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Oral manifestations of HIV infection in homosexual men and intravenous drug users

Study design and relationship of epidemiologic, clinical, and immunologic parameters to oral lesions

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This article describes the baseline findings from a study designed to compare the oral manifestations of HIV infection in homosexual men and intravenous drug users. Both seropositive and seronegative persons were studied. A standard examination instrument was developed to record indexes of oral disease as well as to record the presence of oral lesions. The two groups differed in terms of education, race, socioeconomic status, employment status, housing, and smoking experience. The prevalence and type of oral lesions differed in the two seropositive groups. In seropositive homosexual men, white lesions on the tongue (28.4%) predominated; whereas for the seropositive intravenous drug users, oral candidiasis (43.0%) and gingival marginal erythema (33.3%) were most often detected. We also observed that seronegative intravenous drug users displayed a greater number of oral lesions than seronegative homosexual men. For seropositive homosexual men, lesion presence was significantly associated with decreased levels of CD4; positive associations were seen with current smoking, antiviral drug use, and antibiotic use, and a negative association was observed with current employment. In contrast, only exposure to antiviral drugs was significantly correlated with lesion presence for seropositive intravenous drug users. This baseline analysis from our longitudinal study suggests clear differences in oral manifestations of HIV infection between seropositive homosexual men and intravenous drug users and between seronegative homosexual men and intravenous drug users. Among other parameters, it is apparent that lifestyle, access to health care, and the condition of the oral cavity before infection influence the development of oral lesions in persons with HIV infection. **(ORAL SURG ORAL MED ORAL PATHOL 1994;78:163-74)**

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The development of oral lesions is important in the clinical spectrum that characterizes infection with the human immunodeficiency virus (HIV). The first description of HIV disease contained reference to development of oral lesions, specifically *Candida* infection as a result of the immunodeficiency.[1] Intraoral *Candida* and hairy leukoplakia have been recognized as occurring early in the course of disease,[2-6] and these lesions are included as criteria in different staging systems.[7-11] These lesions are commonly detected in seropositive persons[12-17] and may also be useful as predictors of survival in infected persons.[18-20]

Although much has been written about oral manifestations of HIV infection, certain problems inherent in these studies can be identified. First, the frequency of oral manifestations of HIV infection has not always been evaluated in randomly sampled populations. This may result in prevalence rates that may be higher than the true rate in the population. Second, the occurrence of oral lesions has not been extensively evaluated in the context of the medical and immunologic changes that characterize HIV disease. Third, most of the studies examining oral manifestations of HIV infection have focused on homosexual men. Other cohorts of persons infected with the virus, such as intravenous drug users (IVDU), have not been as extensively studied. This issue is particularly important in consideration of the potential differences between risk groups in terms of income, education, drug use, ethnicity, and access to health care. These differences are likely to influence the condition of the oral cavity.

To address these issues, a longitudinal evaluation of oral manifestations of HIV infection in different cohorts was initiated. Specifically, seropositive (HIV+) and seronegative (HIV−) homosexual men and IVDU men and women were studied. In this article we describe the study protocol, characterize the cohorts, and examine the relationships of clinical, epidemiologic and immunologic parameters to the occurrence of oral lesions in the two cohorts.

MATERIAL AND METHODS

In 1988, the HIV Center for Clinical and Behavorial Studies at the New York State Psychiatric Institute/Department of Psychiatry of Columbia Presbyterian Medical Center was funded by the National Institute for Mental Health (MH 43520). One component of this Center was the semiannual evaluation of seronegative and seropositive homosexual men and IVDU to follow the natural history of HIV disease. An oral/dental examination was added to the semiannual medical and immunologic evaluations. The medical evaluation includes a physical examination, followed by staging of all seropositive persons using the HIV Center Staging System.[9] Drug usage is also recorded. In this analysis, prescription drug usage was tabulated into eight categories (antiviral drugs [with acyclovir considered as a separate category], antifungal drugs, antibiotics, antineoplastic drugs, antihistamines, antiparasitic drugs, and antiulcer drugs). Whole blood is collected at each evaluation for determination of a variety of immunologic/hematologic markers, including the number and percentage of CD4+ lymphocytes (T-helper cells), CD8+ lymphocytes (T suppressor cells), CD19+ lymphocytes (B cells), and the total white blood cell count (WBC).

