



THE SECRETARY OF DEFENSE
WASHINGTON THE DISTRICT OF COLUMBIA

24 OCT 1985

MEMORANDUM FOR SECRETARIES OF THE MILITARY DEPARTMENTS
CHAIRMAN, JOINT CHIEFS OF STAFF
ASSISTANT SECRETARY OF DEFENSE (FM&P)
ASSISTANT SECRETARY OF DEFENSE (RA)
ASSISTANT SECRETARY OF DEFENSE (PA)
ASSISTANT SECRETARY OF DEFENSE (HA)
ASSISTANT SECRETARY OF DEFENSE (LA)
GENERAL COUNSEL

SUBJECT: Policy on Identification, Surveillance, and Disposition of
Military Personnel Infected With Human T-Lymphotropic
Virus Type III (HTLV-III)

The following policy is established relative to infection of military members with Human T-Lymphotropic Virus Type III (HTLV-III). This initial policy is intended to reflect current knowledge regarding the natural history of this disease, the risks to the infected individual incident to military service, the risk of transmission of disease to noninfected personnel, the effect of infected individuals on the function of the unit, and the safety of the blood supply. These policies are adopted as interim guidance which shall be reviewed within one year. This review shall assess developments in the medical management of HTLV-III infections, information obtained through longitudinal epidemiologic studies of the natural history of HTLV-III infection, and the effects of this interim guidance on force management. Appropriate changes to DOD directives shall be promulgated within 30 days of the conclusion of this review.

A. ACCESSION.

Applicants for enlisted service shall be screened for exposure to HTLV-III at the Military Entrance Processing Station or the initial points of entry to military service. Candidates for officer service shall be screened for exposure to HTLV-III during their pre-appointment or pre-contracting physical examinations. Individuals confirmed as HTLV-III antibody positive (Food and Drug Administration-approved enzyme immunoassay (EIA) serologic test and, if positive, a positive immunoelectrophoresis test (Western blot)) are not eligible for military service. The rationale for this policy is

- that the condition existed prior to service,

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- the Department avoids potential medical costs and the possibility that the individual shall not complete his or her service commitment,
- clinical evidence indicates that pre-AIDS patients may suffer adverse and potentially life-threatening reactions to some live virus immunizations administered at basic training,
- an antibody positive individual is not able to participate in battlefield blood donor activities or other blood donation programs, and
- presently, there is no way to differentiate between antibody positive individuals who will progress to clinical disease and antibody positive individuals who will remain healthy.

B. DISEASE SURVEILLANCE.

1. Active duty and reserve component military personnel shall be screened for the presence of HTLV-III antibody. Generally, implementation should be in the following priority order:

- individuals serving in, or subject to deployment on short notice to areas of the world with a high risk of endemic disease or with minimal existing medical capability,
- individuals serving in, or pending assignment to, all other overseas permanent duty stations,
- individuals serving in units subject to deployment overseas,
- other individuals or units deemed appropriate by the respective military department such as medical personnel involved in the care of HTLV-III infectious patients,
- all remaining individuals in conjunction with routinely scheduled periodic physical examinations.

2. Individuals who are confirmed to be antibody positive shall be medically evaluated to determine the status of their infection and the potential adverse consequences to the individual of serving in a particular geographic region. The Assistant Secretary (Health Affairs) shall convene a Tri-Service medical working group to develop a standardized clinical protocol to ensure consistent evaluation and staging of each patient at all military medical treatment facilities.

3. The medical assessment of each exposure to and/or case of HTLV-III infection shall include an epidemiological assessment of the potential transmission of HTLV-III to close personal contacts and family of the patient. This information is vital to provide appropriate preventive medicine counseling and to the continued development of scientifically based information regarding the natural history and transmission pattern of HTLV-III. Therefore, the occurrence of HTLV-III infection shall not be used as a basis for punitive action against an individual.

4. Each military medical service shall conduct ongoing clinical evaluations of each antibody positive individual's health status at least annually, provide appropriate preventive medicine counseling to individual patients, provide public health education materials to the beneficiary population, conduct longitudinal epidemiologic evaluations of antibody positive individuals, and prepare internal reports to facilitate timely review and reassessment of current policy guidelines.

5. Physicians, hospitals, medical clinics, other health care facilities, and clinical laboratories shall notify promptly the cognizant military health authority whenever laboratory examination of any specimen derived from the human body yields microscopic, cultural, immunologic, serologic or other evidence indicative of infection with HTLV-III virus.

C. RETENTION.

1. Individuals who are antibody positive but manifest no evidence of progressive clinical illness or immunological deficiency (physical and laboratory assessment, demonstration of ability to respond to immunizations, and ability to mount a protective immune response to immunizations or exposure to naturally occurring pathogens) shall be retained. The Service Secretaries, in order to protect the health and safety of infected individuals and of other military persons, may limit assignment of such individuals with respect to the nature and location of the duties performed in accordance with operational requirements.

2. All antibody positive persons shall receive a comprehensive clinical and immunological evaluation at least annually. Each individual shall be counseled on the risks of disease transmission, methods of prevention, and informed that they are ineligible to donate blood.

D. SEPARATION.

1. Individuals who are infected with HTLV-III and demonstrate progressive clinical illness shall be referred for medical evaluation for a determination of fitness for continued service in accordance with Title 10 United States Code Section 1201, et seq.

2. Individuals who are infected with HTLV-III and are found not to have complied with preventive medicine counseling for individual patients may be separated for the convenience of the Government.

3. Separation for the convenience of the Government or for misconduct based upon evidence other than HTLV-III infection is unaffected by this policy memorandum.

E. SAFETY OF THE BLOOD SUPPLY.

DOD Military Blood Program Office policies and Food and Drug Administration guidelines shall be followed by the Military Departments Blood Programs and by civilian blood agencies collecting blood on military installation. In the event that units of blood shall not be screened for infectious agents prior to transfusing (contingency or battlefield situations), the DOD Military Blood Program Office in coordination with the Military Departments shall provide guidance to operational units to ensure that potential donors have been screened.

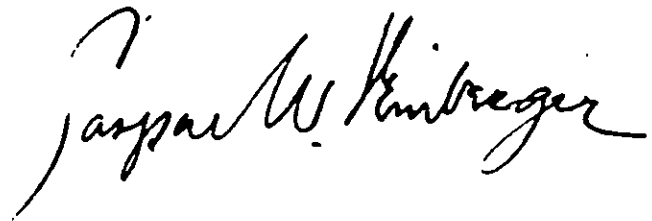
F. LIMITATIONS ON THE USE OF INFORMATION

1. Results obtained from laboratory tests for HTLV-III performed under this memorandum and information concerning personal drug use or consensual sexual activity disclosed by a Service member as part of an epidemiological assessment under this memorandum may not be used against the Service member in actions under the Uniform Code of Military Justice, in a Line of Duty determination, or on the issue of characterization in separation proceedings. Such information may not be used as the basis for separation of the service member except for (a) separation based upon physical disability, or (b) separation for the convenience of the government after a hearing before a board of officers and approval by the Secretary or an Assistant Secretary of the Service concerned.

2. The limitations in paragraph F.1. do not apply to:

(a) The introduction of evidence for impeachment or rebuttal purposes in any proceeding in which the evidence of drug abuse or relevant sexual activity (or lack thereof) has been first introduced by the Service member;

(b) Disciplinary or other action based on independently derived evidence.



- References:
- (a) Armed Forces Epidemiological Board Memorandum, 17 September 1985, Human T-Lymphotropic Virus Type III (HTLV-III) Antibody Positivity
 - (b) Deputy Secretary of Defense Memorandum, 30 August 1985, HTLV-III Testing
 - (c) Assistant Secretary of Defense (Health Affairs) Memorandum, 14 August 1985, Standardization of Reporting Requirements for Blood Collection Agencies on Military Installations
 - (d) Assistant Secretary of Defense (Health Affairs) Memorandum, 17 July 1985, Military Implementation of Public Health Service Provisional Recommendations Concerning Testing Blood and Plasma for Antibodies to HTLV-III
 - (e) DOD Military Blood Program Office Memorandum, 13 March 1985, Military Implementation of Public Health Service Provisional Recommendations Concerning Testing Blood and Plasma for Antibodies to HTLV-III
 - (f) Department of Defense Directive 6200.1, April 27 1973, Policy Concerning the Venereal Disease Control Program of the Armed Forces
 - (g) Department of Defense Directive 1332.18, September 9, 1968, Separation from the Military Service by Reason of Physical Disability
 - (h) Title 10 United States Code Section 1201, et seq.



DEPARTMENT OF DEFENSE
ARMED FORCES EPIDEMIOLOGICAL BOARD

THE EXECUTIVE SECRETARY
ARMED FORCES EPIDEMIOLOGICAL BOARD
OFFICE OF THE SURGEON GENERAL
DEPARTMENT OF THE ARMY
WASHINGTON, D.C. 20310-2300
(202) 695-9115

DASG-AFEB 85-8

17 September 1985

MEMORANDUM FOR THE ASSISTANT SECRETARY OF DEFENSE (HEALTH AFFAIRS)
THE SURGEON GENERAL, DEPARTMENT OF THE ARMY
THE SURGEON GENERAL, DEPARTMENT OF THE NAVY
THE SURGEON GENERAL, DEPARTMENT OF THE AIR FORCE

SUBJECT: Human T-Lymphotropic Virus Type III (HTLV-III) Antibody Positivity

1. At the request of the Assistant Secretary of Defense, Health Affairs, the Armed Forces Epidemiological Board (AFEB) members, consultants and respective military medical service representatives met 11 through 13 September 1985 to consider a set of questions on the above subject (Enclosures 1 and 2).
2. The AFEB traditionally has conceived its mission to be that of rendering advice to the end of ensuring the maintenance of a healthy, effective military service which is ready at all times for rapid deployment. It believes that HTLV-III infections should be addressed in the military services as any other infectious or contagious disease. In this regard it is noteworthy that its similarities to hepatitis B are striking in many respects. The primary objective of the Board must be to protect the health of the individual and simultaneously to prevent the spread of infection to other personnel within the Armed Forces.
3. The Board makes its recommendations relevant to HTLV-III antibody positivity in the light of its evaluation of the current state of knowledge of this complex disease. The Board is well aware of the present threat and of the potential for greater threat based on the comprehensive assessment of several factors to include: a) The risks to the infected individual incident to military service, b) The risk of transmission of illness to non-infected personnel, c) The impact of infected individuals on the function of their unit, and d) The safety of the blood supply.
4. The recommendations of the Board may be subject to change at such time as the natural history of HTLV-III infection becomes more clear. Under these conditions, pertinent and longitudinal studies would be appropriate. Under ideal circumstances the screening of all active duty military personnel for HTLV-III antibody and hepatitis B antigen could be advisable. However, such screening is unnecessary based on information currently available relative

SUBJECT: Human T-Lymphotropic Virus Type III (HTLV-III) Antibody Positivity

to the threat of illness to others or the limitations of personnel to perform their duties. Moreover, the prospect of screening all active military members for HTLV-III antibody at this time is not envisioned as feasible - not only because of the logistical and economical requirements, but especially because of the limited availability of trained personnel and medical resources. The qualifying criterion is simply that it is unknown whether an individual with HTLV-III antibody will progress to active illness. Future studies of the natural history of the syndrome should help clarify this important matter.

5. Based on a thorough review of available information and subsequent discussion, the Board makes the following recommendations:

a. ALL ACTIVE DUTY PERSONNEL PENDING REASSIGNMENT TO OVERSEAS PERMANENT DUTY STATIONS SHOULD BE SCREENED FOR THE PRESENCE OF HTLV-III ANTIBODY. IF THESE INDIVIDUALS ARE FOUND TO BE POSITIVE BY ELISA AND BY AN APPROPRIATE CONFIRMATORY TEST, THE SERVICE MEMBER SHOULD BE MEDICALLY EVALUATED TO DETERMINE THE STATUS OF HIS/HER INFECTION.

