

Substance Abuse™

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- Medical Students' Knowledge About Alcohol and Drug Problems:
Results of the Medical Council of Canada Examination 1
Meldon Kahan, MD, CCFP, FRCPC
Deana Midmer, RN, EdD
Lynn Wilson, MD, CCFP, FCFP
Diane Borsoi, MSc

Purpose: To determine knowledge of a national sample of medical students about substance withdrawal, screening and early intervention, medical and psychiatric complications of addiction, and treatment options.

Methods: Based on learning objectives developed by medical faculty, twenty-two questions on addictions were included in the 1998 Canadian licensing examination.

Results: The exam was written by 858 medical students. The average score on the addiction questions was 64%. Students showed strong knowledge of the clinical features of medical complications. Specific knowledge gaps were identified for withdrawal treatment protocols, low-risk drinking guidelines, taking an alcohol history, substance-induced psychiatric disorders, and Alcoholics Anonymous.

Conclusion: Medical students are knowledge-deficient around key learning objectives in addictions. The deficiencies were in areas of basic knowledge that could be learnt with little difficulty.

KEYWORDS. Medical students, knowledge, substance abuse, addictions

- Preliminary Feasibility and Efficacy of a Brief Motivational Intervention
with Psychophysiological Feedback for Cocaine Abuse 9
Angela L. Stotts, PhD
Geoffrey F. Potts, PhD
Gina Ingersoll, BA
Mary Reeni George, PhD
Laura E. Martin, MS

Motivational interviewing (MI) with personalized feedback, particularly related to biological markers of risk or harm, has been found effective for alcohol use disorders, but has not been fully investigated in cocaine use disorders. A randomized, controlled pilot study evaluating the feasibility and preliminary efficacy of a brief MI intervention using EEG/ERP graphical feedback for cocaine abusers was conducted. Treatment-seeking cocaine abusers (N = 31) were randomly assigned to a two-session MI intervention or a minimal control condition. All participants received EEG assessments at intake and post-treatment. Results indicated that the MI intervention was feasible and the subjective impact of the EEG feedback was positive. Significant group differences in percentage of cocaine positive urine screens across the study were found, favoring the MI group; 84.9% for the control group and 62.6% in the MI group, $p < .05$. Further research must determine the specific conditions under which MI is most appropriate and efficacious.

KEYWORDS. Cocaine, treatment, motivational interviewing, feedback

Inhalant Use and Risky Behavior Correlates in a Sample of Rural Middle School Students

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Jessica Legge Mulenburg, PhD
William D. Johnson, PhD

This study found 20.4% of children attending a middle school located in rural Mississippi had used inhalants to “get high,” a figure that is much larger than the national average. Many (3.4%) students reported they had used inhalants on 10 or more occasions. Inhalant use was most associated with being younger, ever smoking, riding with a driver who had been drinking, and being involved in a fight. Nearly twice as many younger students reported usage in our sample compared to other studies. Longitudinal studies need to be conducted to investigate whether use of inhalants is a precursor to other risky behaviors, and subsequent progression to alcohol abuse or illicit drug use.

KEYWORDS. Inhalants, adolescents, drug use, middle school students, rural health

Inhalant Use in Florida Youth

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Lorena M. Siqueira, MD
Lee A. Crandall, PhD

Purpose: To determine (1) the prevalence of use, (2) risk and protective factors for use of inhalants in Florida youth.

Methods: The Florida Youth Substance Abuse Survey 2004 is a comprehensive assessment of youth substance abuse attitudes and practices obtained by sampling youth from sixty-five counties.

Results: The sample consisted of 60,345 students from 6th to 12th grade; ages 10 to 19 + years (mean 14.5 years \pm 4), 53% were female with 59% White, 19% African-American, 16% Hispanic, 5% Native American, 2% Asian and 7% other. Lifetime use was highest among 14 year olds (16.5%), and current use among 13 year olds (16.7%). Females had significantly ($p < .000$) higher rates than males for lifetime (14.2% vs. 12.7%) and current use (5.1% vs. 4.1%). Native Americans had the highest rates of lifetime use (17%) followed by Whites (15%), mixed/other (15%), Hispanics (14%), Asians (13%), and Blacks (9%). The younger the age of first use of alcohol, cigarettes and marijuana, the higher the lifetime and current prevalence of use of inhalants. Inhalant users were more likely to be depressed, acknowledge deviant behavior and skipping school, have lower grades, have siblings and friends who used illegal substances and parents with a history of antisocial behavior ($p < .000$).

Conclusion: Inhalant use may be a marker for adolescents with a high-risk profile for subsequent illegal drug use. Prevention efforts should be directed to these students at an early age.

KEYWORDS. Adolescents, inhalant use, risk and protective factors

Alcohol and Risks for HIV/AIDS Among Sexually Transmitted Infection Clinic Patients in Cape Town, South Africa

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Leickness C. Simbayi, DPhil
Seth C. Kalichman, PhD
Demetria Cain, BS
Charsey Cherry, MPH
Sean Jooste, MA
Vuyisile Mathiti, BA

Alcohol use is prevalent in South Africa and alcohol use may be associated with higher risk for HIV transmission. This paper reports a study of the association between alcohol use and HIV risk-related behavior among 134 men and 92 women receiving sexually transmitted infection (STI) clinic services in Cape Town, South Africa. Participants completed anonymous surveys of demographic information, substance use, and sexual risk behaviors. Results showed that problem drinking was common among STI clinic patients; 58% of men and 28% of women scored above a cut-off of 9 on the Alcohol Use Disorders Identification Test (AUDIT) suggesting possible problem drinking and 46% of men and 19% of women scored above 12 on the AUDIT indicating probable drinking problems. For men, heavier alcohol use was associated with having multiple sex partners in the past month, less condom use, and having a history of sexually assaulting women. Among women, higher scores on the AUDIT were also related to having multiple sex partners as well as a history of exchanging sex for money or materials. The association between alcohol use and sexual risk behaviors in a population at high-risk for HIV transmission demonstrates the need for integrating alcohol risk reduction counseling with HIV prevention counseling among STI clinic patients in South Africa.

