CHARACTERIZATION OF AFRICAN HUMAN RETROVIRUSES RELATED TO HTLV-III/LAV

ANNUAL/FINAL REPORT

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# Characterization of African Human Retroviruses Related to HTLV-III/LAV

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24

Our data on the biology of HIV-2 suggest that this virus may have a distinct biology from that of its close relative HIV-1. It is therefore relevant to assess these differences in populations infected with significant rates of both HIV-2 and HIV-1. Senegal is such a West African country, and the studies established there have provided important new information on the natural history and epidemiology of HIV-2. The prolonged incubation period for HIVs in general suggests that much can be learned from the evaluation of infected individuals over time. This would include: 1) the dynamics and risk factors and transmission, 2) the immune response parameters evaluated over the course of infection and their correlation with viral burden and clinical course and 3) evolution of HIV pathogenesis. Our studies conducted to date, have already indicated differences in the above virus-host interactions between HIV-2 and HIV-1. Continued comparative studies contribute to our overall understanding of HIV pathogenesis.
FOREWORD

In conducting the research described in this report, the investigator(s) adhered to the "Guide for the Care and Use of Laboratory Animals of the Institute of Laboratory Animal Resources, National Research Council (DEHW Publication No. (NIH) 86-23, Revised 1985).

For the protection of human subjects the investigator(s) have adhered to policies of applicable Federal Law 45CFR46.
Epidemiology and Natural History of HIV-2

In Senegal in 1966, prostitution was legalized in conjunction with a nationally supported program for Sexually Transmitted Disease (STD) prevention. This meant that women could practice prostitution and remain within the law, if they registered at the Institut Hygiene Sociale, an STD outpatient clinic, and were periodically checked for various STDs every 3-6 months. At each visit, the women's carnet (registration book) would be stamped and would therefore "legalize" her for the practice of prostitution, provided the carnet was kept up-to-date. STD centers have been established in Dakar (1970), Kaolack (1978), and Ziguinchor (1978), as well as other major cities in Senegal.

All women attending these clinics in Dakar, Ziguinchor, and Kaolack have been asked to enroll in the study, they have been screened for seropositivity to HIV-1 and HIV-2 beginning in 1985, 1986, and 1987 respectively. The STD centers provide clinical examinations which are required by the government every 3-6 months for legal registration of prostitutes. Blood specimens routinely collected from these women as part of participation in the clinic were also used for HIV serostudies yielding essentially 100% compliance for the screening. Because women return regularly to the clinic to maintain registration and to receive health care, condoms and medications at no cost, they are available for follow-up to determine seroconversion. Additionally, a questionnaire is administered to all women enabling us to study risk factors for seropositivity and for seroconversion. The yearly blood samples allow for evaluation of seroconversion in women regularly attending the clinic.
We have followed several groups of registered female prostitutes in Dakar (n>1500), Ziguinchor (n>200), and Kaolack (n>200), Senegal to better understand the epidemiology of HIV-2 in a high risk populations. All women registered at the various STD centers have been surveyed, with the Dakar study beginning in 1985, Ziguinchor in 1986 and Kaolack in 1987. Counselling and condom distribution began in late 1986 and data regarding behavior modification and potential efficacy of intervention has been obtained subsequently.

Our data has shown wide variation of HIV-2 infection even within a similar risk group category of the same country. The seroprevalence for HIV-2 has varied widely between six different registered prostitute populations in various urban centers (n=1920) throughout Senegal: Ziguinchor (46.2%), Kaolack (28.8%), Louga (21.4%), Dakar (9.8%), Thies (4.6%) and St. Louis (1.5%). We are hopeful that detailed analysis of questionnarie data from these women will help explain why these differences are so marked.

