Using CD4 Counts to Evaluate the Stages and Epidemiology of HIV Infection in South Carolina Public Clinic Patients

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A B S T R A C T

Objectives. CD4 lymphocyte counts decrease with the duration of human immunodeficiency virus (HIV) infection. We used CD4 counts collected for clinical reasons to evaluate the stage of HIV infection and the epidemiology of recent HIV infections among attendees of South Carolina's public health clinics.

Methods. We measured the CD4 T-lymphocyte counts of persons newly diagnosed with HIV infection April 1989 through June 1990 at South Carolina public health clinics who returned for follow-up.

Results. Of 812 newly diagnosed HIV-infected health department patients, 420 (52%) had their CD4 lymphocyte counts measured. Of these 420, 51 (12%) had CD4 counts of <200, the level below which prophylaxis for pneumocystis pneumonia prolongs survival, and 193 (46%) had CD4 counts of <500, the level below which zidovudine may prolong disease-free survival. The highest CD4 counts (≥900), which are associated with more recent HIV infection, were more common in females.

Conclusions. In South Carolina, almost half of newly reported HIV-infected persons who agreed to CD4 testing at the health department might benefit from immediate drug therapy. Within this population, women may be an emerging risk group that requires specifically directed HIV prevention efforts. (*Am J Public Health.* 1994;84:377–381)

Introduction

Several cohort studies demonstrated that CD4 lymphocyte counts decrease with the duration of human immunodeficiency virus (HIV) infection.[1–7] This decrease tends to be linear[8] and predicts opportunistic infection and progression to the acquired immunodeficiency syndrome (AIDS).[2–9] Thus, measuring the CD4 lymphocyte count of HIV-infected persons helps characterize the HIV/AIDS epidemic by staging HIV infection in a population. Indeed, CD4 counts could supplement HIV surveillance by characterizing groups with advanced HIV disease in need of drug therapy as well as identifying those persons most recently infected to evaluate changing demographics and risk groups for HIV transmission.

However, previous studies of CD4 counts in HIV-infected persons have been from restricted populations, including cohorts of homosexual men,[1,3,6,10,11] hemophiliacs,[2,12] attendees at two sexually transmitted disease clinics,[13] and members of the US Army,[14] which is 91% male and attempts to exclude persons who are homosexual, intravenous drug users, or HIV infected.

In March 1989, the South Carolina Department of Health and Environmental Control began offering CD4 lymphocyte testing free of charge at 81 clinics statewide to all HIV-infected persons reported to the health department. South Carolina law requires that all physicians, hospitals, and laboratories licensed by the state report persons with HIV infection to the Department of Health and Environmental Control.

Clinic nurses use these CD4 counts to identify persons who are late in the course of their HIV disease and therefore need immediate medical services. Persons with CD4 counts of <500 who are indigent qualify for Medicaid and are eligible to receive zidovudine through the federal drug reimbursement program. Persons with CD4 counts of <200 receive urgent medical referral to receive zidovudine and prophylaxis against *Pneumocystis carinii* pneumonia.

For this study, we retrospectively reviewed the CD4 lymphocyte counts of newly identified HIV-infected persons in the first 15 months of the South Carolina CD4 testing program. Our objectives were to determine the percentage and characteristics of HIV-infected persons who might benefit from drug therapy and to characterize the population of most recently infected persons.

Methods

Patients

We selected patients newly reported to the state's HIV registry April 1989 through June 1990 whose CD4 T-lymphocyte count was measured in the 90 days after their first positive HIV serology test. Hence, CD4 tests were

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Note. Inclusion of trade names is for identification only and does not imply endorsement by the Department of Health and Human Services or the US Public Health Service.