KEYWORDS. HIV transmission, alcohol use, South Africa, STI clinic

Gail D'Onofrio, MD, MS
Julie B. McCausland, MD
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We conducted a prospective, observational study of patients presenting to an emergency department with suspected use of a street drug known as "illey" to identify the active ingredient in illey and describe the clinical presentation and outcomes associated with its use. Vital signs, mental status, restraint use, and urine toxicology (UT) results were recorded. Patients were interviewed about drug use patterns and co-ingestants. Fifty-nine patients (89.9% males) with a mean age of 22 years (SD ± 4.37) were enrolled over a 34-month period. UT was obtained in 61% of patients; of these 91.7% tested positive for phencyclidine (PCP). Seventy-eight percent of patients were discharged, (15.3%) required psychiatric evaluation; 3 were admitted, one died in the ED. Patients reported concurrent drug use (54%) and at-risk drinking (50%). PCP is likely the active component of illey. Most patients require observation and supportive care only, however major complications including death may occur.

KEYWORDS. Substance abuse, phencyclidine, street drug, urine toxicology

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Yiming Shao, MD, PhD
J. Brooks Jackson, MD

Background: A prospective observational study of HIV seroincidence among high-risk injection drug users (IDU) was carried out in Guangxi, China. The primary objectives of this study were (1) to estimate HIV seroincidence, (2) to estimate participant retention rate, and (3) to evaluate changes in drug use and sexual behavior over a one year period.

Methods: Five hundred HIV seronegative IDU were enrolled. HIV-1 incidence and retention rates were analyzed as a function of sociodemographic, behavioral, and recruitment variables. Changes in drug use and sexual behavior were analyzed at the baseline, 6-month and 12-month follow-up visits.

Results: At 12 months of follow-up, the HIV-1 incidence rate was 3.1 per 100 person years, [95% CI: (1.6%; 5.2%)] and participant retention rate was 87%. Reported changes in high-risk behaviors over 12-months included significant decreases in the frequency of heroin injection, in direct or indirect sharing of injection equipment, and in the number of sexual partners.

Conclusions: HIV incidence is high among IDU in Guangxi, China despite a self-reported decrease in some high risk behaviors over the course of the study.

KEYWORDS. IDU, HIV incidence, retention, Guangxi, China

Mothball Withdrawal Encephalopathy—Case Report and Review
of Paradichlorobenzene Neurotoxicity

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Raymond Cheong, BS

Robin K. Wilson, MD, PhD

Irene C. M. Cortese, MD

David E. Newman-Toker, MD

Paradichlorobenzene (PDB) is a common household deodorant and pesticide found in room deodorizers, toilet bowl fresheners, and some mothballs. Although human exposure to the compound is generally limited and harmless, PDB in larger doses can produce neurotoxic effects, including a chemical “high” similar to that seen with inhalants such as toluene. Although rare, frank addiction to PDB has been reported, and, in such cases, has been associated with gait ataxia, tremor, dysarthria, limb weakness, and bradyphrenia, in various combinations. In such cases, the adverse neurologic consequences have been presumed to result from a direct toxic effect of this small, organic molecule. We report a case of chronic mothball ingestion where profound encephalopathy with cognitive, pyramidal, extrapyramidal, and cerebellar features appears to have been largely the result of PDB withdrawal, rather than direct toxicity. This case raises important questions about the mechanism of PDB neurotoxicity and possible treatment options for PDB-addicted patients. We propose that in cases with clear clinical deterioration after abstinence, readministration and gradual taper of PDB might be considered a therapeutic option.

KEYWORDS. 2-dichlorobenzene, neurotoxicity syndromes, substance-related disorders, substance withdrawal syndrome, basal ganglia diseases, catatonia

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SUBSTANCE ABUSE

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Abstracts

ABOUT THE EDITOR

Marc Galanter, MD, is Professor of Psychiatry at NYU, Founding Director of the Division of Alcoholism and Drug Abuse at NYU and Bellevue Hospital, and Director of the NYU Fellowship Training Program in Addiction Psychiatry. He is also Division Director at NYU's World Health Organization Collaborating Center, and Director of its national Center for Medical Fellowships in Alcoholism and Drug Abuse. In addition to 267 articles, chapters, and books, he is Editor of the "Textbook of Substance Abuse Treatment."

He attended Albert Einstein College of Medicine where he did his residency in psychiatry. After that he was Clinical Associate at the National Institute of Mental Health, and then an NIH Career Teacher. He later served as President of the Association for Medical Education and Research in Substance Abuse (AMERSA) (1976-7), the American Academy of Addiction Psychiatry (1991-2), and the American Society of Addiction Medicine (1999-2001).

Dr. Galanter's research and teaching interests have focused on addiction treatment, spirituality, and improving treatment systems. His current NIH and foundation-funded studies address family therapy for substance abuse, pharmacologic treatment for narcotic addiction, and self-help modalities. His Center at NYU has prepared curricula for 46 teaching hospitals and affiliated medical schools.

Among his awards are the Gold Achievement Award for innovation in clinical care and the Seymour Vestermark Award for Psychiatric Education, both from the American Psychiatric Association, and the McGovern Award for medical teaching from AMERSA.

Medical Students' Knowledge About Alcohol and Drug Problems: Results of the Medical Council of Canada Examination

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ABSTRACT. *Purpose:* To determine knowledge of a national sample of medical students about substance withdrawal, screening and early intervention, medical and psychiatric complications of addiction, and treatment options.

Methods: Based on learning objectives developed by medical faculty, twenty-two questions on addictions were included in the 1998 Canadian licensing examination.

Results: The exam was written by 858 medical students. The average score on the addiction questions was 64%. Students showed strong knowledge of the clinical features of medical complications. Specific knowledge gaps were identified for withdrawal treatment protocols, low-risk drinking guidelines, taking an alcohol history, substance-induced psychiatric disorders, and Alcoholics Anonymous.

