7. The optical system used in the spectral sensitivity experiments was a two-channel Maxwellian view system which formed a 2 degree test field superimposed upon a 10 degree background field. During the scotopic luminosity experiments, the background channel was blocked off and the subject was allowed to dark-adapt before the threshold measurements were made. The stimuli for the spatial modulation sensitivity experiments were vertical sinusoidal gratings generated on the screen of an oscilloscope with a white phosphor by standard procedures.
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New Human T-Lymphotropic Retrovirus Related to Simian T-Lymphotropic Virus Type III ($STLV\text{-}III_{AGM}$)

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This report describes serologic evidence for a virus similar to that known as simian T-lymphotropic virus type III of African Green monkeys ($STLV\text{-}III_{AGM}$) infecting apparently healthy people in Senegal, West Africa, and the isolation of virus from these individuals. Serum samples from selected healthy West African people showed unusual serologic profiles when tested with antigens of HTLV-III/LAV, the etiologic agent of AIDS, and of $STLV\text{-}III_{AGM}$. The samples reacted strongly with all of the major viral antigens of $STLV\text{-}III_{AGM}$ but showed variable or no reactivity with the major viral antigens of HTLV-III/LAV by radioimmunoprecipitation and sodium dodecyl sulfate–polyacrylamide gel electrophoresis. A new human T-lymphotropic virus (HTLV-IV) isolated from these people was grown in vitro and shown to have retroviral type particles, growth characteristics, and major viral proteins similar to those of the STLV-III and HTLV-III/LAV group of retroviruses. The gp120/160, gp32, p64, p55, p53, p24, and p15 proteins precipitated were the same size as and reactive with $STLV\text{-}III_{AGM}$ proteins. The serologic data suggest that this virus shares more common epitopes with $STLV\text{-}III_{AGM}$ than with the prototype HTLV-III/LAV that infects people in the United States and Europe. Further study of this virus and of the origin of the HTLV-III/LAV group of viruses may expand our understanding of the human AIDS virus.

IT HAS RECENTLY BEEN RECOGNIZED that the T-lymphotropic retrovirus family includes not only human retroviruses (HTLV-I, HTLV-II, and HTLV-III/LAV) and bovine leukemia virus but also closely related agents that infect certain nonhuman primate species. The simian T-lymphotropic virus type I (STLV-I) naturally infects most species of Old World monkeys and great apes (*1*). Similar to its human counterpart, STLV-I immortalizes T lymphocytes in vitro and has been linked with spontaneous lymphoid malignancy in the primate host (*1, 2*). STLV-III has been described in both captive ill rhesus macaques (*Macaca mulatta*) and healthy wild-caught African Green monkeys (*Cercopithecus sp.*) (*3–5*). This virus has a cytolytic effect on T4 lymphocytes in culture, Mg^{2+}-dependent reverse transcriptase, and retroviral particles with morphology similar to HTLV-III/LAV, the etiologic agent of AIDS (*3–7*). The major STLV-III proteins have been identified by radioimmunoprecipitation and sodium dodecyl sulfate–polyacrylamide gel electrophoresis (RIP/SDS-PAGE) as 160 kilodaltons (kD), 120 kD, 55 kD, 24 kD, and 15 kD similar to and cross-reactive with the major antigens of HTLV-III/LAV (*3, 5*). Serologic studies on a variety of African primates indicated that approximately 50 percent of African Green monkeys (*Cercopithecus aethiops*) were seropositive for STLV-III ($STLV\text{-}III_{AGM}$), whereas chimpanzees (*Pan troglodytes*), baboons (*Papio sp.*), patas monkeys (*Erythrocebus patas*), and colobus monkeys (*Colobus polykomos*) were seronegative (*5*). Antibodies to $STLV\text{-}III_{AGM}$ have been identified in sera from *Cercopithecus* species sampled as early as 1961 (*8*).

The African Green monkey and other members of the genus *Cercopithecus* are widespread throughout most parts of tropical Africa. The close relation of $STLV\text{-}III_{AGM}$ to HTLV-III/LAV raised the possibility that a family of related viruses may have existed in primates well before the AIDS epidemic began. Therefore, we speculated that STLV-III may have been transmitted to humans at some time during the natural history of these viruses (*5*). AIDS cases may have been present in Central Africa in the mid-1970's (*9*) before the disease was recognized in the United States and Europe. Recent studies indicate that AIDS is endemic in Central Africa with significant transmission occurring in the heterosexual population (*10*). Serologic studies of HTLV-III/LAV indicate that this or a related virus may have been present in Africa as early as 1972 (*11*). We have therefore investigated further the possibility that these viruses may have had a common origin.

By using the differential reactivity of HTLV-III/LAV–positive human sera for $STLV\text{-}III_{AGM}$ viral antigens, we have demonstrated that certain apparently healthy people in Senegal, West Africa, have antibodies that are more strongly reactive with $STLV\text{-}III_{AGM}$ antigens than with the analogous antigens of HTLV-III/LAV by RIP/SDS-PAGE. This reactivity was indistinguishable from that seen in monkeys infected with $STLV\text{-}III_{AGM}$. We subsequently

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isolated and characterized a new virus from these STLV-III antibody–positive individuals. This virus, although similar to HTLV-III/LAV and STLV-III$_{AGM}$ in T4 tropism, is not cytolytic to the target cells in culture and its major proteins are serologically indistinguishable from the major STLV-III$_{AGM}$ proteins.

