

Human T-Lymphotropic Virus Type 4 and the Human Immunodeficiency Virus in West Africa

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A new human T-lymphotropic virus (HTLV-4) was recently described in healthy people from Senegal. This virus has many properties in common with members of the human T-lymphotropic viruses, particularly the human immunodeficiency virus or HIV, the etiologic agent of acquired immune deficiency syndrome (AIDS), but does not appear to be associated with immunodeficiency-related disorders. In the present study, serum samples were obtained from 4248 individuals from six West African countries, including Senegal, Guinea, Guinea Bissau, Mauritania, Burkina Faso, and Ivory Coast. These samples, collected during 1985–1987, were from people categorized as healthy control, sexually active risk, and disease populations. All samples were analyzed for reactivity to HTLV-4 and HIV by radioimmunoprecipitation–sodium dodecyl sulfate–polyacrylamide gel electrophoresis and immunoblotting. Evidence for HTLV-4 infection was found in five of the six countries. The seroprevalence varied markedly from country to country. Healthy sexually active individuals in the risk category had the highest levels of HTLV-4 infection compared to individuals in the healthy control category and the disease category, the latter including AIDS patients. The seroprevalence of HIV infection in most of these countries was quite low, although tightly associated with the rare cases of AIDS. The biology of HTLV-4 infection thus differs from that of HIV in Central Africa or the United States and Europe. The presence of these viruses and their different pathogenicities in several countries of West Africa indicate the necessity for serologic assays that will distinguish between them. Further studies of their origin and distribution as well as of their biology will be important in advancing our understanding of AIDS.

THE HUMAN IMMUNODEFICIENCY virus, or HIV (also called HTLV-III/LAV), is the cause of the acquired immune deficiency syndrome (AIDS) in humans (1). This virus, like the human T-lymphotropic viruses types I and II (HTLV-I and HTLV-II), is tropic to CD4 (T4 helper) lymphocytes. Infection of these cells by HIV leads to the formation of multinucleated syncytia and marked cytolysis. A number of viruses closely related to HIV

infect a variety of nonhuman primates. For example, the simian T-lymphotropic virus type 3 (STLV-3) occurs in African Green monkeys and captive rhesus macaques and is associated with no disease in the former but immunodeficiency in the latter (2, 3). The similarities of STLV-3 to HIV include tropism for CD4 lymphocytes, ultrastructural morphology, and most important, similar viral antigens that are bidirectionally cross-reactive (2, 3). We previously suggested the

possibility that STLV-3 served as a progenitor virus to the human AIDS virus, and hypothesized that there might be other viruses in humans that are more closely related to STLV-3. In 1985 we described a virus termed HTLV-4 that infects apparently healthy people in West Africa (4). This virus is similar to STLV-3 in ultrastructural morphology, CD4-lymphocyte tropism, and major viral proteins. The HTLV-4 viral antigens, identified by radioimmunoprecipitation–sodium dodecyl sulfate–polyacrylamide gel electrophoresis (RIP-SDS/PAGE) as well as immunoblot analysis, include gp160, gp120, gp32, p64, p53, p34, p55, p24, p15, and p31, representing the major *env*, *pol*, *gag* and 3' *orf* gene products, respectively (4, 5). In contrast to HIV, HTLV-4 infection of CD4 cells induces the formation of multinucleated syncytia in vitro without significant cytolysis, and in humans appears not to be associated with immunodeficiency. Clavel *et al.* have described another human retrovirus termed LAV-2 that was isolated from two AIDS patients originating from Cape Verde and Guinea Bissau (6). This virus also cross-reacts with the simian virus STLV-3 but is reported to have pathogenicity equal to HIV.

The study reported here was undertaken to assess the prevalence of HTLV-4 in six West African countries and to study its association with disease. We used highly specific serologic assays that could distinguish among different virus types and analyzed the profiles of viral antigens recognized by serum from infected people. In addition to surveying cases of AIDS and related disorders, we studied patients with a number of other diseases, including cancer, to determine whether they might be associated with HTLV-4 infection. We also hoped to provide preliminary survey information that would aid health policy decisions relative to the prevention and control of human T-lymphotropic virus infection.

A total of 4248 individuals were evaluated between February 1985 and January 1987. Serum samples were obtained by members of our group in 13 major urban areas representing six different West African nations (see Fig. 1 and Table 1) (7). We divided the

Table 1. Distribution of serum samples from six West African countries by health category.