Conclusion: Medical students are knowledge-deficient around key learning objectives in addictions. The deficiencies were in areas of basic knowledge that could be learnt with little difficulty. doi:10.1300/J465v27n04_01 [Article copies available for a fee from The Haworth Document Delivery Service: 1-800-HAWORTH. E-mail address: <docdelivery@haworthpress.com> Website: <http://www.HaworthPress.com> © 2006 by The Haworth Press, Inc. All rights reserved.]

KEYWORDS. Medical students, knowledge, substance abuse, addictions

INTRODUCTION

A number of physician interventions have been shown to reduce substance use and its associated morbidity and mortality. For example, brief advice by physicians has been demonstrated to reduce alcohol consumption, emergency room visits and hospitalizations among problem drinkers.¹⁻³ Medications such as nal-

trexone and methadone are effective in the treatment of alcohol and opioid dependence.⁴⁻⁶

Most research on physician performance has focused on alcohol problems. Physician screening and intervention rates vary with patient gender, specialty, length of office visit, method of measuring physician detection rates and other factors, making generalizations difficult.⁷⁻¹¹ Yet the bulk of research suggests physicians

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perform poorly in screening and counselling patients with alcohol problems. A national population-based survey of 23,000 patients found that physicians asked about and discussed alcohol far less frequently than other health behaviours.¹² Most drinkers with a positive CAGE have not sought help from physicians.¹³ Physicians tend not to rely not on systematic screening but on specific patient characteristics, such as male gender and presenting symptoms.^{14,15} Physician self-report surveys have documented that most do not use formal screening tools,^{16,17} and many do not routinely inquire about alcohol consumption^{18,19} or counsel problem drinkers.²⁰ Women and the elderly are even less likely to receive screening and counselling from their physician.^{10,12,21-23} Patients with milder alcohol problems are less likely to be identified by their physician than patients with more severe alcohol dependence.²⁴ Numerous reviews have called for efforts to improve physician performance in the management of addictions.

The medical school curricula may in part be responsible for this. Several surveys have demonstrated that medical students, residents and physicians have inadequate knowledge about substance use.²⁵⁻²⁸ Physicians commonly report that lack of knowledge and training is a barrier to their detection and management of substance use.²⁹⁻³¹ The amount of curricular time is grossly inadequate compared to the time devoted to problems of similar prevalence.^{32,33} A national survey found that only 56% of residency programs had any required training in addictions; the median number of hours ranged from 3 to 12.³⁴ Another national survey found that only 19% of faculty who taught residents about substance abuse were certified addiction specialists.³⁵

A national survey of practicing primary care physicians in the US, conducted in 1999, found that, compared with other chronic conditions, physicians were less confident of their ability to diagnose substance abuse and more sceptical of the effectiveness of treatment.³⁶ However, if medical curricula on substance abuse have improved over the years, medical trainees may have a greater level of knowledge than practicing physicians. Previous surveys of trainees' knowledge and beliefs about substance use were usually based on a single medical school

or training site with volunteer subjects, using questions testing only a limited scope of knowledge. A MedLine literature search identified one national survey of a representative sample of medical students' knowledge about substance abuse. A survey of 908 family medicine residents in Australia documented relatively good knowledge levels, strong for alcohol and weak for opioids; response rate was 55%.³⁷

As part of five year project to develop and evaluate an enhanced substance abuse curriculum for Ontario's five medical schools (Project CREATE), a set of multiple choice questions was introduced on the 1998 licensing exam of the Medical Council of Canada (MCCQE Part I). This exam, written at the end of medical school, consists of multiple-choice questions and key feature short-answer questions. Its purpose was to measure medical students' knowledge about key aspects of addiction: Withdrawal, screening and early intervention, medical and psychiatric complications, and treatment options.

METHODOLOGY

Learning Objectives. A detailed set of 282 learning objectives was developed, based in part on a review of other medical curricula, such as Project SAEFP and Project ADEPT.³⁸⁻⁴⁰ The objectives covered content areas from the major clinical disciplines. Sixty-eight medical faculty from seven specialties in the five Ontario medical schools then rated each objective according to its importance for medical students in their discipline. A common set of twenty-seven learning objectives was drafted, based on objectives rated as very important by faculty from four or more of the clinical disciplines. This common set included learning objectives on attitudes (3), pharmacology (2), screening and assessment (7), withdrawal (5), benzodiazepine and opioid use (5), physician substance use (4), and overdose (1). Results have been published elsewhere.⁴¹

MCQ's. The common objectives on attitudes were not used for this study because they were felt to be inappropriate for a licensing exam. Based on the remaining common objectives, twenty-six multiple-choice questions were drafted, following the guidelines established

by the Medical Council of Canada. The questions were written and reviewed by medical faculty on Project CREATE, to ensure clarity and relevance. The items, mixed in with other questions, were included in the 1998 MCC licensing examination. The CREATE questions did not count towards the students' score, although students did not know this. For security reasons the MCC used multiple forms of the examination. Eight questions were included on one form of the exam, and nine each on the other two forms.

Data Analysis

The proportion of correct responses and point biserial correlation was tabulated for each question. The 'point biserial correlation' compares the proportion of students who chose the correct answer for those who had high exam scores versus those who had low exam scores. A low correlation indicates that the item is confusing or has more than one right answer. A correlation of 0.10 or higher is considered adequate. 'Proportion correct' is the number of candidates who correctly answered the question. A low proportion of correct responses indicates that candidates found the item difficult.

On reviewing the questions, investigators noted that four of the questions contained more than one choice that could reasonably be considered correct. These questions had a low discrimination index ($-.02$ to $.05$) and the mean correct response rate for these four questions was only 24%. The questions were not included in further analysis.

Questions were grouped into ten subject categories: alcohol and drug withdrawal, medical complications, psychiatric complications, obstetrical complications, prescribing of opioids or benzodiazepines, pharmacology and metabolism, screening and low-risk drinking guidelines, counselling and treatment, brief interventions for problem drinkers, and physician impairment. Two of the investigators categorized each question independently.

