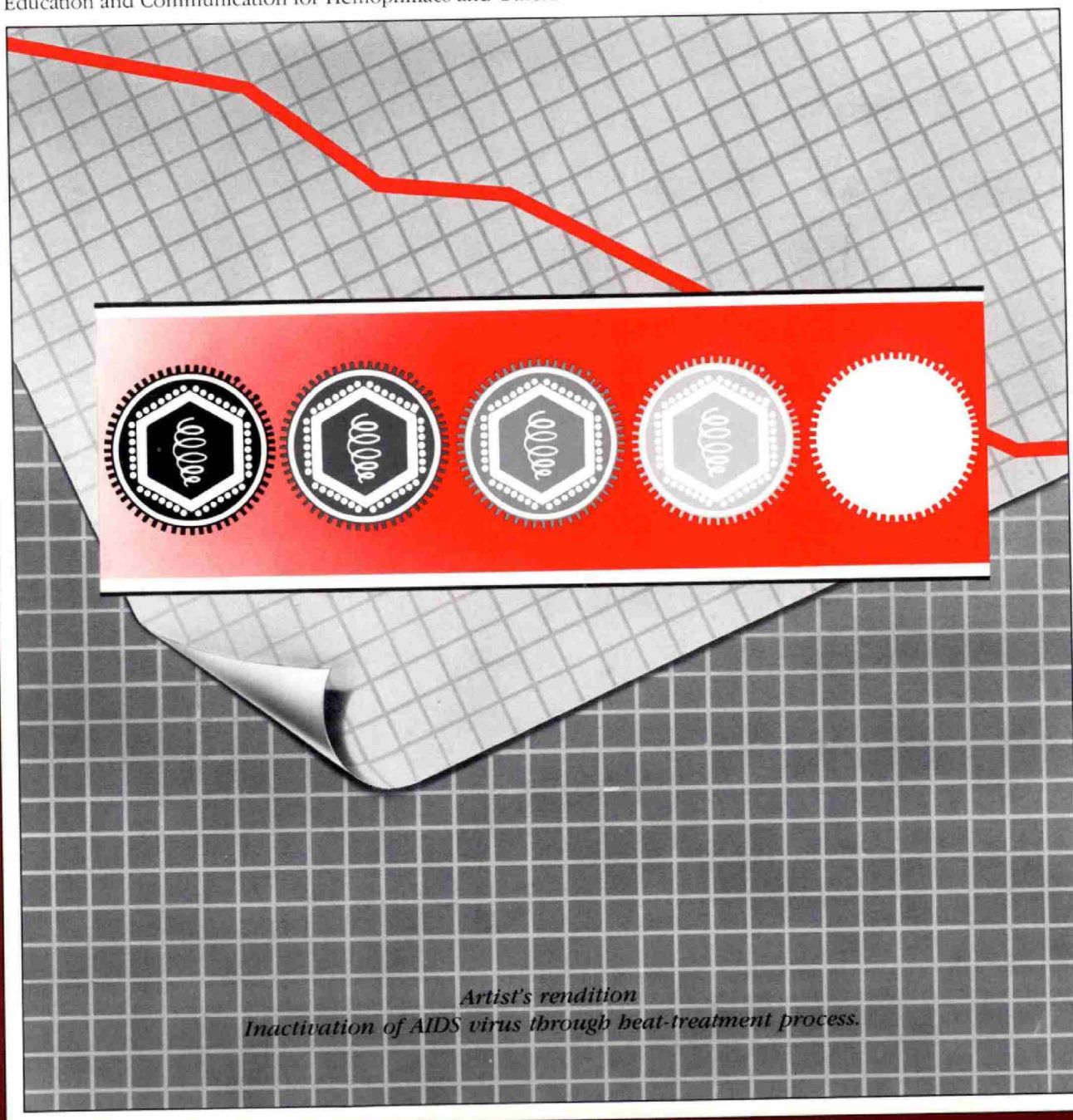
ECHO

Special AIDS Issue

Education and Communication for Hemophiliacs and Others

Volume 6, Number 3 September 1985



Artist's rendition
Inactivation of AIDS virus through heat-treatment process.

An Educational Service of Cutter Biological

FOREWORD

Dear ECHO Reader:

This issue of ECHO is devoted to one topic: Acquired Immune Deficiency Syndrome, or AIDS. AIDS is a disease that causes weakness in or destruction of the body's immune defense mechanisms. AIDS in and of itself is not fatal, but the disease often leaves the person vulnerable to various "opportunistic infections," including *Pneumocystis carinii* pneumonia (PCP) and cytomegalovirus (CMV) infections, as well as malignant tumors, all of which are often fatal in AIDS patients.