This is appropriate to allow identification of those at high risk for progression of infection and at high risk from exotic diseases before an extended overseas tour.

b. INDIVIDUALS WHO ARE ANTIBODY POSITIVE BUT MANIFEST NO EVIDENCE OF PROGRESSIVE CLINICAL ILLNESS OR IMMUNOLOGICAL DEFICIENCY MAY BE CONSIDERED FOR WORLD-WIDE DUTY. ALL ANTIBODY POSITIVE PERSONS SHOULD RECEIVE A COMPREHENSIVE AND IMMUNOLOGICAL EVALUATION AT LEAST ANNUALLY. THEY SHOULD ALSO BE COUNSELED ON RISKS OF TRANSMISSION AND BE DESIGNATED AS DONOR BLOOD INELIGIBLE. MILITARY PERSONNEL WITH PROGRESSIVE CLINICAL ILLNESS OR IMMUNOLOGICAL COMPROMISE SHOULD BE REFERRED TO A MEDICAL EVALUATION BOARD FOR A DETERMINATION OF FITNESS FOR WORLDWIDE DUTY.

c. NEW CANDIDATES FOR ACTIVE DUTY IDENTIFIED AS HTLV-III ANTIBODY POSITIVE (TWO ELISA AND CONFIRMATORY TESTS) AT THE TIME OF INDUCTION WILL BE REJECTED FROM MILITARY SERVICE. THE CANDIDATE WILL BE ADVISED TO CONSULT HIS/HER PERSONAL PHYSICIAN.

This judgment is based on the possibility that such antibody positive persons may have an increased potential to develop the Acquired Immune Deficiency Syndrome - particularly when they are given required live biologic vaccines, when they are exposed to or are infected with agents such as the Plasmodium of malaria or are subjected to other biological

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or physical stresses. It is conceivable that future testing and medical evaluation may show that individuals with positive antibody alone may be healthy and therefore should not be ultimately precluded from consideration for military service.

6. Current evidence indicates that HTLV-III is transmitted to others by blood transfusion from an infected person by the injection of infected blood products or by intimate contact with an infected person. The risk of transmission of HTLV-III is not completely understood and requires further evaluation. However, day-to-day association with infected persons by close household contacts does not pose a threat to the uninfected individuals. There are hundreds of instances where adults or children living with persons with AIDS or positive for HTLV-III antibody have themselves failed to become infected or antibody positive. The same situation has been observed regarding medical contacts with known patients. Moreover, health professionals who have experienced needle puncture with needles contaminated with materials from AIDS patients have very rarely developed illness or serologic evidence of infection. Specifically, only one such case has been reported at present. The Board, therefore, makes the following recommendations relative to military operational settings:

ENVIRONMENTAL CONTACTS IN MILITARY OPERATIONAL SETTINGS SUCH AS TANKS, SUBMARINES AND AIRCRAFT ARE NOT REGARDED AS SIGNIFICANT RISKS FOR INFECTION BY HTLV-III. IN ACCORDANCE WITH UNITED STATES PUBLIC HEALTH SERVICE RECOMMENDATIONS, PERSONNEL WHO ARE HBAG AND/OR HTLV-III ANTIBODY POSITIVE SHOULD BE DESIGNATED AS UNSUITABLE AS BLOOD DONORS.

7. Although generally there is no perceptible risk of transmission by non-sexual person-to-person contact, there are other concerns which are relevant within the military/community setting. The following recommendations by the Board are intended to address these issues:

a. SERVICE PLANNING ON CONTINGENCY BLOOD SAMPLES SHOULD TAKE THE POTENTIAL FOR HTLV-III INFECTION INTO ACCOUNT. THE PERIODIC SCREENING OF ALL MILITARY PERSONNEL IS NOT RECOMMENDED DUE TO EXCESSIVE SCREENING COSTS WEIGHED AGAINST LOW RISK AND THE INABILITY TO ENSURE THE ABSENCE OF INFECTIVITY BY RANDOM TESTING. HOWEVER, THE BOARD RECOMMENDS THAT DONATED BLOOD BE SCREENED TO DETECT HTLV-III ANTIBODY AND HEPATITIS-B ANTIGEN WHEREVER A SIGNIFICANT NUMBER OF BLOOD UNITS ARE TO BE PROCESSED.


b. ALTHOUGH PERSONNEL PENDING OVERSEAS ASSIGNMENT ARE RECOMMENDED FOR THE HIGHEST SCREENING PRIORITY, THOSE CURRENTLY SERVING AT AN OVERSEAS DUTY STATION MAY ALSO BE CANDIDATES FOR SCREENING. SUCH SCREENING SHOULD BE ACCOMPLISHED IN A PRIORITIZED FASHION, WITH THE HIGHEST PRIORITY TO THOSE ASSIGNED AT LOCATIONS WITH A HIGH RISK OF ENDEMIC DISEASE OR WITH MINIMAL MEDICAL CAPABILITY.


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SUBJECT: Human T-Lymphotropic Virus Type III (HTLV-III) Antibody Positivity

C. THE BOARD RECOMMENDS THAT ADDITIONAL EDUCATION BE PROVIDED ON TECHNIQUES TO MINIMIZE THE TRANSMISSION OF THIS INFECTION IN ORDER TO REDUCE UNFOUNDED FEARS REGARDING THE ETIOLOGY AND EPIDEMIOLOGY OF THE DISEASE.

FOR THE ARMED FORCES EPIDEMIOLOGICAL BOARD


THEODORE E. WOODWARD, M.D.
President, AFEB


ROBERT A. WELLS, Ph.D.
LTC(P), USA, MSC
Executive Secretary

2 Encls

CF:

Board Members

Cmdr, HQ USAF SGP

Ch, Prev Med Div, OTSG-DA

Ch, Prev Med Div, OTSG-DAF

Dir, Occup & Prev Med Div, BUMED-DN

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Cmdr, US Army Med R&D Cmd



HEALTH AFFAIRS

OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE

WASHINGTON, D. C. 20301-1200

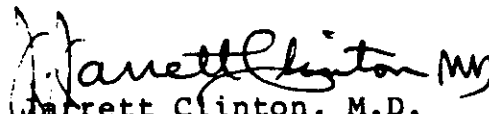
9 SEP 1985

MEMORANDUM FOR EXECUTIVE SECRETARY, ARMED FORCES EPIDEMIOLOGICAL BOARD

SUBJECT: HTLV-III Antibody Positivity

In our June 10, 1985 memorandum to the Armed Forces Epidemiological Board, we requested advice on broad public health issues of HTLV-III antibody positivity in the military. Your specific attention to the following questions in the context of the original request will assist this office in the development of policy guidance:

- 1) Should personnel on active duty be screened for HTLV-III antibody?
- 2) What steps should be taken with respect to active duty personnel who screen confirmed positive for HTLV-III antibody?
- 3) Should confirmed HTLV-III antibody positive individuals, identified through screening of potential active duty accessions, be permitted to join the military services?
- 4) What public health risk does a confirmed HTLV-III antibody positive individual pose in the military operational setting?
- 5) What public health risk does a confirmed HTLV-III antibody positive individual pose in the military community setting?


J. Jarrett Clinton, M.D.
Deputy Assistant Secretary
(Professional Affairs & Quality Assurance)



HEALTH AFFAIRS

OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE

WASHINGTON, D.C. 20301

10 JUN 1985

MEMORANDUM FOR THE EXECUTIVE SECRETARY, ARMED FORCES
EPIDEMIOLOGICAL BOARD

SUBJECT: HTLV-III Antibody Positivity

As introduced at the June 6 meeting of the Subcommittee on Disease Control, request the Board address the issue of the public health significance of HTLV-III antibody positivity.

Specifically, what guidance can the board provide regarding the appropriate implementation of public health surveillance and control measures? Given the spread of HTLV-III infection outside previously identified high-risk groups, what studies should the services conduct and what data should be gathered to better define the natural history of and potential military importance of this infectious agent in active-duty populations? Given the comprehensive health care system of the Armed Forces, a closed system, how might our concerns and approaches differ from those of the civilian sector?

Your considered deliberation of this critical issue is requested.

J. Jarrett Clinton, M.D.
Deputy Assistant Secretary
(Professional Affairs & Quality Assurance)



THE DEPUTY SECRETARY OF DEFENSE

WASHINGTON, D.C. 20301

30 August 1985

MEMORANDUM FOR SECRETARIES OF THE MILITARY DEPARTMENTS
ASSISTANT SECRETARY OF DEFENSE (FM&P)
ASSISTANT SECRETARY OF DEFENSE (HA)
ASSISTANT SECRETARY OF DEFENSE (PA)
ASSISTANT SECRETARY OF DEFENSE (LA)
GENERAL COUNSEL

SUBJECT: HTLV-III Testing

To protect the health of military personnel all potential accessions will be screened for HTLV-III antibody by a Food and Drug Administration-approved enzyme immunoassay (EIA) serologic test and, if positive, an immunoelectrophoresis (Western blot) test.

This testing will be accomplished during the initial physical examination at the Military Entrance Processing Station (MEPS). The blood samples will be drawn by medical personnel at the MEPS. EIA laboratory testing for HTLV-III antibody will be conducted by local civilian facilities.

Individuals with confirmed positive results (repeatedly reactive EIA plus Western blot) will be referred by the MEPS examining physician to their private physician for a more thorough evaluation of their potential for infection with the HTLV-III virus. Individuals who are determined to be negative upon re-evaluation and who demonstrate no signs of immuno-incompetence will be re-evaluated by the MEPS physician and processed for entry.

Until all potential accessions are screened at the MEPS, a similar process will be conducted immediately upon arrival at the initial training center. Those found EIA positive will be withdrawn from training and referred to a military treatment facility for clinical evaluation of immuno-competency.

Accessions processed by other than MEPS or an initial training center will follow a similar process as outlined above at the military point of entry.

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This policy is effective immediately and it should be implemented as soon as possible, but not later than October 1, 1985. Vaccination for protection against smallpox shall not be administered until HTLV III screening is completed and the individual is confirmed as negative. A more complete HTLV-III screening and HTLV-III virus policy will be issued following review of recommendations by the Armed Forces Epidemiological Board.

A handwritten signature in dark ink, appearing to read "William H. Taft, IV". The signature is fluid and cursive, with a prominent "W" and "T".

William H. Taft, IV



HEALTH AFFAIRS

THE ASSISTANT SECRETARY OF DEFENSE

WASHINGTON, D. C. 20301-1200

14 AUG 1985

MEMORANDUM FOR THE SECRETARY OF THE ARMY
SECRETARY OF THE NAVY
SECRETARY OF THE AIR FORCE
CHAIRMAN OF THE JOINT CHIEFS OF STAFF

Subject: Standardization of Reporting Requirements for Blood
Collection Agencies on Military Installations

Reference: ASD(HA) July 17, 1985 Memorandum to the Surgeons
General, "Military Implementation of Public Health
Service Provisional Recommendations Concerning
Testing Blood and Plasma for Antibodies to
HTLV-III"

Effective September 1, all agencies conducting blood
collection operations on military installations will comply
with the following requirements:

1. All potential donors must be informed that, to
assure a safe blood supply, testing is performed for the
presence of hepatitis-B surface antigen, HTLV-III antibody, and
syphilis.

2. All donors must be notified of confirmed positive
results of laboratory testing and advised of the availability
of medical counseling through the military health care system.

3. The blood collection agency will inform the
cognizant local military medical authority of any positive
findings indicative of the presence of hepatitis-B surface
antigen, HTLV-III antibody and syphilis in blood donated by
active duty personnel.

Steps should immediately be taken to notify all commands
of this policy and to ensure timely implementation.

The major national civilian agencies collecting blood on
military installations have indicated their intent to ask
prospective active duty donors to sign a statement giving
informed consent for notification to military doctors of
positive results and to inform those who do not wish to give
consent that they may leave the blood donation site without
providing an explanation.

Bill Mayer
William Mayer, M.D.