RESULTS

Each of the 858 candidates writing the MCCQE Part I completed one of the three

forms of the exam. The three versions were completed by 293, 299 and 266 students, respectively. The average score on the additions questions was 64.5%, with a range of 27% (cannabis and psychosis) to 92% (Fetal Alcohol Syndrome). As shown in Table 1, high average scores (above 70%) were obtained for four categories of questions: pharmacology, opioid prescribing, and medical and obstetrical complications. Students showed strong knowledge (correct responses 70% or above) on several items relating to the clinical features of specific medical complications, including delirium tremens, heroin overdose, fetal alcohol syndrome, opioid withdrawal, and Wernicke's encephalopathy (see Table 2).

Alcohol and drug withdrawal, counselling and treatment and physician impairment had mean scores between 60 and 69%, and problem drinking, low-risk drinking guidelines and psychiatric complications had scores below 60%. Table 3 contains an analysis of incorrect MCQ items ("distracters") chosen by 25% or more of

TABLE 1. Mean scores by category

Category (number of items)	Mean score (range) (%)
Pharmacology (1)	79
Medical complications (4)	74 (54-91)
Opioids and chronic pain (2)	74 (72-76)
Obstetrical complications (3)	72 (61-92)
Motivational interviewing, treatment options (2)	66 (64-68)
Alcohol and drug withdrawal (4)	62 (38-84)
Physician impairment (1)	60
Problem drinking (1)	52
Screening, low-risk drinking guidelines (2)	41 (30-49)
Psychiatric complications (2)	40 (27-53)
Mean score	64

TABLE 2. Knowledge strengths (70%+ correct response rate)

Item	Correct response
Clinical features of fetal alcohol syndrome	92%
Clinical features of delirium tremens	91%
Clinical features of opioid withdrawal	84%
Clinical features of heroin overdose	80%
Alcohol metabolism	79%
Opioids and chronic pain	72%
Clinical features of Wernicke's	70%

TABLE 3. Knowledge gaps (distracters chosen by 25%+; correct responses chosen by < 60%)

Withdrawal treatment protocols	Distracter
Symptom-triggered benzodiazepine treatment of alcohol withdrawal	33% chose scheduled, small doses
Gradual outpatient tapering for benzodiazepine withdrawal	58% chose 2-week taper for woman on long-standing therapeutic dose
Screening and early intervention	
Low-risk drinking guidelines	48% chose 2-3 standard drinks/day for women (Canadian guidelines: 9/week, 2/day)
Heavy drinking and hypertension	Only 49% recommended that a hypertensive patient try reducing drinking to lower blood pressure
Alcohol history	32% stated physicians most likely to miss alcohol problems in men; only 30% recommended asking about maximum daily consumption
Medical complications	
Interpretation of hepatic transaminases	30% chose acetaminophen toxicity as cause of elevated ALT in Hepatitis C +ve patient
Psychiatric complications	
Alcohol and depression	Only 53% recommended alcohol treatment for a heavy drinker with refractory depression
Cannabis and psychosis	Only 27% identified cannabis use as cause of worsening psychosis in a schizophrenic patient
Treatment options	
AA	28% thought being sober was a requirement for attendance
Physician impairment	28% felt informal advice and a suggestion to attend AA was an adequate intervention for an impaired colleague

the sample, and correct items chosen by less than 60% of the sample. Specific knowledge gaps were identified for withdrawal treatment protocols (alcohol and benzodiazepines), screening and early intervention (low-risk drinking guidelines, alcohol and hypertension, alcohol history), interpreting hepatic transaminases, substance-induced psychiatric disorders, treatment options (AA), and interventions for impaired physicians.

DISCUSSION

This study was undertaken to measure the knowledge of medical students about addictions, in order to develop an enhanced curriculum on substance abuse. The study employed a fully representative, national sample of 858

medical students writing their licensing exam. The addiction-related questions were based on learning objectives rated highly by medical faculty from the major clinical disciplines at Ontario's five medical schools.

Students did well in recognizing clinical features of various syndromes. Specific knowledge deficiencies were identified for management of alcohol and benzodiazepine withdrawal. Students were also weak on primary and secondary prevention of alcohol problems, and lacked knowledge about AA and interventions for impaired physicians.

The questions were part of the national exam in the fall of 1998, and, data access and analysis were delayed because of administrative difficulties. Consequently, a limitation of the study is that medical students may have improved their knowledge base in the intervening years, although to our knowledge no new addictions curriculum has been introduced into any of the Canadian medical schools. We were not able to organize a follow-up survey. Another limitation is that students' level of knowledge on a multiple choice exam does not necessarily reflect their actual clinical skills and behaviour.

This study reinforces other studies and reviews that have concluded that medical education is inadequate in addictions. For example, Miller³³ states, "Curricula lack sufficient instruction and experiences in addiction medicine throughout all years of medical education. Programs that have successfully changed students' attitudes and skills for treatment of addicted patients continue to be exceptional and limited in focus rather than the general practice in US medical schools."

There is reason for optimism, however. Evidence from controlled trials suggests that both didactic and skills-based educational interventions are effective in improving the performance of medical students and trainees,⁴²⁻⁴⁷ and faculty development programs are effective in improving faculty's knowledge, attitudes, clinical skills and involvement in teaching.^{48,49}

Information about medical students' deficiencies in knowledge has been useful in planning Project CREATE. For example, CREATE developed seventeen educational modules for use by medical students and faculty. The modules contain evidence-based low-risk drinking

guidelines, simple instructions for providing brief advice to problem drinkers, a review of treatment options for substance users, a review of the simplest and most effective screening strategies, and clear clinical protocols for treating withdrawal. CREATE has had only modest success in introducing the modules into the medical curricula. However, the educational materials have been adapted and disseminated through several initiatives in continuing medical education.

CONCLUSION

Students knew the clinical features of specific addiction-related medical and obstetrical complications. However, their knowledge about management of withdrawal and treatment of addiction was weak. They also had low levels of knowledge of psychiatric complications, screening and low-risk drinking guidelines, problem drinking, and physician impairment.

