

HARDWICK-BURGESS — Rachel Louise Hardwick-Burgess, M.D., of Marstons Mills, died on November 11 at the age of 93.

Dr. Hardwick-Burgess received her degree from the Boston University School of Medicine in 1925. She was a member of the American Medical Association and the American Academy of Pediatrics. Dr. Hardwick-Burgess was a 50-year member of the Massachusetts Medical Society.

HOLMES — Joseph Alexander Holmes, M.D., formerly of Waltham, died on November 28. He was 78.

Dr. Holmes received his degree from Harvard Medical School in 1936. He was a member of the American Medical Association and a fellow of the American College of Surgeons.

LARCHEZ — Henry Francis Larchez, M.D., of South Hamilton, died on December 11. He was 80.

Dr. Larchez received his degree from Middlesex University School of Medicine in 1931. He was a member of the American Medical Association.

MICHELSON — Harry Hirsch Michelson, M.D., of Northampton, died on November 20. He was 85.

Dr. Michelson received his degree from the Medizinische Fakultät der Christian Albrechts Universität in Kiel, West Germany, in 1930. He was a member of the American Medical Association and a fellow of the American Psychiatric Association.

PAUL — Louis Robert Paul, M.D., of Brookline, died on November 28. He was 90.

Dr. Paul received his degree from the Boston University School of Medicine in 1926. He was a member of the American Medical Association and a 50-year member of the Massachusetts Medical Society.

SCHERMAN — Richard Paul Scherman, M.D., formerly of Waban, died on November 14 at the age of 90.

Dr. Scherman received his degree from the Medizinische Fakultät der Ludwig Maximilians Universität in Munich, Germany, in 1922. He was a member of the American Medical Association and the American Thoracic Society.

SMITH — Mary Frances Hayward Smith, M.D., formerly of Boston, died on November 26. She was 82.

Dr. Smith graduated from the Boston University School of Medicine in 1943. She was a member of the American Medical Association.

STERN — Arthur Stern, M.D., of Worcester, died on October 31. He was 78.

Dr. Stern received his degree from Tufts College Medical School in 1934. He was a member of the American Medical Association and the American College of Surgeons. Dr. Stern was a 50-year member of the Massachusetts Medical Society.

WISLOCKI — Florence Clothier Wislocki, M.D., formerly of Milton, died on October 28. She was 83.

Dr. Wislocki received her degree from Johns Hopkins University School of Medicine in 1930. She was a member of the American Psychiatric Association and the American Psychoanalytic Association. Dr. Wislocki was a 50-year member of the Massachusetts Medical Society.

CORRESPONDENCE

INTERPRETATION OF ANTIBODIES REACTING SOLELY WITH HUMAN RETROVIRAL CORE PROTEINS

To the Editor: With more widespread testing for antibodies to human immunodeficiency virus (HIV) in groups at low risk, we sometimes find that confirmatory Western blot assay shows antibodies that react solely with the core proteins of HIV-1. Such antibodies have been interpreted as a false positive finding when they are found in blood donors.¹⁻³ In genuine HIV-1 infection, however, anti-core antibodies are the first to appear in the process of seroconversion.⁴⁻⁶ On the other hand, serum samples from patients infected with HIV-2 recognize the core proteins of HIV-1 and most proteins of STLV-III_{AGM}, a closely related simian retrovirus.^{7,8}

We used Western blotting to look for HIV antibodies in a diverse population at risk for HIV infection and in healthy subjects at low risk. In a cohort of 235 homosexual men living in Finland and followed since 1983, the presence of antibodies that reacted only with HIV-1 core proteins typically preceded full seroconversion by several months and persisted in 20 percent of the HIV-infected subjects' sexual partners then negative on enzyme-linked immunosorbent assay (ELISA) (Fig. 1 and Table 1). These antibodies had a low titer and gave negative or only borderline positive reactions on first-generation ELISAs. The sexual partners, apparently latently infected, periodically had HIV antigen in their serum.⁶ Virus could not be isolated from stored samples of peripheral-blood lymphocytes obtained before overt seroconversion or from the partners with latent infection, but isolation was successful when tried after lymphadenopathy or central nervous system involvement (or both) had developed.