Category and subgroup	Senegal	Guinea	Guinea Bissau	Mauritania	Burkina Faso	Ivory Coast	Total
Control							
Healthy	166	90	50	27	303	184	820
Pregnant women	72	119	40	27	58	365	681
Prisoners					55	282	337
Hospital patients*	188	105	61	86		236	676
Risk							
Prostitutes	403	13	39		308	232	995
STD patients	19			9	32		60
Disease							
Tuberculosis	155	131	150	33		40	509
Hospital patients†	23		123	2	22		170
Total	1026	458	463	184	778	1339	4248
Mean age (years)	32.2	32.6	35.9	32	23.1	30.6	
M:F ratio	1:2.4	1:1.2	1:1.7	1:1.9	1:2.2	1:1.4	

*Includes hospitalized patients from gynecology and surgery wards.

†Includes hospitalized patients from infectious disease and internal medicine wards.

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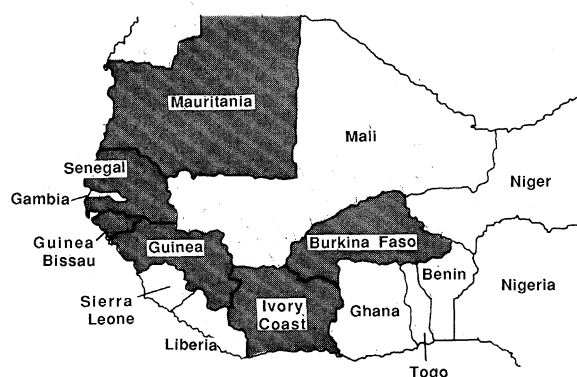


Fig. 1. Map of West Africa. The countries included in this study are shaded. The urban areas surveyed included: in Senegal, Dakar, St. Louis, Ziguinchor, Kaolack, and Bignona; in Guinea, Conakry; in Guinea Bissau, Bissau; in Mauritania, Nouakchott; in Burkina Faso, Ouagadougou; and in Ivory Coast, Abidjan, Tortiya, Adzope, and Khorogo.

populations sampled into three basic categories of health status designated disease, risk, and control. All samples were obtained for the purpose of this study at one point in time. The definitions of the categories used were as follows:

Disease category. Because the clinical spectrum of AIDS in Africa differs from that in the United States (8), we used the World Health Organization's (WHO) provisional clinical case definition for AIDS in Africa (9). All inpatients from a number of hospitals situated in the urban centers (Table 1) were examined by one of our personnel and a venous blood sample was obtained for serology. We categorized all hospitalized patients from internal medicine or infectious disease wards into the disease category. Many of these patients had clinical infections or symptoms consistent with immunosuppression and possible AIDS or a related disorder, as delineated by the WHO. Thus, cases of chronic wasting diarrhea, Kaposi's sarcoma, meningitis-encephalitis, cachexia of unknown etiology, lymphomas, and pulmonary and extrapulmonary tuberculosis were included.

A broad spectrum of clinical abnormalities has also been described for patients

infected with HTLV-I in addition to the development of adult T-cell leukemia lymphoma. Miyoshi and colleagues have described three HTLV-I-infected patients who fit the Centers for Disease Control (CDC) definition of AIDS but were HIV-negative (10). Increased risk for infection by HTLV-I has been observed in patients from infectious disease wards in Miyazaki, Japan, an endemic area for HTLV-I (10). This suggests that human T-lymphotropic viruses may vary widely in their disease outcome. Patients from infectious disease wards therefore provided a large number of individuals that might have been exposed to the immunosuppressive properties of a T-lymphotropic retrovirus.

Risk category. We identified prostitutes and patients visiting outpatient STD (sexually transmitted disease) clinics as being potentially at high risk for infection with a sexually transmitted retrovirus. The health licensure of prostitution in many of these countries allowed for the physical examination and serum sampling at regularly visited STD clinics. All prostitutes and other patients visiting such clinics were sampled.

Control category. Control healthy adult populations from the same geographic lo-

cales as the risk and disease category were obtained, such as blood donors or clinic workers. In addition, healthy pregnant women visiting established pregnancy outpatient clinics, prisoners, and hospitalized patients from gynecology and surgery wards were included. All control individuals were sampled at one point in time; all hospitalized control patients were from the same hospitals sampled for the disease category.