Consequently, medical schools should assign high priority to addressing these deficiencies, given the increasing burden of illness caused by substance abuse, and the positive impact of physician interventions. For the most part, these deficiencies represent discrete and straightforward sets of clinical knowledge and skills that students could learn with little difficulty.

Good curricular materials and educational programs exist for medical students, resident and faculty in various clinical disciplines.⁵⁰⁻⁵⁶ Federally funded programs have been successful in increasing electives and teaching hours on alcohol.⁵⁷ What is needed now is education and political action to ensure that medical programs are responsive to one of the great health problems of our time.

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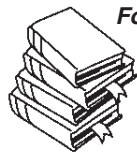
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Preliminary Feasibility and Efficacy of a Brief Motivational Intervention with Psychophysiological Feedback for Cocaine Abuse

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ABSTRACT. Motivational interviewing (MI) with personalized feedback, particularly related to biological markers of risk or harm, has been found effective for alcohol use disorders, but has not been fully investigated in cocaine use disorders. A randomized, controlled pilot study evaluating the feasibility and preliminary efficacy of a brief MI intervention using EEG/ERP graphical feedback for cocaine abusers was conducted. Treatment-seeking cocaine abusers (N = 31) were randomly assigned to a two-session MI intervention or a minimal control condition. All participants received EEG assessments at intake and post-treatment. Results indicated that the MI intervention was feasible and the subjective impact of the EEG feedback was positive. Significant group differences in percentage of cocaine positive urine screens across the study were found, favoring the MI group; 84.9% for the control group and 62.6% in the MI group, $p < .05$. Further research must determine the specific conditions under which MI is most appropriate and efficacious. doi:10.1300/J465v27n04_02 [Article copies available for a fee from The Haworth Document Delivery Service: 1-800-HAWORTH. E-mail address: <docdelivery@haworthpress.com> Website: <<http://www.HaworthPress.com>> © 2006 by The Haworth Press, Inc. All rights reserved.]

KEYWORDS. Cocaine, treatment, motivational interviewing, feedback

INTRODUCTION

Cocaine use continues to be a profound problem, with large individual and societal costs, and remains difficult to treat. Motivating cocaine abusers to change their behavior is a major challenge. However, recent advances in behavioral treatments of cocaine abuse and de-

pendence have resulted in improved cocaine use outcomes. For example, contingency management within the context of a community reinforcement approach has been one of the most successful cocaine treatments, presumably by influencing external motivation for change.^{1,2} References to internal or intrinsic motivation as a mechanism by which behavior change can oc-

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cur, however, have been notably missing in the cocaine treatment literature. Studies of other substances have documented relationships between internal motivation and outcome. In the smoking cessation literature for instance, Curry found that with women who had quit smoking during pregnancy, higher levels of intrinsic relative to extrinsic motivation at baseline were associated with sustained smoking abstinence postpartum.³ Intervention components targeting more individual, internal motivational processes can be developed and may further improve cocaine treatment outcomes.

Objective, normative, and personalized feedback designed to increase internal motivation for change has been used as a primary intervention, as well as an adjunct to more extensive behavioral treatments. In a review of the role of feedback in behavior change, DiClemente et al.⁴ make a distinction between “Generic” and “Personalized” feedback. Generic feedback consists of relevant information that is true for the entire population or subpopulation to which the client belongs (e.g., information on the heart risk of certain dietary behaviors, or the neurological effects/precursors of drug use). By contrast, personalized feedback is individualized in that it is based on personal information acquired through various individual assessment procedures (e.g., providing information on personal risk for certain problems as a result of genetic, biological, or psychosocial assessment). Providing feedback, particularly about biological markers of risk or harm, may be a useful way to motivate or reinforce attempts to change behavior, particularly when compared to normative data.⁵

In the area of addiction, feedback interventions have primarily been developed for the treatment of tobacco and alcohol dependence. In a recent review of randomized trials of feedback interventions for smokers, McClure⁶ reports that there is significant evidence for the efficacy of biological feedback (e.g., CO & cotinine levels; genetic susceptibility to lung cancer) for increasing abstinence or attempts at abstinence from tobacco. Similarly, feedback interventions for alcohol dependence have produced generally positive results. For example, two studies in which personalized biological feedback, such as liver function results, peak blood alcohol estimates, neuropsychological

data and other results from an assessment session, was provided in an empathic therapeutic style, resulted in significant reduction in drinking behavior immediately and at 12-month follow-up.^{7,8} Although there is a significant need for additional research on feedback interventions (e.g., determining which types of feedback are most influential in producing behavior change), the evidence to date indicates that across different health behaviors, personalized feedback, particularly novel and sophisticated biological/physiological feedback, has the potential for increasing the effectiveness of our interventions over standard, generic ways of providing behavior change information.⁴

The manner in which feedback is delivered may be critical to its effectiveness. Motivational Interviewing (MI), a brief treatment approach also designed to increase internal motivation for change, is conducted using an objective, non-judgmental, and empathic style and has commonly been used in conjunction with feedback interventions.⁸⁻¹⁰ Significant evidence supporting the efficacy of MI or brief motivational enhancement interventions delivered as primary or preparatory (prior to more intensive behavior therapy) treatments for alcohol and drug abusers has been indicated in two meta-analytic studies.^{11,12}

For cocaine abuse/dependence, two studies have tested MI with personalized feedback as an adjunct or preparatory treatment.^{13,14} Both studies indicated significant positive effects, but only for a subgroup of patients with lower motivation for change. The feedback component, particularly in the Rohsenow et al. study, was fairly extensive and included results from neuropsychological assessment, but neither study included biological/psychophysiological testing nor corresponding feedback component.

One biological marker found in substance abuse disorders is a reduction in amplitude of the P300 component of the event-related potential (ERP).^{15,16} The ERP is derived from the electroencephalogram (EEG) by averaging fixed-length segments of EEG time-locked to an event or interest (e.g., a task-relevant tone). The classic P300 is a positive voltage deflection over the centroparietal scalp usually elicited by rare, task-relevant stimuli, but seen in studies of many cognitive functions, including selective

attention and working memory.¹⁷⁻¹⁹ The P300 has been associated with multiple cognitive operations and attributed to activity in multiple neural areas.²⁰ One way to conceptualize the P300 is as originating in multiple brain areas and indexing general information processing or cognitive efficiency.