A brief summary of characteristics of the female prostitutes from our cohorts in Dakar, Kaolack and Ziguinchor are provided on Appendix 1. The Ziguinchor study began in 1986, where initial serosurveys indicated close to 40% infection with HIV-2; similarly, the Kaolack cohort of women were sampled in 1987 with a prevalence of 27% HIV-2. The cohorts have a distinct nationality distribution, primarily due to their geographic locations within the country, Ziguinchor being approximately 30 kilometers from the Guinea Bissau border. A significant proportion of the registered prostitutes in this area originate from Guinea Bissau (41%), where HIV-2 rates are reported to be much higher than Senegal. It is therefore not surprising that being of Guinea Bissau origin was highly
associated with HIV-2 seropositivity \( (p < 0.001) \). The Kaolack cohort of women is almost exclusively Senegalese. Risk factor data from the questionnaires provided at all three sites are shown in Appendix tables 2-4.

The data from the Dakar prostitute cohort has been evaluated more extensively than the other cohorts and thus will be presented here. In the current proposal we will be analyzing data from the other two cohorts (Ziguinchor and Kaolack) both separately and together to evaluate common trends in HIV-2 epidemiology and those which may be study site-specific. To date, the overall seroprevalence in 1500 registered Dakar prostitutes has been 9.8% HIV-2, 1.8% HIV-1 and 0.4% HIV-1/2. Serodiagnosis is made by immunoblot analysis on both HIV-1 and HIV-2. Samples that demonstrate envelope antibody reactivity to both viruses are confirmed with radioimmunoprecipitation SDS/PAGE. Dually reactive samples are further studied by virus isolation, polymerase chain amplification (PCR) and antibodies to vpu and vpx.

The majority of women were native Senegalese (73%), with 21% from Ghana and 6% other nationalities. The mean age was 34 yrs, range 21-68, and the mean years of prostitution 6.7 yrs, range 1-19. HIV-2 positive prostitutes were more likely to be older than the mean age of 34 years \( (OR=2.58) \) and to be non-Senegalese \( (OR=1.79) \). The number of years of prostitution was not significantly related to serostatus. Inclusion of these three variables in a multivariate logistic model did not modify these results.

The age-specific prevalence for HIV-2, HIV-1 and HTLV, indicates a dramatic age-specific increase for HIV-2. In contrast, HIV-1 demonstrated peak age-specific prevalence in the 20-30 year old range which is similar to what has
been described in Central African studies of HIV-1. The age-specific prevalence for HIV-2 in Dakar indicates that this cohort has been exposed to the virus for at least 30 years. HTLV antibodies have been assessed by immunoblot showing an overall seroprevalence of 4.3% and also an increase in HTLV with increasing age. In other words, both HTLV and HIV-2 demonstrate age-specific prevalence curves indicative of longer term infection in this population than that of HIV-1. This counters the argument that the lack of AIDS with HIV-2 is due to a recent and rapid introduction of the virus to these West African populations.

The questionnaire administered to each women is aimed at obtaining demographic data, sexual behavior information, antecedent medical problems, and other potential risk factors that may predispose to retrovirus infection. Thus far, history of transfusion, hospitalization, multiple injections, circumcision, tattooing and scarification have not been found to be significant risk factors for HIV-2 infection in this cohort. In addition, there was no difference between positives and negatives with respect to the number of children or mortality in infants or children. Plummer et al. have reported that genital ulcer disease is a significant risk factor for HIV-1 in East Africa. Previous episodes of genital ulcer disease and cervicitis were evaluated in 174 women in our cohort. 37% of the HIV-2 seropositives (n=46) had previous episodes of genital ulcer disease as compared to 31% of the seronegatives (n=128), similarly there was no significant difference in history of cervicitis by serostatus. This indicates again a marked difference between risk factors important for HIV-2 and HIV-1 infection.