HEALTH AFFAIRS

THE ASSISTANT SECRETARY OF DEFENSE

WASHINGTON, D.C. 20301-1200

17 JUL 1985

MEMORANDUM FOR THE SURGEONS GENERAL OF THE MILITARY DEPARTMENTS

SUBJECT: Military Implementation of Public Health Service
Provisional Recommendations Concerning Testing Blood and
Plasma for Antibodies to HTLV-III

Reference is made to the DoD Military Blood Program memorandum dated March 13, 1985, subject as above.

The implementation procedures in the above reference were promulgated to the Services in accordance with Food and Drug Administration (FDA) guidelines for the purpose of insuring a safe blood supply from military donors to military and civilian blood collecting agencies. Additionally, the reference required establishment of a mechanism for providing medical evaluation and counseling to donors found to be positive for HTLV-III antibody.

This memorandum updates policies and procedures promulgated in the March 13, 1985, memorandum.

Donor Information/Screening:

Information concerning other mechanisms available for high risk personnel to obtain HTLV-III antibody test results, rather than through donation of blood, will be included in donor registration literature.

All potential donors must be made aware that testing will be performed to detect the antibody to the HTLV-III virus, which is associated with the acquired immunodeficiency syndrome (AIDS) and that they will be notified should test results prove positive. Donors should be informed that the test is being performed to assure a safer blood supply, that the test is not intended to diagnose AIDS, and the medical significance of a positive test is unknown in terms of its predictive value in an asymptomatic person. (See Enclosure 2 - American Association of Blood Banks recommended publication.) Donors should also be advised that blood products are routinely tested for other infectious agents (Hepatitis B, Syphilis) that may involve obligatory reporting to cognizant public health authorities.

Testing Procedures:

All donor blood collected by military blood collecting agencies will be tested for antibodies to HTLV-III (Enclosure 1).

First, each blood donation will be tested for antibodies to HTLV-III by performing a enzyme-linked immunosorbent assay (ELISA) screening test. All blood products with initially reactive ELISA test results will be discarded. Donors with initially reactive test results are not to be notified and their names are not to be placed on any donor deferral register.

Second, all initially reactive samples will be ELISA retested to assure accurate sample identification and reproducible results. Donors with repeatedly reactive test results will not be notified and their names are not to be placed on any donor deferral register.

Third and final, all repeatedly reactive samples will be retested for antibodies to HTLV-III virus utilizing Western blot testing techniques. Donors with Western blot test reactive results will be notified (see procedures below) and their names will be placed on the local Military Blood Center donor deferral register. Donor deferral registers will be maintained in accordance with established FDA regulation. (21 Code of Federal Regulation 606.160(e)).

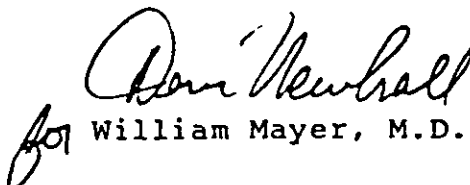
Donor Notification and Reporting Procedures:

Until further notice, civilian blood collection agencies operating on military installations are required to notify the individual donor of any positive HTLV-III findings and to advise the individual of the availability of medical counseling through the military health care system.

The military blood collection programs will continue to advise the responsible military medical authority of any positive HTLV-III findings.

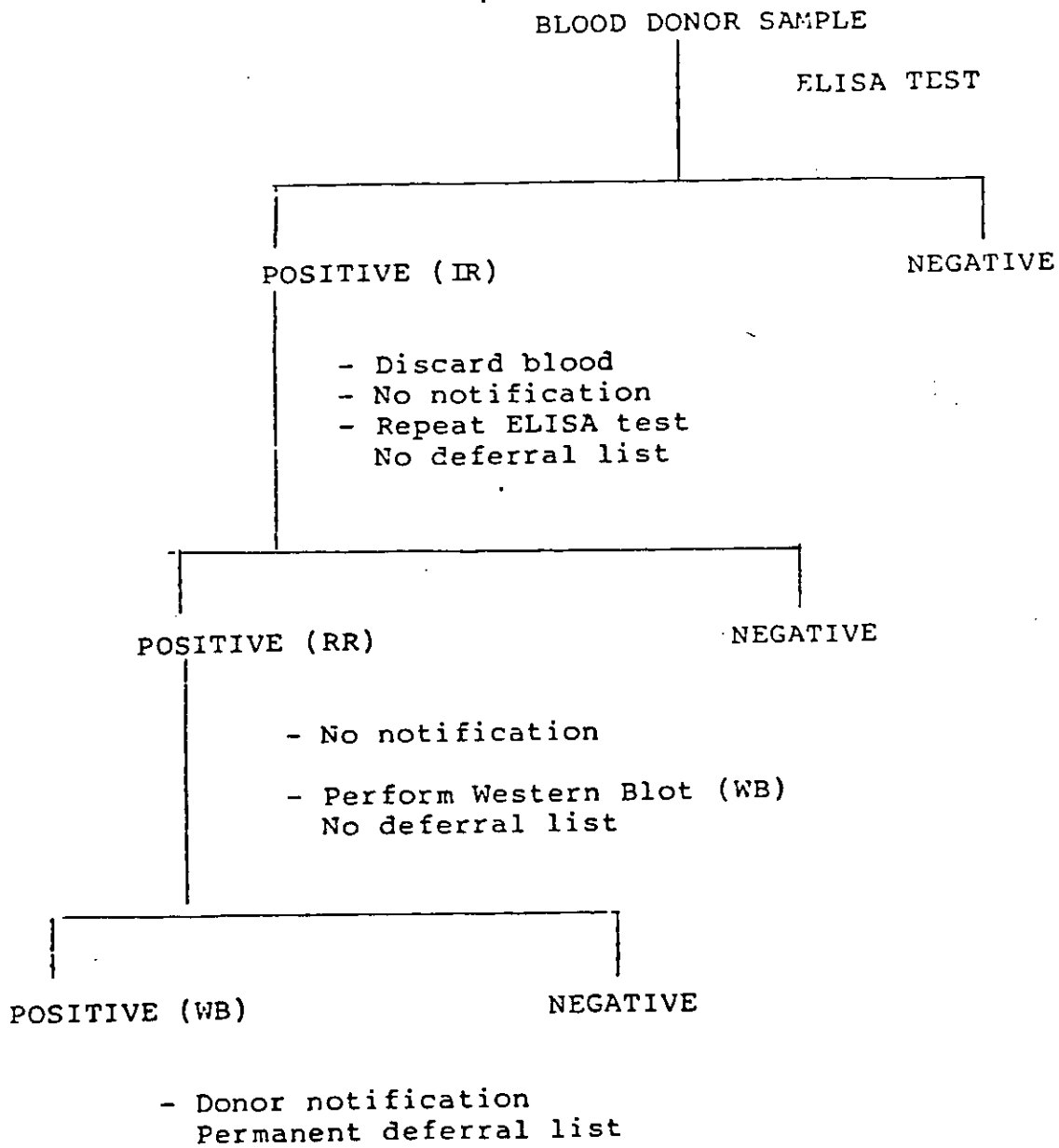
Medical Evaluation and Donor Counseling:

Procedures will be developed and instituted by the military medical services for the education, counseling and treatment of positive Western blot testing donors in accordance with FDA guidelines. Each military location participating in the DoD Military Blood Program will have an individual assigned with the responsibility of donor counseling and education. This assignment will be given only to a trained individual who understands the severe psychological stress that positive Western blot tests may cause in some individuals, the need for confidentiality, and who can provide an accurate explanation of test interpretation.


for William Mayer, M.D.

Enclosures

HTLV-III ANTIBODY TEST AND NOTIFICATION SCHEMATIC



AIDS HAVE TO DO WITH BLOOD TRANSFUSIONS?

AIDS, or Acquired Immune Deficiency Syndrome, is a condition in which the body's normal defense mechanisms against certain diseases or conditions are reduced. As a result, patients often develop unusual infections such as pneumocystis pneumonia or a rare form of skin cancer, Kaposi's sarcoma.

Studies have shown that AIDS may be transmitted through the transfusion of blood or blood products. Although the risk is very low, blood banks must take precautions to help insure the safety of blood. Current research indicates that a virus called HTLV-III (Human T-Cell Lymphotropic III Virus), is the probable cause of AIDS. It is hoped that the identification of this virus will lead to preventative measures and treatment for AIDS.

IS THERE A TEST THAT WILL HELP PROTECT THE BLOOD SUPPLY?

Yes, a test has been developed to detect antibodies to the HTLV-III virus. It is not a test for AIDS, but only a test for prior exposure to HTLV-III or a related virus. This test is used by blood banks to detect individuals with antibodies to HTLV-III because in many cases

that reason, any unit testing positive for antibodies to HTLV-III will not be transfused. These steps will help assure the safety of the blood supply.

WILL MY BLOOD BE TESTED FOR HTLV-III ANTIBODIES?

Yes, before your blood is issued for transfusion, it will be tested for antibodies to the HTLV-III virus. If we find antibodies, the donation will not be used; you will be notified of this finding*, and your name will be included on the blood bank's permanent donor deferral list. This list will be kept confidential and will not indicate the reason for deferral.

If you do not wish to have your blood tested or do not wish to be notified of the results, **YOU SHOULD NOT DONATE BLOOD.**

WHAT DOES A POSITIVE TEST FOR ANTIBODIES TO HTLV-III MEAN?

The meaning of a positive test for antibodies to HTLV-III is unknown, although it has been established that some individuals with HTLV-III antibodies can spread the disease, while others may not. Individuals with a positive test will be advised to seek medical counseling for information about additional testing or special precautions.

TEST DETECT EVERYONE WHO IS POTENTIALLY INFECTIOUS?

A few individuals may have the HTLV-III virus and may be infectious, but will not have the antibodies that are revealed by the test.

Since they will test negative for HTLV-III antibodies and since they may have no signs or symptoms of AIDS, these individuals will not be detected through our testing or routine examinations. For this reason, we continue to require that anyone who is in a risk category as described in the following section not give blood.

WHO IS "AT RISK"?

Certain groups have been shown to be at increased risk of contracting AIDS. The Public Health Service has indicated that these individuals should refrain from donating blood or plasma:

- A. Anyone who has AIDS or one of its signs and symptoms which include: unexplained weight loss; night sweats; blue or purple spots typical of Kaposi's sarcoma on or under the skin, or on mucous membranes; swollen lymph nodes lasting more than one month; persistent white spots or unusual blemishes in the mouth; fever greater than 99°F for more than 10 days; persistent cough and shortness of breath; persistent diarrhea.
- B. Past or present users of intra-

- C. Males who have had sex with more than one male since 1979, and males whose male partner has had sex with more than one male since 1979.
- D. Haitians who have entered the U.S. after 1979. Note: all persons who have resided in Haiti are deferred from blood donation for three years after leaving the country because of the risk of transmitting malaria.
- E. Patients with hemophilia.
- F. Sexual partners of individuals with any of the above categories.

Your time and effort in making a trip to the blood bank is appreciated. We hope that all donors will recognize the necessity of not donating if they are in a group at increased risk for AIDS.

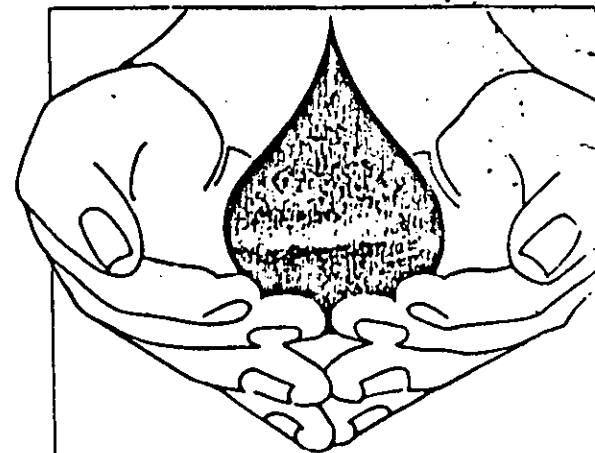
If, for some reason, you feel obligated to proceed with the donation process, even though you are in one of the high risk groups listed above, it is imperative that you inform the blood bank that your donation is not to be used for transfusion to a patient. This can be done either by indication on the confidential form, if one is provided, or by phoning the blood bank as soon as possible after your donation.