The amplitude of the P300 is often reduced in a variety of mental disorders, including substance abuse disorders.²¹ The great majority of the substance abuse related P300 findings come from studies of alcoholism. The P300 is generally seen as stably reduced in patients with alcoholism.^{22,23} P300 amplitude reduction has also been demonstrated in groups at-risk for alcoholism (e.g., sons of alcoholic fathers), and reduced P300 amplitude is sometimes viewed as a phenotypic marker for alcoholism susceptibility.²⁴⁻²⁶ While the reduction is generally more pronounced in males, it has been observed in both sexes.²⁷ It has been suggested that the visual P300 may be a more reliable index of alcoholism risk than the auditory P300.¹⁶

The P300 has been studied less frequently in groups abusing substances other than alcohol. Studies that have examined P300 in substance abuse other than alcohol have found a similar, sustained P300 reduction. For example, abusers of cocaine and/or heroin showed reduced P300 amplitudes during detoxification,²⁸ during the first six months following detoxification,¹⁵ and after at least six months of abstinence,²⁹ although there is some suggestion that the P300 may recover with continued abstinence.³⁰

The purpose of this pilot study was to evaluate the feasibility and preliminary efficacy of a MI intervention, including an EEG-based psychophysiological feedback (ERP) component, for treatment-seeking cocaine abusers. It was our hypothesis that MI with informative biological feedback, based on an individual's own brain activity, has the potential to heighten the impact of messages conveying harmful effects of cocaine use, and provide an impetus for behavior change. Specific research questions included: (1) Will cocaine patients find biologically-based ERP feedback relevant and acceptable? (2) Can ERP data be presented in a way that cocaine patients can understand? (3) Will the ERP feedback have an impact on motiva-

tional process variables and cocaine use outcomes?

METHODS

Participants and Procedures

Thirty-one males seeking outpatient treatment for cocaine use were recruited via community advertising for participation in a research treatment program at the University of Texas-Houston (UT). The UT Treatment Research Clinic is a university medical center based research facility and has been described elsewhere by Elk et al.³¹ To be included in this study, participants had to be English-speaking adults between the ages of 18 and 50, and able to participate in four weeks of outpatient treatment research. The mean age of the participants was 42.5 years (SD = 7.3), with an average of 12.5 years of education. Approximately 22% of participants were married. All participants in this program underwent intake evaluation of medical and psychiatric status prior to inclusion in the study. This included an electrocardiogram, a blood pressure reading, and a psychiatric evaluation. Participants of any age and race who were judged to be in generally good physical and psychiatric health (except for possible acute drug-related problems), and who met cocaine abuse or dependence criteria, determined by the Diagnostic and Statistical Manual of Mental Disorders [DSM-IV: 32], were included. Their mean number of years of cocaine use was 12.6 (SD = 5.9), and mean number of days they used cocaine in the 30 days prior to intake was 14.4 (SD = 8.8). The majority used cocaine via smoking (93.5%). Mean number of alcohol use days was 7.3 (SD = 9.0).

Participants were randomized to either the Motivational Interviewing with ERP Feedback (MI; $n = 17$) or Cocaine Abusing Control (CC; $n = 14$) condition following intake evaluation. Both groups attended the UT Treatment Research Clinic twice weekly for two weeks, during which they met with a research assistant who collected a urine sample, checked their vital signs (blood pressure, pulse, and weight), and administered self-report forms. Posttreatment assessment was conducted at 1-week

post-study by clinic staff blind to study condition. Urine toxicology screening on all urine samples occurred in an on-site analytical neurochemistry laboratory. Quantitative urine benzyolecgonine (BE) was conducted on urine specimens obtained at each visit, including baseline and posttreatment. Reimbursement for patient time and effort expended in purely research aspects of the study was provided: Intake and end of study evaluations (\$20 each), and clinic visits (\$5 each).

Since cocaine use may have an effect on the ERP, additional participants for a third, non-patient control group (NP; $N = 18$) were recruited for comparison on ERP data only. NP men ($n = 15$) and women ($n = 3$) had a mean age of 35 years and were determined to have no substance abuse history. NP group members participated only in the EEG recording procedures, i.e., had no part in the MI intervention (see EEG Recording).

Measurement

Baseline data on demographics, current and past cocaine use and diagnosis, and motivation for change were obtained using self-report forms administered by a research assistant. Demographic information was gathered using an author-constructed questionnaire. Current and past diagnostic information was obtained using the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders [DSM-IV: 32] per the Structured Clinical Interview for DSM-IV [SCID: 33]. SCID assessments were conducted by master's and doctoral level clinicians who were trained by experienced interviewers using standardized training videotapes from Biometrics Research, NY. As recommended, a series of practice interviews was performed to enhance interrater reliability before beginning interviews with study participants. Provisional SCID-based diagnoses were confirmed by the study psychologist or psychiatrist.

The Addiction Severity Index [ASI: 34] was administered during intake and posttreatment assessments to assess substance abuse variables. The ASI also was used to provide feedback on severity of difficulties in several life domains, i.e., medical, legal, employment, psychosocial, psychiatric. In each area a com-

posite score ranging from 0 (no problem) to 1 (most severe problem) was computed.

Drug use was assessed objectively at each clinic visit during treatment, as well as post-treatment, via quantitative urine benzyolecgonine. Urine toxicology screening on all samples occurred in an on-site analytical neurochemistry laboratory.