Since the last time we reported on AIDS in a special supplement of ECHO, there have been *tremendous* gains in the understanding of the disease. Although most persons with hemophilia who have been treated with concentrate, and some who have been treated with cryoprecipitate, have been exposed to the virus in the past, less than 1 percent of the estimated 20,000 persons with hemophilia in the United States have developed AIDS.

As a direct result of intensive research, we have been able to contribute to the scientifically sound and practical recommendations made to the hemophilia community. We now have the ability to screen donors through antibody testing techniques. In addition, our heat-treated factor concentrates achieve a previously unreachable level of safety without altering their stability or effectiveness.

In this issue of ECHO, we offer to you some of the latest information available from scientific research and clinical practice. ECHO presents portions of the valuable information that emerged from the First International Symposium on AIDS in Atlanta this past spring. We also bring you an update on latest research results, and Dr. Margaret Hilgartner shares her clinical expertise in this area. In addition, an historical review of the disease and News from Cutter are also included.

The future appears encouraging. We hope that this issue of ECHO will help you to understand some of the goals and hopes of researchers throughout the world.

Sincerely yours,

GRO-C

G.M. Akin, MD
Director of Medical Services
Cutter Biological

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AIDS:
THE STORY CONTINUES

For most of its short existence, AIDS has been called a mystery disease. Although many unknowns have been clarified, researchers are discovering new answers about AIDS each day.

The story of AIDS began to unfold in the spring of 1981 when physicians in California and New York reported to the Centers for Disease Control (CDC) that they were treating an exceptionally large number of cases of *Pneumocystis carinii* pneumonia (PCP) and of Kaposi's sarcoma in young men. PCP is a rare infection that has been called an opportunistic disease because it only strikes those patients whose immune system has broken down from some other cause. Before AIDS, Kaposi's sarcoma was a relatively uncommon low-grade cancer of older men, but since AIDS, it is now being found in a more malignant form in younger men with this syndrome. The other striking feature was that all of the patients were homosexual men.

These early reports prompted the CDC to search for cases in cities other than New York and Los Angeles. Their findings indicated that there might well be the makings of an epidemic in progress. It was also becoming acutely clear that the disease was not limited to homosexual men, for intravenous drug abusers and Haitians were also developing this mysterious disease. Indeed, these three diverse groups added to the mystery, since they seemed to have nothing in common, and it was even suggested that they did not have the same disease. By the time all of this became known, the disease had picked up a name, acquired immune deficiency syndrome, shortened to AIDS. The name reflects the main characteristics of the disease. The irony is that AIDS itself is not fatal, but it reduces the body's immune system to such a degree that it can no longer defend itself against other diseases, which otherwise would be of no consequence.

Hemophilia and AIDS

In January of 1982, the CDC learned that a person with hemophilia had died in Miami the previous November from PCP. At that time, the CDC did not accept this as a case of AIDS because the patient had liver disease and had received steroids, which are known to impair the immune system. However, two definitely AIDS-associated cases were reported that spring. By the end of the year, six more cases had been added to these. It was later determined from intensive investigations that the only way these men could have gotten the disease was through the infusion of blood, blood components, plasma, and/or clotting factors.

The one positive result that came out of the investigations of the various risk groups was a belief that AIDS was indeed caused by an infectious agent, and most likely a virus.

It was first discovered that AIDS could be transmitted through whole blood when a 20-month-old boy in San Francisco acquired the disease following a transfusion. This case pointed up a major difficulty that was going to plague blood donor centers: one of the 19 persons who had donated the blood for the boy had subsequently developed AIDS.

The ability to screen donors was hampered by not knowing what caused the disease. However, as soon as it became known that there was a possibility of transmitting AIDS through blood products, Cutter Laboratories began to screen donors in an effort to exclude any who were in the high-risk groups. In addition, they stepped up an already intensive research project that was to lead to the heat-treatment process, which would eventually be shown to inactivate the AIDS virus.

The Search Narrows

In the meantime, the CDC was adding the categories of female sexual partners of men with AIDS and the children of intravenous drug abusers, Haitians, and bisexual men to its list of high-risk groups. Haitians have since been removed, but it is expected that the list is still not complete.

The one positive result that came out of the investigations of the various risk groups was a belief that AIDS was indeed caused by an infectious agent, and most likely a virus. This had the effect of channeling all the intense research that was taking place on the cause of AIDS into one area; however, some researchers did not give up their favorite theories until the AIDS viruses were actually isolated.