We previously reported that a certain proportion of serum samples from individuals with antibodies to HTLV-III/LAV cross-reacted with STLV-III viral antigens (*3, 5*). We now further define this cross-reactivity by classifying serum samples on the basis of their antibody reactivity to HTLV-III/LAV and STLV-III$_{AGM}$ viral proteins. All the samples were analyzed by RIP/SDS-PAGE with the use of whole cell lysates prepared from: HTLV-III/LAV–infected Molt-3 cells, uninfected Molt-3 cells, STLV-III$_{AGM}$–infected Hut-78 cells, and uninfected Hut-78 cells. All were metabolically labeled with [^{35}S]cysteine as described (*3, 5*). The RIP/SDS-PAGE technique detects antibodies to the major *gag*-encoded antigens of HTLV-III/LAV, p55, p24, and p17 (*7, 12*), as well as the *env*-encoded gp120 and gp160 (*13*). These *env*-encoded proteins are the most immunogenic species recognized by serum of individuals who have been exposed to HTLV-III/LAV (*13*). Antibody reactivity to gp41, the transmembrane protein of HTLV-III/LAV (*14*), is best visualized by using lentil-lectin preparations of infected whole cell lysates and RIP-SDS/PAGE or by Western blot analysis (*13, 14*). Each serum sample was also analyzed for reactivity to the STLV-III$_{AGM}$ antigens by RIP/SDS-PAGE (*3, 5*). The major viral antigens of STLV-III$_{AGM}$ are the glycoproteins gp160/120 and gp32, and the nonglycosylated species p55, p24, and p15, the last three being the presumed *gag*-related antigens (*5, 15*). Monoclonal or polyclonal antibody to p24 of HTLV-III/LAV recognizes a slower migrating protein species that we have designated p24 of STLV-III$_{AGM}$ (*3, 5*).

Serum samples from HTLV-III/LAV antibody–positive individuals in the United States were selected on the basis of their strong antibody reactivity to all major *env*- and *gag*-encoded antigens of HTLV-III/LAV by RIP/SDS-PAGE. The individuals included patients with AIDS, AIDS-related complex (ARC), and healthy homosexuals. The selection of serum samples was made to enhance our ability to detect antibodies directed to conserved epitopes present on the major antigens of both viruses. To facilitate data presentation we arbitrarily divided all the sera into seven classes of reactivity to HTLV-III/LAV and STLV-III$_{AGM}$ antigens (Table 1). Of 23 U.S. HTLV-III/LAV positive serum samples, 12 (52 percent) showed no reactivity to any known STLV-III$_{AGM}$ antigens (Table 1 and Fig. 1), while 11 showed some cross-reactivity. Five (22 percent) of the samples cross-reacted with the gp160/120 of STLV-III$_{AGM}$, and six (26 percent) with p55 and p24 of STLV-III$_{AGM}$. The representative serologic profiles shown in Fig. 1 were selected on the basis of disease category and class of cross-reactivity.

Serum samples from wild-caught African Green monkeys were selected on the basis of their strong reactivity to all major STLV-III$_{AGM}$ viral proteins by RIP/SDS-PAGE. As with HTLV-III/LAV in humans, the gp120/160 of STLV-III$_{AGM}$ appear to be the most immunogenic proteins in monkeys (*5*). Serum samples from over 50 percent of STLV-III$_{AGM}$ antibody–positive monkeys react only with gp120/160. Of 12 STLV-III$_{AGM}$–positive serum samples, seven (58 percent) showed no reactivity with any HTLV-III/LAV viral antigens (Table 1), and three (25 percent) showed cross-reactivity with the HTLV-III/LAV *gag*-related antigens p55 and p24. The reactivities in classes 6 and 7 were defined by the additional antibody recognition of HTLV-III/LAV *env*-encoded gp160 or gp160 and gp120, respectively.

These results indicate that HTLV-III/LAV and STLV-III$_{AGM}$ share common epitopes in all the major viral antigens and that these are recognized bidirectionally across species lines with many serum samples. In addition, these serologic profiles seem to

