Animal Research Points to Probability

Are Viruses a Cause of Cancer in Man?

Duke has had a long history in cancer research and recently was named as the site for a Comprehensive Cancer Center by the National Cancer Institute.

This is the final article in a series of four written by Yvonne Baskin, medical writer in the Office of Public Relations, about the status of cancer research and treatment, with special emphasis on developments at Duke.

The first article dealt with surgery and therapeutic radiology (INTERCOM Oct. 12, 1973); chemotherapy (Oct. 19); and immunotherapy (Nov. 2).

This article explores research under way with viruses as a key to the cause of cancer.

JOKLIK SPEAKS—Dr. Wolfgang Joklik, (at left) chairman of microbiology and immunology, was photographed during a television interview last fall on the Comprehensive Cancer Center. He was interviewed more recently for the accompanying story on cancer research and viruses. *(Photo by Jimmy Wallace)*

During the past 50 years, more than 100 viruses have been found to cause cancer in animals, but not a single virus has yet been proved to cause cancer in humans.

Still, most scientists believe that viruses will eventually be found to cause at least some of man's cancers.

"The reason we keep working on this is that there is no reason to think that if viruses cause cancers in animals, including primates, they shouldn't also cause cancers in man," said Dr. Wolfgang Joklik, chairman of the Department of Microbiology and Immunology.

Several types of viruses or virus particles have, in fact, been isolated from human cancers. But this is no firm proof that they caused the cancers. And researchers cannot take these isolated viruses and inject them into a healthy human—as they would in animals—to see if they would indeed cause a cancer.

The efforts by Duke researchers to find the causes of cancer will take on new dimensions next spring when a $1.6 million animal isolation laboratory is finished. The facility is being built as part of the new Comprehensive Cancer Center here, one of 11 such centers in the nation designated by the National Cancer Institute.

This will provide Duke with a vastly expanded capability for direct experiments with possible cancer-inducing viruses in laboratory animals.

"There are two groups of viruses for which the evidence of a link to human cancer is good," Joklik said.

One of these groups is the herpes, a DNA-type virus. A herpes virus called EBV has been found in patients with Burkitt's lymphoma, Hodgkin's disease and nasopharyngeal cancer. Another virus called herpes Type 2 has been linked with cervical cancer. Herpes 2 protein and bits of viral DNA have been found in cervical cancer tissue, and the antibody to the virus is found in cervical cancer victims much more frequently than in the general population.

The other group of viruses are the RNA tumor viruses or rousviruses. These viruses are known to cause cancers in all types of animals studied so far, and some people think they may be the root of all human cancers.

"Many rousviruses are incomplete viruses," Joklik said. "They can enter a normal cell and modify it into a cancer cell, but they cannot reproduce themselves without helper viruses. They lack part of the genetic material needed to replicate themselves.

"Once a virus has turned a normal cell into a cancer cell, that cell can multiply rapidly into a tumor with little or no evidence remaining of the virus which started the process," he said.

Rousviruses are the basis for one of the major theories of cancer causation currently held by scientists—the oncogene theory.

This theory says that there are two parts to a rousviruses—the virogene, or the part necessary to multiply itself; and the oncogene, the part necessary to modify normal cells into cancerous ones.

"The theory is that these two parts

(Continued on page 3)

Intercom
duke university medical center
VOLUME 20, NUMBER 47 NOVEMBER 30, 1973 DURHAM, NORTH CAROLINA

Monkeys, Apes May Be Our Best Friends In Disease Diagnosis and Treatment

Monkeys may turn out to be man's best friend when it comes to improving human health.

Monkeys and apes have tissue and blood types so similar to those of man that they are being used as unique models to test innovations in cancer diagnosis and therapy and improvements in organ transplantation.

Leaders in this field include two researchers here who are working on immunological studies of monkeys and apes. The research on these animals is being done at Duke although many of the nonhuman primates are housed at the Yerkes Regional Primate Research Center at Emory University. Dr. Richard S. Metzgar, professor of immunology, and Dr. Hilliard F. Seigler, associate professor of surgery and immunology, are both part time Yerkes faculty members.

One of the major goals of Metzgar and Seigler and other immunologists is to be able to understand the complex human immune system enough to be able to manipulate it.

The immune system of an animal's body is the system which allows it to recognize and react against foreign substances. This is the system which, if not suppressed, will reject a transplanted organ and is largely responsible for our natural ability to resist bacterial and viral infections.

Blood and tissue cells in the body contain substances called antigens. The body through its immune system recognizes its own antigens as "native" and thus fails to make an immune response to its own antigens. The immune system, however, reacts to foreign antigens by producing antibodies or immune cells against them.

Cancer cells also contain foreign antigens, but for reasons not yet fully understood, the human body apparently doesn't react forcefully enough to "reject" a tumor the way it will a heart or kidney transplant from another person.

If enough were known about the immune system, researchers predict better ways could be found to make the body accept transplanted organs and force it to reject malignant tumors.

Metzgar said many of the experiments needed to help decipher the workings of the human immune system could not morally or ethically be attempted in man. Many of the studies, however, are possible in the nonhuman primates and are more meaningful than similar studies in other laboratory animals.

Metzgar and Seigler pioneered work in this field in the early 1960's when human transplantation or tissue antigens were first being studied. They were the first to demonstrate that many of these antigens being defined in man were also present in apes.

In the field of organ transplantation, chimpanzees have become invaluable models for studying transplant rejection and trying out new drugs for suppressing the immune system.

Chimps and men are so immunologically similar, in fact, that before human cadaveric kidney donors were available, kidneys from chimps were transplanted into humans at a few other institutions. But Metzgar said that recent data shows that there are enough other antigenic differences between man and chimpanzees to make this approach impractical.

Trials of new immunosuppressive drugs and combinations of drugs in monkeys and apes during the past five years have been helpful in improving the success of human transplants.

Dr. Seigler believes that within the next decade, as more is learned about the human immune system, transplantation of other major organs such as heart and liver will follow the lead of kidney grafts and become a widespread procedure.

Another dramatic example of the

(Continued on page 3)

HELPING THEIR HUMAN COUSINS—Duke immunologists Dr. Richard S. Metzgar (left) and Dr. H. F. Seigler hold some of the youngest members of the chimpanzee colony at the Yerkes Regional Primate Research Facility in Atlanta. Monkeys and apes have blood and tissue types so similar to those of humans that they are being used by Duke researchers as models to test innovations in cancer diagnosis and therapy and new immunosuppressive drugs for organ transplantation.