The oral/dental examinations are conducted with the use of an 2-part instrument developed for this project (see Appendix). The first part is the two-page history and oral examination component that collects epidemiologic data and records current complaints (pain, oral dryness), the status of the dentition including the number of decayed, missing, and filled teeth (DMF score), indexes of debris and calculus, a half-mouth periodontal examination, and collection of subgingival plaque samples for identification of periodontal pathogenic microorganisms and cytologic smears for evaluation of fungal hyphae. Also noted on this form is the number of specific oral lesions (oral diagnoses) observed. The second part of the instrument is a form completed for each diagnosis. The location of each lesion is noted using the World Health Organization-derived pictogram, and the lesion is characterized in terms of a presumptive or working diagnosis and clinical characteristics (size and color).

Oral lesions were diagnosed on their clinical appearance. In addition, all suspected *Candida* lesions were evaluated microscopically after a surface smear and staining with periodic acid-Schiff. For this article the lesions were grouped into eight diagnostic categories: oral candidiasis, white lesions on the tongue (includes hairy leukoplakia), gingival lesions (specifically identifying marginal erythema [also known as HIV-gingivitis], necrotizing ulcerative gingivitis, and gingival recession with pain [known more commonly as HIV periodontitis]), non-*Candida* red lesions of the mucosa, other white lesions (not located on the tongue), oral ulcers, Kaposi's sarcoma, and papillomas.

An oral/dental examination was offered to all persons in the longitudinal medical study. These examinations were conducted by dentists trained in identification of intraoral lesions associated with HIV infection. After introduction of the oral/dental examination, 129 homosexual men were evaluated at

Table I. Demographic characteristics of the two cohorts not considering serostatus. Mean ± standard deviation is provided for continuous variables. Percentage is given for categoric variables.

Variable	*Homosexual men*	*IVDU*	p-*Value for cohort difference*
Number of subjects	129	138	—
Age (years)	40.6 ± 8.0	41.8 ± 7.2	NS
Education (years)	16.3 ± 2.7	11.7 ± 2.2	<.001
HIV+ (%)	63	57	NS
Race (%)			
White, non-Hispanic	86.8	11.6	
White, Hispanic	8.5	15.9	<.001
Black, non-Hispanic	3.1	72.5	
Black, Hispanic	1.6	0	
Female (%)	NA	35.5	—
Socioeconomic status categories (%)			
Unskilled laborers	0	16.8	
Semiskilled	8.5	30.5	
Skilled	10.9	24.4	<.001
Minor professionals	35.7	26.0	
Professionals	45.0	2.3	
Employment status (%)			
Full-time	55.0	5.3	
Part-time	19.4	2.3	<.001
Unemployed	19.4	9.8	
Other	6.2	82.7	
Housing (%)			
Domiciled	97.7	89.5	
Living in shelter	0	3.8	.02
Other (jail, street, etc.)	2.3	6.8	
Smoking experience (%)			
Never smoked	43.4	8.8	
Past smoker	26.4	4.4	<.001
Current smoker	30.2	86.9	
Edentulous (%)	0	13.0	<.001
DMF score	13.1 ± 6.2	20.9 ± 6.1	<.001

the New York State Psychiatric Institute for their baseline oral/dental examination. The IVDU were seen at the Infectious Disease Clinic at Harlem Hospital Center for their medical examination; 138 received oral examinations. Therefore the baseline data comprise a total of 267 persons. Of the 129 homosexual men, 81 were seropositive and 48 were seronegative. In the IVDU cohort 79 persons were seropositive (51 men and 28 women) and 59 were seronegative (38 men and 21 women).

Statistical methods

In the first part of this analysis, we compared the HIV+ and HIV− homosexual men and IVDU with respect to demographic data, immunologic and medical profile, prescription drug use, and lesion occurrence. Student's t test was used to compare the mean values of continuous variables across two groups. Pearson's χ^2 test was used for categoric variables.

The second part of the analysis focused on identifying correlates of lesion presence. To meet this objective, the number of oral lesions was dichotomized as present (one or more lesions) or absent (no lesions). The association of lesion presence to cohort and serostatus was tested with the adjusted method proposed by Mantel and Haenszel[21] for the analysis of several fourfold tables.

In addition, the Mantel and Haenszel[21] estimate of the common odds ratio was computed as a measure of association between these variables. Associations with other categoric and continuous variables were analyzed bivariately by χ^2 test and Student's t test, respectively. Logistic regression models were used to assess the relationship of lesion presence to several covariates simultaneously.[22] Specifying lesion presence or absence as the outcome variable, logistic regression allowed us to detect significant correlates of lesion occurrence and to compute adjusted estimates of association. For the final models, we present estimated odds ratios and significance levels.