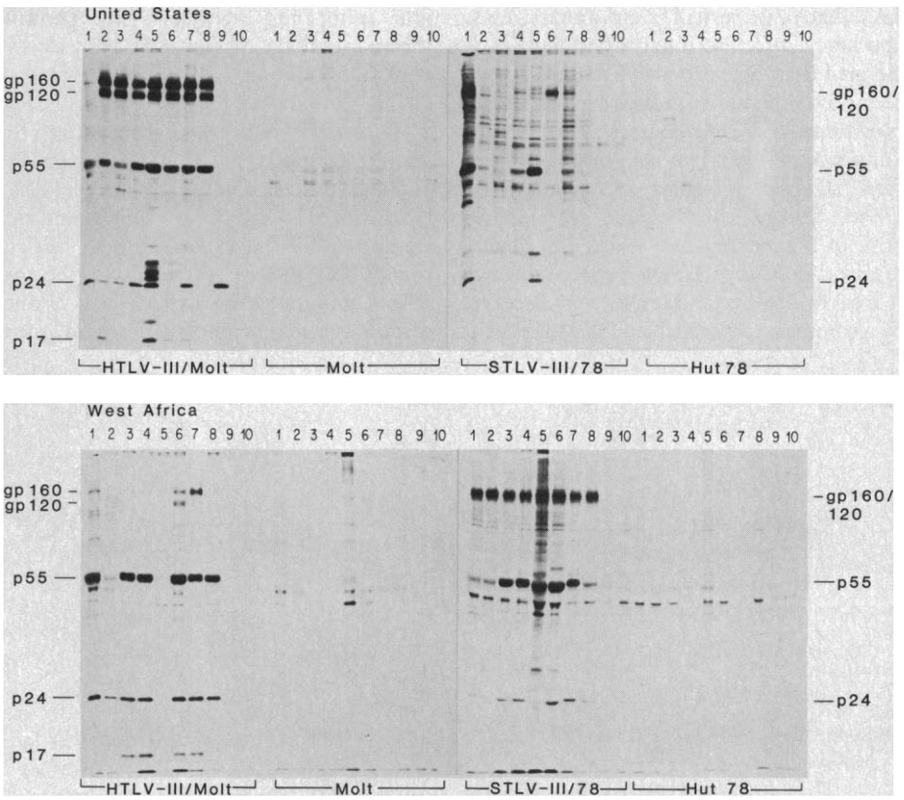

Fig. 1 (top). Cells from HTLV-III/LAV (BH10)–infected Molt-3 cells, uninfected Molt-3 cells, STLV-III$_{AGM}$–infected Hut-78 cells, and uninfected Hut-78 cells were harvested at their peak of log phase of growth and were exposed to [^{35}S]cysteine [150 Ci/ml; specific activity 1000 to 1050 Ci/mmol; New England Nuclear (NEN)] for 4 to 6 hours. A soluble cell lysate was prepared by disrupting cells with RIPA buffer (0.15*M* NaCl, 0.05*M* tris-HCl, *p*H 7.2, 1% sodium deoxycholate, and 0.1% SDS), and clearing by centrifugation for 1 hour at 100,000*g*. Each group of cell lysates was reacted with 10 μl of the following test sera bound to Protein A–Sepharose CL-4B (Protein A–beads, Sigma): lane 1, STLV-III$_{AGM}$ antibody–positive African Green monkey; lanes 2 to 5, U.S. AIDS patients; lanes 6 to 7, ARC patients; lane 8, HTLV-III/LAV antibody–positive healthy homosexual; lane 9, monoclonal antibody to p24 of HTLV-III/LAV; and lane 10, reference HTLV-III/LAV–negative control serum. Immunoprecipitates were eluted in a sample buffer containing 0.1*M* Cleland's reagent, 2% SDS, 0.08*M* tris-HCl, *p*H 6.8, 10% glycerol, and 0.2% bromophenol blue by boiling at 100°C for 2 minutes. Samples were analyzed in a 10.0% acrylamide resolving gel with 3.5% stacking gel according to the discontinuous buffer system of Laemmli (*24*). Fig. 2 (bottom). Serum samples from people in Senegal were analyzed by RIP/SDS-PAGE with the same whole cell lysates as described in Fig. 1. Lanes 1 and 2, STLV-III$_{AGM}$ antibody–positive African Green monkeys; lane 3, healthy Senegalese control with antibodies to STLV-III$_{AGM}$; lanes 4 to 8, sera from Senegalese prostitutes with reactivity to STLV-III$_{AGM}$; lane 9, STLV-III$_{AGM}$ and HTLV-III/LAV seronegative prostitute from Senegal; and lane 10, healthy Senegalese control seronegative for STLV-III$_{AGM}$ and HTLV-III/LAV.

distinguish between infections by these closely related viruses. A serologic profile of class 1, 2, or 3 suggests exposure to HTLV-III/LAV, with antibodies to STLV-III_{AGM} antigens, when present, being cross-reactive antibodies to the shared epitopes of STLV-III_{AGM} antigens. None of the U.S. HTLV-III/LAV antibody–positive serum samples showed the reactivities of classes 4 to 7. The antibody profiles of classes 4 to 7 were more consistent with those of STLV-III_{AGM}–infected monkeys, where a proportion of serum samples from these animals would be capable of cross-reacting with HTLV-III/LAV antigens. In RIP/SDS-PAGE analysis of over 100 STLV-III_{AGM} antibody–positive serum samples from African Green monkeys, we have found no serologic profiles of classes 1, 2, or 3 (*16*).