TABLE 1—Rates of CD4 Testing of HIV-Infected State Clinic Patients, South Carolina, April 1989 through September 1990

	Total	No. (%) CD4 Tested	Relative Rate	95% CI	P
Sex					
Female	223	126 (57)	1.1	1.0, 1.3	.11
Male	589	294 (50)			
Location					
Rural	490	259 (53)	1.1	0.9, 1.2	.47
Urban	322	161 (50)			
Race[a]					
White	186	121 (65)	1.4	1.2, 1.6	<.001
Black	618	296 (48)			
HIV risk factor					
None reported	61	18 (30)	0.6	0.4, 0.8	<.001
Heterosexual contact	412	216 (52)			
Male-to-male sex	245	141 (58)			
Intravenous drugs	85	41 (48)	χ^2 association; $P = .50$		
Transfusion	7	3 (43)			
Hemophilia	2	1 (50)			

[a]Eight persons who reported their race as Hispanic are not included in the racial breakdown.

performed April 1989 through September 1990. A 90-day time frame was chosen to permit timely analysis of the data. We excluded HIV-infected children younger than 13 years old because their absolute CD4 counts are not directly comparable with adult CD4 counts.[15,16]

Specimen Handling

Nurses in the health department clinics collected blood samples from consenting HIV-infected patients. For patients originally identified in these health department clinics, CD4 lymphocyte counts were measured at the first posttest counseling session: that is, when the patient first learned of his or her HIV infection. All blood samples were analyzed by flow cytometry within 20 hours of being drawn with a Coulter Epics–Profile II flow cytometer (Coulter Corporation, Hialeah, Fl). Personnel in the South Carolina Department of Health and Environmental Control Bureau of Laboratories entered the absolute CD4 lymphocyte count (the product of the total lymphocyte count and the percentage of CD4+ lymphocytes) with the patient's name onto the state's mainframe computer, and the result was sent back to the originating clinic.

Data Analysis

The CD4 tests were matched by name, date of birth, county, and race with the Department of Health and Environmental Control surveillance registry of HIV-infected persons by one person working within the HIV/AIDS surveillance section of the department. For analysis we compiled a linked CD4 count/HIV registry microcomputer file with all personal identifiers removed.

We classified persons with absolute CD4 counts of ≥900 as recently infected and persons with CD4 counts of <200 as having advanced HIV infection. We chose a count of 900 as a threshold for defining recent infection because previous researchers found 918 to be the average count for six uninfected control persons who were repeatedly tested.[17] A larger study has since found an average CD4 count of 890 among 63 repeatedly tested HIV-negative control subjects.[18] We chose CD4 counts of <200 to indicate advanced infection because at this level persons have markedly increased risk of opportunistic infection.[9]

We initially evaluated age groups at the standard intervals used for the surveillance of HIV/AIDS—that is, ages 5–12 years, 13–19 years, and at 5-year intervals thereafter.[19] Because children under age 13 years were not analyzed, persons aged 13–19 comprised the youngest group analyzed. Because only 5% of the study population was in this youngest age group, we expanded the youngest category to include persons 20–24 years old to permit a more thorough statistical evaluation of age.

We calculated relative risks (RRs) and confidence intervals (CIs) by the method of Greenland and Robins using Epi Info software.[20] We used StatXact[21] software to perform significance testing of dichotomous outcomes by Fisher's exact chi-square association. Using Kwikstat software,[22] we compared mean ages across two groups by Student's *t* test and assessed the association between age and CD4 cell count using Pearson's correlation.

Results

Of the 1510 newly diagnosed HIV-infected persons more than 12 years old reported to the South Carolina Department of Health and Environmental Control April 1989 through June 1990, 812 (54%) were initially diagnosed as HIV infected at state clinics and 698 (46%) were reported from outside the state clinic system. Persons identified outside the state clinic system were significantly less likely to participate in the CD4 lymphocyte testing program compared with state clinic–identified patients (20% vs 52%; RR = 0.39, 95% CI = 0.33, 0.46) and were 1.9 times more likely to have CD4 counts of <200 (23% vs 12%; RR = 1.9, 95% CI = 1.3, 2.9). Because persons diagnosed outside the clinic system were less completely represented in the database and because those non–public clinic patients who were tested appeared to overrepresent a selected group of persons with more advanced disease, we limited subsequent analysis to the 812 state clinic–identified patients.