The direct measurement of HIV-2 incidence is necessary for the critical understanding of the dynamics of HIV-2 infection at a population level. The
Dakar registered prostitute cohort has now been followed since 1985. Through evaluation of sequential samples from this high risk group we determined HIV-2 incidence. Sequential samples from women were evaluated over the 5 year-period (1953 person-years observation). Seroconversion to HIV-2 was found in 17 women with a mean time of 17 months of observation prior to seroconversion. HIV-2 seroconverters were significantly older than 927 non-seroconverters (p<.025). Nationality or years of prostitution were not significant risk factors for seroconversion. None of the seroconverters have developed AIDS or related signs to date. The annual incidence rate for HIV-2 was found to be 8.7 per 1000 per year in this large high risk population.

Seroconversion for HIV-2 appears quite low despite close to 10% prevalence in this high risk population. The annual incidence was found to be similar over the five-year period of observation. Assuming this rate to remain constant, one would predict that the prevalence for HIV-2 in this cohort would double in 8-10 years. Seroconversion for HIV-1 was 4.0 per 1000 per year in the cohort which represents over one-third of the prevalence or crude cumulative incidence (1.8%). Again, assuming stability of this rate, one would predict that the prevalence for HIV-1 could double in 3 years. This suggests that in this cohort, HIV-1 is spreading more rapidly than HIV-2. Larger numbers and more detailed analysis are required to confirm this preliminary finding. The published data for HIV-1, however, is supportive. Plummer et. al have reported 71% seroconversion over 54 months (157 per 1000 per year) for HIV-1 in a cohort of Nairobi prostitutes. Estimates of HIV-1 incidence among homosexual men from 1985-87 in various urban centers in the US ranged from 9-45 per 1000 per year. The continued study of the Dakar cohort will provide a unique opportunity for direct comparison of the two viruses. The preliminary data, however, is
suggestive of a slower spread of HIV-2 in this high-risk cohort compared to HIV-1.

Since the discovery of HIV-2 we have been involved in a clinical prospective study in Senegal. The follow-up of large numbers of HIV-2 seropositive individuals in a prospective manner has not been duplicated in any other study to our knowledge, and provides a unique opportunity to evaluate the full natural history of HIV-2 infection. We are hopeful that this study will help establish a temporal relationship between HIV-2 exposure and AIDS or other significant pathologies. Due to the inclusion of HIV-1 seropositive individuals we will be able to readily compare the natural history of HIV-2 with that of HIV-1 as well.

The female prostitute cohorts in Dakar, Ziguinchor and Kaolack, Senegal provide the mechanism for identifying study subjects. All seropositive individuals for either HIV-2+, HIV-1+, or HIV-2/1+ have been evaluated for enrollment in this clinical sub-cohort study. At the time of enrollment of the seropositive, two matched seronegatives have also been enrolled. Matching criteria, including age, nationality and years of prostitution, not only allow for controlled comparisons between seropositives and seronegatives but also help equilibrate compliance in the follow-up period. After a baseline epidemiologic and medical questionnaire, these women have been followed semi-annually with an extensive follow-up questionnaire and clinical evaluation. Sexually transmitted disease (STD) diagnostics which are part of the routine clinical exam are also performed, as well as periodic evaluations of immune status. These include delayed-type hypersensitivity skin testing and complete blood counts with T-cell subset typing.
In the Dakar clinical sub-cohort study, with only passive or voluntary follow-up, we have seen greater than 90% compliance in both seropositives and their matched seronegatives.

<table>
<thead>
<tr>
<th>HIV-2+</th>
<th>HIV-1+</th>
<th>HIV-1/2+</th>
<th>HIVnegative</th>
</tr>
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<tbody>
<tr>
<td>N=88</td>
<td>N=18</td>
<td>N=3</td>
<td>N=207</td>
</tr>
<tr>
<td>Person-Years Observed (PYO)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PYO=237</td>
<td>PYO=42</td>
<td>PYO=6</td>
<td>PYO=623</td>
</tr>
</tbody>
</table>

