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The Humphrey Center Report / Humphrey Center News

1986

Humphrey Center News: Spring/Summer 1986 v. 2, no. 2

<https://hdl.handle.net/2144/22159>

Boston University

Humphrey Center NEWS

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

Volume 2, Number 2 Spring/Summer 1986

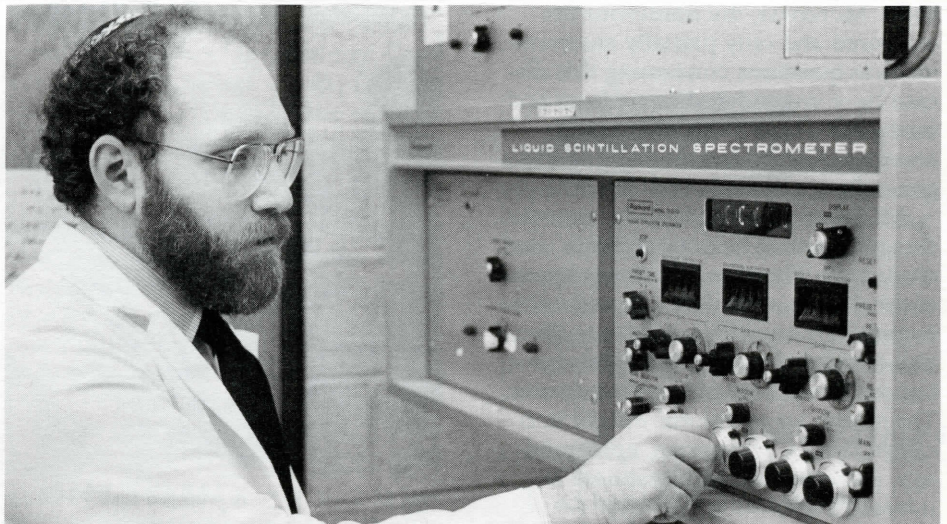
AIDS Research at the HHH Cancer Center

One of the distinguishing features of AIDS is a marked loss of a group of white blood cells called helper cells (cells that help or promote immune reactions). Since the immune system is exquisitely balanced between the presence of helper cells and suppressor cells (cells that suppress or limit immune reactions), a decrease in helper-cell number or function can cause a loss of immune competence. The end result is that the body can't fight infection.

At the Humphrey Center, what researchers observed is that not only are helper cells destroyed by the HTLV-III virus, but the ability to replace cells also is impaired. Because of this diminished capacity for renewal, there must be mechanisms at work in addition to a virus killing off cells. Research carried out by Paul H. Black, M.D., John C. Beldekas, Ph.D. and Elinor H. Levy, Ph.D., is focused on exploring — and, it is hoped, eliminating — those potential other mechanisms through tests with *in vitro* T-cell assays.

In vitro T-cell assays are a means by which to measure the ability of AIDS patients' blood cells to grow and form colonies while a variety of tests are performed on the cells in a test tube. The tests include administration of anti-viral drugs, investigation of the effect of viral proteins on non-infected cells, and exploration of the possibility that affected cells could be producing "impotent" cells.

There are no clear answers yet, but if the range of possibilities can be narrowed, that's progress in research. □



Michael E. Osband, M.D.

The Fight Against Cancer Gets a Shot in the Arm: Adoptive Immunotherapy

Immunotherapy starts with the hypothesis that the immune system can tell that cancer cells aren't a normal part of a patient's body. This is because of substances called antigens that may be on the surface of these cancer cells.

Michael E. Osband, M.D., a member of the Humphrey Center and medical director of the Laboratory for Cellular Immunology and Cancer Diagnosis, is using this hypothesis as a basis for further investigation into the possibility of a cancer treatment called adoptive immunotherapy. The results are promising.

Dr. Osband and his BUSM colleagues Gennaro A. Carpinito, M.D., assistant professor, and Robert J. Krane, M.D., chairman of the Department of Urology, began their investigation with a look at how the immune system re-

sponds to organ transplants. When a transplant is performed, the patient's immune system must be suppressed to prevent rejection of the new organ. "If the body rejects a transplant because the antigens on the cells of the donor organ are different from the patient's," Dr. Osband asks, "wouldn't it follow that the body might reject cancer cells for the same reason?"

Because people continue to develop cancer and die from it, it's apparent that our immune systems, by themselves, do not reject abnormal cancer cells. Dr. Osband and his colleagues *continued on page 3.*

**COMMENTARY:
THE AIDS EPIDEMIC**

COMMENTARY

The AIDS Epidemic: Report on a Frustrating Disease

By Paul H. Black, M.D., John C. Beldekas, Ph.D. and Elinor M. Levy, Ph.D.

Few diseases in the history of medicine have had the social and economic impact that we are currently experiencing with acquired immune deficiency syndrome (AIDS), a condition recognized only in the past few years. Moreover, the numerous unanswered and only partially answered medical questions concerning this disease have engendered many fears and frustrations in the high-risk groups, among medical personnel and in the general population.