Motivation to change was assessed using the University of Rhode Island Change Assessment Scale [URICA: 35], a 28-item self-report scale modified for cocaine, which operationally defines four theoretical stages of change: precontemplation, contemplation, action, and maintenance. Based on this measure, participants were separated into high vs. low motivation groups based on Contemplation (C) and Action (A) subscale scores.^{13,14} Those with scores higher on the C subscale relative to the A subscale were classified as Lower Motivation (LM), while those with relatively higher A than C subscale scores were placed in the Higher Motivation (HM) group. Equal C and A scores were coded as HM. In addition, the Processes of Change Questionnaire,³⁶ a self-report instrument measuring the 5 experiential and 5 behavioral processes of change on a 5-point Likert scale, was used to assess participants' level of cognitive, affective and behavioral strategies engaged in to promote abstinence from cocaine. The Decisional Balance Scale for cocaine,³⁷ a 12-item assessment, was included as a measure of participants' perceived pros and cons of using cocaine, which are important indicators of movement through the early stages of change.³⁸

Finally, to assess patient acceptability and feasibility we administered an author-constructed End of Treatment Survey (ETS) to all patients in the MI condition. The ETS is a self-report measure of patient's perceptions of the treatment (e.g., Was it logical? Will it help? Would they recommend it?), and was delivered after the final MI session. Specific items pertaining to the ERP feedback were completed by both patients and their therapists, including how interesting, confusing, and helpful they found this component.

EEG Recording

All cocaine patients and NP controls participated in two 2-hour EEG recording sessions be-

ested participants could call at the end of study for their results.

Non-Patient Controls (NP)

The non-patient controls received no intervention or meetings with an RA, but simply participated in two EEG acquisition sessions at equivalent intervals, approximately two weeks apart. NP participants were used only to compare P300 effects, and thus not included in outcome assessment.

Data Analysis

Univariate and chi-square procedures tested MI versus CC group differences on baseline sociodemographics and substance use history. Acceptability and subjective impact of the EEG feedback used in the MI condition were analyzed descriptively. Means and standard deviations from the End of Treatment Survey are reported. Repeated measures analysis of variance (ANOVA) procedures were used to determine the effect of treatment (MI or CC) and time (pre- and post-treatment) on the Experiential and Behavioral processes of change and the pros and cons of cocaine use. Only subjects with data at both timepoints ($n = 27$) were included in these analyses. Group effects on the mean percentage of cocaine-positive urine screens and proportion of self-reported cocaine use days during the 3-week treatment and post-treatment period were evaluated using (ANOVA) procedures. Chi-square analysis was used to assess for group differences on urine screen outcome at the post-treatment timepoint. Repeated measures ANOVA procedures with Group (MI, CC, NP) and Session (Intake, Followup) as the factors were used to detect differential changes in P300 amplitude, measured over centroparietal electrodes between 320-420 ms post-stimulus, from pre- to post-treatment. Sample size varies slightly across analyses due to missing or non-useable subsets of data.

RESULTS

Initial comparisons of sociodemographic and substance history data revealed no signifi-

cant differences between the MI and CC conditions. Age, education, gender, race, employment, marital status, cocaine diagnosis, number of cocaine use days in the past 30, and years of cocaine use were comparable between the two cocaine-using groups.

Acceptability and Subjective Impact of EEG Feedback

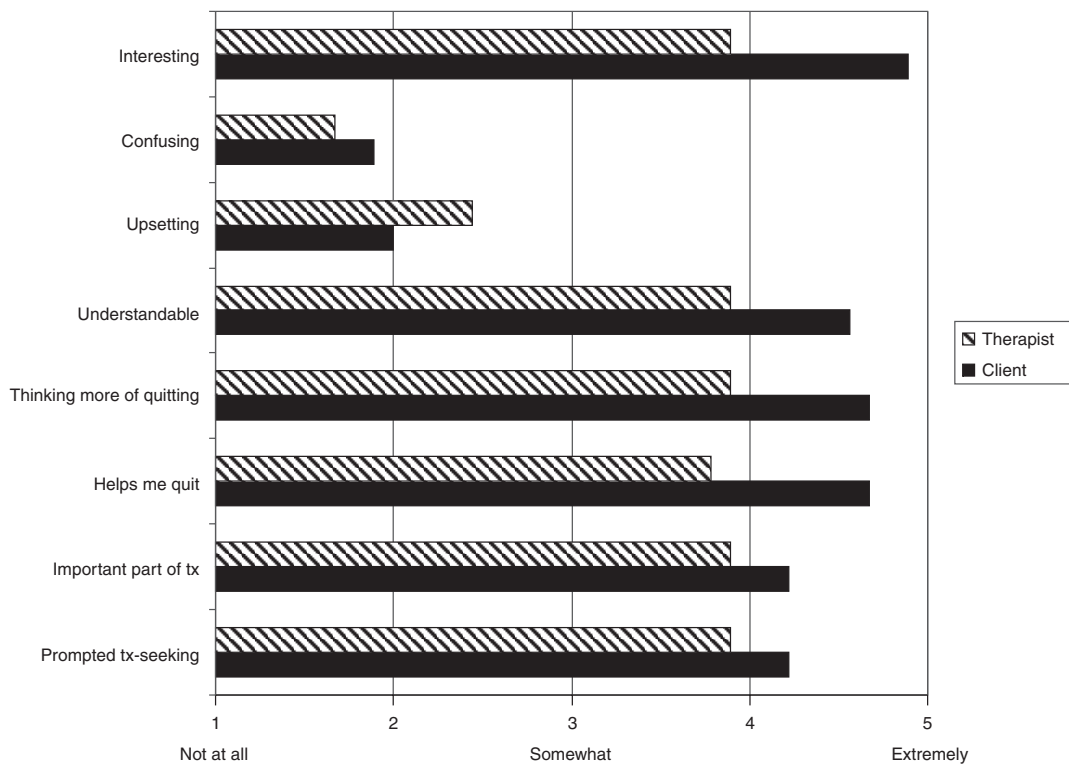
The intervention as a whole was well-received by cocaine patients. Three general items were asked regarding the MI intervention on an 11-point scale (0 = not at all; 10 = extremely). Overall, patients rated the intervention as logical for their drug problem ($M = 7.11$; $SD = 2.03$); were confident that it could help them with their cocaine problem ($M = 6.89$; $SD = 2.03$); and would recommend this type of treatment to a friend with a cocaine or other drug problem ($M = 7.78$; $SD = 2.54$). Although 55.6% of patients agreed that this treatment may be all they needed to help change their drug use, 89% reported that they planned to seek further treatment.