By defining "lost to follow-up" as those prostitutes not seen in the past 12 months or those without travel history of leaving the country with a healthy status, we have been able to account for 90% of those prostitutes initially enrolled in our clinical cohort. From over 237 person-years of observation (p.y.o.) for the 88 HIV-2 seropositives enrolled, we have seen no cases of frank AIDS or ARC in either the seropositives or seronegatives. In general, episodes of other health problems have been equivalent for both seropositives and seronegatives. Of note, one HIV-2 seropositive prostitute has had a clinical diagnosis of tuberculosis and is presently doing well. One seronegative prostitute fits the criteria for generalized lymphadenopathy, without an etiologic diagnosis and one seronegative prostitute has died of an acute diarrheal disease.

As part of the clinical sub-cohort prospective study of HIV-2 infected prostitutes, HIV-2 seropositive, HIV-1 seropositive and stratified HIV seronegative prostitutes were evaluated by certain clinical and immunologic parameters used
to assess integrity of the immune system. These evaluations began in 1988 and are conducted yearly. Immunologic parameters including complete blood counts (Coulter Counter), T-cell subset determinations (Simultest, Becton-Dickinson), and delayed type hypersensitivity (DTH) tuberculin skin testing performed in Dakar. The T-cell subset immunofluorescence assay is routinely evaluated independently, for inter-run variation, which has not been statistically significant.

**RESULTS**

<table>
<thead>
<tr>
<th></th>
<th>HIV-2+</th>
<th>HIV-1+</th>
<th>Negative</th>
</tr>
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<tbody>
<tr>
<td>Number tested</td>
<td>66</td>
<td>10</td>
<td>166</td>
</tr>
<tr>
<td>WBC</td>
<td>$6415 \pm 1539$</td>
<td>$6190 \pm 1654$</td>
<td>$6820 \pm 1629$</td>
</tr>
<tr>
<td>Total lymphs</td>
<td>$2765 \pm 973$</td>
<td>$2441 \pm 1001$</td>
<td>$3144 \pm 869$</td>
</tr>
<tr>
<td>Absol. T4 lymphs</td>
<td>$1257 \pm 521$</td>
<td>$896 \pm 486$</td>
<td>$1712 \pm 525$</td>
</tr>
<tr>
<td>Absol T8 lymphs</td>
<td>$1108 \pm 506$</td>
<td>$1545 \pm 884$</td>
<td>$1027 \pm 393$</td>
</tr>
<tr>
<td>Anergy to PPD</td>
<td>9/31 (29.0%)</td>
<td>6/8 (75%)</td>
<td>21/113 (18.6%)</td>
</tr>
</tbody>
</table>

Comparing HIV-2 and HIV-1 seropositive vs. seronegative women, a trend toward lower T4 counts were noted in both HIV-1 and HIV-2 seropositive women as compared to seronegatives, but this difference was more dramatic in the HIV-1 seropositive (for HIV-2, $p=.01$; for HIV-1, $p=.0001$). On repeat T-cell subset determinations, no significant decreases in T4 counts were noted in HIV-2 positives as compared to negatives.

The presence of cutaneous anergy has been assessed by purified protein derivate (ppd) skin testing on a voluntary basis. The voluntary nature of the testing is to maximize follow-up, since many of the prostitutes object to this procedure. The use of ppd testing was utilized after the first year of the clinical cohort study when CMI-multitest skin testing with 7 different antigens (Merieux)
showed that greater than 90% of the prostitutes were reacting to ppd antigen, probably due to the near uniform immunization with BCG in this region. Initial cutaneous anergy results to ppd testing are shown in the Table above. There was no significant difference in cutaneous anergy between HIV-2 seropositive and seronegatives, but HIV-1 seropositive women were much more likely to be anergic as compared to matched seronegatives (p=.001).

