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limits of AZT's efficacy and now suggest using the drug either sequentially with other drugs or in a kind of AIDS treatment "cocktail" combining a number of drugs to fight the virus all at once. "Treating people with AZT alone doesn't happen in the real world anymore," said Dr. Mark Jacobson of the University of California--San Francisco. Also, with recent findings indicating that HIV replicates rapidly in the lymph nodes after infection, physicians may begin pushing even harder for early treatment of HIV-infected patients.

"New Infectious Disease Push" American Medical News (04/05/93) Vol. 36, No.

The Center for Disease Control will launch a worldwide network to track the spread of infectious diseases and detect drug-resistant or new strains in time to help prevent their spread. The network is expected to cost between $75 million and $125 million but is an essential part of the Clinton administration's health reform plan, according to the CDC and outside experts. The plan will require the CDC to enhance surveillance of disease in the United States and establish about 15 facilities across the world to track disease.

April 13, 1993

"NIH Plans to Begin AIDS Drug Trials at Earlier Stage" Nature (04/01/93) Vol. 362, No. 6419, P. 382 (Macilwain, Colin)

The National Institutes of Health has announced it will start treating HIV-positive patients as soon as possible after seroconversion, resulting from recent findings that show HIV is active in the body in large numbers

much earlier than was previously believed. Anthony Fauci, director of the U.S. National Institute of Allergy and Infectious Diseases (NIAID), said, "We must address the question of how to treat people as early as we possibly can with drugs that are safe enough to give people for years and that will get around microbial resistance." He said any delay would signify questions over safety and resistance rather than a lack of funds. Fauci, who co-authored one of the two papers published last week in Nature, rejects the argument by one of his co-authors, Cecil Fox, that the new discovery indicates that "$1 billion spent on vaccine trials" has been "a waste of time and money" because the trials were started too long after the patients were infected and were ended too quickly. John Tew of the Medical College of Virginia in Richmond claims that the new evidence strongly backs the argument for early treatment of HIV-infected patients. AIDS activists welcomed the new information but said the scientific community has been slow to understand the significance of infection of the lymph tissue. "We've known about this for five years, but we're glad it is now in the public domain," said Jesse Dobson of the California-based Project Inform. But Peter Duesberg, who believes that AIDS is independent of HIV and is a result of drug abuse in the West, said, "We are several paradoxes away from an explanation of AIDS--even if these papers are right."

April 14, 1993

"Risk of AIDS Virus From Doctors Found to Be Minimal" Washington Post

The risk of HIV being transmitted from infected health-care professionals to patients is minimal, according to new research published in today's Journal of the American Medical Association (JAMA). This finding supports previous conclusions by health experts that the chance of

contracting HIV from a health care worker is remote. Three studies in the JAMA demonstrate that thousands of patients were treated by two HIV-positive surgeons and dentists without becoming infected with the virus. The studies were conducted by separate research teams in New Hampshire, Maryland, and Florida. Each study started with an HIV-positive doctor or dentist and tested all patients willing to participate. The New Hampshire study found that none of the 1,174 patients who had undergone invasive procedures by an HIV-positive orthopedic surgeon contracted HIV. In Maryland, 413 of 1,131 patients operated on by a breast surgery specialist at Johns Hopkins Hospital were found to be HIV-negative. Similarly in Florida, 900 of 1,192 dental

patients, who all had been treated by an HIV-positive general dentist, were tested and found to be negative for HIV. The Florida researchers, led by Gordon M. Dickinson of the University of Miami School of Medicine, said, "This study indicates that the risk for transmission of HIV from a general dentist to his patients is minimal in a setting in which universal precautions are strictly observed." Related Story: Philadelphia Inquirer "Alternative Medicine Advocates Divided Over New NIH Research Program" AIDS Treatment News (04/02/93) No. 172, P. 6 (Gilden, Dave)

