneth Janoff, M.D., gather data which helps the Family High Risk Clinic detect persons at risk of cancer.

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