# AIDS Center News

*Published by the World Hemophilia AIDS Center*

*ESTABLISHED UNDER THE AUSPICES OF:*

- WORLD FEDERATION OF HEMOPHILIA MONTREAL, QUEBEC, CANADA
- ORTHOPAEDIC HOSPITAL LOS ANGELES, CALIFORNIA, USA


## CLINICAL MANAGEMENT UPDATE


**APRIL, 1985 - VOL 2, NO. 2**


## APPROACH TO THE CLINICAL MANAGEMENT OF HEMOPHILIA PATIENTS AT RISK FOR AIDS OR THE AIDS-RELATED COMPLEX


**Shelby L. Dietrich, M.D.**


Serologic and epidemiologic evidence of HTLV-III/LAV antibody reactivity in hemophiliacs leads to the conclusion that virtually all hemophilia patients who have received large-pool plasma products (e.g., plasma concentrates) within the past five years have been exposed to the putative agent of AIDS, HTLV-III/LAV. Even when antibody testing for HTLV-III becomes widely available, individual interpretation of results on any given patient is not diagnostic for AIDS or the AIDS-Related complex (ARC) and will not answer pressing questions regarding the individual's possible infectivity to others, the future clinical course, or concurrent perplexing problems. Therefore, until serologic or virologic studies analagous to the hepatitis B antigen test become available, the following guidelines are recommended for patients and families.

### HEALTH CARE GUIDELINES FOR PATIENTS WITH HEMOPHILIA AND THEIR FAMILIES

These general guidelines are similar to those recommended for hepatitis B protection and can help reduce the potential risk factors for patients and their families.

#### *Healthful Living*

Proper diet: Eat from the major food groups each day. Do not share eating utensils or drinking containers.

Rest: Get at least six to eight hours of sleep each night. Don't get overtired.

Exercise: A strong healthy person is less prone to infection and illness. Strong muscles protect joints and decrease the need for concentrate.

Alcohol and other drugs: Avoid street drugs as they suppress the immune system. Take no more than one alcoholic drink per day.

Good hygiene: Wash hands with soap and water before eating and following bathroom use. Do not share toothbrush or razor. Make sure a dentist is examining your teeth and gums on a regular basis.

Management of stress: Keep communication with the family open to reduce stress. Relaxation techniques can be helpful.

#### *Infusion Safety*

Self-protection: Wash hands with soap and water before infusion. Practice proper infusion techniques.

Protection of others: Wash hands with soap and water at the completion of infusion. Clean the work area. Do not infuse near food preparation areas. If blood or concentrate is spilled on the work area, wash the area with hypochlorite solution containing 1000 parts per million available chlorine (household liquid bleach).

Proper disposal of equipment: Use a needle disposal box for all needles. Put syringes, bottles, gloves into a plastic bag and seal the bag.

Needle sticks: Encourage bleeding from the puncture site. Wash the affected area thoroughly with soap and water. Contact the doctor within 24 hours.

#### *Safe Sexual Practices*

All evidence to date indicates that AIDS is transmitted by close and intimate contact involving exchange of body fluids, especially through breaks in the skin or mucous membranes.


*(continued on page 2)*

*(continued from page 1)*

Therefore, we are recommending using condoms even if your partner is pregnant.

The following guidelines are offered for the physician caring for patients with hemophilia.

**MEDICAL SUPERVISION OF PATIENTS WITH HEMOPHILIA PRESUMED TO HAVE BEEN EXPOSED TO HTLV-III /LAV VIRUS**

A review of the definitions of AIDS, ARC, and pediatric AIDS will contribute to the discussion that follows.

A case of AIDS, as defined by the Centers for Disease Control (CDC), U.S. Public Health Service, is a person with a reliably diagnosed disease that is at least moderately indicative of an underlying cellular immune deficiency but who has had no known underlying cause of the deficiency. Diseases at least moderately indicative of underlying cellular immune deficiency lie in five etiological categories: 1) protozoal and helminithic infections (cryptosporidiosis, *Pneumocystis carinii* pneumonia, strongyloidosis, toxoplasmosis); 2) fungal infections (candidiasis, cryptococcosis); 3) bacterial infections ("atypical" mycobacteriosis); 4) viral infections (cytomegalovirus, Herpes simplex, progressive multifocal leukoencephalopathy); 5) cancer (lymphoma, Kaposi's sarcoma).