Therefore, our results suggest that individuals with HIV-2 infection may show some of the humoral and cellular immune alterations seen in HIV-1 infection. These alterations have not correlated to date with significant disease development in the population under study. Our results suggest that immunologic abnormalities such as decreased T4-lymphocytes and anergy may not be as dramatic in HIV-2 infection as seen with HIV-1 infection. Our studies to date have shown distinct differences in the natural history and pathogenic potential for HIV-2 as compared to HIV-1. These differences are further illustrated by predictions generated from natural history studies of HIV-1 asymptomatic seropositive individuals followed for 2 years (200 p.y.o.) in Kinshasa, Zaire. In this HIV-1 cohort, 16% developed ARC and 15% developed or died of AIDS by the end of 2 years. This degree of disease development is markedly different from the results from our HIV-2 clinical cohort in Dakar, where there has been no AIDS or ARC to date. Thus, in contrasting HIV-2 and HIV-1, we have been able to show a distinct difference in the attack rate to AIDS or ARC, namely, that HIV-2 demonstrates a significantly decreased rate of disease induction. The continued follow-up of this cohort is essential to validate this observation and assess the actual latency period of this virus. In addition, we are hopeful that this study will allow for description of early or perhaps unexpected clinical signs of HIV-2 infection.
Inter-run variation and inter-technique variation in our CBC and T-cell subset determinations will continue to be evaluated. In addition, all the seronegatives' T cell values will be plotted against calendar time, to detect any shift in values over time that would indicate a systematic bias.

**Characterization of the Immune response and Viral Carriage of HIV-2.**

We have performed immunoblot for HIV-1 and HIV-2 on over 17,000 serum samples from West Africa. From this large serum bank, we have over 600 HIV-2+ samples available and have tested a panel of 380 HIV-2 positives with 380 HIV negatives matched by nationality, age, and health status on 2 different HIV-2 isolates and SIV. The immunoblot patterns were nondistinquishing, indicating virtual antigenic identity between the viral antigen preparations. Reactivity to at least one protein from each of the 3 structural genes (gag, pol, env) was demonstrated in 98% of the samples, with 2% of the samples only recognizing the env products. We have tested this panel of sera on 3 different commercial HIV-1 ELISAs and found 80% detection by virtue of cross-reactive antibodies with all 3 kits. Reactivity to recombinant-expressed vpx proteins has been evaluated in 1:1 HIV-2+ samples from Dakar with 12% reactivity, in contrast HIV-2+ samples from Guinea Bissau showed 4% reactivity (n=106).

We currently have 6 HIV-2 isolates from West Africa which have been compared to 2 reference HIV-2 isolates from NIH and Sweden. Antigenic characterization has shown polymorphism in env proteins, and variation in expression of vpx and nef. Genetic studies has demonstrated marked genetic variability by restriction enzyme analysis and these isolates have been used to standardize
our PCR primers and probes. Reactivity of DNA prepared from these established HIV-2 infected cell lines has demonstrated the specificity of our HIV-2 primers and these have been tested for sensitivity with dilution series experiments.

We have conducted PCR experiments to assess the specificity of the HIV-2 and HIV-1 primers and probes. Each reagent set tested reacted with the appropriate virus (either HIV-1 or HIV-2) only, when tested with HIV-1 or HIV-2 infected cell lines. Furthermore, the HIV-2 specific reagents amplified seven out of seven HIV-2 isolates tested. These isolates were obtained from a broad range of geographic locations, and from individuals of varying health status. Verification of the PCR-amplified product was performed by ethidium bromide staining, liquid hybridization and southern blot analysis. Negative controls were performed in all experiments. Seropositive DNA was always co-isolated with seronegative DNA, to confirm that samples were not contaminated during the isolation. The PCR experiments described include serial dilutions of viral infected DNA as a positive control, and to determine the sensitivity of a specific reaction. Furthermore, all PCR experiments included at least two negative controls, one where no template DNA was put into the initial reaction to test for contamination of reaction components, and one which included the viral negative cell line DNA used as a background for the dilution series.