AIDS has presented modern medicine with one of its most difficult challenges. The slow but steady spread of the disease will place an ever-increasing proportion of the population at risk unless effective intervention and treatment can be found soon. The search for additional insight into causal factors, prevention, epidemiology, pathogenesis and treatment is intensifying.

Who is at risk?

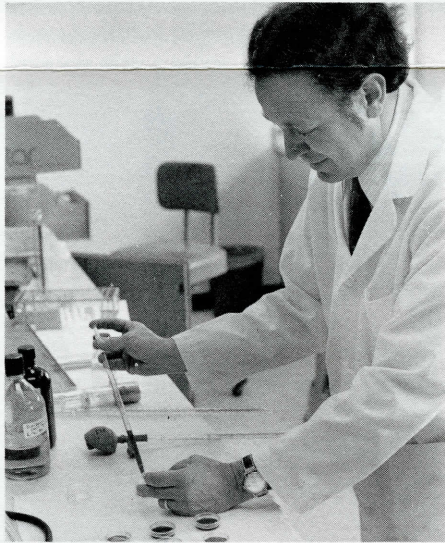
Approximately 75 percent of AIDS patients are homosexual or bisexual males, and about 15 percent are intravenous drug abusers. About 5 percent of AIDS patients are of Haitian descent, hemophiliacs who receive factor VIII preparations, which are required for blood clotting, or patients who receive blood transfusions. Approximately 5 percent of patients with AIDS are not known to belong to any of these risk groups.

A syndrome sometimes seen in high-risk groups is AIDS-related complex (ARC). It is characterized by fever, malaise, weight loss, appetite loss, swelling of the lymph glands and some immune suppression. Approximately 10 to 15 percent of the people with this syndrome have developed full-blown cases of AIDS.

Virus found, test developed

Within the past two years, two groups of scientists — one in France and another in the U.S. at the National Cancer Institute — identified a virus

that seems to be the causal factor in AIDS. Tests have been developed to detect the presence of antibodies to this virus referred to as lymphadenopathy-associated virus (LAV) by the French group and human T-cell lymphotropic virus III (HTLV-III) by the Americans. The test most frequently used is the enzyme-linked immunosorbent assay (ELISA), which recently was approved for use by the Food and Drug Administration.



Paul H. Black, M.D., is professor and chairman of the BUSM Department of Microbiology and a member of the Massachusetts Task Force on AIDS that was established by the governor. He is a former director of the Humphrey Cancer Center. Elinor M. Levy, Ph.D., an associate professor, and John C. Beldekas, Ph.D., a research associate, are members of Black's department and are conducting AIDS-related research.

Limitations of the ELISA test

The current major clinical application of ELISA is to screen blood and blood products, thereby helping to minimize the risk of transfusion-associated AIDS. ELISA is not completely specific for the AIDS virus, however, and it may yield both false positive and false negative results.

A positive test means only that a person has had contact with the virus and has developed antibodies to it. It does not mean that the person has AIDS-related complex or AIDS or that he or she will eventually get these diseases. It is not even certain that every person with a positive test harbors the infectious virus, although some symptom-free people certainly do.

The use of ELISA also presents complex legal, social and ethical issues. These questions mostly arise from fears surrounding the confidentiality of the test results and a concern about whether names of people with positive results would be made available to employers or insurance companies who might use the information to deny jobs or insurance coverage.

With the availability of ELISA and other screening tests, it has become apparent that some healthy people in the high-risk groups are antibody positive and may even harbor the virus. Although these people must be studied for longer periods of time, antibody and/or viral presence without the disease suggests that the virus alone is not sufficient to cause AIDS. This raises questions of whether, and what, co-factors may be necessary for the development of the disease. Much more has to be learned about these co-factors and the role they play in the development of AIDS; this may well be the most important issue facing AIDS researchers.

Contagiousness and treatment

Data from patients with AIDS indicate that the virus is not very infectious. The disease appears to be spread only by intimate sexual contact, by sharing drug needles, or by blood products from infected individuals. The disease is *not* spread by casual contact, or in water or food, or by air or such contaminated objects as books, bedding, combs and clothing. So far it seems unlikely that the disease can be spread by kissing, since the amount of the virus is relatively low in saliva.

It is important to note that there has been no documentation to date of cases in which the disease has been spread to health-care workers who have cared for AIDS patients.

There is no effective treatment for AIDS at present. Many studies are now being carried out with drugs that inhibit enzymes within the virus that are necessary for replication. Many of these drugs, however, may lead to blood cell or kidney damage. Studies of these drugs will continue and they will be tested in patients with AIDS-related complex. In these patients, the immune system has not been so irreparably damaged as it is in people

continued on page 3.

A Day of Celebration



Director Herbert Wotiz, Ph.D., (left) presents an award to Robert C. Gallo, M.D.

Robert C. Gallo, M.D., who was presented with the 1985 Hubert H. Humphrey Cancer Research Center Award by Humphrey Center Director Herbert Wotiz, Ph.D., is renowned for his groundbreaking research efforts into the nature of viruses, especially those related to leukemia. He is well-known in the scientific community for his identification of the biological response modifier, interleukin 2, a molecule potentially able to alert the immune system to tumor cells and, thereby, useful in the treatment of cancer.