All of the 4248 serum samples were analyzed by immunoblot techniques for antibodies to HIV and HTLV-4, as previously described (4). Serum samples with positive reactivity to either HIV or HTLV-4 were also analyzed by RIP-SDS/PAGE with whole cell lysates [HTLV-III_B/Molt 3 and HTLV-4/Hut-78 (PK289) cell lines] metabolically labeled with [³⁵S]cysteine as previously described (4). As shown in Fig. 2, HTLV-4-positive antibodies were most consistently reactive with the gp160/120, p55, and p24 proteins of HTLV-4; reference West African negative sera showed no such reactivity. Similarly, these same sera lacked antibody reactivity to the control uninfected cell lysates.

Studies with HIV have shown that the *env* encoded proteins are the antigens most frequently detected by antibodies from exposed individuals, the gp160/120 by RIP-SDS/PAGE and the gp41 transmembrane protein by immunoblot analysis (11). The *env* related proteins of HTLV-4 are also the most immunoreactive viral antigens (4, 12). The gp32, the presumed transmembrane protein, is readily detected by immunoblot analysis, and the mature envelope protein gp120 is detected by RIP-SDS/PAGE. The *pol* encoded antigens p64, p53, and p34, and *gag* encoded antigens p55, p24, and p15 are less consistently recognized by all groups of HIV or HTLV-4 exposed individuals (4, 5,

Table 2. Detection of antibodies to HTLV-4 in 4248 serum samples as determined by immunoblot analysis and RIP-SDS/PAGE. Results show percentage of samples that were positive; the actual numbers of samples positive and tested are shown in parentheses.

Category and subgroup	Senegal	Guinea	Guinea Bissau	Mauritania	Burkina Faso	Ivory Coast
Control						
Healthy	0.0 (0/166)	0.0 (0/90)	2.0 (1/50)	0.0 (0/27)	0.0 (0/303)	0.5 (1/184)
Pregnant women	4.2 (3/72)	1.7 (2/119)	17.0 (7/40)	0.0 (0/27)	1.7 (1/58)	0.3 (1/365)
Prisoners					0.0 (0/55)	13.5 (38/282)
Hospital patients*	0.5 (1/188)	1.0 (1/105)	10.0 (6/61)	0.0 (0/86)		1.3 (3/236)
Total	0.9 (4/426)	0.9 (3/314)	9.2 (14/151)	0.0 (0/140)	0.2 (1/416)	4.0 (43/1067)
Risk						
Prostitutes	15.0 (62/403)	0.0 (0/13)	64.0 (25/39)		20.4 (63/308)	20.0 (47/232)
STD patients	5.3 (1/19)			0.0 (0/9)	15.6 (5/32)	
Total	14.9 (63/422)	0.0 (0/13)	64.0 (25/39)	0.0 (0/9)	20.0 (68/340)	20.0 (47/232)
Disease						
Tuberculosis	1.3 (2/155)	1.5 (2/131)	12.0 (18/150)	0.0 (0/33)		5.0 (2/40)
Hospital patients†	8.7 (2/23)		15.4 (19/123)	0.0 (0/2)	0.0 (0/22)	
Total	2.2 (4/178)	1.5 (2/131)	13.6 (37/273)	0.0 (0/35)	0.0 (0/22)	5.0 (2/40)

*Includes hospitalized patients from gynecology and surgery wards.

†Includes hospitalized patients from infectious disease and internal medicine wards.

11, 12). Therefore, we interpreted samples as being antibody-positive when there was evidence of reactivity to *env* related antigens of either HIV or HTLV-4, or both. All serum samples were analyzed for reactivity to HTLV-4 by immunoblot analysis (Fig. 3). The typical immunoblot profile of a serum sample that reacts with HTLV-4 shows antibodies to the gp32, p64, p53, p55, and p24, with variable reactivity to the reduced form of gp120 and the NH₂-terminal *gag* protein p15.