One of the researchers who consistently felt that a virus was the culprit was Dr. Robert Gallo of the National Institutes of Health (NIH). He had recently isolated a virus that had been shown to cause a form of cancer in humans. This virus, the human T-cell leukemia virus, or HTLV, belonged to a family called retroviruses. Since there were some similarities between the symptoms of AIDS and those caused by HTLV, Dr. Gallo and his group concentrated on the retroviruses, which invade T-lymphocytes and kill them. Also working with viruses were Dr. Jay Levy of San Francisco and Dr. Luc

Once the virus(es) causing AIDS were known, scientists had a base from which to start looking for ways to prevent and cure the disease.

Montagnier of the Pasteur Institute in Paris.

Gallo and his group called their virus HTLV-III, the French researchers called theirs the lymphadenopathy-associated virus, or LAV, and Levy and his co-workers called their virus the AIDS-related virus, or ARV. These viruses appear to be quite closely related, if not the same virus, and are believed to be the causative agents of AIDS.

Once the virus(es) causing AIDS were known, scientists had a base from which to start looking for ways to prevent and cure the disease. This ambitious prospect seemed to be far off. Of more immediate concern was the need to find a way to detect the virus in blood or plasma donated by persons who unknowingly had AIDS. The screening test for antibodies to the AIDS virus of donated blood and plasma that has recently been developed is discussed elsewhere in this issue of ECHO.

The Future

When the body is invaded by a virus, one of the main lines of defense of the immune system is through white blood cells called lymphocytes. There are two kinds of lymphocytes, T-cells and B-cells. The B-cells produce immunoglobulins that are able to bind with microorganisms and effectively aid in inactivating them. T-cells also can be divided into two types, T-helper and T-suppressor cells. T-helper cells regulate the activation of both B-cells and T-suppressor cells. In a normal individual, T-suppressor cells are present in about half the amount of the helper T-cell group. With AIDS, helper T-cells are destroyed, and the ratio of helper T-cells to suppressor T-cells is reversed. This change may be related to the inability of AIDS patients to fight infection.

One line of research is to find ways of reestablishing the number of T-helper cells in the body. This would allow the body to be its own best defense. Attention too often has centered on patients with severe or fatal AIDS, and less on those who are still surviving. There may well be a subgroup who have a less severe form of the disease and who recover partially or completely. Milder forms of the disease may even go undetected.

Since the recent developments in the production of a vaccine for hepatitis B, interest has been sparked to develop a vaccine for HTLV-III. It took more than six years of intensive research to develop the hepatitis vaccine, but much was learned along the way, and a vaccine for HTLV-III is hoped for in a much shorter time. However, one difference between the HTLV-III and hepatitis B viruses is that HTLV-III has a higher rate of mutation, which means that a vaccine made from one virus type may not be effective.

...a drug may well be able to slow the virus down sufficiently to allow the body to rebuild its defenses.

Antibiotics are ineffective against viruses, but other agents are being tested. The possibility of a drug being developed that will destroy HTLV-III is slim, but a drug may well be able to slow the virus down sufficiently to allow the body to rebuild its defenses.

The studies of the African green monkey are of interest in the unfolding drama of AIDS. It seems that this monkey, common in Africa, harbors a virus closely related to HTLV-III, but it does not become ill. However, this same virus does cause the illness in the rhesus monkey. The reason why the African green monkey does not acquire the disease is unknown, but it may be that the monkey has developed an immunity to the virus. Since HTLV-III might be similar to the virus found in monkeys, an understanding of the protective elements in the African green monkey might prove to be of value in the treatment of AIDS.

Symptoms of AIDS

Since the initial symptoms are very general, they often may be little different from those of other viral diseases. The following are symptoms that should be checked with a physician as soon as they are noted:

- Weight loss for no known reason
- Swollen glands in the neck, armpits, or groin, which may or may not be painful
- Fever that lasts for two or more weeks
- Night sweats that occur for several weeks
- Diarrhea that persists and has no known cause
- Persistent or recurrent headache
- Shortness of breath of recent origin
- Persistent cough
- Skin blotches (purple or red-brown)
- Skin areas that look like bruises but that do not go away

All of these symptoms may not be necessarily present in one person, and most can occur with other diseases, but they all should be investigated as soon as they are noted.■

QUESTIONS & ANSWERS

Dr. Margaret Hilgartner has kindly answered questions about AIDS that ECHO *thought would be of interest. Dr. Hilgartner is Professor of Pediatrics, Chief of the Division of Hematology/Oncology, and Director of the Hemophilia Center, New York Hospital-Cornell Medical Center, New York, New York.*

ECHO: *What should a person with hemophilia do if he notes any of the AIDS symptoms?*

DR. HILGARTNER: Because many symptoms associated with AIDS are vague and may be due to many common infections (eg, cold or flu), the symptoms should not cause undue alarm. However, if they do persist and are severe, the person with hemophilia should consult his treating physician. It is important to note that many of the complications of AIDS are treatable when discovered early.