As chief of the Laboratory of Tumor

Cell Biology, Developmental Therapeutics program, of the National Cancer Institute in Bethesda, Md., Gallo continues to contribute to the understanding of the devastating acquired immune deficiency syndrome (AIDS).

"So far we don't have the vaccine or right treatment for this devastating disease; I am hopeful that soon we will have both. If so then this award may become appropriate in bearing the name of Hubert Humphrey, who gave so much to biomedical science, and who knew so much about courage and personal suffering in cancer." □

AIDS EPIDEMIC

continued from page 2.

with AIDS. (Please see page 1 story about some AIDS-related research being conducted at the Humphrey Center.)

Incidence on the increase

The incidence of the disease is increasing and it appears to be spreading. In the U.S., the disease occurs predominantly among men. However, there is epidemiological evidence in this country that the disease can be transmitted heterosexually. The disease recently has been documented in prostitutes in San Francisco, New York City and Boston. Sexual contact with prostitutes previously exposed to the virus may explain some of the cases classified as being in the "no-known-risk" category.

Approximately 80 to 85 percent of patients with AIDS will have died of their disease within two years of diagnosis. A great challenge to the medical and research community today is to understand the nature and pathogenesis of AIDS. Only through such understanding can we hope to bring about effective prevention and therapy. □

IMMUNOTHERAPY

continued from page 1.

developed a technique called in vitro immunization. Some of a patient's white blood cells, the kind called lymphocytes, are put into a test tube, incubated with some of the patient's cancer cells, then put back into the patient. These sensitized or immunized cells can attack the cancer, similar to the way in which a polio vaccine, for example, stimulates the immune system to fight the polio virus.

To address the second possibility — that the immune response is too weak or has been turned off too early — the question was raised whether any drugs were available that might, in effect, amplify the efforts of the body's immune system. The answer was yes. And the drug was cimetidine, already widely-used for treating ulcers. Cimetidine seems in certain cases to increase an immune response by turning off the suppressor lymphocytes (the cells that regulate the immune system) and so unleashes the immune response. Dr. Osband simply took a known, safe drug and used it in this new application.

QUESTIONS...

Answer to question on back panel.

A. Smoking is the single most preventable cause of cancer today. If everyone were to stop smoking, nearly one-third of all cancer-related deaths could be prevented. Smoking is responsible for 83 percent of all lung cancer, the form of cancer most difficult to treat and cure — 85 percent of lung cancer patients die of the disease. Smoking is also a factor in cancers of the mouth, throat, larynx and pancreas. Cancers related to smoking claim 320,000 lives a year — largely preventable deaths.

Q. Is diet related to cancer?

A. The present evidence linking cancer with diet is based upon laboratory experiments and observation of human populations. A high fat diet, including both unsaturated and saturated fats, may play an important role in cancers of the breast, colon and uterus. In fact, recent studies have shown that obese people have significantly higher death rates from these three types of cancer.

continued on page 4.

In addressing *both* possibilities, Dr. Osband and his colleagues developed a method of treating cancer: adoptive immunotherapy.

Early data on the anti-cancer properties of cimetidine in mice were published by Dr. Osband and his colleagues in 1981. Then 20 terminally ill patients with kidney cancer were treated in what is called a Phase I study, to determine if this treatment was safe. Each patient received three infusions of their in vitro immunized lymphocytes and took cimetidine orally each day. There was no toxicity, Dr. Osband notes, and the tumors shrank in nearly 50 percent of the patients. The results justified expanded clinical trials, and after some additional studies on mice, a study of 60 more terminal cancer patients got under way in February 1986. The study focuses on cancers of the kidney, lung, pancreas, colon and skin.

While it's too soon to know whether adoptive immunotherapy will help all cancer patients, the fact that the treatment continues to be tested in clinical trials — with some positive results — is hopeful. □

QUESTIONS...

continued from page 3.

Consuming fewer fatty foods — such as butter, margarine, vegetable oil, lard, salt pork, shortening, olives and non-dairy creamer — is believed to help reduce your risk of developing cancer. Further, many cancers common to Western nations — such as cancers of the prostate, breast, colon and rectum — are rare or nonexistent among rural Africans, whose diets are much higher in fiber than the American diet. Eating more high-fiber foods is also believed to help reduce your risk of developing cancer. Fiber is the non-digestible carbohydrate found in whole grains, beans, fruit and vegetables. □

CANCER NOTES

CANCER NOTE: More than 400,000 new cases of skin cancer are reported every year, making it the most common form of human cancer. Fortunately, it is one of the most curable forms of cancer when discovered early. Most skin cancer can be prevented since over exposure to the sun is the leading cause. Wearing protective clothing, using strong sunscreens and staying out of strong sunlight are sensible preventive measures, especially for fair-skinned people with red or blond hair — characteristics of people most prone to develop skin cancer.

CANCER NOTE: Cigarettes are not the only form of tobacco known to cause cancer. Cigars, pipes and chewing tobacco have been implicated in cancers of the mouth and throat. Even “second-hand” smoke may cause disease.

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



What is the single most preventable cause of cancer?

ANSWER ON PAGE 3

Address Correction Requested

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