As shown in Tables 2 and 3, we found evidence of HTLV-4 infection in Senegal, Guinea, Guinea Bissau, Burkina Faso, and Ivory Coast. Despite their close geographic proximity, the different countries showed marked variations in seroprevalence to HTLV-4 regardless of health category. In Mauritania, 0 of 184 samples were seropositive to HTLV-4 antigens. Similarly, in Guinea only 5 of 458 samples (1%) were HTLV-4 positive. In Senegal, Guinea Bissau, Burkina Faso, and Ivory Coast the overall HTLV-4 seroprevalence varied from 6.9% to 16%. In these countries the seroprevalence to HTLV-4 was significantly higher in risk populations (14.9% to 64%) than in control groups (0.2% to 9.2%) (prevalence ratio = 7.4; $\chi^2 = 297$, $P < 0.0001$). In Senegal, Guinea, Guinea Bissau, and Mauritania, the seroprevalence to HIV was lower than that to HTLV-4 (Table 3), consistent with the low numbers of reported cases of AIDS in West Africa. The risk category showed a higher seroprevalence to HIV than control populations from the same geographic locales (prevalence ratio = 5.2; $\chi^2 = 106$, $P < 0.0001$).

In Senegal, Guinea, Guinea Bissau, and Mauritania, the seroprevalence to HIV in control populations ranged from 0% to 0.6% and in sexually active risk groups

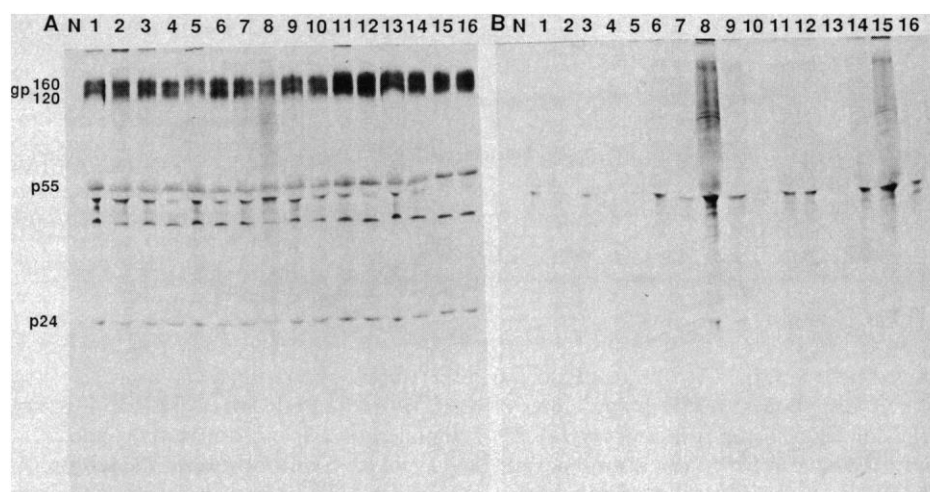


Fig. 2. (A) Radioimmunoprecipitation and sodium dodecyl sulfate polyacrylamide gel electrophoresis of ³⁵S metabolically labeled cell lysates reacted with the following: lane N, reference HTLV-4 seronegative serum from Senegal; lanes 1 to 16, representative HTLV-4-positive sera from Senegal, Guinea, Guinea Bissau, Ivory Coast, and Burkina Faso. (B) The same serum samples as described above reacted with identically prepared cell lysates from uninfected Hut-78 cells.

Fig. 3. Immunoblot analysis of representative HTLV-4 antibody positive serum samples reacted with HTLV-4/Hut-78 (PK289) virus. The majority (85%) of HTLV-4 positive samples showed this profile of reactivity with HTLV-4 antigens, irrespective of health category or geographic origin.

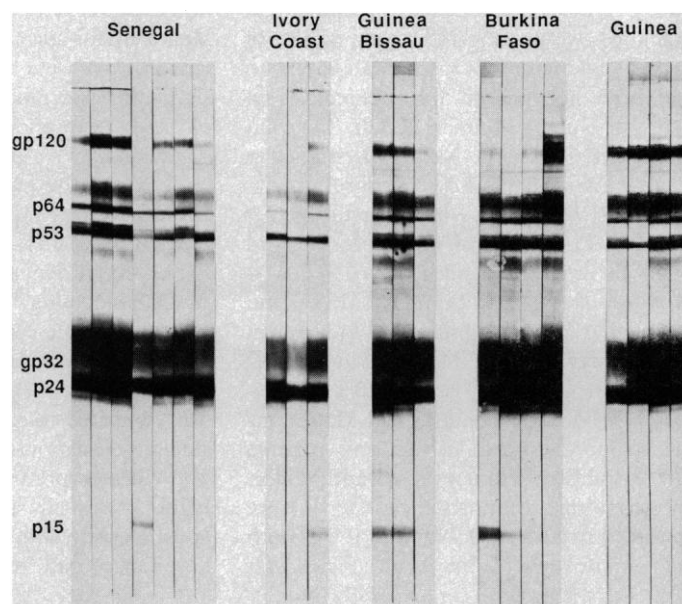


Table 3. Detection of antibodies to HIV (HTLV-III_B) in 4248 serum samples as determined by immunoblot analysis and RIP-SDS/PAGE. Results show percentage of samples that were positive; the actual numbers of samples positive and tested are shown in parentheses.