Please be sure that you understand the information contained in this brochure. If you have any questions, please discuss them with the person who is taking your medical history.

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**AN
IMPORTANT
MESSAGE
TO ALL
BLOOD
DONORS**



DEPARTMENT OF DEFENSE
MILITARY BLOOD PROGRAM OFFICE
OFFICE OF THE SURGEON GENERAL, U.S. ARMY
WASHINGTON, D.C. 20310

REPLY TO
ATTENTION OF

13 MAR 1985

DASG-MEDB

SUBJECT: Military Implementation of Public Health Service
Provisional Recommendations Concerning Testing Blood
and Plasma for Antibodies to HTLV-III

THE SURGEON GENERAL, DEPARTMENT OF THE ARMY
THE SURGEON GENERAL, DEPARTMENT OF THE NAVY
THE SURGEON GENERAL, DEPARTMENT OF THE AIR FORCE

1. The Food and Drug Administration (FDA) has recently licensed several test kits to detect antibody to the HTLV-III Virus, which is associated with the Acquired Immunodeficiency Syndrome (AIDS). Until further notice, each service will initiate a blood donor test and notification system utilizing Food and Drug Administration guidelines (Enclosure) and the following military unique procedures.

a. Each blood donation collected by Military Blood Program facilities will be tested for antibody to HTLV-III Virus.

b. Military and civilian blood agencies collecting blood on military installations will provide positive test results for antibody to HTLV-III to the respective service military health agency responsible for medical evaluation and counseling of reactive donors; i.e. preventive medicine. (BLOOD PROGRAM PERSONNEL WILL NOT RELEASE TEST RESULTS TO NON-MEDICAL PERSONNEL).

c. In addition to Food and Drug Administration labeling requirements it is recommended that a separate label be affixed to each blood bag or a rubber stamped statement on the SF 518 accompanying the blood which bears the wording "Non-reactive By Serologic Test for HTLV-III". As appropriate, the wording "All units non-reactive by Serologic Test for HTLV-III", will be added to the certification section of the DD Form 573 "Blood Shipping Inventory of Blood Products."

d. Donor recruitment and publicity should emphasize that ALTHOUGH THE TEST IS BEING INTRODUCED TO MAKE BLOOD PRODUCTS AND PLASMA DERIVATIVES SAFER, THE TEST IS NOT INTENDED TO DIAGNOSE AIDS, AND THE MEDICAL SIGNIFICANCE OF A POSITIVE TEST IS UNKNOWN IN TERMS OF ITS PREDICTIVE VALUE IN AN ASYMPTOMATIC PERSON.

DASG-MEDB

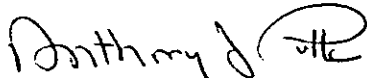
SUBJECT: Military Implementation of Public Health Service
Provisional Recommendations Concerning Testing Blood
and Plasma for Antibodies to HTLV-III

e. Each service Blood Program Officer will develop a system to provide the total number and percentage of positive antibodies to HTLV-III Virus test results, from military donors. This information will be provided to this office on a quarterly basis.

f. Routine testing of all blood supplies by Military Blood Program Activities will commence not later than 30 June 1985.

2. This letter has been coordinated with the OASD(HA).

2 ENCL
As stated


ANTHONY J. POLK
Lieutenant Colonel, MSC
Director

CF:
Commander, Health Service Command



HEALTH AFFAIRS

ASSISTANT SECRETARY OF DEFENSE

WASHINGTON, D.C. 20301

11 October 1985

MEMORANDUM FOR THE SECRETARY OF THE ARMY
SECRETARY OF THE NAVY
SECRETARY OF THE AIR FORCE

SUBJECT: Reporting of HTLV-III Antibody Status of Pre-Accession
Individuals Determined at the Military Entrance Processing
Stations

It is Department of Defense policy that communicable disease reporting requirements of civil authorities be complied with through liaison between the military public health jurisdiction and the appropriate local, state, or Federal health jurisdiction, unless such reporting would compromise the national security.

Media accounts report that the Department of the Army, through its role as Executive Agent of the Military Entrance Processing Station (MEPS) system, has offered to supply to local health departments individual recruit information that has not been requested to be reported to civilian health authorities.

Although Acquired Immune Deficiency Syndrome (AIDS) is a reportable condition in most states, HTLV-III antibody positivity does not constitute a reportable condition in virtually all jurisdictions. In fact, some states prohibit entities subject to state control from reporting antibody status alone. It is not the intent of the Department to interfere with the application of duly constituted state rules and regulations nor with the inherent constitutional and statutory rights and privileges of private citizens.

It is contrary to DoD policy to report HTLV-III antibody positivity to civilian authorities except in response to a valid civilian health authority request. The determination of whether a valid civilian requirement to report HTLV-III positivity actually exists can be made only by the ASD(HA) upon receipt of a formal request for such reporting from the civilian health authority.

Please direct the Commander, Military Entrance Processing Command and any other involved Commands to comply with this policy immediately.

William Mayer, M.D.



HEALTH AFFAIRS

THE ASSISTANT SECRETARY OF DEFENSE

WASHINGTON, D. C. 20315-2000

22 OCT 1985

MEMORANDUM FOR THE DOMESTIC POLICY COUNCIL
WORKING GROUP ON HEALTH POLICY

SUBJECT: Proposed DoD Policy and Program on HTLV III Screening

This memorandum outlines the proposed Department of Defense policy and program for HTLV III screening and disposition. I expect the Secretary to act on the proposal this week.

KEY POLICY AND PROGRAM ISSUES

Accessions

Applicants for service shall be screened for exposure to HTLV-III at the Military Entrance Processing Station or the initial points of entry to military service. This will involve approximately 300 thousand individuals per year. The laboratory tests will be conducted through civilian contract labs. Current policy is that those repeatedly reactive by enzyme immuno-assay and confirmed as positive by Western blot immunoelectrophoresis will not be accepted into service.

Results of pre-admission medical examinations and laboratory tests are considered confidential medical information. Release of individual patient information outside the Department is restricted to valid civilian health authority requests.

Disease Surveillance

Active duty and reserve component military personnel (approximately 3.6 million) shall be screened for the presence of HTLV-III antibody. The general priority of screening will be:

- o Individuals in or going to areas of endemic disease or limited medical facilities.
- o All others in or pending overseas assignments.
- o Other unique groups such as individuals involved with medical care of HTLV-III infected personnel.
- o All others on routine physical exams.

The testing will be done predominantly by Service medical personnel in Service medical facilities. Contract labs for Western Blot confirmation may be used.

Retention

Individuals who are antibody positive but manifest no evidence of progressive clinical illness or immunological deficiency shall be retained. For operationally related safety or health reasons, the Service Secretaries have discretionary authority to restrict the assignment and duties of active duty HTLV-III antibody positive individuals who manifest no symptoms of disease. All antibody positive persons shall receive a comprehensive clinical and immunological evaluation at least annually.

Separation

Individuals who are infected with HTLV-III and demonstrate progressive clinical illness shall be medically discharged if determined medically unfit for continued service. Persons who are infected with HTLV-III and are found not to have complied with preventive medicine counseling for individual patients may also be separated for the convenience of the Government.

Safety of the Blood Supply

DoD Military Blood Program policies and Food and Drug Administration guidelines shall be followed by the Military Departments Blood Programs and by civilian blood agencies collecting blood on military installations.



William Mayer, M.D.



HEALTH AFFAIRS

THE ASSISTANT SECRETARY OF DEFENSE

WASHINGTON, D. C. 20301-1200

31 OCT 1985

MEMORANDUM FOR ASSISTANT SECRETARY OF THE ARMY (M&RA)
ASSISTANT SECRETARY OF THE NAVY (M&RA)
ASSISTANT SECRETARY OF THE AIR FORCE (MRA&I)

SUBJECT: Testing of Military Personnel for Human T-Lymphotropic
Virus Type III (HTLV-III)

Reference: SECDEF memo, dated 24 October 1985, Policy on
Identification, Surveillance, and Disposition of
Military Personnel Infected With Human T-Lymphotropic
Virus Type III (HTLV-III)

I have been tasked by the referenced policy memorandum to convene a Tri-Service medical working group to develop a standardized clinical protocol for the HTLV-III testing of military personnel to ensure consistent evaluation and staging of each patient at all military medical treatment facilities. The chairman for this working group will be Colonel George Stebbing, MC, USA, Office of Professional Affairs and Quality Assurance. The first meeting of this working group is scheduled for 5 November 1985 at 0930-1100 hours. The meeting place will be provided to your representative.

I am also establishing a separate working group to oversee the quality control aspects of the HTLV-III testing. This HTLV-III working group on testing will focus attention on appropriate internal quality assurance procedures, external proficiency testing procedures, methodologies for HTLV-III testing, and developments in new technology for identifying the HTLV-III. Commander Walter Vogl, MSC, USN, Office of Professional Affairs and Quality Assurance, will chair this group. The first meeting of this working group will also be held on 5 November 1985 at 1330-1500 hours. The meeting place will be provided.

Please provide this office with the name, rank, job title, address, and telephone number of your representative to each of these working groups. If you have any questions regarding these meetings, please have your staff contact Colonel Stebbing (695-6800) or Commander Vogl (695-7116).

In addition, you are requested to submit documents implementing the policies established in the referenced memorandum by 6 December 1985. The documents must include the policy regarding any plans to limit assignment with respect to the nature and location of duties performed by an individual who is HTLV-III antibody positive but has no progressive disease or immunological deficiency.

A handwritten signature in cursive script that reads "Bud Mayer".

William Mayer, M.D.

ENLISTED HOMOSEXUAL ADMINISTRATIVE SEPARATIONS
(DOD DIRECTIVE 1332.14)

YEAR FY	ARMY	NAVY	MARINE CORPS	AIR FORCE	DOD
FY71	243	571	63	355	1232
FY72	190	368	96	325	979
FY73	193	398	82	279	952
FY74	206	429	104	284	1023
FY75	172	516	95	154	937
FY76	248	709	89	250	1296
FY77	275	822	88	257	1442
FY78	314	548	88	358	1308
FY79	333	866	85	372	1656
FY80	439	992	79	456	1966
FY81	439	1115	90	332	1976
FY82	473	1134	123	339	2069
FY83	383	887	149	390	1809
FY84	478	885	124	314	1801
FY85 (3QT)	321	602	94	213	1230



REPLY TO
ATTENTION OF

DEPARTMENT OF THE ARMY
OFFICE OF THE DEPUTY CHIEF OF STAFF FOR PERSONNEL
WASHINGTON, D.C. 20310

DAPE-HRP

29 AUG 1985

MEMORANDUM THRU ~~CHIEF OF STAFF, ARMY~~ *29 Aug 85*
~~ASSISTANT SECRETARY OF ARMY (MANPOWER AND RESERVE AFFAIRS)~~ *WOL*
FOR ASSISTANT SECRETARY OF DEFENSE (HEALTH AFFAIRS)
SUBJECT: HTLV III Testing--INFORMATION MEMORANDUM

1. Reference memorandum dated 29 August 1985, SAB. Concur with subject policy as revised by the attached.
2. It should be noted that the contracting out for testing will require extraordinary measures to meet the 1 October 1985 implementation date.

Attachment

John S. Crosby
JOHN S. CROSBY
Major General, GS
Assistant Deputy Chief of Staff
for Personnel

LTC Quay/54707
Typed by B. Smith

MEMORANDUM FOR SECRETARIES OF THE MILITARY DEPARTMENTS

SUBJECT: HTLV-III Testing

To protect the health of military personnel, all potential accessions will be screened for HTLV-III antibody by an FDA-approved enzyme immunoassay (EIA) serologic test.

This testing will normally be accomplished during the initial physical examination at Military Entrance Processing Station (MEPS). While blood samples will be drawn by MEPS medical personnel, laboratory testing for HTLV-III antibody will be conducted by local civilian facilities with close proximity to the MEPS. Applicants not processed by MEPS (i.e., National Guard, Officer Candidates, etc.) will also be screened by EIA and processed as outlined below.