In some regions of Africa, HTLV-III/LAV, like other sexually transmitted agents, appears to infect both males and females at elevated rates. The prevalence of such agents seems to be higher in groups such as female prostitutes and their contacts (*10*). Serum samples were obtained from healthy prostitutes at routine medical examinations in Dakar, Senegal. At the time of sampling none of the individuals showed any clinical manifestations of AIDS or a related disease. A total of 289 serum samples was screened by a commercially available HTLV-III/LAV ELISA kit assay, and 20 samples were found to be antibody-positive (*15*). These 20 samples were examined for antibodies to HTLV-III/LAV and STLV-III_{AGM} by RIP/SDS-PAGE and 15 of them showed antibodies to one or both viruses. The remaining five samples were judged to be false positives by ELISA. All of the 15 serum samples reacted strongly with all the STLV-III_{AGM} antigens. Two of these 15 (13 percent) samples showed no detectable antibodies to any major HTLV-III/LAV antigens (Fig. 2); four (27 percent) showed antibodies only to p24 and p55 *gag*-related antigens of HTLV-III/LAV (Fig. 2). Class 6 seroreactivity was demonstrated in six (40 percent) prostitute serum samples, where antibodies were directed to all major STLV-III_{AGM} viral antigens and gp160 and *gag*-encoded antigens of HTLV-III/LAV. The four remaining samples (27 percent) showed serologic profiles defined by class 7, with antibodies to all major antigens of STLV-III_{AGM} and HTLV-III/LAV (Fig. 2). These samples were characterized by strong reactivity to STLV-III_{AGM} gp120/160 and relatively faint reactivity to HTLV-III/LAV gp120 and gp160. This diminished reactivity with the HTLV-III/LAV *env*-encoded gp120 and gp160 relative to the *gag*-related antigen seroreactivity was distinct from any serologic profile observed previously in our laboratory, where we have analyzed more than 800 serum samples for antibodies to HTLV-III/LAV. This qualitative difference in reactivity was confirmed by the lack of detectable antibodies to gp41 when the sera were analyzed by Western blot (*15*). However, all 15 samples reacted strongly with all major STLV-III_{AGM} viral antigens, including the gp120/160, p55, and p24, and these bands were not precipitated from lysates similarly prepared from the uninfected Hut-78 cell line (Fig. 2). Representative serum samples demonstrating each category of seroreactivity (classes 4 to 7) are shown in Fig. 2 together with control serum samples from STLV-III_{AGM} antibody positive African green monkeys (lanes 1 and 2).

We also screened serum samples from a group of 122 inpatients hospitalized for surgery in Dakar, Senegal, using the HTLV-III/LAV ELISA (*15*). One serum sample from a surgery patient reacted with the HTLV-III/LAV antigens p55, p24, and p17 when analyzed by RIP/SDS-PAGE. This same sample, when reacted with STLV-III_{AGM} antigens, reacted strongly with all the simian viral antigens, and thus had a serologic profile similar to the profiles of healthy prostitutes from this same geographic locale that were categorized as class 5. A similar pattern of serologic reactivity

