

Letters to the Editor

Presence of SIV Antibodies in the Sera of Infants Born to SIV-Seronegative Monkeys

To the Editor: Several studies have been conducted on the transmission of retrovirus infections from infected mothers to infants (1-3). Previously, serologic techniques were used to demonstrate the transmission of infection by the detection of specific antibodies against HIV, HTLV-1, etc., but the passive transfer of maternal antibodies in the infant sera posed problems in the analysis of the data. More recently, however, the highly sensitive polymerase chain reaction (PCR) has been adopted to demonstrate more accurately the presence of retrovirus infection in infants born to HIV- and HTLV-1-infected mothers (4,5).

Our laboratory has conducted studies on blood samples from a human population in Atlanta, Georgia, at high risk for HIV-1 infection and from the sooty mangabey (*Cercocebus atys*) monkey colony at the Yerkes Regional Primate Research Center of Emory University, a large number (>75%) of which are naturally infected with a simian immunodeficiency virus (SIV/smm). Peripheral blood mononuclear cells (PBMC) from 30 of the 165 HIV-1-seronegative high-risk humans (6) and from 16 SIV-seronegative monkeys, when cultured in vitro with pokeweed mitogen (PWM), secreted antibod-

ies against HIV-1 and SIV/smm, respectively (unpublished observation). In addition, of the samples that were positive by the PWM assay, PBMC from at least 12 of the 26 HIV-1-seronegative humans and from all 16 mangabeys (unpublished observation) were found to be infected with HIV-1 and SIV/smm, respectively, using PCR techniques.

Of interest is our observation of three infant monkeys (ages 26, 19, and 9 months), seropositive for SIV/smm, that were born to two SIV-seronegative mothers (Table 1). Previous serum samples from the two mothers were retrieved from the frozen inventory and analyzed repeatedly in parallel with current serum samples and with serum samples from the infants and appropriate negative and positive controls, using ELISA and Western blot. Results demonstrated that none of the sera samples from the two mothers contained detectable levels of SIV-reactive antibodies as far back as 3 years. However, serial sera from all three infants contained high levels of SIV-reactive antibodies and demonstrated multiple (*gag*, *pol*, *env*) SIV-specific bands by Western blot analysis. PBMC from the two mothers and infants were (a) cultured in vitro with PWM with and without depletion of CD8⁺ cells prior to culture; (b) co-cultured with human PHA-P blasts, and supernatant fluids were analyzed for reverse transcriptase (RT) activity; and (c) ana-

TABLE 1. Results of sera and in vitro cultures samples from two SIV-seronegative female monkeys with seropositive infants

Blood samples	Date of birth	Date of first SIV-seropositive sample	ELISA Ab titer ^a	Supernatant fluid from PWM cultures ^b (OD 405 nm)	PCR results ^c	RT activity by the co-culture assay ^d
Mother 1 (FHe)	7/82	— ^e	>1:10	0.28 ± 0.03	+	18,711
Infant 1.1 (FYh)	8/86	11/88	1:8000	0.97 ± 0.03	+	35,253
Infant 1.2 (FVj)	6/88	3/89	1:2000	0.68 ± 0.05	+	22,498
Mother 2 (FOe)	1/83	— ^e	>1:10	0.22 ± 0.01	+	15,966
Infant 2.1 (FRi)	7/88	3/90	1:4000	0.89 ± 0.04	+	24,595
Negative control ^f	—	—	>1:10	0.01 ± 0.01	—	452
Positive control ^f	—	—	1:4000	0.76 ± 0.05	+	31,211

Ab, antibody; PWM, pokeweed mitogen; PCR, polymerase chain reaction; RT, reverse transcriptase; OD, optical density; PBMC, peripheral blood mononuclear cells.

^a Reciprocal of the highest dilution with an OD (405 nm) value 2 SD above background control. All samples were tested 3/90.

^b Supernatant fluid of PBMC cultured with pokeweed mitogen for 4 days and tested undiluted by the ELISA assay for anti-SIV antibody.

^c PCR analysis performed using two sets of *gag* region primer pairs.

^d PBMC from each animal co-cultured with human PHA-P blasts and supernatant fluid analyzed for RT activity.

^e All serum samples up to 3 years prior to 3/90 were negative by serology.

^f Negative and positive controls consisted of sera and PBMC from an uninfected rhesus macaque and a macaque experimentally infected with SIV/smm-9.

lyzed for the presence of SIV-specific sequences using two sets of *gag*-specific primer pairs. Data obtained demonstrate that in spite of being serologically negative, both the mothers were in fact infected with SIV/smm.

The sexual route has previously been considered to be the principal mode of transmitting retrovirus infections in these monkeys, based on the coincidence of the rate of seroconversion with the onset of sexual maturity. The infants might get scratches and be bitten by other monkeys, but this is a highly unlikely route of infection, since most infants remain seronegative. The data resulting from our studies not only demonstrate the possible transmission of retrovirus infections from seronegative but infected monkeys to offspring but, more important, also provide evidence that SIV is not transmitted only by the sexual route in these nonhuman primate species. These data should prompt caution concerning the use of serology as the sole criterion for the evaluation of HIV-1 infection, at least in mothers at high risk for HIV-1 infection.

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Increased Plasma Prostacyclin in AIDS

To the Editor: Prostanoids, including prostacyclin (PGI₂), through their ability to increase the intracellular cyclic AMP level, have been shown to have a significant role in immune suppression (1-3). On the other hand, thromboxane A₂ (TXA₂) is reported to augment cell-mediated immunity (1). We determined the plasma PGI₂ and TXA₂ levels in 15 AIDS patients (all males; between the ages of 24 and 69 years, median age of 44 years; 12 patients had Kaposi's sarcoma), and in 15 age- and sex-matched normal controls. At the time of the study, none of the patients was taking any medication. Both PGI₂ and TXA₂ are unstable compounds. PGI₂ is readily hydrolyzed to 6-ketoprostaglandin F_{1α} and TXA₂ is rapidly converted to thromboxane B₂ (4,5). In our study, PGI₂ and TXA₂ were determined in their 6-ketoprostaglandin F_{1α} and thromboxane B₂ forms, respectively, by radioimmunoassay (4,5). It was found that the plasma PGI₂ level in the AIDS patients was significantly increased ($p < 0.0001$, $n = 15$) when compared to that of the normal controls (Table 1). In contrast, the plasma TXA₂ level in these patients (7.60 ± 2.22 pM) remained similar to that of the normal controls (6.21 ± 1.22 pM; $p > 0.5$; $n = 15$). The increased plasma PGI₂ level was not, however, related to the stage of the disease (6), or to the age of the patients. Although the majority of the patients had Kaposi's sarcoma, the increase in plasma PGI₂ level in these patients was similar to that of the other patients without Kaposi's sarcoma. As such, these results do not indicate that the increase in plasma PGI₂ level was due to the occurrence of Kaposi's sarcoma in AIDS patients.

We do not know the mechanism of the specific increase in plasma PGI₂ level over the TXA₂ level in these AIDS patients. However, since endothelial cells are the major source of PGI₂, and TXA₂ is primarily produced by the activation of platelets (4,5), it is possible that the increased plasma PGI₂ level in AIDS patients was the consequence of the interaction of HIV with endothelial cells.

Since AIDS is due to HIV-induced immunosuppression, and prostaglandins are known to impair immune response, it is possible that the elevated level of