Individuals with positive results will be referred by the examining physician to their private physician (non-DOD affiliated) for a more thorough evaluation of their potential for infection with the HTLV-III virus and information will be referred to appropriate public health service agencies for follow-up in accordance with the laws of the jurisdiction concerned. Individuals who are determined to be negative upon re-evaluation by an immunoelectrophoresis (Western blot) test and who demonstrate no signs of immuno-incompetence will be re-evaluated and processed for entry.

Until all potential accessions are screened, a similar process will be conducted immediately upon arrival at the initial training site. Those found EIA positive will be withdrawn from training and referred to a military treatment facility for clinical evaluation of immuno-competency.

This policy is effective on October 1, 1985. A more complete HTLV-III screening and HTLV-III virus policy will be issued following review of recommendations by the Armed Forces Epidemiological Board.

The estimated unprogrammed cost (\$30-100 million) will be shared proportionately by the services.



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

Dear Doctor:

The Public Health Service (PHS) recently published provisional recommendations for screening donated blood and plasma for antibodies to the HTLV-III virus which causes the acquired immunodeficiency syndrome (AIDS). A copy of those recommendations is attached to this letter for your information, and I strongly suggest that you keep this letter and the attachments on file for future reference. Test kits using the ELISA* technology for detecting HTLV-III antibodies will soon be licensed by FDA and will be commercially available. Blood and plasma collecting facilities will begin testing soon thereafter.

Although this is NOT a test for AIDS, there will be individual donors who are found to be reactive in a test for antibodies to the HTLV-III virus and, as suggested in the PHS recommendation, those donors will be referred to a physician for further evaluation. The purpose of this letter is to alert you to the possibility that one or more such donors may be referred to you, and to provide you with as much information as we currently have on how to evaluate such an individual. Based on preliminary information, we expect that less than 1 percent of donors will be reactive for HTLV-III antibodies after repeat testing at the blood or plasma collecting facility. Reactive HTLV-III tests may be due to subclinical infection, to immunity, to an active carrier state, or may represent biologically false-positive reactions such as cross-reactivity to antigens or other viruses. We do not yet know how many blood and plasma donors will fall into each category.

Additional PHS suggestions for the medical evaluation of referred donors are included with this letter. You will also find a sample information sheet which will serve as a model to educate donors at blood and plasma collecting facilities about the antibody test and a sample information sheet for donors with a positive antibody test.

The PHS has placed a very high priority on expediting the development and approval of the HTLV-III antibody test so that it could be used

*ELISA is an acronym for enzyme-linked immunosorbent assay. This assay utilized the principle of a solid phase (e.g., beads or microtiter plate wells) coated with antigen or antibody and an indicator reagent, antibody or antigen, respectively, to which an enzyme has been conjugated or "linked".

A typical ELISA test such as that used for the detection of antibody to HTLV-III utilizes beads or microtiter wells coated with disrupted, inactivated HTLV-III virus antigens and goat anti-human Ig conjugated or "linked" to an enzyme which on incubation with the appropriate substance will produce a color.

When an unknown serum or plasma sample is tested for the presence of antibodies, it is placed in the antigen-coated wells; the antibody in the sample links to the antigen on the solid-phase carrier and is detected by the anti-human antibodies conjugated to the enzyme.

to screen blood and plasma prior to use. Used in that context, the test achieves an important public health goal. However, it is vital that both physicians and patients understand that the antibody test is NOT a test for AIDS. As with any serologic test, there will be some false-positive results, even in samples which are repeatably reactive. When true HTLV-III antibody is present in an otherwise asymptomatic individual, it could mean that infection with the virus has occurred without any clinical evidence of disease. Limited observations indicate that only a small proportion of those individuals will go on to develop AIDS. The natural history of HTLV-III infection is not completely understood at present, and it is not possible to identify by laboratory or other means those asymptomatic persons with antibody to HTLV-III who will eventually develop AIDS. Therefore your clinical judgement is the most important aspect of the evaluation of individuals with antibody to HTLV-III, especially since the test is primarily designed to screen blood and plasma.

Whenever there is a reactive test for antibody to HTLV-III in blood and plasma donors, the PHS recommends that additional serologic testing be considered to clarify the significance of the screening test results. The Western blot* technique has been the most extensively used test for HTLV-III antibody specificity in the research setting. Based on data available to date, minimal criteria that define a positive Western blot test have been established by the PHS, as described in the attached Provisional Recommendations. Western blot testing will be available through most of the manufacturers of the antibody test kits. Further information about the availability of Western blot testing can be obtained through your local blood bank. You may also be able to get additional information through your State Health Department. It is important to recognize, however, that the Western blot test is still considered a research tool which has not yet been fully standardized. Furthermore, when the HTLV-III screening test is positive, negative Western blot result does not necessarily mean that antibody specific to HTLV-III is absent because the relative sensitivity of each of the tests varies among laboratories. In addition to blood or plasma donors who might be referred to you as the result of a reactive screening test for HTLV-III antibody other patients may ask you to determine their HTLV-III antibody status because of concern that they may be at risk of

*The term "Western blot" refers to a technique for identifying antibodies to proteins of specific molecular weight. The technique therefore allows the identification of antibodies to specific proteins associated with the HTLV-III virus. Based on available data, the Western blot should be considered positive for antibody to HTLV-III if band p24 or gp41 is present (alone or in combination with other bands). In general this test is less sensitive than the ELISA but more specific if positive.

developing AIDS. Such individuals should be given information about the implications of the ELISA test BEFORE being tested, with particular emphasis on the significance of a positive result. In addition, physicians and other health professionals should recognize the need for assuring the confidentiality of test results because disclosure could lead to serious social and employment consequences. Loss of employment or insurability may occur if positive test results become a part of the medical record.

Because, as noted above, the natural history of the disease is not completely understood at the present time, the medical significance of a positive result is unknown in terms of its predictive value for an asymptomatic individual. Furthermore, there may be biologically false-positive reactions due to cross-reactivity to antigens of other viruses. Individuals who seek testing should also recognize that a negative antibody test result does not necessarily mean that they are free of virus. Antibody may not have developed, or be undetectable, if exposure was recent. There is at least one report that 4 of 96 individuals carried the virus for 6 months without developing detectable antibodies. Because a positive test result can be difficult to interpret for an asymptomatic individual, consideration also should be given to the severe psychological stress which would be placed on the individual if the test for antibody to HTLV-III is positive. Appropriate counseling should be available if HTLV-III testing is done.

As significant new information is developed and new products become available to help in the diagnosis and treatment of AIDS, we will continue to take steps to inform the medical community.

Sincerely yours,

A handwritten signature in dark ink, appearing to read "Frank E. Young", written in a cursive style.

Frank E. Young, M.D., Ph.D.
Commissioner of Food and Drugs

**IMPORTANT
AIDS
INFORMATION**

MOR

MORBIDITY AND MORTALITY WEEKLY REPORT

- 1 Provisional Public Health Service Inter-Agency Recommendations for Screening Donated Blood and Plasma for Antibody to the Virus Causing Acquired Immunodeficiency Syndrome
- 5 Poliomyelitis - Finland
- 6 Update: Influenza Activity - United States
- 11 Phytophotodermatitis among Grocery Workers - Ohio
- 13 Reye Syndrome - United States, 1984

Provisional Public Health Service Inter-Agency Recommendations for Screening Donated Blood and Plasma for Antibody to the Virus Causing Acquired Immunodeficiency Syndrome

In March 1983, the U.S. Public Health Service issued inter-agency recommendations on the prevention of acquired immunodeficiency syndrome (AIDS) (1). Included was the recommendation that members of groups at increased risk for AIDS should refrain from donating plasma and/or blood. That recommendation was made to decrease the risk of AIDS associated with the administration of blood or blood products, which accounts for about 2% of all reported AIDS cases in the United States.

Evidence has shown that a newly recognized retrovirus is the cause of AIDS. Although this virus has been given several names, including human T-lymphotropic virus type III (HTLV-III) (2), lymphadenopathy-associated virus (LAV) (3), and AIDS-associated retrovirus (ARV) (4), it is referred to as HTLV-III in this discussion. Tests to detect antibody to HTLV-III will be licensed and commercially available in the United States in the near future to screen blood and plasma for laboratory evidence of infection with the virus. The antibody tests are modifications of the enzyme-linked immunosorbent assay (ELISA), which uses antigens derived from whole disrupted HTLV-III (5).

There is considerable experience with the ELISA test in research laboratories, but much additional information will be gathered following its widespread application. In the early phases of testing, a number of false-positive tests may be encountered. Adjustments in interpretation are anticipated as more is learned about the performance of the test in an individual laboratory and about the specific proportion of falsely positive or falsely negative tests in the screening setting where the test is used.

The present recommendations concern the use of these tests to screen blood and plasma collected for transfusion or manufactured into other products. They are intended to supplement, rather than replace, the U.S. Food and Drug Administration's recently revised recommendations to blood and plasma collection facilities and the earlier inter-agency recommendations (1). Additional public health applications of these tests in the understanding and control of AIDS will be described in a subsequent report.

BACKGROUND

Antibody Detection Studies

The ELISA test has been used in many research programs for detecting antibodies to HTLV-III in patients with AIDS and with AIDS-related conditions. In different studies, HTLV-III antibody was found to range from 68% to 100% of patients with AIDS, and in 84%-100% of persons with related conditions, such as unexplained generalized lymphadenopathy (5-7). Serologic surveys have yielded variable seropositivity rates in groups at in-

creased risk for AIDS (13,14), and 35% of women who were sexual partners of men with AIDS (15). In contrast to the above groups, HTLV-III antibody has been detected in fewer than 1% of persons with no known risks for AIDS (4-10).

The time needed to develop a positive antibody test following infection is not known. Data regarding the interval between infection with HTLV-III and seroconversion are limited. A nurse who sustained a needle-stick injury while caring for an AIDS patient developed antibody between 4 and 7 weeks following exposure (16). Additionally, a recent study described several asymptomatic individuals infected with HTLV-III for more than 6 months in the absence of detectable antibody (17,18). Nonetheless, currently available ELISA tests can be expected to identify most persons with HTLV-III infection.

Virus Isolation Studies

HTLV-III has been isolated from blood, semen, and saliva and has been recovered from many individuals in the presence of antibody (19,20). HTLV-III has been isolated from the blood of 85% or more of seropositive individuals with AIDS (21), lymphadenopathy, or other AIDS-associated conditions (2) and from three of four mothers of infants with AIDS (2). The virus has also been isolated from asymptomatic seropositive homosexual men and hemophiliacs, and has been recovered from 95% of seropositive high-risk blood donors who had been implicated in the transmission of AIDS through transfusion (21). The recovery of HTLV-III from these high-risk donors 2 or more years after their initial donation provides evidence that viremia may persist for years in both asymptomatic and symptomatic individuals. HTLV-III has also been isolated from some asymptomatic seronegative persons, but this is the exception (17).

Modes of Transmission

Epidemiologic data suggest that the virus has been transmitted through intimate sexual contact; sharing contaminated needles; transfusion of whole blood, blood cellular components, plasma, or clotting factor concentrates that have not been heat treated; or from infected mother to child before, at, or shortly after the time of birth. No other products prepared from blood (e.g., immunoglobulin, albumin, plasma protein fraction, hepatitis B vaccine) have been implicated, nor have cases been documented to occur through such common exposures as sharing meals, sneezing or coughing, or other casual contact.

Natural History of Infection

Information about the course of infection with HTLV-III is incomplete, but the majority of infected adults will not acquire clinically apparent AIDS in the first few years after infection. In some studies 5%-19% of seropositive homosexual men developed AIDS within 2-5 years after a previously collected serum sample was retrospectively tested and found to be seropositive. An additional 25% developed generalized lymphadenopathy, oral candidiasis, or other AIDS-associated conditions within the same interval (11,22). The long-term prognosis for most persons infected with HTLV-III is unknown.