Table II. Mean (± standard deviation) immunologic and medical staging variables for homosexual men and IVDU stratified by serostatus

	HIV −		*HIV +*	
	Homosexual men	*IVDU*	*Homosexual men*	*IVDU*
CD4 cell count	896 ± 314	919 ± 307	305 ± 232	355 ± 253
CD4 % lymphocytes	46 ± 7	44 ± 7	20 ± 13	20 ± 10
CD8 cell count	528 ± 215	580 ± 234	880 ± 559	900 ± 545
CD8 % lymphocytes	27 ± 7	27 ± 7	54 ± 12	53 ± 12
CD19 cell count	216 ± 72	285 ± 171*	125 ± 84	179 ± 109*
CD19 % lymphocytes	11 ± 4	13 ± 6	9 ± 5	11 ± 6*
White blood cell count ($\times 10^4$)	6.1 ± 1.5	6.2 ± 2.0	4.5 ± 1.6	4.9 ± 2.1
State of disease (%)				
Asymptomatic	—	—	9.9	3.8
Lymphadenopathy	—	—	25.9	11.4
ARC	—	—	50.6	78.5*
AIDS	—	—	13.6	6.3

*Significant cohort difference, $p < 0.01$

RESULTS

Demographic characteristics

The demographic characteristics of the two cohorts are presented in Table I. As anticipated, the homosexual and IVDU cohorts differ significantly with respect to education, race, socioeconomic status, employment status, type of housing, smoking experience, and oral health status (as measured by DMF score and proportion of persons with no teeth). They are comparable, however, with respect to age and percentage of the cohort that are seropositive. There are no significant differences between seropositive and seronegative persons within each cohort.

Immunologic/medical profile

Table II compares mean levels of various immunologic measures (CD4, CD4 percentage [%], CD8, CD8%, CD19, CD19%, WBC) between cohorts within serostatus and gives the medical stage of disease by cohort among HIV+ subjects with the use of the system developed by the HIV Center for Clinical and Behavioral Studies.[9] The two cohorts appear surprisingly comparable with respect to all of the immunologic parameters with the exception of CD19 (raw count or percentage), which is lower for homosexual men whether HIV+ or HIV−. The two HIV+ groups also differ with respect to medical stage of disease, with a greater proportion of IVDU who have progressed to more advanced disease (84.8% of IVDU versus 64.2% of homosexual men have progressed to Stage 3 or Stage 4 [AIDS]) at the first dental visit.

Prescription drug use

Table III compares reported rates of prescription drug use during the previous 6 months stratified by cohort within serostatus. With respect to the five categories that may be related to serostatus (antiviral drugs, acyclovir, antifungal drugs, antibiotics, and antineoplastic drugs), HIV+ homosexual men and IVDU are comparable in three (antiviral drugs, antifungal drugs, and antibiotics). HIV+ homosexual men and HIV+ IVDU differ significantly in the use of acyclovir, and this difference is also seen for the two seronegative groups. The two HIV+ groups also differ significantly with respect to exposure to antineoplastic drugs as eight HIV+ homosexual men and no HIV+ IVDU reported use of these agents.

Types of lesions observed

The types of lesions detected varied by cohort and serostatus (see Table IV). Among seronegative subjects, the most frequently observed lesions in homosexual men were marginal erythema (12.5%) and oral ulcers (10.4%), whereas the most common lesions in IVDU were marginal erythema (33.3%), white lesions on the tongue (22.0%), and oral candidiasis (10.2%). The most common lesions observed in the HIV+ homosexual men were white lesions on the tongue (28.4%), oral candidiasis (17.3%), non-*Candida* red lesions (17.3%), and marginal erythema (16.1%). For seropositive IVDU, the most common lesions were oral candidiasis (43.0%), marginal erythema (33.3%), and white lesions on the tongue (29.1%).