ECHO: *What are LAV and HTLV-III?*

DR. HILGARTNER: These abbreviations stand for the lymphadenopathy-associated virus and the human T-cell lymphotrophic virus-III. These are retroviruses that have been isolated by the French and American workers, respectively, and in all probability, they are the same virus. This virus is believed to be the causative agent of AIDS. These viruses appear to attack the lymphocytes, particularly the T-helper lymphocytes, and thereby destroy the function and balance of the immune system.

ECHO: *What is the AIDS-related complex?*

DR. HILGARTNER: The AIDS-related complex, or ARC, is a milder condition than AIDS, but it is suspected that it may be a precurser of AIDS.

ECHO: *Why is it believed that HTLV-III may be the cause of AIDS?*

DR. HILGARTNER: These viruses have been isolated from the lymphocytes and tissues of people who have developed AIDS. They are known to reside in the T-helper lymphocytes and kill those lymphocytes that they have infected. This is very similar to the course of disease in the patient with AIDS and is therefore suggestive evidence that this virus causes AIDS. The antibodies against HTLV-III/LAV have also been found in the plasma of asymptomatic persons who have been exposed to these viruses.

ECHO: *Is there a blood test for HTLV-III/LAV antibody?*

DR. HILGARTNER: There is currently a screening test for the HTLV-III/LAV antibody, which is used for research purposes and to screen blood donors. Because there are still some uncertainties concerning the accuracy of the screening tests and because of the social problems that may occur if the results become public property, the test has been reserved for these purposes only.

ECHO: *Does a person have AIDS if he has antibodies to HTLV-III/LAV?*

DR. HILGARTNER: If an individual has antibodies to HTLV-III/LAV (a positive test), it does *not* mean that that person has AIDS. It only means that he or she had been exposed to the virus and has made antibodies to the virus.

ECHO: *What is the risk of a person with hemophilia getting AIDS?*

DR. HILGARTNER: The current risk of persons with hemophilia developing AIDS is directly related to their need for blood products to stop bleeding. The risk is extremely low. Although most persons with hemophilia who have been treated with concentrate and some who have been treated with cryoprecipitate have been exposed to the virus in the past, less than 1 percent of the 20,000 persons with hemophilia in the United States have developed AIDS. The risks for developing AIDS should be even less with the screening procedures for blood donors and the testing of all plasma donations for HTLV-III/LAV antibodies. The risk is further reduced when the factor concentrate has been subjected to a heat-treatment process.

ECHO: *What can persons with hemophilia do to lessen the chance of getting AIDS?*

DR. HILGARTNER: They should use the product considered most pure for their factor replacement and type of disease. Of course, they should also observe good rules of hygiene for themselves, eat a well-balanced diet, get plenty of rest, and avoid exposure to infection. These simple rules of living appear to be important in decreasing the cofactors that may predispose the person to the virus.

ECHO: *Are people in contact with persons with hemophilia at risk of developing AIDS?*

DR. HILGARTNER: Persons who have usual social, work, or school-related casual contact and household contact do not appear to have an increased risk of developing AIDS, since the AIDS virus appears to be transmitted only through blood and certain body secretions.

Studies of homosexual men indicate AIDS is spread by intimate sexual contact with anal intercourse as a significant mode of viral transmission. Studies of drug abusers have shown that using a needle contaminated with the virus may also transmit the disease.

Family members in close contact with a person with hemophilia do not appear to have an increased risk of developing immune suppression or AIDS. However, there

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MEDILOGUE

Last spring, scientists and researchers from all over the world met in Atlanta to pool their findings on the multifaceted aspects of the acquired immune deficiency syndrome, or AIDS. This was the largest group ever to be brought together to discuss this important new disease entity. ECHO *reviews some of the important developments that emerged from this conference.*

A positive trend away from the steadily increasing number of AIDS cases being reported is among persons with hemophilia. The Centers for Disease Control (CDC) has announced that the number of new cases is decreasing, or at least staying the same. This trend probably reflects the improved methods of screening blood and plasma donors and the increased usage of heat-treated factor concentrates. Therefore, it is particularly important that a person with hemophilia not withhold medically indicated treatment for fear of AIDS, especially in view of the safety data concerning the heat-treated factor concentrates.

A positive trend away from the steadily increasing number of AIDS cases being reported is among persons with hemophilia.