A case of ARC is a person with one or more of these signs or symptoms without known cause: palpable lymphadenopathy involving two or more extrainguinal sites of at least three months duration; weight loss/anorexia of at least one month duration (weight loss of ten percent or more of body weight); fatigue/malaise of at least one month duration; fever greater than 39°C. of at least one month duration; and diarrhea lasting longer than two weeks. Laboratory findings may include: decreased helper T-cells; depressed helper/suppressor ratio; at least one of the following: leukopenia, absolute lymphopenia, thrombocytopenia, or anemia; elevated serum globulins; depressed blastogenesis.

A case of pediatric AIDS is defined as a child with a reliably diagnosed disease indicative of underlying cellular immunodeficiency and no known cause of that cellular immunodeficiency. Specific conditions that must be excluded in a child are primary immunodeficiency diseases (severe combined immunodeficiency, DiGeorge syndrome, Wiskott-Aldrich syndrome, ataxia-telangiectasia, graft versus host disease, neutropenia, neutrophil function abnormality, agammaglobulinanemia, or hypogammaglobulinemia with raised IgM) or secondary immunodeficiency associated with immunosuppressive therapy, lymphoreticular malignancy, or starvation. Because children are subject to a variety of congenital immunodeficiencies, confirmation of AIDS diagnosis in children is more complex than in adults. Laboratory testing to exclude cogenital conditions is required.

***Medical Examination***

Each hemophilia patient should have a carefully performed annual physical examination including a complete history with a review of blood product consumption. Certain clinical signs and symptoms should always receive careful attention.

1. Dermatologic: severe and recurrent infectious processes such as Herpes simplex; recurrent bacterial or fungal infections; seborrheic dermatitis; unexplained diffuse hyperpigmentation.
2. Pulmonary: A dry nonproductive cough, often accompanied by fever and shortness of breath (associated with *Pneumocystis carinii* or viral pneumonitis); a productive, persistent cough (may be linked to bacterial or other etiology).
3. Hematopoietic: Fluctuating adenopathy associated with aching discomfort; variable lymph node size and consistency; soft, moderately enlarged spleen. A large, firm spleen and/or very large lymph nodes are suggestive of intracellular infections.
4. Gastrointestinal: oral thrush; recurrent pharyngitis; odynophagia; candida esophagitis; protracted diarrhea.
5. Neurologic: persistent headache; memory loss; confusion; ataxia; irrational behavior.
6. General: Fatigue; unexplained malaise; weight loss; night sweats; diffuse myalgia.

Many of these symptoms are subjective in nature. Suggestible patients may be alarmed and apprehensive over the possibility of having ARC or AIDS. A careful examination and explanation accompanied by supportive follow-up will do much to allay unnecessary apprehension.

Laboratory tests for immune system dysfunction are part of the examination. *First-line* tests include complete blood count, differential and platelet count and skin testing for common allergens. If skin anergy is present and/or leukopenia, lymphopenia or thrombocytopenia are found, further evaluation of phenotypes of T-cell subsets is advisable. The absolute numbers of helper T-cells (T4) are often decreased while the numbers of suppressor T-cells (T8) may be normal, increased, or decreased. The helper/suppressor ratio is often decreased. HTLV-III antibody tests should be included when testing is available. Hemophiliacs receiving blood products are exposed to viruses in addition to the HTLV-III virus: hepatitis B, non-A non-B hepatitis, and cytomegalovirus. Evidence for these infections should be sought clinically and serologically.

*(continued on page 3)*

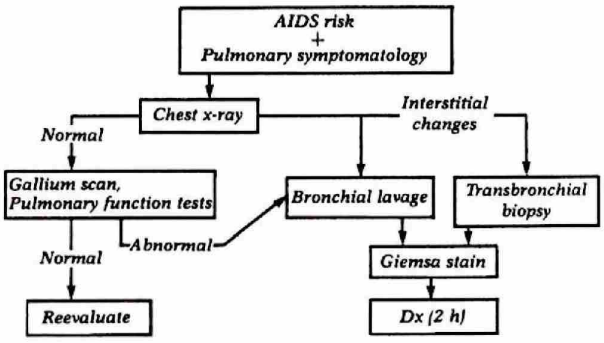
(continued from page 2)

### *Medical Follow-up*

Based on the results of the laboratory studies and the physical examination, patients can be categorized into three follow-up groups:

1. Patients with normal clinical findings and normal or near-normal absolute numbers of helper T-cells and helper/suppressor ratios may be followed on an annual basis.
2. Patients with ARC or patients with absolute numbers of helper T-cells ranging beteen 200 cells/mm$^3$ and 400 cells/mm$^3$ appear to be at a somewhat increased risk to develop AIDS. They should be followed regularly every four to eight weeks. Clinical and laboratory signs of ARC and the presence of lymphadenopathy tend to fluctuate. Careful, persistent follow-up of these patients is most important since patients whose coping mechanisms include disease denial may attempt to avoid the physician and the treatment center unless severe illness occurs.
3. Patients with fewer than 200 helper T-cells/mm$^3$ are in a high-risk group for the development of opportunistic infections. These patients may experience recurrent oral candidiasis, weight loss, fever, and generalized malaise. Herpes simplex, other skin infections, recurrent oral candidiasis, minor opportunistic infections, and parasites should be treated vigorously with available agents. Bacterial infections should be treated with antibiotics after cultures are taken. Patients with pulmonary symptoms should be evaluated according to the pictured algorithm.[1] A patient presenting with a dry, nonproductive cough should be evaluated immediately by a chest radiograph. Even if the radiograph is negative, which it is in about five percent of patients with *Pneumocystis* pneumonia, careful monitoring of the patient is indicated.

**EVALUATION OF SUSPECTED AIDS PATIENT WITH PULMONARY PRESENTATION**




Patients with thrombocytopenia may be treated with oral prednisone therapy if the thrombocyte count drops to a level considered dangerous by the physician or if excessive bruising, petechiae, or other classic signs appear. If the condition is severe and unresponsive, splenectomy may be indicated. Consideration of this surgery assumes that adequate hemostatic coverage is available including sufficient supplies of platelets and clotting factor replacement therapy.

In areas of the world where tuberculosis and intestinal parasites are common, patients with these conditions may be *a priori* immune suppressed. Then, the HTLV-III virus may act as an opportunistic infection. Treatment of tuberculosis and parasites is urgent when these sources of infection are found in a person with hemophilia. Another important factor leading to immune suppression is prolonged protein and calorie malnutrition. Children are particularly vulnerable to the problem. Malnourished hemophilia children may be at excessive risk.

Based on present information, we must emphasize that the natural history of AIDS and ARC is as yet unknown. Longitudinal follow-up studies are currently needed to define the course of this syndrome, which is as yet undetermined. A high percentage of hemophilia patients appear to have a well-defined clinical course which will resolve in spite of the continued presence of HTLV-III antibodies. Only a small, yet unknown percentage of patients go on to develop ARC or AIDS.

We must further emphasize, to the hemophilia patient, the importance of prompt treatment of bleeding episodes. Hemorrhage still remains the leading cause of mortality and morbidity in hemophilia. Though no effective treatment has yet been found to overcome the immune deficiency in AIDS, patients need to be reassured about the substantial amount of ongoing research directed toward this end. Hemophilia patients must have the opportunity to express their fears and anxieties about AIDS and to have their questions answered. Most important of all, they must have an ongoing, close physician-patient relationship.

**References:**

1. Wofsy, C.B.: Opportunistic Infections in AIDS in Symposium Proceedings: Focus on AIDS, Ocober 8, 1984.

**Other sources of information for this article:**

2. Public Health Service, Food and Drug Administration: Clinicians Guide to Evaluation of HTLV-III Antibody Positive Individuals, 1985.
3. Center for Interdisciplinary Research in Immunology and Diseases: AIDS Reference Guide for Medical Professionals, University of California, Los Angeles, 1985.

(continued on page 4)

*(continued from page 3)*

**Suggested Background Reading:**

4. Devita, V.T., Jr.; Hellman., R.A. (Eds): AIDS, Lippincott, Philadelphia, 1985.
5. Ebbesen, P., Biggar, R.J., Melbye, M. (Eds): AIDS A Basic Guide for Clinicians, Munksgaard/Saunders, Philadelphia, 1984.

• • •

*Dr. Dietrich is Director of the World Hemophilia AIDS Center; Chairman of the Medical Board, World Federation of Hemophilia; and Director of the Hemophilia Treatment Center, Orthopaedic Hospital, Los Angeles, CA.*

## TESTING FOR HTLV-III ANTIBODIES IN HAEMATOLOGY STAFF

**(Summarized from P. Jones and P. Hamilton in Letters to the Editor, The Lancet, Vol. 1, No. 8422: 217, January 2, 1985)**

The staff of a haemophilia reference centre were tested for HTLV-III antibodies. The 21 people tested were 10 medical laboratory scientific officers, three nurses, three doctors, three secretarial staff, one physiotherapist, and one social worker. All the staff were HTLV-III antibody negative. Blood from one severely affected haemophilic patient previously exposed to multidonor factor VIII concentrates was sent for testing at the same time; this specimen was HTLV-III antibody positive.

While clearly important that blood specimens from at-risk groups continue to be handled appropriately, these results should reassure staff working in similar circumstances.