Relationship of cohort and serostatus to the occurrence of oral lesions

To relate lesion occurrence to HIV serostatus and cohort membership, we dichotomized all subjects as to the presence or absence of oral lesions (one or more lesions versus no lesions). HIV+ subjects have oral

Table III. Prescription drug use by cohort and serostatus

Drug	*HIV −*			*HIV +*		
	Homosexual men (%)	*IVDU (%)*	*p*	*Homosexual men (%)*	*IVDU (%)*	*p*
Antiviral	0	0	—	47.5	61.5	NS
Acyclovir	8.3	0	0.03	33.8	5.1	<0.001
Antifungal	0	1.7	NS	23.8	15.4	NS
Antibiotic	20.8	17.2	NS	51.3	48.7	NS
Antihistamine	22.9	3.5	0.002	18.8	3.9	0.003
Antineoplastic	0	0	—	10.0	0	0.004
Antiparasitic	0	0	—	13.8	2.6	0.011
Antiulcer	0	6.9	NS	7.5	6.4	NS

Table IV. Prevalences of oral lesions among HIV+ and HIV− homosexual men and IVDU

Type of lesion	*HIV−*		*HIV+*	
	Homosexual men (%)	*IVDU (%)*	*Homosexual men (%)*	*IVDU (%)*
Oral candidiasis	4.2	10.2	17.3	43.0
White lesions on the tongue	2.1	22.0	28.4	29.1
Gingival lesions				
Marginal erythema	12.5	33.3*	16.1	33.3*
Necrotizing ulcerative gingivitis/gingival recession with pain	0	2.0*	6.2	5.8*
Non-*Candida* red lesions	8.3	5.1	17.3	10.1
Oral ulcers	10.4	8.5	13.6	7.6
Other white lesions (not on tongue)	0	3.4	0	3.8
Kaposi's sarcoma	0	0	4.9	0
Papilloma	0	1.7	0	2.5

*Among nonedentulous subjects: 51 HIV− and 69 HIV+ IVDU.

lesions significantly more often than HIV− subjects adjusted for cohort (Table V). The odds of a lesion being present were 2.7 times greater for HIV+ than for HIV− subjects. Within the homosexual cohort, a greater percentage of HIV+ subjects displayed one or more oral lesions than HIV− subjects. However, among IVDU, the occurrence of one or more oral lesions was not significantly greater in the HIV+ subjects. Overall, a significant cohort difference was observed. Adjusted for serostatus, IVDU were more likely than homosexual men to have lesions. The cohort effect was not as large as the serostatus effect yielding an estimated odds ratio of 1.7. Among HIV+ subjects, homosexual men and IVDU did not differ significantly with respect to lesion occurrence. There was, however, a significant cohort difference among HIV− subjects.

Table V. Percentage of subjects who display one or more oral lesions by serostatus within cohort

*Cohort**	*HIV serostatus†*	*Percentage with lesions*	*n*
Homosexual men	HIV+	64.2	81
	HIV−	31.3	48
IVDU	HIV+	69.6	79
	HIV−	54.2	59

*Cohorts differ significantly with respect to lesion presence controlling for serostatus (Mantel & Haenszel[21] $x^2 = 4.4$, df = 1, $p = 0.04$).
†HIV− and HIV+ subjects differ significantly with respect to lesion presence controlling for cohort (Mantel & Haenszel[21] $x^2 = 14.8$, df = 1, $p < 0.001$).

Correlates of oral lesions in all subjects

Table VI presents the percentage of subjects with one or more lesions by covariate level within cohort and serostatus. No significant correlates of lesion presence were found in either of the seronegative groups. However, significant associations between lesion presence and current smoking, current employment, and antiviral use were found among the HIV+ homosexual men. In the HIV+ IVDU, only antiviral use was significantly related to lesion presence. On the basis of these results, we performed adjusted analysis in the HIV+ cohorts only with special attention to the aforementioned variables.

Table VI. Percentage of subjects who display one or more oral lesions by covariate level stratified by cohort and serostatus

Covariate	*Homosexual men*		*IVDU*	
	HIV− (%)	*HIV+ (%)*	*HIV− (%)*	*HIV+ (%)*
Age decade				
20-29	75.0	100.0	33.3	100.0
30-39	36.8	59.5	60.0	75.8
40-49	25.0	75.0	50.0	63.6
≥50	11.1	40.0	57.1	66.7
Race				
White	26.2	61.4	62.5	37.5
White/Hispanic	75.0	85.7	66.7	84.6
Black	50.0	100.0	50.0	70.7
Black/Hispanic	—	50.0	—	—
Current smoking				
No	32.4	57.1*	50.0	50.0
Yes	28.6	80.0	55.1	72.9
Currently employed				
No	40.0	82.6*	57.7	70.4
Yes	29.0	56.9	28.6	33.3
Antiviral use				
No	31.3	47.6†	53.5	56.7*
Yes	—	81.6	—	79.2
Acyclovir use				
No	29.6	60.4	53.5	70.3
Yes	50.0	70.4	—	75.0
Antibiotic use				
No	26.3	53.9	58.3	62.5
Yes	50.0	73.2	30.0	79.0