SCREENING BLOOD AND PLASMA

Initial Testing

Persons accepted as donors should be informed that their

test is positive and that they may be placed on the collection facility's donor deferral list, as is currently practiced with other infectious diseases, and should be informed of the identities of additional deferral lists to which the positive donors may be added.

All blood or plasma should be tested for HTLV-III antibody by ELISA. Any blood or plasma that is positive on initial testing must not be transfused or manufactured into other products capable of transmitting infectious agents.

When the ELISA is used to screen populations in whom the prevalence of HTLV-III infections is low, the proportion of positive results that are falsely positive will be high. Therefore, the ELISA should be repeated on all seropositive specimens before the donor is notified. If the repeat ELISA test is negative, the specimen should be tested by another test.

Other Testing

Other tests have included immunofluorescence and radio-immunoprecipitation assays, but the most extensive experience has been with the Western blot technique (22), in which antibodies can be detected to HTLV-III proteins of specific molecular weights. Based on available data, the Western blot should be considered positive for antibody to HTLV-III if band p24 or gp41 is present (alone or in combination with other bands).

Notification of Donors

If the repeat ELISA test is positive or if other tests are positive, it is the responsibility of the collection facility to ensure that the donor is notified. The information should be given to the donor by an individual especially aware of the sensitivities involved. At present, the proportion of these seropositive donors who have been infected with HTLV-III is not known. It is, therefore, important to emphasize to the donor that the positive result is a preliminary finding that may not represent true infection. To determine the significance of a positive test, the donor should be referred to a physician for evaluation. The information should be given to the donor in a manner to ensure confidentiality of the results and of the donor's identity.

Maintaining Confidentiality

Physicians, laboratory and nursing personnel, and others should recognize the importance of maintaining confidentiality of positive test results. Disclosure of this information for purposes other than medical or public health could lead to serious consequences for the individual. Screening procedures should be designed with safeguards to protect against unauthorized disclosure. Donors should be given a clear explanation of how information about them will be handled. Facilities should consider developing contingency plans in the event that disclosure is sought through legal process. If donor deferral lists are kept, it is necessary to maintain confidentiality of such lists. Whenever appropriate, as an additional safeguard, donor deferral lists should be general, without indication of the reason for inclusion.

Medical Evaluation

The evaluation might include ELISA testing of a follow-up serum specimen and Western blot testing, if the specimen is positive. Persons who continue to show serologic evidence of

ual or his/her sexual contacts and examined for signs of AIDS or related conditions, such as lymphadenopathy, oral candidiasis, Kaposi's sarcoma, and unexplained weight loss. Additional laboratory studies might include tests for other sexually transmitted diseases, tests of immune function and, where available, tests for the presence of the virus, such as viral culture. Testing for antibodies to HTLV-III in the individual's sexual contacts may also be useful in establishing whether the test results truly represent infection.

RECOMMENDATIONS FOR THE INDIVIDUAL

An individual judged most likely to have an HTLV-III infection should be provided the following information and advice:

1. The prognosis for an individual infected with HTLV-III over the long term is not known. However, data available from studies conducted among homosexual men indicate that most persons will remain infected.
2. Although asymptomatic, these individuals may transmit HTLV-III to others. Regular medical evaluation and follow-up is advised, especially for individuals who develop signs or symptoms suggestive of AIDS.
3. Refrain from donating blood, plasma, body organs, other tissue, or sperm.
4. There is a risk of infecting others by sexual intercourse, sharing of needles and, possibly, exposure of others to saliva through oral-genital contact or intimate kissing. The efficacy of condoms in preventing infection with HTLV-III is unproven, but the consistent use of them may reduce transmission.
5. Toothbrushes, razors, or other implements that could become contaminated with blood should not be shared.
6. Women with a seropositive test, or women whose sexual partner is seropositive, are themselves at increased risk of acquiring AIDS. If they become pregnant, their offspring are also at increased risk of acquiring AIDS.
7. After accidents resulting in bleeding, contaminated surfaces should be cleaned with household bleach freshly diluted 1:10 in water.
8. Devices that have punctured the skin, such as hypodermic and acupuncture needles, should be steam sterilized by autoclave before reuse or safely discarded. Whenever possible, disposable needles and equipment should be used.
9. When seeking medical or dental care for intercurrent illness, these persons should inform those responsible for their care of their positive antibody status so that appropriate evaluation can be undertaken and precautions taken to prevent transmission to others.
10. Testing for HTLV-III antibody should be offered to persons who may have been infected as a result of their contact with seropositive individuals (e.g., sexual partners, persons with whom needles have been shared, infants born to seropositive mothers).

Revised recommendations will be published as additional information becomes available and additional experience is gained with this test.

National Institutes of Health: Health Resources and Services Administration.

References

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AIDS Information for Health Professionals

Clinicians Guide to Evaluation of HTLV-III Antibody Positive Individuals

The Virus that Causes AIDS

The etiologic agent of the acquired immunodeficiency syndrome (AIDS) is human T-cell lymphotropic virus type III (HTLV-III), also known as LAV and ARV. This distinctive class of RNA virus shares some features with retroviruses previously linked to various disorders in animals, including leukemias, neurologic diseases, and immunodeficiency disorders and to a human virus, HTLV-I, linked to an unusual form of human leukemia. HTLV-III has a cytotoxic effect on T-lymphocytes of the helper type. The diverse infections and tumors which are the ultimate cause of death for AIDS patients result from the fact that the virus renders the immune system incompetent.

Clinical Significance of HTLV-III Seropositivity

Over 90% of patients with full-blown AIDS are positive for HTLV-III antibodies in the screening test, and with the application of additional research techniques close to 100% of such individuals are virus-positive. Among seropositive persons, the risk for developing frank AIDS may vary depending upon risk group and possibly other factors such as additional environmental exposures and genetic background. Preliminary estimates in cohorts of homosexual men followed prospectively for two to five years indicate that between 5% and 20% of persons with detectable HTLV-III antibodies may go on to develop AIDS. However, information that pertains to one risk group may not directly translate to other risk groups. The lack of precise data on the clinical significance of HTLV-III antibody positivity for an individual patient coupled with the fact that many persons in high-risk groups have detectable HTLV-III antibodies, creates a dilemma for the physician confronted with evaluating and counseling such antibody-positive patients. If this virus follows patterns seen in other viruses, the majority of exposed individuals will remain clinically healthy. However, this is a new class of human virus and the long-term implications of exposure to the health of an individual are unknown. Furthermore, the implications of seropositivity in the individual to the potential for transmitting the virus to others are unknown. Epidemiologic data do document that homosexual and probably heterosexual sexual relations, needle sharing, blood transfusion and transplacental and/or perinatal exposure are modes of transmission. Finally, it should be emphasized that the current antibody test is licensed as a blood bank screening and not a diagnostic tool. In this regard, the absence of antibody in a high-risk person does not necessarily mean that the patient is virus negative, since the virus has been isolated from a few at-risk individuals who were antibody negative. Conversely, as with all antibody tests of this type, a few biologic false positives will be detected due to antibodies to non-HTLV-III cross-reactive antigens.

Dynamics of HTLV-III Infection

Seroconversion generally antedates the development of clinical or subclinical laboratory signs of viral infection by several years, necessitating extended follow-up. The first sign of subclinical infection may be a laboratory perturbation associ-

ated with HTLV-III seropositivity.

The laboratory parameter most frequently linked to HTLV-III infection is a depressed number of peripheral blood lymphocytes bearing the helper T-cell phenotype. Other laboratory parameters which have been associated with this process include elevated immunoglobulin levels; high titers to a variety of viral agents (particularly Epstein Barr virus and cytomegalovirus); and elevated beta-2 microglobulin, thymosin, and acid-labile alpha interferon. Although these various observations are of some research interest and reflect the variety of laboratory perturbations which result from fundamental virus-associated immunodeficiency, their relevance in the clinical setting is not sufficiently well-defined to be of practical diagnostic benefit. These are currently a focus of ongoing research studies.

Range of Clinical Manifestations

Another condition recognized as being associated with HTLV-III infection is the lymphadenopathy syndrome, a medical complex characterized by the occurrence of persistent, unexplained lymph node enlargement in several extra-inguinal lymph node groups. The relationship of the lymphadenopathy syndrome to progression to overt clinical AIDS is uncertain but probably is as high as 10%.

Another lesser manifestation is the AIDS related complex (ARC), a clinical and laboratory syndrome characterized by minor conditions clinically associated with immunosuppression (e.g., oral thrush) and laboratory evidence of immunosuppression. In addition, unexplained idiopathic thrombocytopenia is probably associated with HTLV-III infection, as are a variety of non-life-threatening fungal, viral, and bacterial infectious processes which probably represent manifestations of virus-induced immunologic perturbation. These manifestations are sometimes termed lesser AIDS.

The clinical presentation of clinical AIDS, as originally defined, follows four major patterns:

- 1) A febrile prodrome of weeks to months followed by opportunistic infection.
- 2) Abrupt onset of opportunistic infection.
- 3) Presentation with Kaposi's sarcoma.
- 4) Progression from the AIDS-related complex.

Approach to Clinical Evaluation

AIDS and its diverse related clinical disorders challenge the diagnostic acumen of physicians in all branches of medicine. The prospective clinical evaluation of HTLV-III seropositive individuals who may be at risk for AIDS requires a careful multi-system approach to evaluate signs and symptoms. Clearly, it is important to take a careful medical and social history and perform thorough physical examinations on these individuals. Listed below is a broad overview of recognized clinical signs and symptoms. A more thorough review of the published literature is strongly recommended (see Background Reading).

Medical History: Possible source of exposure, identification of risk group exposure, blood transfusion, acupuncture, tattoos, needle stick exposure, foreign travel, and sexual history.

Dermatologic: Kaposi's sarcoma (purple or reddish nodules), which may appear anywhere in the skin and on mucocutaneous surfaces (e.g., mouth and rectum), infectious processes (e.g.,

Herpes simplex or zoster), seborrheic dermatitis, unexplained diffuse hyperpigmentation, alopecia.

Ophthalmologic: Ocular lesions (retinitis due to cytomegalovirus or toxoplasmosis), cottonwool spots, retinal hemorrhages.

Hematopoietic: Fluctuating adenopathy associated with aching discomfort. Variable lymph node size and consistency. Soft, moderately enlarged spleen. Large, firm spleen and/or very large lymph nodes are suggestive of intracellular infections (e.g., mycobacterium avium), lymphoma or Kaposi's sarcoma.

Gastrointestinal: Oral thrush, candida esophagitis associated with xerostomia and pharyngitis or odynophagia. Watery diarrhea due to various protozoan infestations and lower GI pain due to herpes proctitis.

Pulmonary: Non-productive cough and dyspnea (associated with *Pneumocystis carinii* or viral pneumonitis), productive cough linked to bacterial or other etiology.

Musculoskeletal: Diffuse arthralgias and myalgias associated with febrile prodrome suggestive of vasculitis, autoimmune and rheumatologic diseases.

Neurologic: Persistent headache, memory loss, ataxia, confusion, irrational behavior, personality change, focal neurologic signs, and seizure.

General: Fatigue, asthenia, night sweats or sweating, decreased libido, withdrawal and other signs of depression, fever including Pel-Ebstein fever pattern.

Laboratory tests that could be helpful in evaluating antibody positives include a complete blood count, differential and platelet count, VDRL, tests of hepatitis B infection, and baseline routine chemistries, including gamma globulin levels. Additional, specific tests should be directed by the clinical findings.

Therapeutic Intervention

Therapeutic interventions that are specific for the virus or for the immunodeficiency do not yet exist, although there is considerable research being done attempting to develop such modalities. However, rapid diagnostic evaluation and intervention with appropriate antimicrobials in specifically documented illnesses may be lifesaving. Some clinicians have advocated use of prophylactic therapy to prevent common protozoan and fungal diseases (i.e., trimethoprim-sulfamethoxazole and ketoconazole), but there is also a substantial amount of drug-related dermatologic and hematologic toxicity for some of these agents and implementation of such therapy without consulting a specialist would not be recommended.