Treatment Modalities

Research for the treatment of AIDS is being concentrated mainly in two areas: finding an agent or agents to destroy HTLV-III itself or a mechanism by which the immune system can be revitalized. At the present time, most patients are being treated for the secondary conditions that result because of the defective immune system. One resource open to all patients with AIDS or those at risk is good nutrition, which is as essential to the functioning of the immune system as it is to the body as a whole. Often, patients with AIDS are found to be malnourished, and this condition has to be corrected in conjunction with treatment for the secondary condition.

The most common AIDS-associated opportunistic infection, with respect to persons with hemophilia, is *Pneumocystis carinii* pneumonia (PCP). The symptoms are usually rapid and labored breathing, a nonproductive cough, and anxiety elicited by the inability to breathe. Treatment consists of skilled nursing care and drug therapy, usually a combination of trimethoprim-sulfamethoxazole or pentamidine, an experimental drug available only from the CDC. (In fact it was through requests for pentamidine that the CDC was able to trace some of the earliest cases of AIDS.)

Studies Compared

Because of the high rate of toxicity with the use of trimethoprim-sulfamethoxazole in AIDS patients, the use of pentamidine has increased. Dr. Jose Dryjanski and his colleagues of the Memorial Sloan-Kettering Cancer Center in New York City administered pentamidine intravenously (instead of intramuscularly), which they found to be safe and effective. Dr. David Hardy from the University of California, Los Angeles tested the drug combination of pyrimethamine and sulfadoxine in a 1 to 20 ratio. The investigators concluded that this combination is a safe and effective prophylactic agent against PCP relapse.

Reports of experimental drugs had mixed reactions. The drug ICRF-159 is a very active agent in the treatment of Kaposi's sarcoma in patients without AIDS in Africa. However, in the treatment of patients with AIDS in the United States, there was a low response rate, which highlights the different biologic manifestations of this cancer in the presence of immune deficiency. Dr. Willy Rozenbaum and his colleagues in France treated patients with AIDS with tungstoantimoniate. In a patient with hemophilia and AIDS, therapy with this drug prevented the recurrence of opportunistic diseases at one year, despite low numbers of T-cells.

Research for the treatment of AIDS is being concentrated mainly in two areas: finding an agent or agents to destroy HTLV-III itself or a mechanism by which the immune system can be revitalized.

One resource open to all patients with AIDS or those at risk is good nutrition...

Virology

Dr. Donald Francis of the CDC reported on the natural history of HTLV-III. As part of the study of the virus at the CDC, the period of incubation was determined. This was possible because of their previous

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RESEARCH UPDATE

Cutter's Heat Treatment

The saga of the search for a safer factor concentrate began in Cutter's laboratories several years ago, well before late 1981 when the acquired immune deficiency syndrome (AIDS) began to be a threat to the hemophilia community. Indeed, the problem of an infectious virus being transmitted through blood and blood products had been apparent with several viruses. By the time that AIDS came along, various experimental approaches had already been explored, such as the removal of viruses through heating, chemical inactivation agents, and ultraviolet irradiation.

It was discovered that Koāte® and Konȳne®, if modified in certain respects, could be heated with stabilizers and under carefully defined conditions without affecting the safety or the efficacy of the product, and studies showed that some of the model viruses, such as herpes simplex, that were being studied were effectively eliminated by this method. When it was first suspected that a family of viruses called the retroviruses might be implicated in AIDS, Cutter began working with this virus group.

It was discovered that Koāte® and Konȳne®, if modified in certain respects, could be heated with stabilizers and under carefully defined conditions without affecting the safety or the efficacy of the product ...

Eventually, the AIDS virus was isolated by three independent research groups and was variously named the human T-cell lymphotrophic virus, type III (HTLV-III), the lymphadenopathy-associated virus (LAV), and AIDS-related virus (ARV). It is believed that these viruses are the same or at least closely related, and it was these viruses that were tested to see if they could withstand being treated with heat.

Testing Techniques

The studies to determine the effectiveness of the heat treatment were conducted in the following way. A known amount of virus was added to the clotting factor concentrate, and then it was freeze-dried (a process called lyophylization). The concentrate with the virus was then heated at 68°C for 72 hours. At various time intervals, the concentrate was tested to determine how much, if any, virus was detectable. A portion of the concentrate containing the virus was not heated in order to serve as a control.

This type of study was done by Cutter Laboratories in collaboration with the Centers for Disease Control (CDC). Doctors J. Steven McDougal and Bruce Evatt and their colleagues at the CDC provided HTLV-III/LAV virus to Cutter, where it was added to Factor VIII concentrate and heated at 68°C. After the heat treatment, the virus was not detectable.