*$p < 0.05$
†$p < 0.01$

Table VII. Mean levels (± standard deviation) of HIV-related immunologic/hematologic measures stratified by lesion presence/absence in HIV+ homosexual men and IVDU

	Homosexual men		*IVDU*	
	Lesion present	*Lesion absent*	*Lesion present*	*Lesion absent*
CD4 cell count	243 ± 205	416 ± 240*	332 ± 256	411 ± 240
CD4 % lymphocytes	17 ± 14%	25 ± 10%*	19 ± 10%	22 ± 10%
CD8 cell count	872 ± 609	895 ± 465	847 ± 514	1033 ± 608
CD8 % lymphocytes	56 ± 13%	52 ± 10%	53 ± 11%	51 ± 13%
CD19 cell count	130 ± 85	116 ± 83	169 ± 109	210 ± 106
CD19 % lymphocytes	9.4 ± 5.8%	7.2 ± 4.5%	11.2 ± 5.4%	11.4 ± 6.2%
White blood cell count ($\times 10^3$)	4.5 ± 1.7	4.4 ± 1.5	4.6 ± 2.1	5.6 ± 2.2

*$p < 0.01$

Correlates of oral lesions in HIV+ subjects

For this portion of the analysis, we examined the demographic and exposure variables considered earlier, but also included disease-related immunologic/hematologic measures such as CD4, CD8, CD19, and WBC. Table VII presents the mean levels of these variables stratified by lesion presence or absence within each cohort.

Homosexual men. Among HIV+ homosexual men, lesion presence is significantly associated with decreased levels of CD4 cells (both absolute count and percentage of total lymphocytes). Our sample failed to produce any significant correlations between lesion presence and CD8, CD19, or WBC. As noted previously, we found positive associations between lesion presence and demographic/exposure variables, with respect to current smoking, antiviral drug use, and antibiotic use, and a negative association with current employment.

IVDU. Among the IVDU, we were unable to

discover any significant hematologic/immunologic correlates of lesion presence by bivariate analysis in the HIV+ group. Although we did observe a decrease in the mean number and percentage of CD4 cells among those with one or more lesions, these results were not as strong as in the homosexual male cohort. As noted previously, among the demographic and exposure variables, the only significant correlation of lesion presence in HIV+ IVDU was exposure to antiviral agents.

Regression analysis of lesion occurrence in HIV+ subjects

Finally, we used logistic regression modeling to assess the associations of covariates to lesion presence while adjusting for potential confounders. As a result of apparent cohort differences, we present results separately for homosexual men and IVDU (see Table VIII).

Homosexual men. In the HIV+ homosexual male cohort, we found five significant correlates of lesion presence: current smoking, employment status, antiviral drug use, CD4 percentage, and WBC. Although CD4 cell count is more commonly found in the literature than CD4%, we used CD4% in the logistic models because it is less variable than the raw CD4 count in repeated laboratory measurements. The parameter estimate from the logistic model indicates that current smoking increases the odds of lesion presence by a factor of 10. In contrast, holding a full-time or part-time job reduces the odds of oral lesions by a factor of 0.2. The odds ratio for antiviral drug use was close to 11, which reveals greatly increased odds of lesion presence among those taking antiviral drugs. As seen in Table VIII, lesion presence is associated with lower CD4%; a decrease of 10 points on the CD4% scale is indicative of an odds ratio of 2.5. We were surprised to discover a relationship between lesion presence and WBC, undetected in bivariate analysis. A significant effect of WBC, on the order of two times the risk, was found only after adjustment for CD4% in the HIV+ homosexual male cohort.

To describe the relationship between WBC and lesion occurrence, we stratified by CD4% (0 to 13, 14 to 28, ≥29) and calculated the mean WBC by lesion presence or absence within the cohort. The average WBC ($\times 10^3$) for subjects with lesions compared with those without lesions within CD4 categories were: 4.2 versus 3.4 for 0 to 13 CD4%, 4.5 versus 4.8 for 14 to 28 CD4% and 5.6 versus 3.9 for ≥29 CD4%. In the lowest and highest CD4% categories, lesion presence was accompanied by an increased WBC corresponding to the positive association found by means of regression. There seems to be no WBC effect in the middle category.