Category and subgroup	Senegal	Guinea	Guinea Bissau	Mauritania	Burkina Faso	Ivory Coast
Control						
Healthy	0.0 (0/166)	0.0 (0/90)	0.0 (0/50)	0.0 (0/27)	0.0 (0/303)	2.2 (4/184)
Pregnant women	0.0 (0/72)	1.7 (2/119)	0.0 (0/40)	0.0 (0/27)	1.7 (1/58)	0.5 (2/365)
Prisoners					1.8 (1/55)	6.7 (19/282)
Hospital patients*	0.0 (0/188)	0.0 (0/105)	0.0 (0/61)	0.0 (0/86)		5.5 (13/236)
Total	0.0 (0/426)	0.6 (2/314)	0.0 (0/151)	0.0 (0/140)	0.5 (2/416)	3.7 (38/1067)
Risk						
Prostitutes	0.5 (2/403)	0.0 (0/13)	0.0 (0/39)		14.6 (45/308)	19.8 (46/232)
STD patients	5.3 (1/19)			0.0 (0/9)	0.0 (0/32)	
Total	0.7 (3/422)	0.0 (0/13)	0.0 (0/39)	0.0 (0/9)	13.2 (45/340)	19.8 (46/232)
Disease						
Tuberculosis	0.0 (0/155)	0.8 (1/131)	0.0 (0/150)	6.0 (2/33)		10.0 (4/40)
Hospital patients†	8.7 (2/23)		0.0 (0/123)	0.0 (0/2)	4.5 (1/22)	
Total	1.1 (2/178)	0.8 (1/131)	0.0 (0/273)	5.7 (2/35)	4.5 (1/22)	10.0 (4/40)

*Includes hospitalized patients from gynecology and surgery wards.

†Includes hospitalized patients from infectious disease and internal medicine wards.

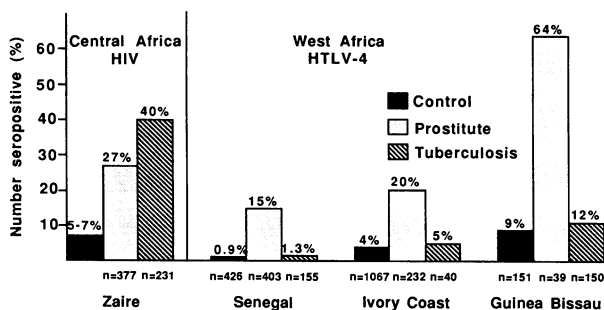


Fig. 4. Seroprevalence of HTLV-4 in control, prostitute, and tuberculosis patients in Senegal, Ivory Coast, and Guinea Bissau compared to the seroprevalence of HIV in Zaire (14) in similar groups. Only HTLV-4 seroprevalence in prostitutes (as opposed to all risk groups) is given to compare with seroprevalence with HIV in Zairian prostitutes.

ranged from 0% to 0.7%. Burkina Faso and Ivory Coast showed relatively high rates of HIV infection in the risk category (13.2% and 19.8%) compared to control populations (0.5% and 3.7%). It is of interest that the five HIV-positive individuals sampled in Senegal for this study were either Central Africans or Senegalese recently traveling in Central Africa.

Because we found only five cases of diagnosed AIDS among the 4248 individuals examined, we investigated a total of 509 of these individuals in the disease category who had been hospitalized for tuberculosis in Senegal, Guinea, Guinea Bissau, Mauritania, and Ivory Coast. Numerous studies in Central Africa have shown a close association of HIV infection with tuberculosis (13, 14) (Fig. 4). In Senegal, Guinea Bissau, and Ivory Coast the seroprevalence of HTLV-4 in tuberculosis patients (1.3%, 12%, and 5%; Table 2) was significantly lower than the seroprevalence of HTLV-4 in the risk categories (14.9%, 64%, and 20%, respectively; Table 2). In Guinea and Mauritania the seroprevalence in tuberculosis patients (1.5% and 0%) was not significantly different from the seroprevalence rates in the control categories (0.9% and 0%), both being quite low (Table 2 and Fig. 2). It

therefore appears that, unlike HIV and AIDS in Central Africa, HTLV-4 is not significantly associated with tuberculosis.