Patients with cutaneous T-cell lymphoma or its prodromes have been found to have antibodies crossreacting with the core proteins of HTLV-I (human T-cell lymphotropic virus Type I) (55 percent) or HIV-1 (24 percent)⁹ (Table 1). In randomly selected dermatol-

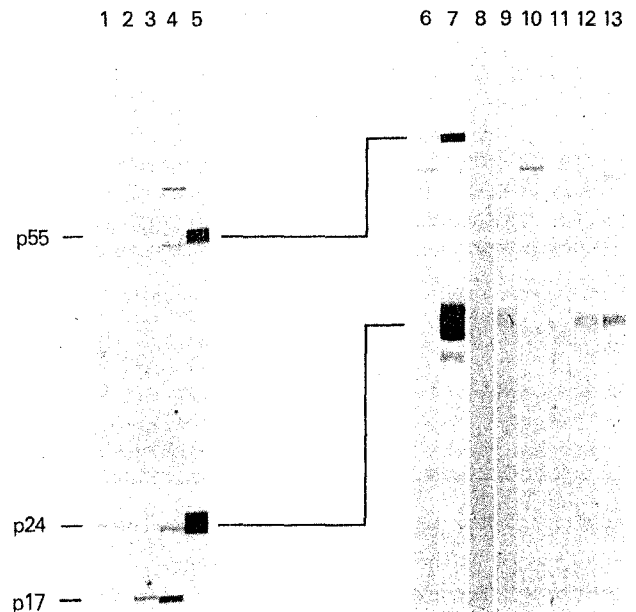


Figure 1. Reactivity on Western Blot Testing of Representative Serum Samples from Subjects Studied for HIV-1.

Lanes 1 through 4 represent samples from subjects with HIV infection before whole-virus ELISA seroconversion; Lanes 6 and 8 through 13, samples from patients with multiple sclerosis; and Lanes 5 and 7, monoclonal anti-24 antibody recognizing p24 and p55 core proteins.

Table 1. Frequency of Anti-HIV Antibody Response Restricted to Core Antigens in Different Groups Studied by Western Blot Assay.

GROUP	HTLV-I		HIV-1*		HIV-2†
	CORE	OTHER‡	CORE	OTHER‡	
	<i>no. of serum samples reacting/no. studied</i>				
Homosexual men, before seroconversion§	Not tested	Not tested	9/9	0/9	Not tested
Seronegative sexual partners of HIV-infected men	Not tested	Not tested	5/25	0/25	Not tested
Patients with cutaneous T-cell lymphoma and prodrome	12/22	2/22	6/25	1/25	3/9
Patients with dermatologic disorders	3/55	1/55	7/55	1/55	4/17
Patients with multiple sclerosis	2/17	0/17	7/17	1/17	2/16
Healthy subjects	0/150	1/150	1/150	0/150	0/30

*HTLV-III_B isolate.

†SBL 6669 isolate.

‡Polymerase and envelope proteins.

§Seronegative by whole-virus ELISA kits.

logic patients, such antibodies were found in a few cases with generalized warts without underlying systemic disease and in some cases with autoimmune connective tissue disease (Table 1). As reported earlier,¹⁰ we found crossreacting antibodies to the core of HTLV-I but also to HIV-1 in patients with multiple sclerosis (Fig. 1 and Table 1). Among 150 healthy Finnish persons, 1 (a woman) had antibodies to p24 and p55 of HIV-1 (Table 1). Some patients with multiple sclerosis, cutaneous T-cell lymphoma, or dermatologic disorders had antibodies that also reacted with the viral proteins of an HIV-2 isolate (Table 1).

Thus, an antibody response restricted to HIV core proteins detected by Western blotting may indicate either an infection with some as yet unidentified virus immunologically related to the known human retroviruses or an early phase of HIV-1 infection in persons at risk. Against this background, it is important for the laboratory to know whether a person belongs to a high-risk group, and consequently to perform additional tests — e.g., viral antigen assay¹¹ or careful immunologic studies — and to suggest extended follow-up. Isolating virus from persons with latent infection seems to be rarely successful.

ANNAMARI RANKI, M.D., PH.D.

EIJA JOHANSSON, M.D., PH.D.

University of Helsinki

00170 Helsinki, Finland

KAI KROHN, M.D., PH.D.