Of these 812 newly reported HIV-infected patients, 420 (52%) had their CD4 lymphocyte counts measured at a state clinic within 90 days of their first positive HIV serology test. The mean age of clinic patients whose CD4 counts were measured was 30.7 years, which was similar to the mean of 30.2 years among HIV-infected clinic patients whose CD4 counts were not measured. Gender and urban or rural residence were not significantly associated with undergoing CD4 testing (Table 1). Whites were 1.4 times more likely than Blacks to participate in the lymphocyte testing program. Persons who reported no HIV risk factors were significantly less likely to undergo follow-up CD4 testing. No defined risk group for acquiring HIV infection was significantly more or less likely to be CD4 tested.

Within the study population of 420 newly diagnosed HIV-infected persons

TABLE 2—Distribution of CD4 Counts of HIV-Infected State Clinic Patients, South Carolina, April 1989 through September 1990

	Total	No. (%) with CD4 of <200	No. (%) with CD4 of >199 and <500	No. (%) with CD4 of >499 and <900	No. (%) with CD4 of ≥900	P (χ^2)
All patients	420	51 (12)	142 (34)	158 (37)	68 (16)	
Age, y						
>24	322	50 (16)	109 (34)	109 (34)	54 (17)	<.01
≤24	98	1 (1)	33 (34)	49 (50)	15 (15)	
Sex						
Female	126	10 (8)	34 (27)	53 (42)	29 (23)	.014
Male	294	41 (14)	108 (37)	105 (36)	40 (14)	
Race[a]						
Black	299	38 (13)	99 (33)	112 (37)	50 (17)	.871
White	119	12 (10)	43 (36)	45 (38)	19 (16)	
Location						
Rural	259	35 (14)	78 (30)	105 (41)	41 (16)	.145
Urban	161	16 (10)	64 (40)	53 (33)	28 (17)	
HIV risk factor						
None reported	18	5 (28)	4 (22)	4 (22)	5 (28)	
Heterosexual contact	216	24 (31)	73 (34)	83 (38)	36 (17)	
Male-to-male sex	141	16 (11)	52 (37)	55 (39)	18 (13)	
Intravenous drugs	41	6 (15)	11 (27)	15 (37)	9 (22)	.520
Transfusion	3	0 (0)	1 (33)	1 (33)	1 (33)	
Hemophilia	1	0 (0)	1 (0)	0 (0)	0 (0)	

[a]Two Hispanic persons are not included in the racial breakdown. Totals for racial groups differ slightly from those reported in Table 1 because five persons were recorded as a different race when they were HIV tested than they were during subsequent CD4 testing.

from state clinics, 51 (12%) had what we defined as advanced HIV disease (CD4 counts of <200). One hundred ninety-three persons (46%) had CD4 counts of <500. At the other end of the CD4 spectrum, 69 persons (16%) had CD4 counts of ≥900. The mean CD4 count for the population was 588 with a standard deviation of 347.

The distribution of CD4 counts by age, sex, race, location, and HIV risk factor is shown in Table 2. Females were 1.7 times more likely than males to have CD4 counts of ≥900 (95% CI = 1.1, 2.6). No significantly increased risks for recent infection were associated with age, race, urban versus rural residence, or risk group for acquiring HIV infection.

Reported risk factors for acquiring HIV infection for the 29 females who had CD4 counts of ≥900 are listed in Table 3. Among these 29 women, 21 (72%) reported heterosexual contact as their primary risk behavior for acquiring HIV infection. The proportional distribution of reported risk factors is not significantly different between females with CD4 counts of ≥900 and those with CD4 counts of <900.

At the other extreme of CD4 counts, persons more than 24 years old had a 15.2 times greater prevalence of advanced HIV disease than persons 24 years of age or younger (95% CI = 2.1, 108.7). Males were 1.8 times more likely than females to have advanced infection (95% CI = 0.9, 3.4). Persons who did not report an HIV risk factor were 2.4 times more likely to have CD4 counts of <200, but there were no other significant differences by HIV risk group, race, or urban versus rural location. There was no statistically significant Pearson correlation between age and CD4 count ($R^2 = 0.004, P = .18$).

TABLE 3—HIV Risk Factors for Females Whose CD4 Counts Were Tested, South Carolina, April 1989 through September 1990

HIV Risk Factor	Total	No. (%) with CD4 of ≥900
Heterosexual contact		
HIV-positive partner	31	7 (23)
Partner with HIV risk factors	14	4 (29)
Partner without known HIV risk factors	60	10 (17)
Intravenous drug use	13	5 (38)
No reported risk factor	8	3 (38)
Total	126	29

Note. χ^2 association; $P = .31$ for all factors.

