Workshop papers

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WORKSHOP IN HEALTH ADMINISTRATION STUDIES

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Recreational drug use and sexual behavior change in a cohort of homosexual men

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The relationship between use of recreational drugs and high-risk (HIV-transmitting) homosexual behavior was examined in the Multicenter AIDS Cohort Study (MACS) population. Among the 3916 men who completed both the baseline (1984) and first 6-month follow-up evaluations and were sexually active during the 6 months prior to enrollment, self-reported use of each of 10 classes of recreational drugs in conjunction with sexual activity was analyzed for both cross-sectional and prospective relationships with pattern of sexual behavior using a four-level sexual risk behavior index. At baseline, the proportion of men in the highest risk category (unprotected anal exposures with multiple partners) increased from 36 to 85% when men not using any drugs to men using three or more drugs plus volatile nitrites were examined. In multivariate logistical analyses, volatile nitrite use was significantly associated with failure to maintain or attain lower sexual risk levels after controlling for the effects of age, educational level and numbers of high-risk partners. These results suggest that volatile nitrite use may play an important role in the association between recreational drug use and high-risk sexual behavior among homosexual/bisexual men.

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Keywords: Sexual behavior, homosexual men, recreational drugs, volatile nitrites, HIV transmission.

Introduction

Since the discovery of AIDS in 1981 there has been increasing attention to methods for decreasing the sexual spread of the etiological agent, HIV [1,2]. In response to the growing numbers of AIDS cases and the need for definite prospective information regarding the routes of transmission and actual history of the syndrome, a multicenter study of approximately 5000 homosexually active men was begun in 1984. The Multicenter AIDS Cohort Study (MACS) involves semi-annual medical, epidemiological and laboratory evaluations, as described elsewhere [3,4]. A major finding of the MACS is the verification of unprotected receptive anal intercourse as the principal mode of HIV infection in homosexually active men [5,6]. There has been a progressive decline in reported levels of this particular sexual practice, as well as a substantial decrease in HIV seroconversion rates over the first 4 years of observation [6–8], consistent to a large degree among the individual MACS sites (Pittsburgh, Baltimore/Washington DC, Chicago, and Los Angeles).

Since we are interested in the potential role of recreational drugs and alcohol as cofactors for either HIV infection or clinical consequences of HIV exposure, a series of questions about recreational drug use is included

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Note: The results of this study were presented in preliminary form at the 1986 Annual Meeting of the American Public Health Association and the III International Conference on AIDS, Washington DC, 1987.

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in each semi-annual MACS evaluation. While drug use was associated with increased risk of HIV seropositivity in previous analyses of the MACS cohort [4], we could not detect any adverse effects of substance use on either immunological or clinical sequelae of HIV infection [9]. The current study was undertaken to see whether relationships between drug use and persistence of high-risk (i.e. HIV-transmitting) sexual behaviors could explain the initially observed association between drug use and seropositivity in our study population. Such a finding could have significant implications for interventions aimed at reducing the sexual spread of HIV to population groups in all risk categories.

Methods

The study population consists of the entire MACS cohort in all four metropolitan areas (Los Angeles, Chicago, Pittsburgh, and Baltimore/Washington DC). For these analyses we have eliminated subjects who did not complete both baseline (April 1984 through March 1985) and the first 6-month follow-up evaluations, subjects who reported no sexual activity during the 6 months prior to baseline, and those for whom data on drug use or sexual behavior were not available.

Drug use and sexual activity were assessed using an interviewer-administered questionnaire which specifically probed for use of each of 10 different classes of recreational drugs — marijuana or hashish, volatile nitrites ('poppers'), cocaine, methylenedioxyamphetamine (MDA), hallucinogens, sedatives or hypnotics ('downers'), stimulants ('uppers'), inhaled ethyl chloride, opiates and 'other kinds of street drugs' — plus alcohol ingestion and details of sexual activity. At baseline, the questionnaire asked the frequency of use of each substance over the past 2 years and the past 6 months, and for use of each specific class with sexual activities during the past 6 months. At follow-up, frequency of use of each class, as well as use of each with sex, during the intervening 6 months was assessed. The reliability of the questionnaire was evaluated in pretesting and questions considered unreliable or ambiguous by respondents were eliminated or revised.