The new Office of Alternative Medicine at the National Institutes of Health has raised questions about the NIH's commitment to an effort that uses unorthodox or holistic therapeutic methods. The OAM is a small division of the NIH, with its budget only at $2 million dollars compared to more than $10 billion for the NIH as a whole. In addition, the money for available research grants is even smaller. About $500,000 to $600,000 total will be

available this year for 10 or 20 grants. Kaiya Montaocean, of the Center for Natural and Traditional Medicine in Washington, D.C., says the OAM is afraid to become involved in AIDS. "They have to look successful and there is no easy answer in AIDS," she said. There is also a common perception that the OAM will focus on fields the NIH establishment will find non-threatening, such as relaxation techniques and acupuncture. When the OAM called for an advisory committee conference of about 120 people last year, the AIDS community was largely missing from the meeting. In addition, activists' general lack of contact with the Office has added suspicion that the epidemic will be ignored. Jon Greenberg, of ACT-UP/New York, said, "The OAM advisory panel is composed of practitioners without real research experience. It will take them several years to accept the nature of research."

Nevertheless, Dr. Leanna Standish, research director and AIDS investigator at the Bastyr College of Naturopathic Medicine in Seattle, said, "Here is a wonderful opportunity to fund AIDS research. It's only fair to give the Office time to gel, but it's up to the public to insist that it's much, much more [than public relations]."

"Herpesvirus Decimates Immune-cell Soldiers" Science News (04/03/93) Vol. 143, No. 14, P. 215 (Fackelmann, Kathy A.)

Scientists conducting test tube experiments have found that herpesvirus-6 can attack the human immune system's natural killer cells. This attack causes the killer cells to malfunction, diminishing an important component in the immune system's fight against diseases. Also, the herpesvirus-6 may be a factor in immune diseases, such as AIDS. In 1989, Paolo Lusso's research found that herpesvirus-6 attacks another white cell, the CD4 T-lymphocyte, which is the primary target of HIV. Lusso also found that herpesvirus-6 can

kill natural killer cells. Scientists previously knew that the natural killer cells of patients infected with HIV do not work correctly. Lusso's research represents the first time scientists have indicated that natural killer cells are vulnerable to any kind of viral attack, according to Anthony L. Komaroff, a researcher with Harvard Medical School. Despite the test-tube findings, scientists are uncertain whether the same result occurs in the body. Lusso's team also found that herpesvirus-6 produces the CD4 receptor molecule that provides access for HIV. CD4 T-lymphocytes express this surface receptor, making them vulnerable to HIV's attack. Researchers concluded that herpesvirus-6 cells can exacerbate the affects of HIV.

April 15, 1993

"AIDS and Priorities in the Global Village: To the Editor" Journal of the American Medical Association (04/07/93) Vol. 269, No. 13, P. 1636 (Gellert, George and Nordenberg, Dale F.)

All health-care workers are obligated and responsible for not only ensuring that politicians understand the dimensions of certain health problems, but also to be committed to related policies, write George Gellert and Dale F. Nordenberg of the Orange County Health Care Agency, Santa Ana, Calif., and the Emory University School of Public Health in Atlanta, Ga., respectively. Dr. Berkley's editorial on why American doctors should care about the AIDS epidemic beyond the United States details several reasons for the concerted interest that all countries share in combating AIDS. It should be noted that while AIDS leads in hastening global health interdependence, it is not the only illness doing so. Diseases such as malaria and many

respiratory and intestinal pathogens have similarly inhibited the economic development of most of humanity and acted to marginalize large populations. Berkley mentions the enormous social and economic impact that AIDS will have on many developing countries, and the increased need for international assistance that will result. Berkley also cites the lack of political aggressiveness toward the AIDS epidemic in its first decade. But now there is a new administration with a promise of substantial differences in approach to international health and development in general, and HIV/AIDS in particular. Vice President Al Gore proposes in his book "Earth in the Balance" a major environmental initiative that includes sustainable international development, with programs to promote literacy, improve child survival, and disseminate contraceptive technology and access throughout the developing world. If enacted, this change in policy could drastically change the future of worldwide health.