In all six countries studied the seroprevalence for HTLV-4 was higher in people in the risk category who were apparently healthy at the time of sampling compared to all patients in the disease category. As described, the disease category included many different infectious diseases, tumors, and other clinical syndromes; each was analyzed separately for association with HTLV-4 infection. We were unable to establish any significant association of HTLV-4 with any of these disease entities either analyzed alone or as a group.

To assess the potential pathogenicity of HTLV-4 it was important for us to examine populations with a significant prevalence to HTLV-4. In Senegal, all five of five HIV-positive individuals were either Central Africans or Senegalese who had recently traveled in Central Africa. The overall seroprevalence to HTLV-4 in Senegal by health category was compared to seroprevalence to HIV in similar populations in Zaire (13, 14) (Table 4). The seroprevalence to HTLV-4 was higher in sexually active risk groups (15%) in comparison with healthy controls (0.9%), hospitalized patients from infectious disease

wards (2.2%), or diagnosed AIDS cases (0%). Five additional cases of AIDS in Senegal have been reported, and these patients were HIV-positive (15). In comparison, the seroprevalence of HIV in Zaire was previously found to be 27% in Zairian prostitutes (14); among hospitalized patients from infectious disease wards in the same urban area the HIV seroprevalence was 45% (13). Among diagnosed AIDS cases in Zaire the HIV seroprevalence was 90.4% (13), and among CDC-defined AIDS cases in West Africa the HIV seroprevalence was 100%, and none of these patients was HTLV-4 positive.

A total of 330 HTLV-4 antibody positive samples representing five West African countries were evaluated for their serologic profiles as shown in Fig. 5. Both RIP-SDS/PAGE and immunoblot analyses of these samples appeared sensitive and specific with total concordance on HTLV-4 antigen. A similar result was obtained with samples from HIV-positive individuals when we used the same two assays with HIV antigen. The HTLV-4-positive individuals usually showed a strong titer in response to the gp120/160, gp32, p64, p53, p55, and p24 antigens of HTLV-4. The cross-reactive antibody response to HIV antigens was generally directed to the *gag* and *pol* encoded antigens, p55, p24 and p64, p53 and p34. This type of response was seen in 280 (85%) of the 330 samples studied, with representative individuals from each country. All of the HTLV-4 reactive samples from native Senegalese demonstrated this typical reactivity.

An atypical response to HTLV-4 and HIV antigens was shown by individuals from Burkina Faso and Ivory Coast. In both countries a number of individuals showed specific reactivity to the *env* related antigens of HIV and HTLV-4 by RIP-SDS/PAGE (Fig. 5). It is not known whether this serologic profile is indicative of dual infection or infection by a novel T-lymphotropic virus with highly cross-reactive *env* protein epitopes (7). All of the individuals with these serologic profiles were apparently healthy at the time of sampling. In vitro studies have shown that HIV can superinfect HTLV-4-infected Hut-78 cells and lead to characteristic syncytia formation at 7 days after infection. However, such dually infected cells showed no early burst of CD4 cell cytolysis normally observed in HIV-infected Hut-78 cells (12). This suggests that HTLV-4-infected individuals may also become infected with HIV but that the characteristic CD4 directed cytolytic effects become attenuated by prior infection with HTLV-4. Further studies in vitro and in natural populations of people exposed to