A second study was conducted by Dr. Jay Levy of the University of California, San Francisco. Dr. Levy and his group added titers of ARV to human plasma. A Factor VIII filtrate was separated from the "spiked" plasma, which was found to have infectious ARV virus after lyophilization. The Factor VIII was then heat-treated at 68°C. ARV was undetectable after 48 hours. Dr. Levy recommends that heating lyophilized Factor VIII "will eliminate infectious ARV" from plasma-derived coagulation products (Lancet 1: 1456-1457, 1985).

From the data presented above, along with the results of other studies, Dr. McDougal and colleagues concluded: "... both in vitro and in vivo data indicate that the use of heat-treated products will reduce (and hopefully terminate) AIDS transmission by anti-hemophilic factor" (Journal of Clinical Investigation, August 1985).

Cutter Laboratories uses its unique heat-treatment regimen on both Koāte®-HT and on Konȳne®-HT. Contact your hemophilia treatment center for additional information on Koāte®-HT and Konȳne®-HT.

Antibody Screening Test

As soon as the first reports appeared that it was possible to contract AIDS indirectly through blood products, ways in which to screen blood and plasma donors were considered. When first implemented, this was done mainly through history taking. Members of high-risk groups were requested not to give blood voluntarily. Nonetheless, Cutter Laboratories obtains plasma from areas which are not considered high risk for AIDS. Also, Cutter implemented the use of hepatitis B core antibody testing as a surrogate AIDS screening test, but now uses the recently FDA-approved testing for HTLV-III antibodies.

In order to develop a screening test to prevent AIDS from being transmitted through blood products, it was necessary to find out what caused the disease. Once it was determined that the human T-lymphotrophic virus, type III, or HTLV-III was the most likely cause of the disease, the search was intensified for an effective screening technique. What was needed was a test that could be readily available, could be used for large numbers of samples, was accurate, and was reasonably priced.

Five companies have been approved by the government to develop the screening test, or the enzyme-linked immunosorbent

assay (ELISA) kits; three have placed these kits on the market. Each company was supplied by the government with samples of HTLV-III virus. Although not directly helped by the government, several other companies are also developing screening tests.

The first antibody test kits to receive government approval were those being produced by Abbott Laboratories. In the clinical trials, these tests were able to detect the presence of the antibody to the HTLV-III virus 95 percent of the time, and they were able to determine that the blood donor lacked the antibody to the HTLV-III virus 99.8 percent of the time. The test is designed only as a method for screening donor blood and plasma.

In the meantime, several companies are working on a second generation of tests developed through genetic engineering techniques. The ultimate goal for future research, of course, is the development of a vaccine.

...a positive test result does not mean that the person will actually get AIDS.

Practical Value

The recently developed screening test for HTLV-III antibody cannot be used to diagnose AIDS or to detect the AIDS virus in the blood. What it can do is indicate that the antibody to the AIDS virus is present in the blood and that persons who have a positive test have been exposed to the virus at some point in their lives.

Some controversy has developed over who is to be notified if the blood sample proves to be positive. State law may require notification of regulating health agencies. If the donor is to be notified of test results in accordance with state laws, the donor is strongly encouraged to consult a physician, since there is the possibility of transmitting the disease to others and the advice of a physician is extremely important. But more importantly, many of the complications of AIDS are treatable when discovered early, and it is important to be alert to the signs and symptoms, such as persistent fever, unexplained weight loss, swollen glands, shortness of breath, diarrhea, headache, skin ulcers, or persistent cough.

A Positive Test

What does it mean if the test is positive? First of all, that person will be permanently excluded from giving blood and plasma. However, a positive test result does not mean that the person will actually get AIDS. Although the test could indicate a subclinical infection, it could also be due to immunity or to cross-reactivity, or it could even be an error made in the testing. Although the majority of persons with hemophilia test positive for the AIDS antibody, fewer than 1 percent have developed AIDS.