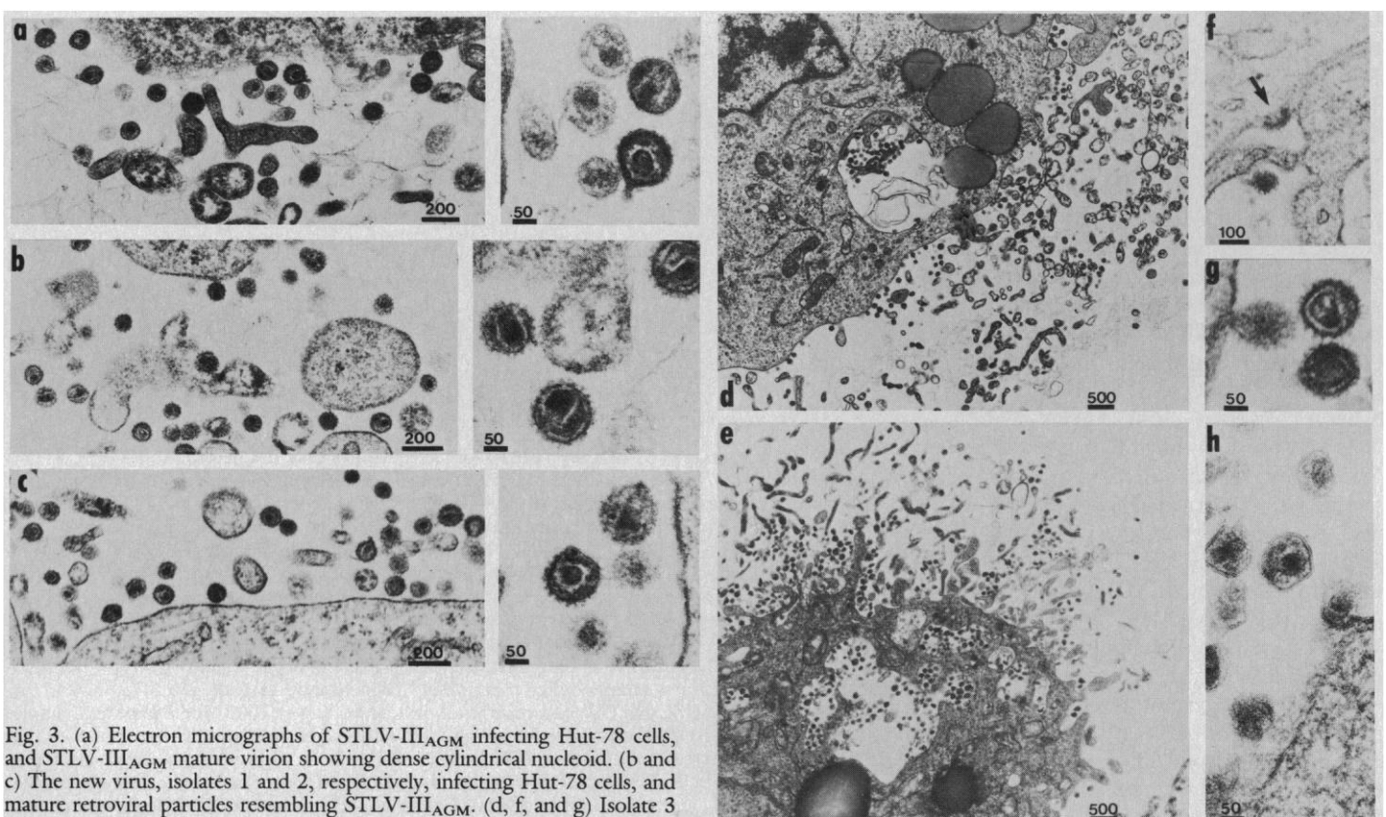

Fig. 3. (a) Electron micrographs of STLV-III_{AGM} infecting Hut-78 cells, and STLV-III_{AGM} mature virion showing dense cylindrical nucleoid. (b and c) The new virus, isolates 1 and 2, respectively, infecting Hut-78 cells, and mature retroviral particles resembling STLV-III_{AGM}. (d, f, and g) Isolate 3 infecting Hut-78 cells showing an abundance of retrovirus particles, budding particle, and extracellular virions approximately 120 nm in diameter. (e and h) Electron micrographs of HTLV-III/LAV (BH-10) infecting H9 cells, and extracellular mature virions. All bars show nanometers. Electron microscopy performed with a GEOL 1200 EX microscope.

Table 1. Serologic profiles of human and monkey sera assayed on HTLV-III/LAV and STLV-III$_{AGM}$ proteins. Seven classes of seroreactivity to HTLV-III/LAV and STLV-III$_{AGM}$ were designated on the basis of RIP/SDS-PAGE. Human serum samples from the United States and Senegal as well as African Green monkey sera were evaluated by RIP/SDS-PAGE for antibodies directed to both viruses. Representative serum samples from each category of seroreactivity are illustrated in Figs. 1 and 2, in the lanes indicated.

Class	Antibodies to		Serum donors			Figure references
			Human		African Green monkey	
	HTLV-III/LAV	STLV-III$_{AGM}$	United States	West Africa		
1	p24, p55, gp160, gp120	Negative	12/23	0	0	(Fig. 1, lanes 3, 8)
2	p24, p55, gp160, gp120	gp120/gp160	5/23	0	0	(Fig. 1, lane 6)
3	p24, p55, gp160, gp120	p55, p24	6/23	0	0	(Fig. 1, lane 5)
4	Negative	p24, p55, gp120/gp160	0	2/16	7/12	(Fig. 2, lane 5)
5	p24, p55	p24, p55, gp120/gp160	0	4/16*	3/12	(Fig. 2, lanes 1–4, 8)
6	p24, p55, gp160	p24, p55, gp120/gp160	0	6/16	1/12	(Fig. 2, lanes 7)
7	p24, p55, gp160, gp120	p24, p55, gp120/gp160	0	4/16	1/12	(Fig. 2, lanes 6)

*Includes one serum sample from a surgical patient.

was also observed in one individual from Dakar sampled in 1976 (*17*).

All of the serologic profiles of these individuals from West Africa were categorized into classes 4, 5, 6, or 7. These human sera thus react with STLV-III$_{AGM}$ antigens in a manner similar to that observed with STLV-III$_{AGM}$–infected monkeys. There are at least two possible interpretations of these data. For example, these sera might show an unusual reactivity with the conserved epitopes of HTLV-III/LAV and STLV-III$_{AGM}$ as a result of exposure to prototype HTLV-III/LAV, or the virus infecting these West Africans might be more closely related to STLV-III$_{AGM}$. To address this question, we isolated and characterized virus from healthy, antibody positive individuals in Senegal.

Peripheral blood lymphocytes were obtained from eight STLV-III$_{AGM}$ antibody–positive people and were cocultivated with Hut-78 cells, a well-defined human mature T-cell line (*18*). The procedure for virus isolation was the same as that described for STLV-III$_{AGM}$ (*5*). Remarkably, the cytolysis of target cells in vitro was not observed. Such cytolysis had occurred with other isolates from four macaques and seven African Green monkeys and was generally observed with isolates of HTLV-III/LAV (*3–6*). Because of this lack of cytolysis, Hut-78 cells were added only once to each culture, at day 5. At days 21 to 28, cellular atypia and multinucleated giant cells were evident. Beginning at day 14 after initiation, all cell cultures were monitored for viral protein expression by membrane immunofluorescence (MIF) and RIP/SDS-PAGE with the use of a battery of reference sera with known antibody reactivity to STLV-III$_{AGM}$, HTLV-III/LAV, and HTLV-I viral proteins. At days 28 to 35, viral proteins related to STLV-III$_{AGM}$ were detected in three cultures by both MIF and RIP/SDS-PAGE. The remaining five cultures that were weakly positive or negative for viral proteins at day 35 were not further characterized.