Table VIII. Results from the final logistic regression models for HIV+ homosexual men and IVDU

	Homosexual men		*IVDU*	
Co-variate	*Odds ratio*	p-*Value*	*Odds ratio*	p-*Value*
Smoking	10.4	0.003	2.0	0.45
Current employment	0.2	0.03	0.5	0.69
Antiviral use	10.8	0.002	2.5	0.12
CD4%*	0.4	0.003	0.9	0.72
WBC†	2.1	0.046	0.8	0.29

*Odds ratio corresponds to a 10 point increase in CD4% (approximately one standard deviation).
†Odds ratio corresponds to a 1.5 point increase in WBC (approximately one standard deviation in homosexual men; 0.75 standard deviation in IVDU).

A number of other variables were tested in regression models for association with lesion presence, but were found to be nonsignificant. These included age, race, sex, socioeconomic status, homelessness, exposure to acyclovir, antibiotic use, antifungal use, edentulousness, CD 8 cells (number or percentage) and CD 19 cells (number or percentage).

IVDU. Using regression, we were not able to detect any statistically significant correlates of lesion presence for seropositive IVDU. For comparison purposes, however, we present logistic regression results for the IVDU in Table VIII. For the smoking, employment, antiviral, and CD4% variables, the relationships to lesion presence had the same tendencies for the IVDU as for the homosexual men, but in each case the magnitude of the association was much weaker (and nonsignificant). The only difference of note was the estimated effect of WBC. Among IVDU, WBC seems to have a weak negative correlation with lesion presence.

DISCUSSION

This preliminary report has presented an overview of a study designed to examine the relationship of oral lesions to the immunologic and medical findings in HIV disease. The occurrence of oral lesions in HIV disease has been examined in the literature, and a number of these studies were shown to be flawed as a result either of selection bias or the lack of an appropriate control group. This issue has been reviewed for periodontal manifestations of HIV infection.[23]

This study reduced bias by examining persons at various stages of disease who are participating in a longitudinal study of the natural history of HIV disease. None of the persons was selected for study on the basis of the condition of their oral cavity. Recruitment of an appropriate study population is a critical consideration for proper study design. Specifically, if persons in a population are preselected on the basis of

some characteristic to be studied, the true prevalence rates of HIV-associated oral lesions will be artificially inflated compared with the general population.

Among the important findings from this analysis of the baseline data is that the homosexual men and IVDU differed in the occurrence of oral lesions in both seronegative and seropositive persons. The percentage of seronegative IVDU with oral lesions was higher than the percentage observed for seronegative homosexual men. For both of the seronegative groups, marginal gingival erythema was the lesion most often detected, but this lesion occurred much more frequently in the IVDU (33.3%) compared with the homosexual men (12.5%). Interestingly, white lesions on the tongue were frequently seen in the seronegative IVDU, and 10% of these persons had *Candida* infection. Focusing on the seropositive subjects, approximately 70% of IVDU displayed oral lesions compared with 64% of the homosexual men. Although the percentage of seropositive subjects with lesions did not differ on the basis of cohort, the types of lesions seen in these two groups did differ. Seropositive IVDU displayed a much higher percentage of *Candida* infection than did the seropositive homosexual men (43% versus 17.3%). This finding may relate more to differences in the oral cavity before infection, that is, more plaque, calculus, caries, and periodontal disease, and the higher percentage of *Candida* infection before infection with HIV than to systemic differences in terms of route of infection or frequency of exposure.

Intravenous drug use has been associated with increased oral disease.[24-27] An increase in both the caries rate and the severity of periodontal disease have been observed in IVDU. Furthermore, Rees[28] has suggested that intravenous opiate use may result in depressed cellular immunity, which can predispose IVDU to oral fungal and viral infections. In this study we observed an increased prevalence of oral fungal infections in both seropositive and seronegative IVDU compared with seropositive and seronegative homosexual men. This was observed despite the fact that CD4 count or CD4% were not different between seronegative and seropositive persons in the different cohorts. In addition to the potential influence of intravenous opiates on intraoral *Candida* infection in IVDU, other potential contributing factors observed in IVDU include poor access to health care, poor diet, and heavy accumulation of dental plaque.

Furthermore, it is interesting to observe that other lesions also appear to occur more frequently in one or the other cohort, that is, intraoral Kaposi's sarcoma was only seen in seropositive homosexual men whereas papilloma-like lesions were seen only in seronegative and seropositive IVDU. These differences emphasize the importance of defining the populations to be studied to determine the occurrence and significance of oral lesions in HIV infection.