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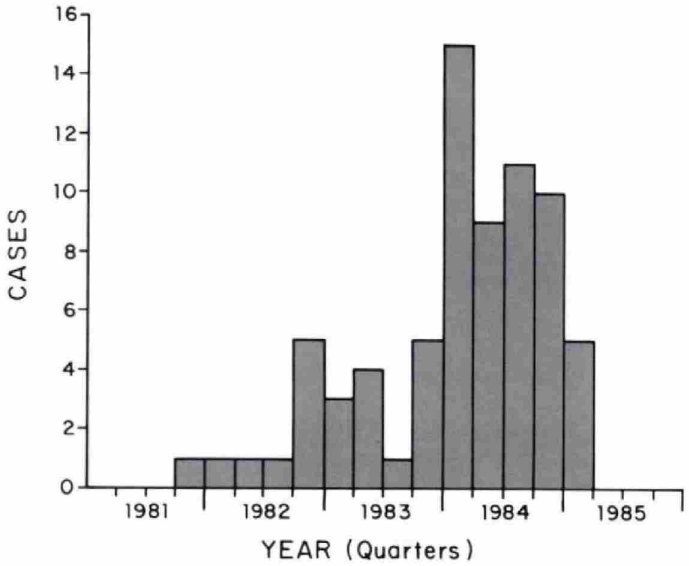
The Centers for Disease Control reported recently that the number of new cases of AIDS in persons with hemophilia is declining or is, at the very least, remaining the same.



Hemophilia-associated acquired immunodeficiency syndrome, by year—United States, 1981-1985.
From: *Morbidity and Mortality Weekly Report*, May 3, 1985.

NEWS FROM CUTTER

Cutter Biological Steps Forward

On February 14, 1985, the Medical and Scientific Advisory Council of the National Hemophilia Foundation announced its recommendations concerning AIDS and the treatment of hemophilia. They supported the use of heat-treated concentrate for Factor VIII and Factor IX. The Centers for Disease Control in Atlanta endorsed this view. Cutter Biological has stepped forward once more in response to these recommendations and to the needs of the hemophilia community. Effective June 21, 1985, Cutter discontinued the distribution of all non-heat-treated antihemophilic concentrate, both Factor VIII and Factor IX. This action is consistent with the results of the collaborative research performed and sponsored by Cutter.

This very positive decision follows course with the previous sound and prudent action by Cutter. In early 1983, Cutter voluntarily intensified plasma donor screening procedures and then was the only commercial manufacturer to begin and use hepatitis B core antibody testing of donated plasma. In early 1984, they announced the time and temperature parameters used in the heat-treatment processes at the same time that Koāte®-HT and Konȳne®-HT became available to the hemophiliac community.

A Matter of Factors

"A Matter of Factors," a recently developed slide/tape presentation for the person with hemophilia and his family, discusses the topic of AIDS. This educational service, sponsored by Cutter Biological, provides the latest information on the safety and efficacy of the various coagulation products.

The blood-screening process and heat treatment are explained in relationship to the AIDS issue. Three physicians well known in the field of hematology also express their opinions on these preventive measures. A review of the disease of hemophilia, the historical development of the coagulation products, and the importance of early treatment for the person with hemophilia are also presented.■

For more information on "A Matter of Factors," contact your local Cutter sales representative or hemophilia center.

MEDILOGUE
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studies on hepatitis, from which semen samples were still available dating back to the 1970s. Once HTLV-III was identified as the cause of AIDS, the reseachers were able to examine the semen taken at different times and to follow the course that the disease took in the patient. They determined that the incubation period ranged from 16 to 65 months, with a mean of 35 months.

Several studies were reported in which HTLV-III was inactivated by chemical, photochemical, and other means. Dr. Linda Martin reported the inactivation of the virus with several chemicals, including household bleach, and then heating the preparation at 56°C for five minutes.

Dr. Milton Mozen from Cutter Laboratories, in a study with Dr. Jay Levy of the University of California Medical Center, San Francisco, reported on the recovery of the AIDS-related retrovirus, or ARV, from cryoprecipitate after the virus has been added to the plasma. They found that the virus remains even throughout the subsequent fractionation procedure, including acid precipitation and filtration, with about a 100-fold reduction in titer in the final lyophilized product. However, when the latter is heated at 68°C, no virus is detectable after 48 hours. Mozen points out that in the manufacture of Factor VIII concentrate, Cutter's heat-treatment process leaves an even wider margin of safety because of a longer treatment period. These results confirm their previous studies with the mouse xenotropic retrovirus.

Dr. Lawrence Kaminsky, in association with Dr. Jay Levy, also reported the serological evidence linking ARV to AIDS and related conditions. Using a highly sensitive indirect immunofluorescent assay, they detected antibodies to the virus in all 133 patients with AIDS. In their study, 68 of 72 persons with the lymphadenopathy syndrome, 15 of 18 sexual contacts of patients with AIDS, and 33 of 51 homosexual controls tested positive for the antibodies. Of 343 persons not belonging to any risk group for AIDS, none was positive. Their data support the conclusion that ARV is responsible for AIDS. ■

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QUESTIONS & ANSWERS
Continued from page 6

have been reports of immune suppression and AIDS in sexual partners of patients who have developed AIDS, one of whom was the wife of a hemophilia patient. Overall, we believe that *if there is a risk of heterosexual transmission* of AIDS by otherwise healthy persons with hemophilia, *it appears to be remote.*

The AIDS virus can be transmit-

Dear Reader: We would like to know more about you and others who may read this issue of ECHO. Your response will help us to present articles that will be of interest to you. Your cooperation is very much appreciated.