For the purpose of analysis, each participant was categorized into one of four levels of sexual risk behavior which reflected *a priori* conceptions about AIDS risk generally shared by investigators and the gay community at that time. The levels are:

(1) no risk: no anal insertive or receptive intercourse, no oral receptive, and no fecal–oral ('rimming') or manual–anal ('fisting') activity during the prior 6 months;
(2) low risk: only receptive oral and/or insertive anal intercourse (with or without condoms) during the prior 6 months;
(3) modified high risk: receptive anal intercourse limited to one partner or the consistent use of condoms with all partners and/or fecal–oral or manual–anal intercourse limited to one partner during prior 6 months;
(4) high risk: receptive anal intercourse, fecal–oral, or manual–anal intercourse with multiple partners and without the consistent use of condoms during prior 6 months.

The empirical utility of these categories in measuring risk of HIV-1 exposure was assessed by computing HIV-1 seroconversion rates by category during the 6-month follow-up period. Potential modifications of the sexual risk behavior categorization which incorporated insertive oral intercourse were also examined in relation to seroconversion, as were needle-using behaviors. Seroconversion was defined as change from negative to positive in both enzyme-linked immunosorbent assay (ELISA) and Western blot test results [12] in the 6-month time period. People with indeterminant antibody tests were excluded from these analyses.

Prospective analyses examined the *change* in sexual risk behavior category from initial to follow-up intervals as the outcome. Increase in risk was defined as changing from the no- or low-risk category pre-entry to the modified-high- or high-risk category during follow-up or from the modified-high level pre-entry to high risk during follow-up. For men initially in the high-risk category, continuation of HIV risk practices was defined as remaining in the high-risk category during follow-up.

The importance of usage of all 10 categories of illicit substances was analyzed by identifying the particular combinations (patterns) of the 10 drug categories which were most frequently reported, first for overall use and then separately for drugs used in conjunction with sexual activity. The association of these patterns with initial risk and change in risk were examined and, where similarities among patterns were found, the patterns were further collapsed and simplified for analysis. In order to assess the importance of mode of drug delivery, men were classified as using needles if they reported injecting any drug in any manner (intradermal, intramuscular, or intravenous) during the relevant period.

Statistical analyses were performed using standard statistical software (SAS and BMDP). For univariate analysis the chi-square test was used to test for association between dichotomous variables. Continuous variables were categorized and tested with chi-square analysis for differences and trend and were examined for possible curvilinear relationships. In order to evaluate other aspects of recreational substance use, including alcohol use, frequency of use of each illicit drug, injection of drugs by needle and rectal administration of drugs, all of which were themselves associated with the pattern of drugs used, the Mantel–Haenszel chi-square test [13] was used to test for the significance of their association with sexual risk level independent of the pattern of drugs used. Multiple logistic regression was employed to assess the relative contributions of factors to odds of reporting increased risk and

o odds of continuing to report high-risk practices dur-ng follow-up. All factors whose individual associations had P values < 0.05 were initially included in the models; stepwise backward fitting was employed to select the final models, retaining only variables with P values < 0.05 by the F test for partial association with the end-point. Pairwise interactions between significant variables were similarly tested, using a P value cut-off of 0.01.

Results

Of the 4954 men enrolled in the MACS, 36 reported no sexual activity during the prior 6 months, 478 failed to report for follow-up at 6 months, another 171 provided incomplete data on sexual risk, and 353 others provided incomplete drug use data. Thus, a total of 3916 men were available for primary analysis. The men who were not followed were somewhat younger and less well educated, but they did not differ with respect to sexual behavior risk-level categorization. Table 1 gives the distribution of sexual risk level in the 6-month period preceding entry into the study and in the subsequent 6 months among the men with complete data; it shows that the proportion reporting high-risk behaviors declined from 56.3 to 43.4% over the 6 months, while the proportions in each of the remaining categories increased. Table 1 also shows the rates of seroconversion among initially HIV-1-seronegative men during the 6-month period between evaluations by sexual risk level, reported during the same period. Of the five seroconverters whose sexual activity during the 6 months post-entry was classified as no risk or low risk, four were in the modified-high-risk group during the preceding 6-month period and may therefore have been initially tested for HIV antibody during the window period between infection and antibody production. The fifth reported unprotected insertive anal intercourse with one partner during each of the two 6-month periods and with many partners before then. Furthermore, since none of these five used needles during a 2.5-year period, recent sexual exposure is the plausible explanation even for their seroconversions.