The identification of marginal erythema in this study provides an example of another potential pitfall when attempting to determine the prevalence of oral manifestations of HIV infection. HIV-gingivitis has been defined as an oral lesion associated with HIV infection. The lesion is described as a demarcated band of intense tissue erythema present at the gingival margin. The lesion is not associated with plaque accumulation and does not respond to traditional periodontal therapy including routine plaque control measures and mechanical debridement. As the clinical investigators in this study are not aware of the serostatus of persons being examined, a definition of "HIV-gingivitis" is inappropriate. Consequently in this study marginal erythema was defined as a band of significant erythema at least 2 mm in thickness, distinctly demarcated from the adjacent gingiva and continuous from papilla to papilla. One third of both seronegative IVDU and seropositive IVDU displayed marginal erythema. For seronegative and seropositive IVDU virtually all tooth surfaces displayed plaque accumulation (data not shown), and it is not possible to tell true HIV-gingivitis from plaque-associated marginal erythema. A modest difference was seen in the prevalence of marginal erythema in seronegative (12.5%) versus seropositive (16.1%) homosexual men. These persons tended to have a much lower percentage of tooth surfaces with plaque (data not shown). Although the definition of HIV-gingivitis may be useful for persons with better plaque control, the definition may have little practical application.

Examining correlates of lesion presence in HIV+ homosexual men and IVDU, we observed that in seropositive homosexual men, lesion presence was significantly associated with a decrease in CD4 count. This result is expected because the association between progression of HIV disease and CD4 depletion is well established. The association of lesion occurrence with smoking was of interest, particularly in light of the well-defined health risks associated with smoking cigarettes and the more recently defined association between cigarette smoking and increased risk for periodontal disease.[29, 30] In the homosexual cohort, the positive association of oral lesions and the use of antiviral drugs and antibiotics and the negative association of lesions with current employment are indirect measures of the health of the person. When examining these three variables for seropositive IVDU, however, none approached significance. These data emphasize the difference between the two seropositive groups and suggest that some beliefs regarding

the occurrence of oral lesions in HIV infection, which were developed by studying homosexual men, may not be valid for other cohorts. There are many potential reasons for this, but one important reason identified in this study is simply that before infection, persons in a lower socioeconomic status group will tend to have more oral disease than persons in a higher socioeconomic status group.[24]

There are many reasons to identify the relationship of oral lesions in HIV infection to the immunologic and medical changes that characterize the disease. First, oral lesions may be important early identifiers of HIV infection.[18, 19] Second, certain oral lesions (*Candida* infection, hairy leukoplakia) are important in the staging of HIV disease.[7-11] Third, dental professionals need to be aware of different patterns of disease that may characterize different persons with HIV infection. Familiarity with these patterns may have potential therapeutic implications. Later reports will examine the relationship of specific oral lesions associated with HIV infection to the medical and immunologic changes that occur with disease.

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Appendix: Examination instrument for oral manifestations of HIV infection

ORAL EXAM AND HISTORY

Medical Staging ☐

1. Subject ID: ___ ___ ___ ___-___ ___
2. Dental Visit #: ___ ___
3. Today's Date (Mo/Da/Yr): ___ ___/___ ___/___ ___
4. Examiner's initials: ___ ___ ___
5. Date of Birth (Mo/Da/Yr): ___ ___/___ ___/___ ___
6. Oral complaint — Circle Yes or No
   a. Pain (present at time of examination) — Yes 1 No 0
      If yes, explain and list location:

      _____

      _____

   b. Frequent oral dryness ..... Yes 1 No 0
   c. Other (pain since last examination) — Yes 1 No 0
      If yes, explain and list location:

      _____

      _____

   d. Antibiotic prophylaxis given ..... Yes 1 No 0
      Rx: _____

EXAMINATION

7. a. Oral soft tissue findings: ..... Yes 1 No 0
   b. If yes, enter number of lesions: ___ ___

   If YES, enter information on soft tissue pathology form—one form for each lesion noted. Then continue with the oral exam and history form.
   If NO, continue with this form.