"AIDS and Priorities in the Global Village: In Reply" Journal of the American

Medical Association (04/07/93) Vol. 269, No. 13, P. 1636 (Berkley, Seth)

Every nation should tackle HIV as early and aggressively as possible before the disease reaches an endemic state, even at a cost of diverting less attention to some other illnesses, writes Seth Berkley of the Rockefeller Foundation in New York, N.Y., in reply to a letter by Drs. Gellert and Nordenberg. Although it is true that diseases other than AIDS, such as malaria and respiratory and intestinal illnesses, have similarly inhibited economic development in developing countries and deserve much more attention than they are getting, Berkley disagrees with the contention that AIDS is

receiving too much attention. HIV differs from other diseases, in most developing countries because it is continuing to spread. For most endemic diseases, the outcome of neglecting interventions for one year is another year of about the same level of needless disease and death. But with AIDS and its increasing spread, the cost of neglect, not only in disease burden but financially, is much greater. Interventions in the early part of a rampantly spreading epidemic like HIV are highly cost-effective because each individual infection prevented significantly interrupts transmission. Berkley says he agrees with Gellert and Nordenberg about the gigantic social and economic effects of AIDS and about the need for political leadership. But he concludes that not only is assertive political leadership needed in the United States for the AIDS epidemic, but even more so in developing countries with high rates of HIV infection and where complacency about the epidemic has been the rule.

AIDS/HIV Articles

First HIV Vaccine Trial Begins in HIV-Infected Children

March 29, 1993

First HIV Vaccine Therapy Trial Begins In HIV-Infected Children

The National Institutes of Health has opened the first trial of experimental HIV vaccines in children who are infected with the human immunodeficiency virus (HIV), the virus that causes AIDS.

The trial will compare the safety of three HIV experimental vaccines in 90 children recruited from at least 12 sites nationwide. Volunteers must be HIV-infected but have no symptoms of HIV disease.

HHS Secretary Donna E. Shalala said this initial study can be seen as "a hopeful milestone in our efforts to ameliorate the tragedy of HIV-infected children who now face the certainty they will develop AIDS."

Anthony S. Fauci, M.D., director of the National Institute of Allergy and Infectious Diseases and of the NIH Office of AIDS Research, said the trial "is the first step in finding out whether vaccines can help prevent or delay disease progression in children with HIV who are not yet sick." If these vaccines prove to be safe, more sophisticated questions about their therapeutic potential will be assessed in Phase II trials.

The Centers for Disease Control and Prevention estimates 10,000 children in the United States have HIV. By the end of the decade, the World Health Organization projects 10 million children will be infected worldwide.

The study will enroll children ages 1 month to 12 years old. NIAID, which funds the AIDS Clinical Trials Group network, anticipates conducting the trial at nine ACTG sites around the country and three sites participating in the ACTG but funded by the National Institute of Child Health and Human Development.

Preliminary evidence from similar studies under way in infected adults shows that certain vaccines can boost existing HIV-specific immune responses and

stimulate new ones. It will be several years, however, before researchers know how these responses affect the clinical course of the disease.

The results from the pediatric trial, known as ACTG 218, will be examined closely for other reasons as well. "This trial will provide the first insight into how the immature immune system responds to candidate HIV vaccines," said

Daniel Hoth, M.D., director of NIAID's division of AIDS. "We need this information to design trials to test whether experimental vaccines can prevent HIV infection in children."

In the United States, most HIV-infected children live in poor inner-city areas, and more than 80 percent are minorities, mainly black or Hispanic. Nearly all HIV-infected children acquire the virus from their mothers during pregnancy or at birth. An infected mother in the United States has more than a one in four chance of transmitting the virus to her baby. As growing numbers of women of childbearing age become exposed to HIV through injection drug use or infected sexual partners, researchers expect a corresponding increase in the numbers of infected children.

HIV disease progresses more rapidly in infants and children than in adults. The most recent information suggests that 50 percent of infants born with HIV develop a serious AIDS-related infection by 3 to 6 years of age. These infections include severe or frequent bouts of common bacterial illnesses of childhood that can result in seizures, pneumonia, diarrhea and other symptoms leading to nutritional problems and long hospital stays.

At least half of the children in the trial will be 2 years of age or younger to enable comparison of the immune responses of the younger and older participants. All volunteers must have well-documented HIV infection but no symptoms of HIV disease other than swollen lymph glands or a mildly swollen liver or spleen. They cannot have received any anti-retroviral or immune-regulating drugs within one month prior to their entry into the study.

Study chair John S. Lambert, M.D., of the University of Rochester Medical School, and co- chair Samuel Katz, M.D., of Duke University School of Medicine, will coordinate the trial assisted by James McNamara, M.D., medical

officer in the pediatric medicine branch of NIAID's division of AIDS.