Reanalysis of potential risk factors for recent HIV infection with absolute CD4 counts of 800 or 1000 as a cutoff for recent infection or 30 years as a cutoff for age did not substantially change the results.

Discussion

This study of CD4 lymphocyte counts among HIV-infected persons newly diagnosed in public health clinics in South Carolina found that 46% of tested persons had CD4 counts of <500,

the level below which zidovudine may improve disease-free survival.[23–25] This percentage corresponds with (1) the US Army estimate that 58% of their HIV-infected persons have CD4 counts of <500[14] and (2) the 50% of persons with newly diagnosed HIV infections in a Baltimore sexually transmitted disease clinic who had CD4 counts of <500.[13] Although none of these figures is generalizable to the HIV-infected US population, the figures provide evidence across different cohorts that a substantial proportion of HIV-infected persons have far enough advanced HIV disease to potentially benefit from pharmacologic therapy.

Although the majority of persons with HIV infection (even recent HIV infection) were male, a disproportionate number of more recent HIV infections occurred in females. This finding is consistent with other current data. The Centers for Disease Control reports that newly diagnosed cases of AIDS in females increased by 29% from 1988 to 1989 compared with an 18% increase for males.[26] St. Louis and colleagues recently reported US Job Corps data that noted a higher HIV seroprevalence among 16- and 17-year-old females than among males, which the authors suggest may reflect a recent increase in HIV infection in young women nationally.[27]

There are limitations to these results. First, CD4 lymphocyte counts are an imperfect measurement of the duration of HIV infection. There is considerable variability in the normal level of CD4 counts in uninfected persons[17,28] and in the rate of decline of CD4 counts among HIV-infected persons.[2,4] If different groups have different normal values or different rates of decline of CD4 counts, that could distort our extrapolation of the duration of infection from CD4 counts.

However, the limited data that are available suggest that CD4 counts in persons without HIV infection do not differ by gender or ethnicity,[18] and the only data on the effect of age on CD4 counts that we are aware of concern differences in young children, who were excluded from this evaluation. Indeed, if rates of decline of CD4 counts differed among different groups, the duration of infection would be extrapolated most accurately early in the course of the illness before differential rates of decline produced increasingly larger differences (CD4 count decline is linear in individuals with HIV infection[8]). Thus, our data on recently infected persons would be less susceptible to this potential distortion.

A second concern is that the apparent increased prevalence of recent infections in females could reflect their earlier use of health care. More recent infection among females would then reflect earlier diagnosis rather than a trend in disease transmission. However, we have no evidence that females were seeking health care earlier than males. Because the data abstraction methods used did not recover the type of program that a person was tested under, we cannot determine whether recently infected females were disproportionately identified through, for example, prenatal screening efforts, which are not equally accessed by men. We do know, however, that once identified, HIV-infected females were not significantly more likely than males to return within 90 days for follow-up CD4 testing. Continued surveillance of CD4 counts among HIV-infected persons will answer this question. If higher CD4 counts reflect increased rates of new infection among females, then the differences in CD4 counts between the sexes will narrow as the relative numbers of infected females and males stabilize.

A third study limitation is that the study population is not representative of the entire HIV-infected population in South Carolina and so the results may not be generalizable. It included only persons who attended public health clinics and so likely underrepresents higher socioeconomic groups. Further, Blacks and persons who reported no risk factor for HIV transmission were less likely to have follow-up CD4 testing, which could permit an unmeasured selection bias that might affect our findings. Nevertheless, this study population is more diverse than previously reported study populations and so offers the opportunity for a more complete comparison of CD4 counts across age, sex, and HIV risk groups than was previously available.

In conclusion, CD4 counts reflect the duration of HIV infection and so can enhance the characterization of HIV disease in a population. In South Carolina, among HIV-infected persons newly reported to the health department who agreed to CD4 lymphocyte testing, 46% might benefit from immediate drug therapy. Within this study population females may represent an emerging risk group that requires specifically directed HIV prevention efforts. □

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