## IMMUNOLOGIC DYSFUNCTION IN INFANTS INFECTED THROUGH TRANSFUSION WITH HTLV-III

**(Summarized from R.F. Wykoff, E.R. Pearl, F.T. Saulsbury; New England Journal of Medicine 312: 294-296, January 31, 1985)**

Three infants with transfusion-acquired HTLV-III infections had a broad spectrum of diseases. The three infants were in a neonatal intensive care unit at the same time and all three received a single transfusion from a common donor. Analysis of donor blood revealed presence of HTLV-III antibodies and an abnormal helper/suppressor T-cell ratio. The donor was asymptomatic at time of the donation.

One of the infants developed AIDS and died at 14 months of age. During the course of his illness he evidenced hepatosplenomegaly, underweight, generalized adenopathy, oral and perineal candidiasis, persistent lymphopenia, abnormal helper/suppressor T-cell ratio, polyclonal hyperimmunoglobulinemia. Serologic tests for cytomeglovirus, Epstein-Barr virus, and hepatitis B virus were negative. A lung biopsy specimen was positive for *Pneumocystis carinii.*

A second infant, at nine months of age, evidenced anemia, cutaneous petechiae and purpura, lymphadenopathy, hepatosplenomegaly, and oral candidiasis. She had thrombocytopenia, neutropenia, polyclonal hyperimmunoglobulinemia, a positive Coombs' test and positive antinuclear antibody. Tests for Epstein-Barr virus and cytomegalovirus were negative. At 20 months of age, following glucocorticoid therapy, the patient was well. Platelet and neutrophil counts had risen but the direct Coombs' test was still positive.

The third infant had developed chronic diarrhea, weight loss, generalized lymphadenopathy and hepatosplenomegaly by the age of four months. Serologic tests for Epstein-Barr virus, cytomegalovirus and hepatitis B virus were negative. Polyclonal hyperimmunoglobulinemia and altered helper/suppressor ratios were found. The diarrhea abated but the lymphadenopathy, lymphocytosis, and hyperimmunoglobulinemeia have persisted.

## IMMUNE STATUS OF BLOOD PRODUCT RECIPIENTS

**(Summarized from J. Jason, M. Hilgartner, R.C., Holman, G. Dixon, et al., Journal of the American Medical Association 253: 1140-1144, February 22, 1985)**

Persons with hemophilia are at risk of the acquired immunodeficiency syndrome (AIDS), and clinically asymptomatic hemophiliacs have shown a high incidence of AIDS-like immune abnormalities, facts leading to speculations that many hemophiliacs have been exposed to the AIDS agent through their blood products. The immune status was evaluated in three groups of blood product recipients without AIDS in New York City, including 47 persons with hemophilia A receiving factor VIII concentrate, 50 persons with homozygous B (Beta)-thalassemia, and 27 persons with sickle cell anemia receiving frozen-packed RBCs and in 20 healthy persons who had not received a transfusion. Hemophiliac participants had significantly lower lymphocyte counts than did the thalassemic or anemic participants, had lower numbers of T-helper lymphocytes, and had a lower T-helper/suppressor ratio. These differences remained after adjustment for age and sex. Thus. AIDS-like immune abnormalities were found in patients receiving factor concentrate, but not in those receiving RBCs. These defects could be due to both an immunosuppressive effect of the lyophilized factor itself and to contact with the AIDS agent.

## HTLV-III ANTIBODY DETECTION TESTS APPROVED BY FDA

Test kits to screen for the presence of HTLV-III antibody were approved March 2, 1985 by the U.S. Food and Drug Administration (FDA). Three firms, Abbott Laboratories, Electro-Nucleonics, Inc., and Litton-Bionetics have been licensed to market the kits. Two other companies have applied also for FDA approval to produce the test.

Underscoring the rapid pace at which the blood banking industry is expected to use the test voluntarily, the American Red Cross immediately signed an agreement with Abbott and announced plans to begin phasing-in the assay within days. Nationwide implementation is anticipated to take from 2 to 6 weeks. Sometime later this year, use of the test will be mandated by the FDA under its statutory authority to regulate blood and blood products.

Government officials stress that the new blood test must be used cautiously *since it is neither errorproof nor a diagnostic test for AIDS.*

The U.S. nationwide market for the HTLV-III antibody screening test will reach 20 million on an annual basis. About 1.5 million kits per month will be used by blood banks and plasma centers; most of the remainder will go to commercial laboratories and physician offices.