What to Tell the Seropositive Patient

From a clinical perspective, counseling a seropositive, clinically healthy individual presents a challenge since the risk of clinical disease is not well characterized. The possibility that the test reactivity represents a biologic false positive should be discussed particularly in the patients without definable risk exposure. It is inevitable that substantial psychological stress will derive from the knowledge of antibody positivity, and judicious reassurance is supported by the current data which suggests that the vast majority of antibody positives are clinically well. However, given the fact that clinical problems may take some years to become manifest clinically, *long-term follow-up with careful assessment of symptomatology* as described above are in order. HTLV-III has also been linked to hematologic and neurologic disorders, a focus of active investigation. With this in mind, clinical symptoms in antibody-positive persons should be pursued vigorously to assure optimal care. The risk for an antibody-positive individual being infectious for another person is not quantified. As summarized above, certain factors (e.g., sexual contact, needle sharing, pregnancy) are linked to virus transmission and may serve as the basis for tailoring recommendations to the antibody positive individual to decrease the likelihood of transmission of the virus.

Summary

The practicing physician encountering an HTLV-III antibody-positive person must deal with incomplete knowledge about the natural history of the disease. Preventive measures and practical advice to the individual are summarized in attached documents. Clinical long-term follow-up of antibody-positive persons should be a commitment for physicians confronted with such patients. Careful monitoring of the fast-moving medical literature concerning this condition is important to provide optimal care. Where feasible, consideration of referral to a center organized to follow such patients may be appropriate.

Background Reading

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Information for Individuals About AIDS and the Antibody Blood Test

[For use in educating donors BEFORE collecting blood or plasma]

Information About the Test for Antibodies to the HTLV-III Virus

WHAT IS AIDS?

Acquired immunodeficiency syndrome (AIDS) is a serious disease which reduces the body's ability to fight infection. Over the past several years increasing numbers of persons in certain high-risk groups developed the disease, and by early 1985 about 9,000 cases had been reported. During 1984, a virus (HTLV-III) was discovered which is the cause of AIDS, and a test was developed to detect antibodies to the virus. More detailed information about AIDS is available in *Facts About AIDS*, which is provided by the U.S. Public Health Service.

WHAT IS THE ANTIBODY TEST?

When a person is infected by a virus, the body's white blood cells normally begin to fight the infection by producing substances called antibodies. Antibodies can therefore be used to indicate whether or not a person has been infected by a virus. Research has shown that antibodies to the HTLV-III virus are usually found in the blood of persons who have AIDS or AIDS-related conditions, and in many people who are members of groups at increased risk for AIDS. However, a negative antibody test does not guarantee that a person is free of the virus, especially if he or she is a member of a group at increased risk for AIDS. Antibodies may not have developed if exposure to the virus was recent. That is why it is very important for members of groups at increased risk for AIDS to continue to refrain from donating blood or plasma. It is also possible that other factors, including other viruses, could cause the test to be positive even though the person was never infected with HTLV-III.

WHAT IS THE ANTIBODY TEST BEING USED FOR?

Until recently, the antibody test was limited to use in research to gain a better understanding of AIDS as an infectious disease. For example, some of those studies showed that 68% to 100% of patients with AIDS had been exposed to the HTLV-III virus. During the past year, commercially available tests for HTLV-III antibody were being developed, and such tests were recently approved by the Food and Drug Administration.* The primary purpose of these antibody tests is to screen blood which is donated for use in transfusion and in the production of other blood products.

WHY IS THE ANTIBODY TEST BEING USED TO SCREEN BLOOD?

Because a positive antibody test means that a person may have been infected by the HTLV-III virus, it is now possible to use the test to identify blood which should not be used for transfusion. By not using blood from people who may have been infected by HTLV-III, we believe that transfusions will be even safer than they are now.

WHAT DOES A POSITIVE ANTIBODY TEST MEAN?

The most important thing to understand is that the antibody test is

NOT a test for AIDS, and that a positive test does *NOT* mean that the person definitely will develop AIDS. The test does provide an extra safety check on blood so that the risk of getting AIDS from transfusions will be even lower than it already is. As with many other blood tests, there will be some people who have test results which are called "false-positives"; that is, for some reason the test indicates that HTLV-III antibody is present when, in fact, it is not really HTLV-III antibody which is causing the test to register positive. For this reason it is especially important for persons with positive antibody tests to have follow-up tests to try to determine whether or not the screening test really means that HTLV-III antibody is present.

Based on what is known so far, probably only a small proportion of people infected with the virus will develop AIDS. In fact, many infected people may not develop any illness at all. But there is no information at the present time to be able to predict which persons with the antibodies are more likely or less likely to develop AIDS-related conditions or AIDS itself. For that reason, follow-up medical evaluations are strongly recommended.

WHAT WILL BE DONE WITH THE TEST RESULTS?

If the test for HTLV-III antibody is positive when repeated, and we are satisfied that there has not been a laboratory error, we will inform you (insert method to be used, e.g., by letter) and advise you regarding a follow-up medical evaluation. Donors with positive HTLV-III antibody tests will be placed on a list of persons who may not give blood, and the reason for being deferred as a donor will be kept in a confidential file. Only authorized individuals will have access to this information. In the future we may have to report HTLV-III positive test results to the Health Department as is now required for some other tests.

A Special Note to Persons Who May Be At Increased Risk for Aids

It is vital to the safety of the blood supply that persons who are in groups at increased risk for AIDS continue to follow the U.S. Public Health Service recommendations and to voluntarily refrain from donating. These groups are: 1) anyone who has AIDS or one of its signs and symptoms; 2) males who have had sex with more than one male since 1979, and males whose sexual partner has had sex with more than one male since 1979; 3) past or present abusers of intravenous drugs; 4) Haitians who entered the USA after 1977; 5) hemophiliacs; and 6) sexual partners of persons in these groups.

Even though we are now testing blood for antibodies to the HTLV-III virus, the test will not detect all people who may be carriers of the virus because not everyone who is infected with the virus will have antibodies. If you think you are at increased risk for AIDS, or that you may have been exposed to the virus, **DO NOT DONATE BLOOD** even if you feel perfectly healthy. There is a possibility that antibody for the virus may not be detected when your blood is tested even though you may have been infected. If that were to happen, the blood would be used to treat patients who would then be at risk for infection by HTLV-III and for AIDS.

If you are interested in knowing whether or not you have antibody to HTLV-III, see your physician or [insert name and location of other testing site].

*This information sheet was prepared on 2/14/85 (before any test was licensed), and it is intended to be used *after* tests are commercially available.

Information for Individuals (continued)

Information for Persons Who Have a Positive Test for HTLV-III Antibody

[To be used in conjunction with the pre-donation information which should be offered again with the test results]

A positive HTLV-III antibody test does not always mean that a person has been infected by the virus which causes acquired immunodeficiency syndrome (AIDS). Positive tests in blood and plasma donors may be caused by other things, and that is why a follow-up medical evaluation is important in order to get a better understanding of the meaning of your test results. Your doctor is in the best position to decide what additional tests, if any, need to be done. It is important that you have as open and frank a discussion as possible regarding any possible exposures that you may have had to the virus, so that your physician can make the best evaluation.

Until your doctor has made a medical evaluation, it is best to be cautious, even though you have no symptoms, and to assume that you may have been exposed to the virus, that you may be contagious, and that you might unknowingly spread the virus to others. You will want to take responsible steps to prevent the possibility of spreading the virus to other people, especially your family and close contacts.

- Do not donate blood or plasma, sperm, body organs, or other tissues.
- You should let your doctor and dentist know that you have a positive HTLV-III antibody test so that they can do their best in caring for you and in preventing spread of the virus.

- Limit your sexual contacts, and be frank with your sexual partner(s) about steps you are taking to prevent the spread of the virus. Using a condom may help in this regard.
- Sexual practices in which exchange of body fluids such as semen takes place should be avoided.
- Virus has been found in saliva of some infected people, and it is possible that it could be transmitted by open-mouthed, or "French," kissing and by oral sex.
- There is no evidence that the virus can be spread through casual kissing or other casual social contacts such as hugging. Such contacts with other people at work or in the community do not need to be modified.
- Toothbrushes, razors, or other implements that could become contaminated with blood should not be shared.
- If you are a drug user:
 - limit your drug use
 - do not let others use needles you have used and do not use someone else's needles
 - do not leave your "works" around where others might pick up needles
- If you are a woman with a positive antibody test or the sexual partner of a man with a positive antibody test, it would be advisable to avoid pregnancy or to postpone pregnancy until more is learned. Some infants have developed AIDS from their infected mothers.

February 19, 1985

FROM: Director, Office of Biologics Research and Review

SUBJECT: Implementation of Public Health Service Provisional Recommendations
Concerning Testing Blood and Plasma for Antibodies to HTLV-III

TO: All Registered Blood Establishments

The Food and Drug Administration (FDA) will soon license tests to detect antibody to the HTLV-III virus which is associated with the acquired immunodeficiency syndrome (AIDS). Provisional recommendations to screen blood and plasma were issued by the U.S. Public Health Service (PHS) on 11 January 1985, and blood and plasma collection facilities are encouraged to voluntarily begin performing the test as soon as supplies are commercially available. Excluding reactive units from use in transfusion or from further manufacturing into injectable products is expected to significantly reduce exposure to HTLV-III virus from this source. IT IS IMPORTANT FOR DONORS TO UNDERSTAND THAT ALTHOUGH THE TEST IS BEING INTRODUCED TO MAKE BLOOD PRODUCTS AND PLASMA DERIVATIVES SAFER, THE TEST IS NOT INTENDED TO DIAGNOSE AIDS, AND THE MEDICAL SIGNIFICANCE OF A POSITIVE TEST IS UNKNOWN IN TERMS OF ITS PREDICTIVE VALUE IN AN ASYMPTOMATIC PERSON. Please note that all of the 14 December 1984 Revised Recommendations to Decrease the Risk of Transmitting Acquired Immunodeficiency Syndrome (AIDS) still apply, and this memo supplements rather than replaces existing requirements for donor education and medical screening.

The following information is intended to answer many of the questions which may arise when establishments begin applying the new test. The models given here represent acceptable approaches but are not meant to exclude other alternatives. The anticipated public health benefit of testing blood and plasma for HTLV-III antibodies has dictated an unusually rapid test development, and continuing evolution of methodology and refinement of procedures are expected.

Prior to mandatory testing, a voluntary phase-in period will exist. Information updates will be provided as necessary. It is recognized, however, that not every potential problem can be anticipated and communication with test kit manufacturers is encouraged. In addition, a working group has been established

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to help in responding to problems, and one of the members of this group can be contacted if additional assistance is needed (see attached).

- I. Blood and Plasma Testing
 - II. Medical Follow Up and Donor Counseling
 - III. Alternative Mechanisms for Obtaining HTLV-III Antibody Testing
 - IV. Informed Consents, Donor Deferral Registers, Donor Notifications and Confidentiality Requirements
 - V. Definition of Reactive Results
 - VI. Additional Testing of Reactive Samples
 - VII. Standard Operating Procedure Revision, Use of Outside Testing Laboratories and Biosafety
 - VIII. Blood Product Labeling
- Glossary; References

I. Blood and Plasma Testing

The 11 January 1985 Morbidity and Mortality Weekly Report (attached) explains the basis for the PHS recommendation to screen all blood and plasma for antibodies to HTLV-III. The FDA plans to propose regulations mandating that an approved test for HTLV-III be performed on each unit of blood, blood component or plasma collected for any purpose. However, the rule making procedure requires time and final regulations are not expected for several months. Therefore, the interval between first reagent availability and mandatory testing will be a period during which voluntary testing will occur.

Laboratories should begin immediately to acquire the necessary equipment and to train personnel to assure accurate, routine test performance. Because of the potentially serious impact that a positive test result may have on individual donors, it is very important that staff are adequately trained, and that consistently reproducible results are assured before any positive results are communicated to donors. Preliminary testing with unlinked samples may be a very useful first step. This may be done without informing donors provided that any linkage with donor identity has been broken. Following that period of preliminary testing, we recognize that an appropriate phase-in period will be essential.

