

Oral Lesions in Primary/Acute and Recent/Early HIV Infection

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BACKGROUND

- Oral lesions are increasingly common as HIV disease progresses.^{1-5, 8-11}
Are they also common during the acute HIV syndrome?
- Oral lesions (especially, oral candidiasis and hairy leukoplakia) decrease in prevalence with the use of antiretroviral therapies.¹²⁻¹⁴
Is this also true of the oral manifestations in primary/early HIV infection?

OBJECTIVES

- To determine the type and prevalence of oral lesions during acute/primary and recent/early HIV disease.
- To examine the association between oral lesion diagnoses and use of antiretroviral therapy for the treatment of primary/early HIV infection.

METHODS

- Since August 2000, we have performed standardized oral clinical examinations on adults who enrolled in the prospective OPTIONS STUDY in San Francisco because of suspected primary or recent HIV infection.

Oral Lesions:

- The oral lesion criteria and definitions of Greenspan et al., 1992 and the EC-Clearinghouse, 1993 were used.⁶⁻⁷
- Calibration of examiners (nurse practitioners or physicians):
 - A videotaped training session, which included color slides and diagnostic criteria of the selected oral disease outcomes, was reviewed by all examiners annually, with pre- and post-testing.

Subject Eligibility for the OPTIONS STUDY:

INCLUSION

- Self-presented or provider network referred.
- Adult males/females, age > 17
- Suspected primary or recent HIV infection OR documented seroconversion in the past 6 months.
- Group 1: HIV negative: negative HIV EIA and HIV RNA tests.
- Group 2: Primary/Acute HIV infection: negative HIV EIA and positive HIV RNA tests, or positive EIA < 30 days
- Group 3: Recent/Early HIV Infection: positive EIA and either a documented negative antibody test within 6 months or a negative detuned EIA (<0.75), which represents a stage up to 6-7 months after primary/acute infection.
- Ability to provide written consent.
- Ability for follow-up period for at least 96 weeks.

EXCLUSION

- Documentation of an AIDS-defining clinical condition (Epstein Barr virus or CMV mononucleosis syndrome, acute streptococcal pharyngitis)
- Any prior antiretroviral therapy beyond four weeks, except for post-exposure prophylaxis.
- Persons of procreative potential not practicing single-barrier contraception.
- Neoplastic disease requiring systemic cytotoxic or radiation therapy or participants who have had these therapies within one month of baseline and have not completely recovered from the effects of these therapies.
- Unstable or severe intercurrent medical conditions

Study Visits:

- HIV(-): Baseline visit only
- HIV(+): Longitudinal Follow-up
 - Baseline
 - 4 weeks
 - 12 weeks
 - 24 weeks
 - every 24 weeks thereafter

Treatments

- HIV + subjects have the option to undergo therapy at any time during the study. Therapy options:
 - Triple drug therapy consisting of Combivir® (zidovudine [AZT], lamiduvine [3TC] and nelfinavir (Viracept®)), which are all approved by the FDA for treatment of HIV infection.
 - IL-2 is a synthetic copy of a protein growth factor normally produced in the body, which in other research studies has been shown to increase some types of cells of the immune system. It is not approved by the FDA for the purpose for which it is used in this study.

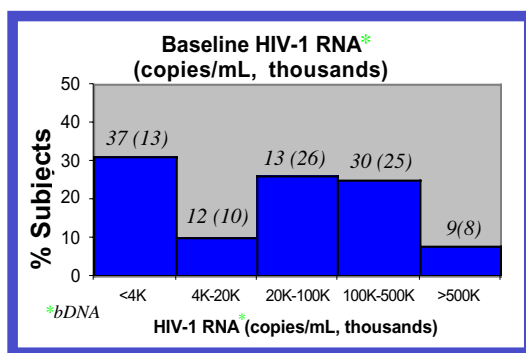
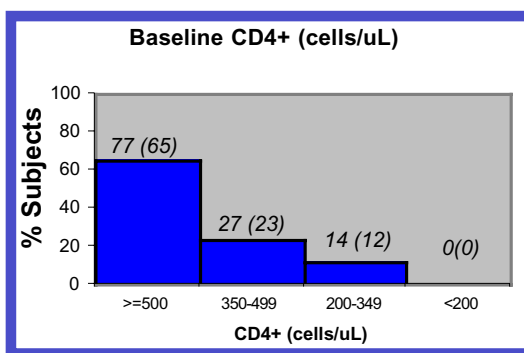
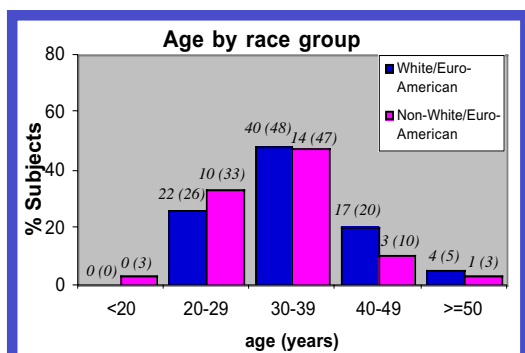
RESULTS