Cell-free supernatants from the three cultures were monitored for Mg^{2+}-dependent reverse transcriptase as described (*6*). High reverse transcriptase levels (3,500 to 93,000 cpm) over background (76 to 860 cpm) were observed in the three cell cultures expressing STLV-III$_{AGM}$ proteins and not in cultures that were negative for viral proteins.

Cell cultures expressing antigens cross-reactive with STLV-III$_{AGM}$ were examined by electron microscopy. For this purpose, 5×10^6 cells were fixed in 4 percent paraformaldehyde and 1 percent glutaraldehyde in a phosphate buffer. Particles characteristic of a retrovirus were observed budding from infected cell membranes (Fig. 3f). Extracellular virions had an electron-dense cylindrical core (Fig. 3, b, c, g) similar to that described for both simian and human T-lymphotropic viruses (Fig. 3, a, e, h). The ultrastructural morphology of the retroviral particles in all three cultures derived from STLV-III$_{AGM}$ antibody–positive people in Senegal was similar to that of a reference STLV-III$_{AGM}$ cell line derived from an African Green monkey. It is notable that the spike proteins of STLV-III$_{AGM}$ type virions of both monkey and human origin were more prominent than those usually observed with HTLV-III/LAV virions. The level of virus production in cultures from STLV-III$_{AGM}$ antibody–positive individuals (Fig. 3d) was similar to that observed with HTLV-III/LAV–infected H9 cells (Fig. 3e), based on both visual examination and reverse transcriptase activity.

Virus isolation was also attempted on peripheral blood lymphocytes from seven STLV-III$_{AGM}$ antibody–negative prostitutes, surgery patients, and cancer patients from Senegal. These cultures did not produce detectable virus by the methods described above.

The three cell cultures derived by cocultivation of lymphocytes from three STLV-III$_{AGM}$ antibody–positive prostitutes from Senegal were analyzed for viral protein expression and compared to STLV-III$_{AGM}$ by RIP/SDS-PAGE and Western blot analysis. Each culture was metabolically labeled with [^{35}S]cysteine and whole cell lysates were prepared as described (*3, 5*). Lysates from Hut-78 reference cells persistently infected with STLV-III$_{AGM}$ (Fig. 4, lane S) and uninfected Hut-78 cells (Fig. 4, lanes C) were similarly prepared and subjected to RIP/SDS-PAGE.

As shown in Fig. 4, serum from a negative control individual who lacked antibodies to both STLV-III$_{AGM}$ and HTLV-III/LAV did not recognize any specific proteins in any of the five lysates. Conversely, lysates from cultures 1, 2, and 3 showed bands of about 120, 160, 55, and 24 kD when reacted with sera of the individuals from which they were derived, or serum from a reference STLV-III$_{AGM}$ antibody–positive African Green monkey (Fig. 4, lanes 1, 2, and 3). These bands were indistinguishable from proteins with similar electrophoretic mobility precipitated from reference STLV-III$_{AGM}$ whole cell lysate (Fig. 4, lane S), but they were not detectable when the same sera were reacted with uninfected Hut-78 cell lysates or similarly prepared whole cell lysates from cultures derived from antibody negative people from Senegal. Serum from a reference U.S. AIDS patient recognized the 55- and 24-kD proteins of STLV-III$_{AGM}$ and reacted similarly with the same proteins in cultures 1 to 3; only faint reactivity to gp120/160 was observed.

The viral antigens of STLV-III$_{AGM}$ recognized by the Western blot procedure are similar to those described by RIP/SDS-PAGE. The smearing band at 32 kD found with the Western blot technique (*15*) correlates with a similar 32-kD glycoprotein observed with lentil-lectin preparations and

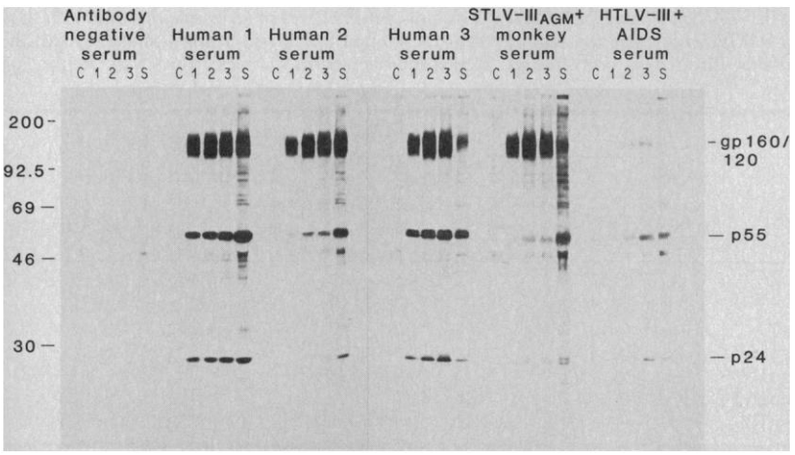

Fig. 4 (left). Whole cell lysates from cultures of the three isolates (lanes 1 to 3), STLV-III$_{AGM}$ reference infected Hut-78 cells (lanes S), and uninfected Hut-78 cells (lanes C) were prepared as described above and analyzed by RIP/SDS-PAGE. Each group of cell lysates was reacted with the following test sera: serum sample from prostitute in Senegal who was virus- and antibody-negative for STLV-III$_{AGM}$ and HTLV-III/LAV; STLV-III$_{AGM}$ antibody–positive sera from the individuals who yielded virus isolates 1, 2, and 3; reference STLV-III$_{AGM}$ antibody–positive serum from an African Green monkey; and reference HTLV-III/LAV antibody–positive serum from a U.S. AIDS patient.