We recognize the shortcomings of determining sensitivity by using serial dilutions of virus infected tissue culture in non-infected DNA, these studies are in progress currently. However, if one assumes that there are less than 30 proviral copies per cell (a reasonable assumption), than we would be detecting less than 10 molecules of HIV DNA in a background of 2 micrograms of HIV
negative genomic DNA. The exact proviral load in various HIV infected cell lines is not known and this has been a technique used by others for rough estimation of sensitivity.

The sensitivity was not perfect in our assays, when using DNA derived from peripheral blood cells of HIV-2 infected people and the sample size was small. Two of the 9 people tested were dual-reactive for HIV-1 and HIV-2 by antibody studies and were PCR negative -- perhaps these people harbor an unusual virus rather than harboring both HIV-1 and HIV-2, which could explain the fact that they were PCR negative. Fourteen of twenty people (70%) who were seropositive for HIV-2 only were also PCR positive, fifteen of fifteen seronegative individuals were PCR negative.

These results are comparable to those published by others when using PCR to screen healthy risk populations for HIV-1. For example, Ehrlich et al. found 19/65 (29%) HIV-1 EIA positive individuals to be PCR negative. (Ehrlich et al., Blood 74, 1658-64 (1989)). While other groups are reporting a better correlation between seropositives and PCR positives (90-95%), frequently these studies are done on people who are symptomatic AIDS patients. In HIV-1 infection, the virus is probably present at significantly lower levels in healthy people, and therefore harder to detect with PCR. There is little published data on the use of PCR to detect sequences in HIV-2 infected people. Given the recognized differences between HIV-2 and HIV-1 from a variety of perspectives, it is perhaps premature to judge HIV-2 PCR data from HIV-1 PCR data. Finally, studies with HTLV-2 have shown that using greater amount of input DNA can enhance a PCR signal (using 6-12 ug. rather than 2 ug. (Korber, unpublished)).
Further studies can be done to determine if this will increase our sensitivity with the HIV-2 seropositive samples.

Our collaborators in Tours, France have developed synthetic peptides corresponding to a specific immunodominant domain of the carboxyl-terminus of HIV-2 and SIV\textsubscript{mac} gp120. As seen on Appendix table 5, we have been able to demonstrate a geographic difference among serum samples collected from different West African countries and their reactivity to SIV and HIV-2 synthetic peptides (SIV SP34 and HIV-2 SP33). By also comparing African green monkey (AGM) sera, we hypothesize that individuals from Senegal were reacting as if they had been exposed to a "variant" that more closely resembled the HIV-2\textsubscript{rod}, prototype and that individuals from Ivory Coast were reacting more closely to what would be expected with SIV. With these synthetic peptides, it might be possible to use this "site-directed" serology to determine subtypes among the various immunodeficiency viruses and thereby be able to create "serotypes." These serotypes would then identify groups of individuals infected with a certain strain of HIV-2. The clinical or immunologic correlates of groups of people with a particular serotype could then be determined to see if varying pathogenic potentials could be delineated.

**Interactions of HIV-1 and HIV-2**

Superinfection studies of HIV-1 into HIV-2 infected cells has shown that superinfection can occur with co-expression of both viruses. Of interest however, is that the apparent cytolytic effect of acute HIV-1 infection appeared to be diminished with low concentration of virus and totally abrogated at high concentration of virus. Our interpretation of these preliminary results includes the possibility that prior HIV-2 infection of CD4+ cells may provide some
protective effect to the acute cytolytic properties of HIV-1 virus although virus-attachment interference did not appear to occur. It is also possible that a small number of cells in our persistantly HIV-2 infected culture were expressing CD4 and were therefore available for HIV-1 infection. This appears unlikely since virtually all the cells were positive for HIV-2 antigens and CD4 was not detectable. Furthermore, since the RIP-SDS/PAGE assay requires a significant proportion of the cells to be expressing specific viral antigens (>40%), the expression of HIV-1 proteins by day 7 post-infection is highly suggestive of superinfection.