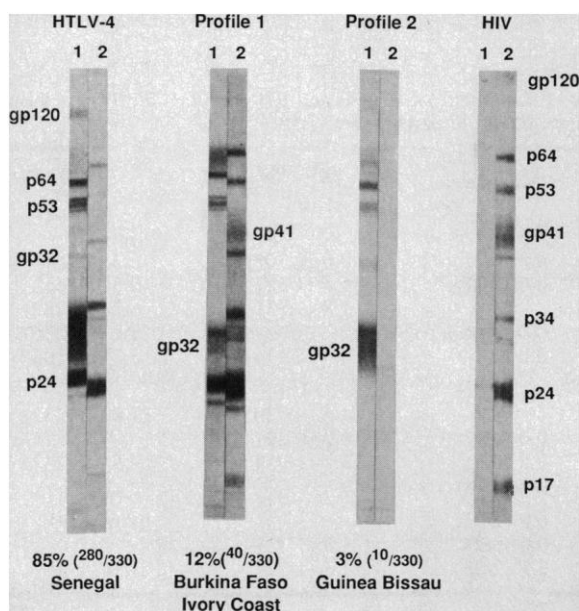


Fig. 5. Immunoblots of characteristic serologic profiles on HTLV-4 (lanes 1) and HIV (lanes 2). A total of 330 HTLV-4-positive serum samples were analyzed. The percentages of samples with the characteristic HTLV-4 profile and atypical profiles 1 and 2 are indicated. All of the HTLV-4 positive samples from Senegal demonstrated the characteristic profile. Atypical profile 1 was seen in samples from Burkina Faso and Ivory Coast. Atypical profile 2 was seen in a small number of samples from Guinea Bissau.

these viruses will be necessary to understand the clinical significance of HTLV-4 and HIV interactions.

A second atypical response to HTLV-4 antigens was shown by a small proportion of serum samples (10 of 330; 3%) that reacted strongly to the gp120/160 and gp32 of HTLV-4 but gave faint or no response to the *gag* and *pol* related antigens of HTLV-4. It is of interest that nine of these samples were from people sampled in Guinea Bissau; the tenth sample was from a patient hospitalized in Senegal with chronic weight loss and diarrhea; however, this individual was also native to Guinea Bissau. There are several interpretations for this type of response. First, it is possible that these individuals are infected with HTLV-4 and that, similar to AIDS patients with HIV, they have lost their antibody response to the *gag* related antigens. Second, this atypical response and its tight geographical distribution may indicate the existence of another closely related virus in the HTLV-4 group.

Our data suggest that HTLV-4 is the more prevalent T-lymphotropic virus in West Africa. Sexually active groups showed a sevenfold increased risk for infection with HTLV-4, suggesting that this T-lymphotropic virus is also sexually transmitted. The serologic evidence for the presence of HIV was low in Senegal, Guinea, Guinea Bissau, and Mauritania; however, increased seroprevalence to both HTLV-4 and HIV was seen in Ivory Coast and Burkina Faso, countries that are closer to Central Africa. In the risk category, seroprevalence to HTLV-4 was 20% in both countries, and to HIV was 19.8% in Ivory Coast and 13.2% in Burkina Faso. In the control category, seroprevalence to both viruses was significantly lower, 0.2 to 4.0%, as would be expected for sexually transmitted viruses. The reported cases of AIDS in Senegal and most other West African countries are quite rare. The few documented cases of AIDS that we have observed in this geographic area have been uniformly associated with HIV, and the affected individuals have been of Central African descent or have recently traveled in Central Africa.

There is serologic evidence that HTLV-4 was present in the mid-1970s in Dakar, Senegal (4). The seroprevalence to HTLV-4 in risk groups in Senegal is now 5 to 15%. The relatively high seroprevalence to HIV in Central African patients with sexually transmitted diseases and prostitutes has often been observed in conjunction with clinical and immunologic abnormalities and high numbers of AIDS cases in the same regions (8, 13, 16). An ongoing clinical prospective study conducted in Senegal over a 24-month period indicates no significant clinical

Table 4. Comparison of seroprevalence to HTLV-4 and HIV in Senegal and Zaire by health category. Results show percentage of samples that were positive; the actual number of samples positive and tested are shown in parentheses.

Category and subgroup	Senegal		Zaire* HIV
	HTLV-4	HIV	
Control	0.9 (4/426)	0.0 (0/426)	8.8 (15/170)
Risk	15.0 (63/422)	0.7 (3/422)	27.0 (101/377)
Disease			
Hospital patients	2.2 (4/178)	1.1 (2/178)	45.0 (99/219)
AIDS cases	0.0 (0/5)	100.0 (5/5)	90.4 (132/146)

*See (13, 14).

cal or immunological abnormalities in HTLV-4 seropositive prostitutes compared with seronegative prostitutes (17), suggesting that the pathogenicity of HTLV-4 is quite different from that of HIV. HTLV-4 infection was not significantly higher in tuberculosis patients, hospitalized patients from infectious disease wards, or diagnosed AIDS cases. This suggests that the pathogenic potential of HTLV-4 is markedly reduced from that of HIV, the prototype AIDS virus. Our data from Guinea Bissau revealed some unusual features in that the control, risk, and disease categories showed a relatively high seroprevalence to HTLV-4. In addition, many of the HTLV-4-positive sera from individuals in this country showed an atypical reactivity with the HTLV-4 antigens.