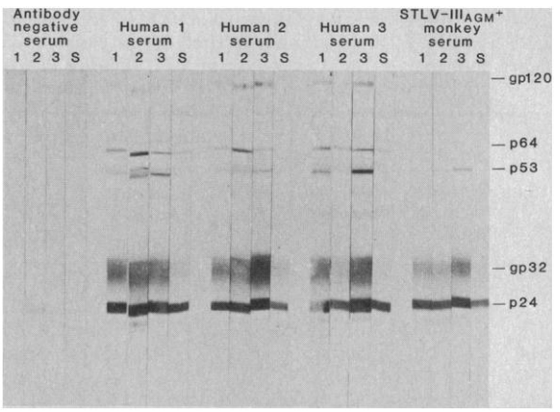

Fig. 5 (right). Western blot analysis of cell cultures with the three virus isolates (lanes 1 to 3), and an STLV-III$_{AGM}$ reference infected cell line (lanes S). Each group of strips was reacted with: Serum sample from a prostitute in Senegal who was virus- and antibody-negative for STLV-III$_{AGM}$ and HTLV-III/LAV; STLV-III$_{AGM}$ antibody–positive sera from the individuals who yielded virus isolates 1, 2, and 3; and reference STLV-III$_{AGM}$ antibody–positive serum from an African Green monkey.

RIP/SDS-PAGE (*16*). It has been speculated that gp32 may represent the transmembrane glycoprotein of STLV-III$_{AGM}$, by analogy with gp41 of HTLV-III/LAV. The p53 and p64 of STLV-III$_{AGM}$ are analogous to the p53 and p64 *pol* gene products of HTLV-III/LAV (*19*).

Cell-free virus from cultures 1 to 3, as well as STLV-III$_{AGM}$ from a reference cell line, was collected from supernatant fluid and subjected to Western blotting as described (*15*). Strips were incubated with the same serum samples as described (Fig. 5). STLV-III$_{AGM}$–positive reference serum from an African Green monkey showed reactivity with the gp32, p24, p53, and p64 of STLV-III$_{AGM}$ as well as similar bands with the three virus preparations from the prostitutes (Fig. 5). Similar proteins were recognized with serum samples from the individuals who had yielded STLV-III$_{AGM}$–related viruses with some variability in recognition of the gp120. Control antibody negative serum did not detect these bands in the three human or STLV-III$_{AGM}$ virus preparations.

The heterogeneity of different HTLV-III/LAV isolates has been reported earlier on the basis of both restriction fragment analysis and primary nucleotide sequence data (*20*). The most divergent portion of the HTLV-III/LAV genome appears to lie within the exterior glycoprotein portion of the *env* gene (*20*). We therefore propose that variant strains of HTLV-III/LAV should be detectable with the use of serum from STLV-III$_{AGM}$–infected monkeys, since it has been demonstrated that this virus is related to the human virus by major antigen cross-reactivity, bidirectionally across species lines (*3, 5, 15*).

It appears that serum from HTLV-III/LAV antibody–positive individuals in the United States with AIDS or ARC or in a high-risk category for AIDS can recognize STLV-III$_{AGM}$ antigens in approximately 50 percent of the cases studied. The serologic studies of the healthy Senegalese prostitutes and controls described here revealed an unusual antibody profile that had not been described previously in humans. By both Western blot analysis and RIP/SDS-PAGE these sera showed reactivity to *gag*-related antigens of HTLV-III/LAV with minimal or no reactivity to the *env*-encoded antigens (*15*). They also showed reactivity with all of the major antigens of STLV-III$_{AGM}$. Their reactivity with HTLV-III/LAV antigens may therefore result from cross-reactive antibodies directed to the conserved epitopes in the two viruses. We postulated that a virus infecting apparently healthy people in West Africa would be closely related to STLV-III$_{AGM}$, with more epitopes shared with the simian virus than with the representative U.S. strain of HTLV-III/LAV. Our present knowledge of the biology and epidemiology of this family of viruses indicates that such variant strains may not be unique to Senegal. In fact, our data suggest that earlier reports of antibody reactivity directed only to the p24 *gag* protein in various human populations could reflect exposure to such variant strains (*11*).

Data from a retrospective study suggest that this new virus, which for now we will refer to as HTLV-IV, was present in Dakar, Senegal, in the mid-70's (*17*). Thus, the evidence to date indicates that HTLV-IV may have been present in at least a small proportion of people in West Africa for over a decade in the absence of AIDS or a related disorder. To our knowledge, AIDS has not been observed in Dakar, Senegal. All of the individuals in the present study with evidence of exposure to HTLV-IV were subjected to a physical examination and were apparently healthy at the time of sampling. This is in sharp contrast to the seroepidemiologic data from other parts of the world, where evidence of exposure to HTLV-III/LAV is closely linked with the development of AIDS and related clinical syndromes.