8. a. DMF Score: ___ ___ or 8b. Missing teeth: ___ ___
9. Microbiology
   a. Tooth number: ___ ___ ___ ___ ___ ___ ___ ___
10. OHI-S: Tooth #: ___ ___ ___ ___ ___ ___ ___ ___
    a. *Debris Index* (0-3): ___ ___ ___ ___ ___ ___
    b. *Calculus Index* (0-3): ___ ___ ___ ___ ___ ___

Visit #: __ __ DATE: __ __/ __ __/__ __
ID # __ __ __ __- __ __

11. Periodontal Screening Examination (97 = Missing; 98 = Other; 99 = Error)

TOOTH	SITE	POCKET DEPTH	BLEEDING	(Circle Yes or No)
02	DB	__ __	Yes 1	No 0
	MB	__ __	Yes 1	No 0
03	DB	__ __	Yes 1	No 0
	MB	__ __	Yes 1	No 0
04	DB	__ __	Yes 1	No 0
	MB	__ __	Yes 1	No 0
05	DB	__ __	Yes 1	No 0
	MB	__ __	Yes 1	No 0
06	DB	__ __	Yes 1	No 0
	MB	__ __	Yes 1	No 0
07	DB	__ __	Yes 1	No 0
	MB	__ __	Yes 1	No 0
08	DB	__ __	Yes 1	No 0
	MB	__ __	Yes 1	No 0
31	DB	__ __	Yes 1	No 0
	MB	__ __	Yes 1	No 0
30	DB	__ __	Yes 1	No 0
	MB	__ __	Yes 1	No 0
29	DB	__ __	Yes 1	No 0
	MB	__ __	Yes 1	No 0
28	DB	__ __	Yes 1	No 0
	MB	__ __	Yes 1	No 0
27	DB	__ __	Yes 1	No 0
	MB	__ __	Yes 1	No 0
26	DB	__ __	Yes 1	No 0
	MB	__ __	Yes 1	No 0
25	DB	__ __	Yes 1	No 0
	MB	__ __	Yes 1	No 0

12. Smear Taken — Yes 1 — No 0
13. Removable denture(s): — Yes 1 — No 0
    Circle: FU, FL, PU, PL
14. Prophy since last visit: — Yes 1 — No 0
15. a. Mouthwash: — Yes 1 — No 0
    If yes, b. Product: _____
    c. Frequency: _____

COMMENTS:

ORAL SOFT TISSUE PATHOLOGY

1. Subject ID: ___ ___ ___ ___- ___ ___
2. Dental Visit#: ___ ___
3. Today's Date (Mo/Da/Yr): ___ ___/ ___ ___/ ___ ___
4. Examiner's initials: ___ ___ ___
5. Date of Birth (Mo/Da/Yr): ___ ___/___ ___/___ ___
6. a. Lesion Number: ___ ___b. Out of: ___ ___

FOR EXAMINER'S USE ONLY (NOT FOR DATA ENTRY)

Location of Lesion		
(1) ___ ___	(6) ___ ___	(11) ___ ___
(2) ___ ___	(7) ___ ___	(12) ___ ___
(3) ___ ___	(8) ___ ___	(13) ___ ___
(4) ___ ___	(9) ___ ___	(14) ___ ___
(5) ___ ___	(10) ___ ___	(15) ___ ___

7. Total number of locations
   1-5 = 01
   6-10 = 02 ___ ___
   11-15 = 03

	Circle Yes or No
8. a. Is this a NEW diagnosis?	Yes 1 No 0
b. Is lesion painful?	Yes 1 No 0
9. Is this a new location for an old diagnosis?	Yes 1 No 0

10. Clinical diagnosis _____ # ___ ___

11. Lesion character	Circle Yes or No
a. lump	Yes 1 No 0
b. flat	Yes 1 No 0
c. hairy	Yes 1 No 0
d. corrugated	Yes 1 No 0
e. plaques	Yes 1 No 0
f. raised	Yes 1 No 0
g. vesicles	Yes 1 No 0
h. fissured	Yes 1 No 0
i. exudate	Yes 1 No 0
j. ulcerated	

12. a. Size: <0.5cm = 01
    0.5-1.0 cm = 02 ___ ___
    >1.0 cm = 03
    12. b. # surface ___
    12. c. # papillae ___

13. Color:	Circle Yes or No
a. white	Yes 1 No 0
b. red	Yes 1 No 0
c. black	Yes 1 No 0
d. purple	Yes 1 No 0
e. brown	Yes 1 No 0
14. Photos taken?	Yes 1 No 0
15. Laboratory procedures for diagnosis:	
a. smear taken	Yes 1 No 0
b. biopsy needed	Yes 1 No 0
c. sample taken	Yes 1 No 0

If yes, d. Tooth #___ ___ Surface: ___ ___
e. Control #___ ___ Surface: ___ ___