Name _____ Age _____ Sex _____

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Do you have hemophilia? _____ If so, what type? _____

Are you a patient? _____ Doctor? _____ Other healthcare professional? _____

Relative of a hemophiliac? _____

Are you associated with a treatment center? _____ If so, which one? _____

Please give location _____

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ted when semen comes in contact with the circulatory system through tears in the mucous membrane. The National Hemophilia Foundation has suggested that it may be advisable for heterosexual couples to avoid anal intercourse and consider the use of condoms until more is known about the natural history of AIDS and the significance of antibodies to HTLV-III/LAV.

ECHO: *Should the person with hemophilia modify or stop treatment with Factor VIII or IX?*

DR. HILGARTNER: *Absolutely not. Persons with hemophilia are urged not to withhold treatment if it is medically indicated.* There is no evidence to warrant changing the current use of Factor VIII or Factor IX. In fact, if treatment is withheld, the crippling complications of the disease well known to all of the adult population with hemophilia will develop, and life-threatening hemorrhage may not be controlled. These complications could then lead to a *greater* use of blood products. If prophylactic treatment is necessary, the use of heat-treated product should be used for replacement.

As previously stated, the current screening of blood donors and the testing of the blood itself has markedly improved the products and made them safer to use. If there are questions about the product prescribed by the physician, they should be discussed with the physician or treatment center.

ECHO: *How do the heat-treated products offer protection from AIDS?*

DR. HILGARTNER: The methods for heat treatment of factor concentrate have shown the ease with which the HTLV-III/LAV virus can be killed. In scientific tests, the manufacturers of concentrate have demonstrated that virus added to concentrate before heat treatment is destroyed by the treatment process. Therefore, the heat-treated products appear to offer protection from the AIDS virus.

ECHO: *What is the treatment for AIDS?*

DR. HILGARTNER: There is no treatment for the immune deficiency caused by the AIDS virus itself. However, there are treatments for some of the opportunistic infections. Some physicians believe that regular treatments with intravenous gamma globulin will provide the patient who has AIDS with antibodies, which may help to fight infections. The experimental drugs or replacement products of the immune system have, for the most part, not provided effective therapy. A preliminary report from France suggests that one such experimental drug has been useful in repairing the immune system of a person with hemophilia, but more testing is necessary to verify this treatment.

ECHO: *What research is being done about AIDS?*

DR. HILGARTNER: Clinical research to understand the course of AIDS is being undertaken in many clinics throughout the country. This includes following the general health status of symptomatic persons with hemophilia, those with HTLV-III/LAV antibodies, patients with some of the symptoms of the AIDS-related complex (ARC), as well as heterosexual contacts of these patients. These studies are vital to tell us about the spectrum of the disease and protective capacity of the antibodies.

Basic research is being done in many laboratories in this country and abroad, particularly at the National Institutes of Health and the Pasteur Institute. It is hoped that the research will help us to learn more about the virus and its patterns of growth so that we can produce a vaccine or drugs that may impede its growth, prevent its spread, or destroy it.■

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The screening technique that is now being used has greater significance for the person receiving whole blood, since whole blood is not pretreated prior to transfusion. However, the person with hemophilia who is using heat-treated factor concentrate derived from plasma is protected by the heat-treatment technique, which destroys the AIDS virus.

AIDS in Hemophilia Decreasing

The Centers for Disease Control reported recently that the number of new cases of AIDS in persons with hemophilia is declining or is, at the very least, remaining the same. As of last May, there were 73 cases of AIDS associated with hemophilia. The first case occurred in 1981, followed by eight in 1982, 13 in 1983, 45 in 1984, and six in the first five months of 1985. The majority of these patients, 71 percent, have hemophilia A, which may reflect the fact that they are more apt to use blood products.

Ten of the 23 patients diagnosed since August 1984 have disorders in addition to hemophilia. The CDC also reported that the most common infection occurring in patients with hemophilia and AIDS is *Pneumocystis carinii* pneumonia (PCP). Sixty-one of the 73 patients had PCP alone or in combination with another opportunistic infection. These patients lived in 27 different states, and the number of cases per state ranged from one to nine.

The decline in the number of cases undoubtedly reflects the steps taken in the medical community: the elimination of high-risk blood donors and the development and increased use of the heat-treated factor concentrates.■

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