*(Editor's Note: Readers are cautioned that this antibody test is a good screen for blood and blood products but is a poor test for diagnosis of patients. "It screens blood not patients.")*

## IMPLEMENTING HTLV-III ANTIBODY TESTING OF BLOOD AND PLASMA

**(Summarized from the ABRA Newsletter, American Blood Resources Association, Annapolis, Maryland, March 1985)**

Blood and plasma collection facilities in the United States are preparing to implement HTLV-III antibody testing. All major fractionators have stated their intent to test. Some reagent companies have decided to require testing. The German Bundesgesundheitsamt (BGA) has decreed that plasma and plasma products exported to Germany after October 1, 1985 must be tested (that amounts to 15 to 20 percent of American plasma activities). By April or May, a blood/plasma industry standard will have been established so that anyone who is not testing will be potentially at risk to adverse legal consequences.

The U.S. Food and Drug Administration (FDA) is expected to call for testing of all blood and plasma collections used for transfusion and for further manufacture into both injectable and non-injectable products.

Fully operational testing means: testing all blood and plasma collections; informing donors of testing program in advance of donation; rejecting and destroying reactive blood or plasma; permanently deferring reactive donors from further donation; placing reactive donors on deferral list; advising reactive donors of test results; referring donors to local medical or public health officials for more extensive tests, counselling, and medical evaluation; and where appropriate, reporting reactive donors to state or local agencies.

Plasma units found reactive will be destroyed in a manner similar to that of reactive hepatitis plasma units. Plasma units in inventory at the center collected from donors subsequently found reactive will most likely be pulled and destroyed as well. Notification to manufacturers who have received shipments of plasma units from donors subsequently found anti-HTLV-III reactive is currently under discussion. A policy will likely evolve that will require that manufacturers be notified of such shipments. Additional or confirmatory testing should be done as a component of a reactive individual's further medical evaluation by appropriate persons in the medical community or public health service.

Plasma centers will need to establish notification procedures taking into account confidentiality interests of anti-HTLV-III reactive individuals. When donors are informed of reactive findings they should be encouraged to seek additional medical evaluations. A donor should be advised that he will be permanently deferred from donation and that his name will be added to a permanent deferral list.

It will be extremely important to protect the confidentiality of donor identity in relation to test results and restrict access of information concerning both laboratory results and donor referral registries. The misuse of such information could have serious consequences for both the donors and the plasma establishments.

In the interpretation of test results, "initial reactive" means whatever the test kit manufacturer defines as the final interpretive result. Product decisions will be made from the initial test. Notification of the donor should be made only after the tests have been found to be repeatedly reactive.

## PROVISIONAL RECOMMENDATIONS FOR SCREENING DONATED BLOOD AND PLASMA

Provisional U.S. Public Health Service inter-agency recommendations have been issued for screening donated blood and plasma for antibody to the HTLV-III virus.

The recommendations concern the use of these tests to screen blood and plasma collected for transfusion or manufactured into other products.

## CASE SURVEILLANCE REPORT

More than 100 centers have responded to the second international survey of AIDS and ARC in hemophilia. We are still receiving several replies each week. Early returns show an increase of three AIDS and 19 ARC cases among the 49 centers that have responded to both surveys. We urge all centers who have not already done so to complete and return this second survey as soon as possible. Comple returns will be published in the next issue of *AIDS Center News*.

## NEW BOOK

**AIDS and The Blood, Peter Jones, M.D.; 1985; published at the Newcastle Haemophilia Reference Centre and distributed by the Haemophilia Society, P.O. Box 9, 16 Trinity Street, London SE1 1DE. (Each copy cost 1.50 *pounds* plus postage and packing as follows: UK add 50p for the first copy and 10p each thereafter. Overseas add 1 *pound* for the first copy and 50p for each additional copy. NB Please remit in sterling. Overseas orders will be sent AIRMAIL.)**

This booklet provides a wealth of timely , practical information about AIDS and hemophilila. A brief historical review of AIDS and the present knowledge about this syndrome set the stage for further discussion of signs and symptoms, associated diseases, and general guidelines for care of people with AIDS.

A major section of the book is directed toward management of hemophilia in the face of the AIDS problem. The necessity of continuing to treat bleeding episodes is emphasized. Home therapy, heat treatment of concentrates, the importance of follow-up, transmission risks, and family planning as well as other areas of concern are objectively and sensitively discussed. General questions about blood transfusion and donation, sexual contacts, and HTLV-III antibody testing are thoughtfully answered in the third portion of the booklet.


# WORLD HEMOPHILIA AIDS CENTER

*2400 So. Flower Street*
*Los Angeles, CA 90007 USA*
*Phone (213) 742-1354*
*TELEX (VIA WUI): 6502283270*