Characteristics of OPTIONS STUDY Subjects, n (%):

- Among all persons with suspected HIV infection, 81% were indeed infected.
- Most subjects were White; 3% were Black and 12% were Hispanic. The median age of study subjects was 35 years (range, 18 to 59 years).
- Most subjects were males who acquired HIV infection through sex with men (89%).
- Among HIV-infected subjects, CD4 T-cell counts and HIV RNA levels are consistent with early HIV infection.

Baseline Status	Primary/acute	Recent/early	All
HIV-	14 (12)	82 (69)	119 (100)

	Transmission Group			
	Sex w/ men (n=107)	IDU (n=2)	Other (n=5)	All (N=119)
Gender				
Male	102 (95)	2 (100)	5 (100)	109 (92)
Female	5 (5)	0 (0)	0 (0)	5 (4)
Missing	--	--	--	5 (4)



Study Visits:

- Among HIV-infected subjects, the median number of study visits within 18 months of baseline was 4 (range, 1 to 7). On average, 95% of the HIV-infected subjects opted to begin antiretroviral therapy.

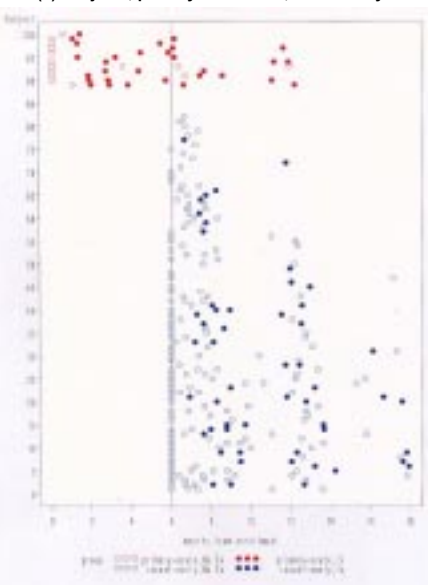
Oral Lesion Prevalence by HIV Status:

- Oral candidiasis tended to increase with the duration of HIV infection, even within 18 months of infection.
- Aphthous ulcers appeared to be unrelated to HIV infection.
- Papilloma/warts occurred primarily in HIV-negative subjects.
- No episodes of oral hairy leukoplakia were diagnosed.

Effect of Antiretroviral Treatment on Oral Lesion Prevalences:

- One AU oral lesion and no OC lesions were diagnosed while subjects were on antiretroviral medications. The odds ratios and 95% confidence intervals were AU, 0.144 (0.008 to 2.55) and OC, 0.195 (0.025 to 1.54).
- In the absence of a treatment effect, 4 AU lesions and 2 OC lesions were expected
- Because few lesions have been diagnosed to date, the decreases in lesions prevalence with treatment were not statistically significant.

Options Study Follow-up
HIV(+) Subjects; primary-acute n=14, recent-early n=82



	Prevalence* by HIV Status at Enrollment			Repeated measures p-value** (one-sided)
	HIV negative (n=23)	Primary/Acute (n=14)	Recent/Early (n=82)	
Oral candidiasis (OC)	1.0%	1.6%	2.6%	0.25
Aphthous ulcer (AU)	5.0%	4.9%	4.7%	0.47
Papilloma/Wart (PW)	3.6%	1.1%	0.3%	0.09
Hairy leukoplakia (HL)	0.0%	0.0%	0.0%	--

*Prevalence estimates are based on the proportion of subjects diagnosed with a given lesion type during the 20-month study period (August 2000-April 2002) on 119 HIV- and primary/early HIV subjects.
**p-values, corresponding with trends in prevalence, are based upon repeated measures models (generalized estimating equation).

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OC in primary/acute HIV infection

CONCLUSIONS

- Oral lesions notably OC, are seen in both primary/acute and early/recent HIV infection, but this trend does not reach a statistically significant level.
- Oral lesions notably OC, are seen less frequently once antiretroviral therapy has been initiated.

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