Extensive screening of univariate associations between the pattern of drug use and sexual risk level or change in level produced no evidence for a role of drugs used exclusively apart from sexual partners. For this reason we present information on only those patterns of usage which occurred in conjunction with sexual activities. Second, analysis of the 10 individual classes of illicit drugs showed that all but the opiates had associations with the end-points which were positive and of similar magnitude, and differences between particular combinations were generally small. Nevertheless, the presence of some distinctions between poppers and the other drugs, in addition to the fact the popper drug group was the one most often used with sex, have led us to describe patterns of use by popper use and total number of other classes of drugs used.

Table 2 displays the association between pattern of drugs used and sexual behavior during the 6-month interval preceding entry into the study. While even among non-users many men reported having engaged in high-risk behaviors, the trend toward higher sexual risk levels with heavier drug use shown by this crude analysis is strong. The focus of further analyses was to attempt to show that this association could not be attributed to confounding relationships with demographic characteristics or other characteristics of recreational drug use, such as frequency of use and drug injection by needle, and to evaluate the association of drug use with subsequent changes in sexual behavior.

Injection of drugs by needle was reported during lifetime by 7.5% and during the 6 months post-entry by only 1.9% (61) of the men. Although needle-using and non-using men reported similar numbers of sexual partners, those using needles during the 6 months post-entry were more likely to report sexual behavior classified as high risk during the interval (65 versus 46%, respectively; $P < 0.01$). However, since 55% of needle-users versus only 12% of non-users ($P < 0.001$) reported using four or more different drugs with sex prior to entry, their higher level of sexual risk behaviors could be primarily attributed to their greater overall use of recreational drugs with sex. Needle-users were similar in age to non-users but tended to have less education (29% of users versus 59% of non-users had college degrees; $P < 0.001$). Among needle-users, the classes of drugs most commonly injected were uppers (62%), cocaine (36%), MDA (18%) and opiates (10%). Nearly half (44%) of needle-users reported that they shared needles during the same time period; their

Table 1. Proportion of men in categories of reported sexual risk behavior and associations with HIV-1 serconversion in 6-month periods pre- and post-entry, 1984–1985 (n = 3916).

		Post-entry		
Risk category*	Pre-entry (%)	%	Change in %	HIV-1 seroconversion [No.† (%)]
None	1.1	4.2	+3.1	5/735 (0.7)
Low	14.9	19.7	+4.8	
Modified high	27.7	32.6	+4.9	23/853 (2.7)
High	56.3	43.4	−12.9	59/846 (7.0)

*See definition in Methods section. †Number seroconverted in 6 months/number initially seronegative.

Table 2. Sexual risk behavior category by pattern of illicit drugs used with sex partners (n = 3916).

Pattern of drugs*	Number	Risk category: High n	High %	High or modified high n	High or modified high %
None with sex partners					
No drug use	699	263	37.6	507	72.5
Some drug use	473	161	34.0	329	69.6
Drugs with sex partners					
No poppers, one or more others	480	226	47.1	387	80.6
Poppers only	601	344	57.2	519	86.4
Poppers and one other	808	532	65.8	722	89.4
Poppers and two others	382	274	71.7	359	94.0
Poppers and three or more others	473	403	85.2	464	98.1

*Counts all drugs used with at least one sex partner in past 6 months; combinations may reflect drugs used at the same or different times. Classes of drugs included poppers (volatile nitrites), cocaine, marijuana, upper, (stimulants) downers (sedatives, hypnotics), MDA (methylenedioxyamphetamine), hallucinogens and others.

characteristics did not differ greatly from the total group of needle-users.

The pattern of recreational drugs used was found to vary significantly by number of sex partners as well as with age. At least one drug was used with sex in 47% of men with one partner, in 63% of men with two to nine partners, and in 79% of men with 10 or more partners; among the users the proportion who reported heaviest use (poppers and at least two other drugs) were 19, 22 and 37%, respectively. Among men aged 40 years or more, only 60% used any drugs with sex, while among younger men 73% did; among the older users 68% reported relatively lighter usage (poppers and one other drug at most) compared with only 48% of younger users. Significant but somewhat smaller differences in drug use pattern were also found by level of education.