Studies of LAV-2 have linked this virus to the cause of AIDS in four patients (6, 18). These patients had a strong antibody response to a gp33-36 and a gp41 protein of LAV-2, the latter being very similar to the transmembrane envelope protein of the prototype AIDS virus, HIV (6, 18). We have analyzed many of the HTLV-4-positive serum samples with LAV-2 antigen by RIP-SDS/PAGE and immunoblot. In general, the degree of reactivity to the LAV-2 *env* related proteins was diminished compared to the reactivity with HTLV-4 antigen (12). It is therefore imperative that the biology of this new group of STLV-3 related human viruses be better defined through population based cross-sectional and prospective studies using assays that clearly distinguish among LAV-2, HTLV-4, and HIV.

The study described here indicates that HTLV-4 and HIV are both present in West Africa, and that HIV infection appears to be low in most of the urban centers studied except in Burkina Faso and Ivory Coast. HTLV-4 appears to be more widespread, with rates of infection elevated in sexually active risk categories but not tightly associated with disease. Studies in vitro indicate that HTLV-4 may interfere with some of the pathogenic effects of HIV. It is not known if this reflects an interaction between the two viruses that will alter the pathogene-

sis of AIDS in Africa, and it may be necessary to monitor infection rates in these countries for several years in order to obtain epidemiological data that would resolve this question. Since the pathogenesis of HTLV-4 infection appears to differ from the pathogenesis of HIV-induced AIDS in Central Africa, Europe, and the United States, the differences in the distribution of the two viruses may need to be taken into consideration by those formulating health policies designed to halt the spread of AIDS.

REFERENCES AND NOTES

1. R. C. Gallo *et al.*, *Science* **224**, 500 (1984); M. Popovic, M. G. Sarngadharan, E. Reed, R. C. Gallo, *ibid.*, p. 497; F. Barré-Sinoussi *et al.*, *ibid.* **220**, 868 (1983).
2. P. J. Kanki *et al.*, *Lancet* **1985-I**, 1330 (1985); P. J. Kanki, J. Alroy, M. Essex, *Science* **230**, 951 (1985).
3. P. J. Kanki *et al.*, *Science* **228**, 1199 (1985); M. D. Daniel *et al.*, *ibid.*, p. 1201.
4. F. Barin *et al.*, *Lancet* **1985-II**, 1387 (1985); P. J. Kanki *et al.*, *Science* **232**, 238 (1986).
5. J. S. Allan *et al.*, *Blood* **69**, 331 (1987); J. Allan and P. Kanki, in preparation.
6. F. Clavel *et al.*, *Science* **233**, 343 (1986).
7. F. Denis *et al.*, *Lancet* **1987-I**, 408 (1987).
8. T. C. Quinn, J. M. Mann, J. W. Curran, P. Piot, *Science* **234**, 955 (1986).
9. World Health Organization, *Weekly Epidemiol. Res.* **61**, 69 (1986); Centers for Disease Control, *Morbidity Mortal. Weekly Rep.* **34**, 373 (1985).
10. I. Miyoshi, paper presented at ARC International Symposium on Viruses and Cancers, Martinique, 1986; M. Essex *et al.*, in *Human T-cell Leukemia Viruses*, R. C. Gallo, M. Essex, L. Gross, Eds. (Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, 1984), pp. 355-362.
11. F. Barin *et al.*, *Science* **228**, 1094 (1985); J. S. Allan *et al.*, *ibid.*, p. 1091. F. Veronese *et al.*, *ibid.* **229**, 1402 (1985).
12. P. J. Kanki and F. Barin, unpublished data.
13. P. J. Kanki *et al.*, in preparation.
14. J. Mann, paper presented at International Conference on AIDS, Paris, France, 1986.
15. A. Sow, paper presented at Human Viral Diseases and AIDS Prevention, Dakar, Senegal, 1986.
16. N. Clumeck *et al.*, *Lancet* **1985-II**, 524 (1985); N. Clumeck *et al.*, *J. Am. Med. Assoc.* **18** (no. 254) 2599 (1985); J. K. Kreiss *et al.*, *N. Engl. J. Med.* **314**, 414 (1986).
17. R. Marlink *et al.*, in preparation.
18. F. Brun-Vezinet *et al.*, *Lancet* **1987-I**, 128 (1987).
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