"We will compare the safety of the vaccines by closely monitoring the children for any side effects, to see if one vaccine produces more swollen arms or fevers, for example, than another," said Dr. McNamara. "We'll also look at whether low or high doses of the vaccines stimulate immune responses or other significant laboratory or clinical effects." He emphasized that the small study size precludes comparing these responses or effects among the three

products.

The trial will test two doses each of three experimental vaccines made from recombinant HIV proteins. These so-called subunit vaccines, each genetically engineered to contain only a piece of the virus, have so far proved well-tolerated in ongoing trials in HIV-infected adults.

One vaccine made by MicroGeneSys Inc. of Meriden, Conn., contains gp160--a protein that gives rise to HIV's surface proteins--plus alum adjuvant. Adjuvants boost specific immune responses to a vaccine. Presently, alum is the only adjuvant used in human vaccines licensed by the Food and Drug Administration.

Both of the other vaccines--one made by Genentech Inc. of South San Francisco and the other by Biocine, a joint venture of Chiron and CIBA-Geigy, in Emeryville, Calif.--contain the major HIV surface protein, gp120, plus adjuvant. The Genentech vaccine contains alum, while the Biocine vaccine contains MF59, an experimental adjuvant that has proved safe and effective in other Phase I vaccine trials in adults.

A low dose of each product will be tested first against a placebo in 15

children. Twelve children will be assigned at random to be immunized with the experimental vaccine, and three children will be given adjuvant alone, considered the placebo. Neither the health care workers nor the children will be told what they receive.

If the low dose is well-tolerated, controlled testing of a higher dose of the experimental vaccine and adjuvant placebo in another group of 15 children will begin.

Each child will receive six immunizations--one every four weeks for six months--and be followed-up for 24 weeks after the last immunization.

For more information about the trial sites or eligibility for enrollment, call the AIDS Clinical Trials Information Service, 1-800-TRIALS-A, from 9 a.m. to 7 p.m., EST weekdays. The service has Spanish-speaking information specialists available. Information on NIAID's pediatric HIV/AIDS research is available from the Office of Communications at (301) 496- 5717.

NIH, CDC and FDA are agencies of the U.S. Public Health Service in HHS. For press inquiries only, please call Laurie K. Doepel at (301) 402-1663.

News from the National Institute of Dental Research

There is new evidence that the human immunodeficiency virus can cause disease independently of its ability to suppress the immune system, say scientists at the National Institues of Health.

They report that HIV itself, not an opportunistic infection, caused scaling skin conditions to develop in mice carrying the genes for HIV. Although the HIV genes were active in the mice, they did not compromise the animals' immunity, the researchers found. This led them to conclude that the HIV

itself caused the skin disease.

Our findings support a growing body of evidence that HIV can cause disease without affecting the immune system, said lead author Dr. Jeffrey Kopp of the National Institute of Dental Research (NIDR). Dr. Kopp and his colleagues described their study in the March issue of AIDS Research and Human Retroviruses.

Developing animal models of HIV infection has been difficult, since most animals, including mice, cannot be infected by the virus. To bypass this problem, scientists have developed HIV-transgenic mice, which carry genes for HIV as well as their own genetic material.

NIDR scientists created the transgenic mice by injecting HIV genes into mouse eggs and then implanting the eggs into female mice. The resulting litters contained both normal and transgenic animals.

Institute scientists had created mice that carried a complete copy of HIV genetic material in l988. Those mice, however, became sick and died too soon after birth to study in depth. In the present study, the scientists used an incomplete copy of HIV, which allowed the animals to live longer.

Some of the transgenic animals developed scaling, wart-like tumors on their necks and backs. Other transgenic mice developed thickened, crusting skin lesions that covered most of their bodies, resembling psoriasis in humans. No skin lesions developed in their normal, non-transgenic littermates.

Studies of tissue taken from the wart-like skin tumors showed that they were a type of noncancerous tumor called papilloma. Although the papillomavirus can cause these skin lesions, laboratory tests showed no sign of that virus in the animals.

Tissue samples taken from the sick mice throughout the study revealed the

presence of a protein-producing molecule made by the HIV genetic material.