Controlling for pattern of drugs used, few other characteristics of recreational drug use showed significant additional association with sexual risk. The relatively small group (fewer than 5%) of men who administered drugs or alcohol rectally were more likely to have reported high-risk behaviors than other men. Also, men who used poppers more frequently (weekly or more often) were more likely to have reported high-risk behaviors than less frequent users of poppers but, for other illicit substances, a dose-dependent association with high-risk sexual practices could not be found. Lastly, our data on alcohol consumption, which was limited to data on total use rather than on use during sex, gave no suggestion of association between any alcohol use or frequency of use and sexual risk, once we controlled for use of other drugs.

Multivariate analysis of these data showed that the strong cross-sectional association between pattern of recreational drugs used and high-risk sexual behavior was nearly unchanged after accounting for age and education, frequency of use, and whether drugs were taken rectally or by needle (data not shown).

While the strong cross-sectional association may suggest a causal relationship, it was in order to provide evidence more indicative of a causal association that we chose the *change* in sexual risk level between the two successive 6-month periods as the primary end-point of study. Among men initially in the high-risk category, 66% remained in the high-risk category during follow-up, while 22% of men initially in lower risk categories reported increased risk. Table 3 reports the findings for these outcomes in MACS participants in the two categories of initial risk. For the men classified as high risk prior to entry, the strongest predictor of continuation of high-risk sexual behavior was the number of partners with whom they had engaged in high-risk sex during the 6 months prior to entry. Nevertheless, frequent use of poppers, rectal administration of drugs and the number of other illicit drugs used were all independently associated with a higher rate of failure to reduce risk. Younger men were also more likely to maintain high-risk behaviors. Education level was related to risk continuation in a less straightforward way; men who never attended college had the lowest while men with less than 4 years of college had the highest rates of continuing high-risk behaviors. Finally, there was some evidence that men who injected drugs by needle were more likely to continue their high-risk sexual practices (relative odds = 2.0), but the result was not significant given the small number of men who used needles (n = 43) in this analysis.

For men initially in lower risk categories, increased risk at follow-up was related in a similar pattern although even more strongly to age and education. Change in risk was not independently related to number of sexual partners. Among the drug factors studied, only popper use was significantly associated with increased risk during follow-up, and this association was independent of frequency of popper use.

le 3. Multivariate models for failure to maintain/attain lower sexual risk during 6-month follow-up, 1984–1985*.

	Initial risk category					
	Less than high risk (n = 1686)			High risk (n = 2130)		
Baseline risk factor	n	Odds ratio†	*P* value	n	Odds ratio†	*P* value
Number of high-risk partners						
2–3	(Not applicable)			917	1.0	< 0.001
4–7				609	2.3	
8–19				377	4.8	
20+				227	14.4	
Used poppers with sex						
Total	703	1.6	< 0.001	–	–	(NS)
Used at least weekly	–	–	(NS)	656	1.4	0.004
Number of other drugs (3+ versus 0)	–	–	(NS)	416‡	1.7‡	< 0.001
Rectal administration of drugs	–		(NS)	110	2.0	0.03
Age (years)						
40+	358	1.0	< 0.001	393	1.0	0.006
30–39	819	1.3		986	1.2	
< 30	509	2.0		751	1.6	
Education						
High school or less	203	1.0	0.04	266	1.0	0.01
College, no degree	419	1.8		677	1.7	
College degree	1064	1.5		1187	1.4	

*Behavioral risk factors pertain to the 6 months pre-entry; outcome represents change from that period to subsequent 6-month period (see text for details). †Odds of maintaining high-risk level (if initially high risk) or increasing risk (all others) by multivariate logistic regression: dashes indicate variables whose *P* values were above the cut-off for inclusion in the final models. ‡A linear term relationship was employed; results given are for men who used three or more other drugs compared with those who used none.

Discussion

The present study confirms, in the largest multisite study of sexual behavior in homosexual/bisexual men, both cross-sectional and sequential relationships between recreational drug use and high-risk sexual behavior previously reported in single-city cohorts [14–17]. It should be noted that these findings apply only to the extent to which drug use was associated with occurrence of sexual behaviors considered as having a high risk of transmitting HIV-1; we have not attempted to evaluate whether sexual exposure while under the influence of drugs or alcohol might alter the risk of infection associated with specific behaviors. While such hypotheses might be plausible given the known immunosuppressive effects of alcohol [18] and some recreational drugs [19], they have not been supported by findings from this study.