During the phase-in period, it will best serve public health goals to discard products with unvalidated positive test results although concomitant donor notification may be inappropriate due to uncertainties in test results. Product labeling for HTLV-III antibody should not begin until the establishment is routinely testing all of its blood supply. Any reactive samples identified during the phase-in period may be frozen for retesting after the facility has the test established on a routine basis. We recommend deferring donor notification until such retesting has been done and proficiency is assured. With this approach, initial donor information forms should explain that test results will not be available until that later time. Consistent with the provisional PHS recommendations, donors should be informed when blood is routinely tested following validation of the test system in each establishment.

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Recommendations for phase-in period:

- Donor information concerning phase-in testing is optional
- Discard presumptively positive blood or plasma products
- Do not notify donors of uncertain results
- Do not defer donors based on uncertain HTLV-III test results
- Do not put HTLV-III results in product labeling

If presumptively positive samples are frozen for repeat testing following phase-in period:

- Inform donor appropriately
- Defer donor notification and entry in deferral register until repeat testing verifies test is reactive

II. Medical Follow-Up and Donor Counseling

Mechanisms for educating and counseling donors also need to be identified and coordinated with local health facilities. Suggestions for medical evaluation and counseling of reactive donors are explained in detail in the attachments to this memorandum. The major blood and plasma collecting organizations will also be good resources for guidance in the development of written information for donors and notification procedures. Many donors will respond best to a personal interview and the donor's preference concerning a notification procedure should be observed if possible. Each blood establishment will want to assign responsibility for providing donor information to trained individuals who understand the need for confidentiality and the severe psychological stress that reactive tests will cause in some individuals. Accurate explanation of test interpretation is also essential.

III. Alternative Mechanisms for Obtaining HTLV-III Antibody Testing

Information concerning other mechanisms for obtaining HTLV-III antibody tests should be available to individuals who may not qualify as donors but who appear as prospective donors because of concern about their antibody status. We recommend that whenever possible procedures for referring persons to these alternative sites be worked out locally in advance of mandated testing. Ideally, clear instructions concerning this alternative should be available to every prospective donor along with the information concerning tests to be performed and the educational material identifying high risk groups. IT IS IMPORTANT FOR DONORS TO UNDERSTAND THAT ALTHOUGH THE TEST IS EXPECTED TO MAKE BLOOD PRODUCTS AND PLASMA DERIVATIVES SAFER, THE TEST IS NOT INTENDED TO DIAGNOSE AIDS. Even repeatedly reactive tests may be false-positives. It is important for individuals who seek testing to understand that the natural history of the disease is not currently well defined, and the medical significance of a positive result is unknown in terms of its predictive value for an asymptomatic individual. Also, a negative antibody test result does not mean that one is free of virus. Antibody may not have developed, or be undetectable, if infection was recent. There is at least one report that 4 of 96 individuals carried the virus for 6 months without developing detectable antibodies.

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IV. Donor Information, Donor Deferral Registers, Donor Notifications and Confidentiality Requirements

When the HTLV-III antibody screening test is performed routinely in your establishment, all blood and plasma donors should be informed that:

- A sample of their blood will be tested
- After the phase-in period, donors will be notified if the ELISA test for HTLV-III antibody is positive initially and when repeated
- Individuals with reactive tests will be deferred from future blood or plasma donation
- The names of HTLV-III antibody reactive persons will become part of donor deferral registers as required by 21 CFR 606.160(e)

In addition, some health departments may require reporting of positive test results and the donor consent should include this information if applicable. We recommend that testing information be put in the context of explaining which required laboratory tests are routinely performed on all blood products before distribution for use, and that donors be given a choice as to how the blood establishment will notify them of reactive test results. The analogy to HBsAg test requirements and deferral policies may be useful. See the attached MMWR for additional information.

It is not required that the donor consent be a part of medical history forms but it is strongly recommended that the donor's signature acknowledging receipt of pre-donation information be a part of each establishment's records. Donor consent may not be feasible and is not required by FDA for testing blood already in inventory during the phase-in testing period. The number of donors who may have reactive test results is expected to be small, and these few individuals could be asked to return later for follow-up to confirm test results. The donor's consent could then be obtained before repeat testing. In all cases, it will be extremely important to protect the confidentiality of donor identity in relation to test results and to restrict access to information concerning both laboratory results and donor deferral registers. The misuse of such information could have serious consequences for both donors and blood establishments because positive test results could result in loss of employment or insurability.

There is no requirement that deferral registers identify the cause for deferral or list donors by name. Donor deferral records do not have to be available at blood collection sites but there must be a mechanism to link entries on the deferral list to individual donors and the reason for deferral. Information concerning reasons for deferral of individual donors in the register should be restricted to selected personnel to protect confidentiality. The mechanics of assuring that unsuitable products are not distributed need to be carefully thought out and documented in the procedure manual. An expected minimum precaution will be a clerical re-check to assure accurate identification of units quarantined.

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V. Definition of Reactive Results

It is very important that both donor and blood establishment staff understand that the HTLV-III antibody test is NOT a test for AIDS. As with any serologic test, there will be some false-positive results, even in samples which are repeatedly reactive. When true HTLV-III antibody is present in an otherwise asymptomatic individual, it could mean that infection with the virus has occurred without any clinical evidence of disease. Limited observations indicate that only a small proportion of those individuals will go on to develop AIDS. It is not possible to identify by laboratory or other means those asymptomatic persons with antibody to HTLV-III who will eventually develop AIDS.

The procedures required to establish that a sample is initially reactive in the test for HTLV-III antibody will be defined by each manufacturer's package insert. Invalid test results due to procedural errors should be eliminated before classifying a sample as having an "initial reactive" test result. All initially reactive samples should be at least retested to assure accurate sample identification and reproducible results. Consideration should be given to performing the repeat test on a sample integrally attached to the blood container. Donors should not be notified of positive test results until there is clear agreement that the initial and repeat ELISA tests are reactive (see glossary); the tests may be done with a single manufacturer's reagent. If discrepant results occur and procedural error can be ruled out, the sample should be reported to the HTLV-III reagent manufacturer.

At the present time, all blood products with an initial reactive test result must not be distributed for transfusion or further manufacturing into injectable products.

In addition, you are reminded that the 14 December 1984 donor screening recommendations preclude the use of blood products collected from healthy members of high risk groups for transfusion or routine manufacturing into injectable plasma derivatives. Clearly explain to these donors, and HTLV-III antibody reactive donors, that they will not be eligible for routine blood or plasma collection at any facility in the foreseeable future. In areas where multiple blood or plasma collection sites exist in close proximity, it may also be prudent to share donor deferral registers, to assure blood product safety. Although it may be difficult to explain the reasons for deferral to apparently healthy individuals, it is important that they understand the public health goal so that they can cooperate in achieving the safest possible blood supply.

VI. Additional Testing of Reactive Samples

Blood and plasma establishments currently will have no testing obligation beyond repeating the procedure described by the HTLV-III test manufacturer to arrive at a decision that a sample is positive. However, medical evaluation is recommended for individuals with repeatedly reactive

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ELISA tests and such persons should be advised to consult a physician, clinic, or public health facility. Because there is no fully standardized confirmatory test currently available, the PHS recommends that additional testing of the individual be considered as part of the medical evaluation to clarify the meaning of positive HTLV-III screening test results. The Western blot technique (see glossary) has been the most extensively used test for HTLV-III antibody specificity in the research setting.

Therefore, the Western blot test for antibodies to HTLV-III virus will be available through most of the licensed manufacturers of the antibody test kits. Based on the data available to date, minimal criteria defining a positive Western blot test have been established by the PHS. It is important to recognize, however, that the Western blot test is still considered a research tool rather than a confirmatory test. When the ELISA screening test is positive, a negative Western blot result does not mean that antibody specific to HTLV-III is absent, because the relative sensitivity of each of the tests varies among laboratories.

VII. Standard Operating Procedure (SOP) Revision, Use of Outside Testing Laboratories and Biosafety

To comply with existing good manufacturing practices requirements, it will be necessary for each blood establishment to revise their procedure manual to include HTLV-III antibody testing, quarantine and disposition procedures for reactive units, procedures for notifying donors of positive test results, and record keeping procedures including the maintenance of donor deferral registers. Licensed establishments do not need to submit these revised SOPs to the Office of Biologics Research and Review (OBRR). Compliance with the regulatory requirements will be determined on site at the time of FDA inspections.

The use of outside testing laboratories to perform required HTLV-III antibody tests is permissible but licensed establishments must obtain prior approval for this shared responsibility. The blood or plasma collecting facility must maintain written records of all test results. The written record must be available before any product distribution occurs except for Source Leukocytes or in emergency situations when the blood product is clearly labeled to indicate that the test has not been performed.

The handling, storage and disposition of reagents, samples and blood products should be in accordance with existing biosafety precautions for HBsAg reactive materials.

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VIII. Blood Product Labeling

Information concerning HTLV-III antibody test results should appear in the package insert (circular of information) for blood and blood components intended for transfusion. However, the test results must appear on the container label of Source Plasma, Recovered Human Plasma and other products intended only for further manufacture. An acceptable container statement is "Non-reactive by serologic test for HTLV-III" or "Non-reactive when tested for HBsAg and HTLV-III by FDA required tests." Licensed blood establishments should submit to OBRR file copies of package insert or container label changes concomitant with implementation of the new labeling. Any variation from the above statements must be approved by OBRR prior to use.

Because all blood products are to be tested and found negative for HTLV-III antibody prior to distribution, informing consignees by letter of the date routine testing will begin in a blood establishment will be considered adequate notification. This can best be accomplished near the end of the phase-in period when total blood component inventories can be included in such a notification. Once HTLV-III antibody testing is routine practice in any establishment, it will be necessary to label the containers of any blood products that have not been so tested. These untested products will generally be emergency shipments or old inventory of products with long dating periods, e.g., Frozen Red Blood Cells, Plasma and Cryoprecipitated ABF. The corresponding label statements are:

CAUTION: Required test for HTLV-III has not been done.

or CAUTION: This product was prepared before testing for HTLV-III was required and the HTLV-III status of the donor is not known.

or CAUTION: This product was prepared before testing for HTLV-III was required. The donor was tested for HTLV-III (insert date) and found to be non-reactive.

Blood products may be collected from donors with reactive HTLV-III antibody tests for research or further manufacturing into special in vitro diagnostic products only with prior approval from OBRR. Such units must bear the statement "Reactive by serologic test for HTLV-III" and a prominent cautionary statement such as "Caution: the risk of transmitting HTLV-III is present."

The major blood collecting organizations will be notified at the time each manufacturer is licensed for this product and this information will appear in each organization's news letters. Individual inquiries concerning the list of approved licensees may be directed to the Division of Product Certification, 301-443-5433.



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Glossary

ELISA (screening) test:

ELISA is an acronym for enzyme-linked immunosorbent assay. This assay utilizes the principle of a solid phase (e.g., beads or microtiter plate wells) coated with antigen or antibody and an indicator reagent, antibody or antigen, respectively, to which an enzyme has been conjugated or "linked".

A typical ELISA test such as that used for the detection of antibody to HTLV-III utilizes beads or microtiter wells coated with disrupted, inactivated HTLV-III virus antigens and goat anti-human Ig conjugated or "linked" to an enzyme which on incubation with the appropriate substance will produce a color.

When an unknown serum or plasma sample is tested for the presence of antibodies, it is placed in the antigen coated wells, and the antibody in the sample links to the antigen on the solid-phase carrier and is detected by the anti-human antibodies conjugated to the enzyme.

Western blot technique:

The term "western blot" refers to a technique for identifying antibodies to proteins of specific molecular weight. The technique therefore allows the identification of antibodies to specific proteins associated with the HTLV-III virus. Based on available data, the Western blot should be considered positive for antibody to HTLV-III if band p24 or gp41 is present (alone or in combination with other bands).

References

See enclosed 11 January 1985 Morbidity and Mortality Weekly Report.

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