Evidence of HIV protein production proved that the viral genes were "turned on," or active, said Dr. Kopp.

The scientists found no evidence, however, of compromised immunity in the mice: no increase in their white blood cell count and no signs of common infections. The fact that HIV genes were active but the animals' immune systems were not suppressed confirms that the virus itself was causing the skin lesions, Dr. Kopp said.

Further proof of HIV gene involvement came from a test in which the scientists exposed the transgenic animals to ultraviolet light. The light increased HIV genetic activity causing papillomas to develop on formerly healthy skin. Papilloma formation in response to increased HIV genetic activity proved the genes were responsible for the skin condition, the scientists said. No lesions appeared on normal mice exposed to the UV light.

The transgenic mice used in this study were developed at NIDR by Dr. Peter Dickie, who is now with the National Institute of Allergy and Infectious Diseases.

Collaborating on the study with Dr. Kopp were Mr. Charles Wohlenberg, Drs. Nickolas Dorfman, Joseph Bryant, Abner Notkins, and Paul Klotman, all of NIDR; Dr. Stephen Katz of the National Cancer Institute; and Dr. James Rooney, formerly with NIDR and now with Burroughs Wellcome.

Clinical Consultation Telephone Service for AIDS

March 4, 1993

HHS Secretary Donna E. Shalala today announced the first nationwide clinical consultation telephone service for doctors and other health care professionals who have questions about providing care to people with HIV infection or AIDS.

The toll-free National HIV Telephone Consulting Service is staffed by a physician, a nurse practitioner and a pharmacist. It provides information on drugs, clinical trials and the latest treatment methods. The service is funded by the Health Resources and Services Administration and operates out of San Francisco General Hospital.

Secretary Shalala said, "One goal of this project is to share expertise so patients get the best care. A second goal is to get more primary health care providers involved in care for people with HIV or AIDS, which reduces treatment cost by allowing patients to remain with their medical providers and community social support networks. Currently, many providers refer patients with HIV or AIDS to specialists or other providers who have more experience."

Secretary Shalala said, "This clinical expertise should be especially helpful for physicians and providers who treat people with HIV or AIDS in communities and clinical sites where HIV expertise is not readily available."

The telephone number for health care professionals is 1-800-933-3413, and it is accessible from 10:30 a.m. to 8 p.m. EST (7:30 a.m. to 5 p.m. PST) Monday through Friday. During these times, consultants will try to answer questions immediately, or within an hour. At other times, physicians and health care providers can leave an electronic message, and questions will be answered as quickly as possible.

Health care professionals may call the service to ask any question

related to providing HIV care, including the latest HIV/AIDS drug treatment information, clinical trials information, subspecialty case referral, literature searches and other information. The service is designed for health care professionals rather than patients, families or others who have alternate sources of information or materials.

When a health care professional calls the new service, the call is taken by either a clinical pharmacist, primary care physician or family nurse practitioner. All staff members have extensive experience in outpatient and inpatient primary care for people with HIV-related diseases. The consultant asks for patient-specific information, including CD4 cell count, current medications, sex, age and the patient's HIV history.

This national service has grown out of a 16-month local effort that

responded to nearly 1,000 calls from health care providers in northern California. The initial project was funded by HRSA's Bureau of Health Professions, through its Community Provider AIDS Training (CPAT) project, and by the American Academy of Family Physicians.

"When providers expand their knowledge, they also improve the quality of care they are able to provide to their patients," said HRSA Administrator Robert G. Harmon. M.D., M.P.H. "This project will be a great resource for health care professionals and the HIV/AIDS patients they serve."

"This service has opened a new means of communication between health care professionals and experts on HIV care management," said HRSA's associate administrator for AIDS and director of the Bureau of Health Resources Development, G. Stephen Bowen, M.D., M.P.H. "Providers who treat people with

HIV or AIDS have access to the latest information on new drugs, treatment methods and therapies for people with HIV or AIDS."

HRSA is one of eight U.S. Public Health Service agencies within HHS.

AIDS Hotline Numbers for Consumers

CDC National AIDS Hotline -- 1-800-342-AIDS

for information in Spanish - 1-800-344-SIDA

AIDS Clinical Trials (English & Spanish) -- 1-800-TRIALS-A

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