The associations between recreational drug use and high-risk sexual behavior observed in the MACS cohorts at baseline and 6-month follow-up (1984–1985) were not related to participants' possible knowledge of their HIV infection status, because these test results were not available to the men during this interval [20]. While continuation of high-risk sexual behaviors was clearly related to baseline numbers of sexual partners, recreational drug use (especially the use of volatile nitrites or 'poppers') was independently associated with it in this cohort in the interval 1984–1985. Injection of drugs by needle could not account for a significant portion of high-risk sexual behavior in this cohort because of the rarity with which it was reported (fewer than 2% during the 6-month follow-up) and because the effect seen in these users was modest (relative odds of 2.0 in the initially high-risk group). We have not examined the relationship between recreational drug use and high-risk sexual behavior in the MACS beyond that initial time period because information concerning drug use with sexual partners was collected by only a subset of centers during waves two and three and by none thereafter. This study therefore should not be interpreted as implying that a similar relationship between recreational drug use and HIV-transmitting sexual behaviors still exists today among homosexual/bisexual men of similar socioeconomic status to the MACS cohorts.

Nevertheless, these findings, along with those of other researchers [15,17,21], suggest a rather strong relationship between recreational drug use and high-risk sexual activity among high-socioeconomic-status homosexual/bisexual men during the period of time (1984–1985) when HIV-1 transmission was at its peak among such men [22]. We have previously reviewed the various mechanisms which might explain these observations [15,16], noting that the apparent non-specificity of the relationship across drug classes would argue against any specific psychopharmacological or aphrodisiac effect. The current study modifies our early observations by showing an independent effect of popper use on maintenance of high-risk behavior and a lack of relationship between alcohol use and unsafe sexual practices. It has long been known that volatile nitrites are frequently used by some

men to facilitate receptive anal intercourse [23], presumably because of their ability to relax the smooth muscles of the anal sphincter. Our inability to demonstrate any relationship between alcohol use and high-risk sexual practices may be the result of the near universal use of alcohol in these cohorts and our lack of specific measures of alcohol use with sexual partners. Ultimately, interest in understanding the mechanism(s) linking recreational drug use to HIV-transmitting behaviors may be of practical benefit in the design and implementation of AIDS prevention activities. Although sexual behavior change among homosexual/bisexual men in major cities of the USA has been dramatic, there are still men who participate at least occasionally in unprotected anal intercourse capable of transmitting HIV [24].

Studies aimed at understanding the mechanism(s) which may link sexual and drug-use behaviors in some homosexual/bisexual men are beyond the scope of the MACS, but are being pursued in several individual MACS cohorts as well as in a variety of other cities and populations. Such studies need to examine not only the behavioral phenomena but also their determinants, both contextual and psychological. For example, is the apparent strengthening of the relationship between drug use and sexual behavior seen when drug use *with* sexual partners is measured the result of the settings in which these behaviors take place, the timing of the intoxication, or the effects of drug use on individual judgement in exercising sexual restraint? Are there individual expectations or personality characteristics which predict the effect of drug use on sexual behavior? And how can these findings be applied to interventions aimed at people at greatest risk of HIV infection and AIDS? Furthermore, as our prevention efforts turn increasingly to heterosexual transmission, we need to know whether or not recreational drug use is a significant factor contributing to HIV transmission among heterosexual men and women. Surprisingly, very little is known about the potential rate of non-intravenous drug use as a cofactor in heterosexual behaviors. Recently, Stall and McKusick [25] reported that the combination of alcohol and drug use was a predictor of reported unprotected sexual intercourse among male and female heterosexuals in an exit survey of pick-up bar patrons in San Francisco. This suggests that recreational drug use may play a role in heterosexual as well as homosexual HIV transmission. If the use of recreational drugs is related to the continuance of or relapse to unsafe behaviors, then efforts to 'unlink' sexual and drug-use behaviors might significantly improve AIDS prevention among all adults at risk through sexual activities.

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Appendix

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