We have demonstrated that chimpanzee lymphocytes can be infected in vitro with HIV-2. 8 different HIV-2 isolates were evaluated and the virus with highest infectivity was used for the inoculum. This was the criteria for choice of the HIV-2 isolate for inoculation. A weak-titered antibody response was seen in both chimpanzees by 1.5 months post-inoculation. However, during this time period, we were unable to isolate virus. PCR evaluation has also shown HIV-2 positive sequences in both chimpanzees at 1 and 2 months post-inoculation, respectively. At 10 months post-inoculation it appeared that antibody titer was falling and both animals were re-inoculated with a similarly prepared inoculum. Again, only a transient antibody response could be demonstrated and virus was not re-isolated. After multiple antibody, PCR and virus isolation attempts the study was discontinued. Despite in vitro evidence of the susceptibility of the chimpanzee for HIV-2 infection, we were unable to establish a persistant viral infection in this primate species.
<table>
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<tr>
<th>Total Cohort</th>
<th>Dakar (n=1463)</th>
<th>Ziguinchor (n=250)</th>
<th>Kaolack (n=214)</th>
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<tr>
<td><strong>HIV Distribution</strong></td>
<td></td>
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<tr>
<td>138 (9.4%)</td>
<td>1286 (84.5%)</td>
<td>31 (2.1%)</td>
<td>8 (0.5%)</td>
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<td><strong>Senegalese</strong></td>
<td><strong>Ghanian</strong></td>
<td><strong>Other</strong></td>
<td><strong>Senegalese</strong></td>
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<td>(n=1051)</td>
<td>(n=313)</td>
<td>(n=90)</td>
<td>(n=143)</td>
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<td>Serosatus by HIV-2</td>
<td>8.7%</td>
<td>11.5%</td>
<td>8.9%</td>
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<tr>
<td>Nationality HIV-1</td>
<td>1.1%</td>
<td>5.1%</td>
<td>3.3%</td>
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<td>-1986-</td>
<td>-1987-</td>
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<tr>
<td><strong>Sub-cohort</strong></td>
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<td>Ziguinchor (n=166)</td>
<td>Kaolack (n=136)</td>
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<td><strong>HIV-1+</strong></td>
<td><strong>HIV-2+</strong></td>
<td><strong>HIV-1+</strong></td>
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<td>Enrolled Clinical Study</td>
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<tr>
<td>Person-Years of Observation (PYO)</td>
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<td>30</td>
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<td>Average PYO</td>
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<td>2.8 yr.</td>
<td>1.9 yr.</td>
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<td>-1987 to present-</td>
<td>-1988 to present-</td>
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<tr>
<td>DAMD Start Date:</td>
<td>-1988-</td>
<td>-1988-</td>
<td>-1990 proposed-</td>
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## DAKAR COHORT

### Appendix 2

<table>
<thead>
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<th></th>
<th>Total</th>
<th>Senegalese</th>
<th>Guinea</th>
<th>Other</th>
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<td></td>
<td>(1031)</td>
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<tr>
<td></td>
<td>HIV</td>
<td>HIV2</td>
<td>HIV1</td>
<td>HIV D</td>
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<tr>
<td></td>
<td>(884)</td>
<td>(107)</td>
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<td>(6)</td>
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<td>(715)</td>
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<td>32</td>
</tr>
<tr>
<td>Years of Prostitution</td>
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<td>5.7</td>
<td>6</td>
</tr>
<tr>
<td>Mean</td>
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<td>4.2</td>
</tr>
<tr>
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**Origin of Sera**

- \(\text{Reactivity to SIV SP34}\)
- \(\text{Reactivity to both SIV SP34 and HIV SP33}\)
- \(\text{Reactivity to HIV2 SP33}\)
PUBLICATIONS under DAMD 17-87-C-7072 contract (9/16/90)


REVIEWS AND BOOK CHAPTERS