University of Tampere

33101 Tampere, Finland

1. Biberfeld G, Bredberg-Rådén U, Böttiger B, et al. Blood donor sera with false-positive western blot reactions to human immunodeficiency virus. *Lancet* 1986; 2:289-90.
2. van der Poel CL, Reesink HW, Tersmette T, Lelie PN, Huisman H, Miedema F. Blood donations reactive for HIV in western blot, but non-infective in culture and recipients of blood. *Lancet* 1986; 2:752-3.
3. Couroucé A-M, Muller JY, Richard D. False-positive western blot reactions to human immunodeficiency virus in blood donors. *Lancet* 1986; 2:921-2.
4. Biggar RJ, Melbye M, Ebbesen P, et al. Variation in human T lymphotropic virus III (HTLV-III) antibodies in homosexual men: decline before onset of illness related to acquired immune deficiency syndrome (AIDS). *Br Med J* 1985; 291:997-8.
5. Lange JMA, Coutinho RA, Krone WJA, et al. Distinct IgG recognition patterns during progression of subclinical and clinical infection with lymphadenopathy associated virus/human T lymphotropic virus. *Br Med J* 1986; 292:228-30.
6. Ranki A, Valle S-L, Krohn M, et al. Long latency precedes overt seroconversion in sexually transmitted human-immunodeficiency-virus infection. *Lancet* 1987; 2:589-93.

7. Kanki PJ, Barin F, M'Boup S, et al. New human T-lymphotropic retrovirus related to simian T-lymphotropic virus type III (STLV-III_{AGM}). *Science* 1986; 232:238-43.
8. Brun-Vezinet F, Rey MA, Katlama C, et al. Lymphadenopathy-associated virus type 2 in AIDS and AIDS-related complex: clinical and virological features in four patients. *Lancet* 1987; 1:128-32.
9. Ranki A, Krohn K. Crossreacting antibodies to gag proteins of HTLV-I and HTLV-III in patients with Mycosis fungoides or its prodrome large-plaque parapsoriasis. In: Gallo RC, Haseltine W, Klein G, zurHausen H, eds. *Viruses and human cancer*. New York: Alan R. Liss, 1987:43-57.
10. Koprowski H, DeFreitas EC, Harper ME, et al. Multiple sclerosis and human T-cell lymphotropic retroviruses. *Nature* 1985; 318:154-60.
11. Allain J-P, Laurian Y, Paul DA, et al. Serological markers in early stages of human immunodeficiency virus infection in haemophiliacs. *Lancet* 1986; 2:1233-6.

FETAL HEMOGLOBIN AND ERYTHROPOIETIN

To the Editor: In their study of the stimulation of fetal hemoglobin synthesis by human erythropoietin in primates, Al-Khatti et al. (Aug. 13 issue)¹ speculate that the use of recombinant erythropoietin may be of benefit to patients with sickle cell anemia.

Our experience² with renal transplantation in patients with sickle cell anemia has demonstrated that the presence of abnormally high erythropoietin levels in patients who have received a kidney can lead to disastrous episodes of sickling, which may cause loss of the allograft or death. Unlike the anemic animals studied by Al-Khatti et al., which have high levels of erythropoietin, patients with sickle cell anemia have levels of erythropoietin that are abnormally low for their degree of anemia. The response to exogenously administered erythropoietin may therefore be quantitatively and qualitatively different. Thus, we would urge extreme caution in the administration of recombinant erythropoietin to patients with sickle cell anemia. In the last paragraph of their report, the authors acknowledge the possibility of the induction of sickling crises; we believe, however, that this point deserves special emphasis.

W. HENRY BARBER, M.D., D.PHIL.

University of Alabama Hospital

Birmingham, AL 35294

1. Al-Khatti A, Veith RW, Papayannopoulou T, Fritsch EF, Goldwasser E, Stamatoyannopoulos G. Stimulation of fetal hemoglobin synthesis by erythropoietin in baboons. *N Engl J Med* 1987; 317:415-20.
2. Barber WH, Deierhoi MH, Julian BA, et al. Renal transplantation in sickle cell anemia and sickle disease. *Clin Transplant* 1987; 1:169-75.

To the Editor: The recently reported use of recombinant human erythropoietin to stimulate production of fetal hemoglobin¹ is an important development, with potential for the management of sickle cell anemia¹ and perhaps also for the treatment of malaria. Per-

Letters to the Editor are considered for publication (subject to editing and abridgment), provided that they are submitted in duplicate, signed by all authors, typewritten in double spacing, and do not exceed 40 typewritten lines of manuscript text (excluding references). Submission of a letter constitutes permission for the Massachusetts Medical Society, its licensees, and its assignees to use it in the *Journal's* various editions (print, data base, and optical disk) in anthologies, revisions, and any other form or medium. Letters should not duplicate similar material being submitted or published elsewhere, and they should not contain abbreviations. Financial associations or other possible conflicts of interest should always be disclosed.

Letters referring to a recent *Journal* article must be received within six weeks of the article's publication. We are unable to provide pre-publication proofs, and unpublished material will not be returned to authors unless a stamped, self-addressed envelope is enclosed. Receipt of letters is not acknowledged, but correspondents will be notified when a decision is made.