Present data on the biology of STLV-III$_{AGM}$ in the African Green monkey indicate that virus-positive, antibody-positive infected monkeys are healthy (*5, 16*); this is in sharp contrast to the biology of STLV-III$_{mac}$ in the macaque host where this virus appears to be closely associated with an immunodeficiency syndrome resembling human AIDS (*3, 4, 16, 21*). We therefore speculate that there are a number of related T-lymphotropic viruses that differ in their pathogenicity to their respective hosts.

The occurrence of common epitopes in all the major viral antigens of STLV-III$_{AGM}$ and HTLV-III/LAV, including those of the *env* region, suggests that despite the genetic variation in this region, conserved sequences between these viruses may be identified, expressed, and evaluated as potential vaccines. STLV-III$_{AGM}$ of primates and HTLV-IV are similar to HTLV-III/LAV in their propensity for growth in T4 lymphocyte populations, and recent evidence indicates that the mature envelope protein of

HTLV-III/LAV directly interacts with the T4 molecule on the target cell (*22*). This also suggests that conserved epitopes of the *env* proteins of these viruses may be critical to virus infection and thus appropriate candidates for vaccine development.

The occurrence of an STLV-III$_{AGM}$–related virus in healthy Senegalese may provide clues as to how this family of viruses has evolved. It is well recognized that HTLV-III/LAV shares some sequence homology with various ungulate retroviruses, most notably visna (*23*). However, the degree of homology in genes other than *pol* is negligible, suggesting a more ancestral relationship. The similarities and cross-reactivity of STLV-III$_{AGM}$ with the *env*, *gag*, *pol*, and *3'orf* products of HTLV-III/LAV indicate that these are more closely related members of the family of T-lymphotropic viruses. STLV-III$_{AGM}$ naturally infects only a limited number of primate species, unlike STLV-I, suggesting that STLV-III$_{AGM}$ may have arisen in more recent times. It is therefore conceivable that STLV-III$_{AGM}$ or HTLV-IV may have served as the progenitor virus to the human AIDS virus, HTLV-III/LAV; alternatively they may have had a common progenitor. Continued study of the origin of this group of viruses may provide a better understanding of how they acquired their pathogenicity and how we can effectively interfere with HTLV-III/LAV infection.

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El Niño: A Chaotic Dynamical System?

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Most of the principal qualitative features of the El Niño–Southern Oscillation phenomenon can be explained by a simple but physically motivated theory. These features are the occurrence of sea-surface warmings in the eastern equatorial Pacific and the associated trade wind reversal; the aperiodicity of these events; the preferred onset time with respect to the seasonal cycle; and the much weaker events in the Atlantic and Indian oceans. The theory, in its simplest form, is a conceptual model for the interaction of just three variables, namely near-surface temperatures in the east and west equatorial ocean and a wind-driven current advecting the temperature field. For a large range of parameters, the model is naturally chaotic and aperiodically produces El Niño–like events. For a smaller basin, representing a smaller ocean, the events are proportionally less intense.

EL NIÑO MAY BE DEFINED AS THE appearance of anomalously warm water in the eastern equatorial Pacific. Associated with this is a weakening, and sometimes a reversal, of the trade wind field (Fig. 1). Major El Niño–Southern Oscillation events occurred in 1957, 1965, 1972, and 1982, and their occurrence for the past 100 years can be inferred from proxy data (*1*). The various events differ in detail and intensity but appear to have broadly similar overall features (*2–4*). Although occurring aperiodically, the events also appear to be at least partially phase-locked to the seasonal cycle. As well as engendering much purely scientific interest, El Niño has major economic consequences and possibly global climatic effects (*5*). Much observational and modeling effort has therefore been devoted to it, with various degrees of success (*6–12*).

In this report I show that all the broad qualitative features may be explained with a simple but realistic model. Other models for El Niño exist, varying in complexity from relatively elaborate coupled ocean-atmosphere models (*10*) to relatively simple stochastic dynamic or probabilistic models (*12*). To forecast El Niño, a coupled general circulation model is probably needed. However, to understand the phenomenon a simpler theory is needed. The theory, or model, presented here differs from others in that no stochastic or seasonally varying forcing is required to produce the aperiodicity, no explicit wave dynamics are required to explain the time scales, and no mid-latitude influences are needed to explain variations in intensity. Instead, these phenomena arise naturally and deterministically within a simple framework. It has been conjectured (*6, 10, 13*) that El Niños may be generated internally, but no mechanism for the complete cycle of events has been isolated.

Imagine an equatorial ocean to be a box of fluid characterized by temperatures in the east and west (T_e and T_w) and a current u (Fig. 2). The current is driven by a surface wind, which is in part generated by the temperature gradient $(T_e - T_w)/\Delta x$, so describing a parameterized Walker circulation (*14*). A cooler temperature in the east ($T_e < T_w$) produces a westward surface

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