Specific evaluations regarding the MI-based individual therapy and the ERP procedures and feedback were sought. When assessed relative to one another, 71.4% said that the individual therapy and 28.6% said that the ERP procedures and information about their brain functioning was more helpful. Evaluation items specifically related to the ERP feedback component by both patients and therapists were very positive (Figure 2). Overall, clients thought the ERP feedback was interesting and reported that it helped them to think more seriously about quitting cocaine and to seek further treatment. Most rated the ERP information as "not at all" confusing. Therapist ratings were comparable, although slightly lower. All subjects recommended that the ERP information and "brain picture" be kept as a regular part of cocaine treatment.

Motivational Process Measures

A significant treatment \times time effect was found for mean level of behavioral processes, $F(1, 25) = 4.00, p \leq .05$, but not for the experiential processes of change, $F(1, 25) = .39, p \leq .39$. Subjects who received the MI intervention sig-

FIGURE 2. Summary ratings of the acceptability, comprehensibility, and impact of the ERP feedback as reported by the MI-treated cocaine patients and their therapists.



nificantly increased their use of behavioral processes from pre- to post-treatment [$M = 2.76 (.4)$ to $M = 3.12 (.6)$] relative to those assigned to the CC group [$M = 2.99 (.8)$ to $M = 3.03 (.8)$]. Although the MI intervention group slightly increased their report of cons for cocaine use [$M = 2.09 (.9)$ to $M = 2.29 (.9)$] and the CC group decreased their reported cons [$M = 2.24 (.9)$ to $M = 1.87 (.9)$], a statistically significant effect was not found, $F(1, 25) = 2.5, p < .12$. No differential change by group was found for the pros of cocaine use, nor for the URICA measure of motivation.

Cocaine Use Outcomes

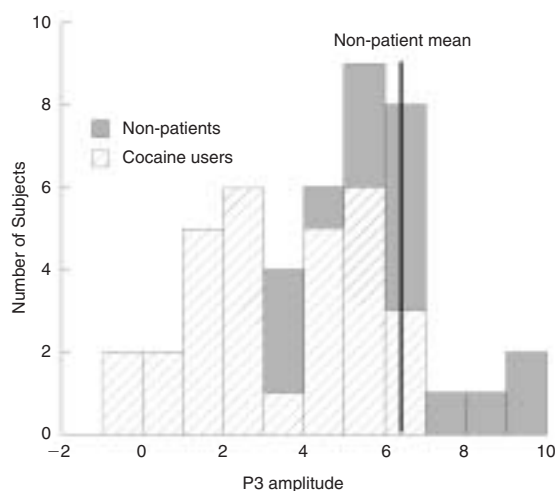
Analysis of urine drug screens across treatment and post-treatment periods revealed significant group differences favoring the MI group. The MI group submitted a mean of 62.6% cocaine-positive urine samples across the five treatment and post-treatment timepoints, while the CC group averaged 84.9%, $F(1, 29) = 4.7, p < .05$. Self-report data of cocaine

use failed to differentiate the 2 conditions. At the post-treatment timepoint alone, 56.3% of the MI group and 84.6% of the CC condition submitted a urine sample that was positive for cocaine, although this difference failed to meet statistical significance. A treatment by motivation level interaction, reported in two larger studies,^{13,14} was not detected; however, baseline level of motivation based on the URICA was a strong predictor of reported cocaine use, $F(1, 30) = 12.1, p \leq .002$. Patients in the higher motivation group ($n = 10$) reported using cocaine on 16.5% of days, while those with lower motivation ($n = 21$) reportedly used cocaine on 41.1% of days.

P300 Outcomes

Thirty cocaine users and 16 non-patients provided useable data at intake. In these data there was a main effect for Group indicating that the non-patients had a significantly larger P300 than the cocaine users, $t(44) = 4.31, p < .001$ (Figure 3). In the participants who sup-

FIGURE 3. Distribution of P300 amplitudes at initial test in the cocaine users (both those who subsequently underwent the MI intervention and the cocaine-using controls) and in the non-patients showing the usual P300 reduction in the cocaine-using group. The line marked "Non-patient mean" shows how many patients showed a P300 reduction and thus could have a feedback instrument showing abnormal brain activity.

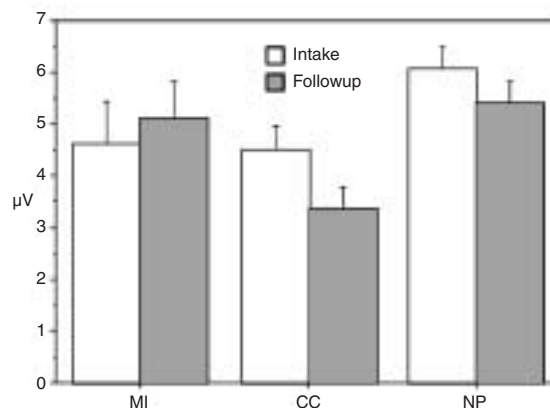


plied useable P300 data at both intake and post-treatment (MI = 12; CC = 13; NP = 16), there was a Group \times Session interaction, $F(2, 38) = 8.97, p < .02$, indicating a smaller P300 at post-treatment in the CC and NP groups, but not in the MI group (Figures 4 and 5). Thus, non-patients and cocaine control participants, but not motivational interviewing participants, demonstrated a reduction in P300 amplitude from pre- to post-treatment consistent with reductions that have been seen both from early to late trials within a session,³⁹ and initial to later recording sessions separated by days or weeks.⁴⁰

DISCUSSION

This study developed and tested the acceptability, subjective impact, and preliminary efficacy of a brief motivational interviewing and psychophysiological (ERP) feedback intervention for the treatment of cocaine abuse. Overall, treatment-seeking cocaine patients found the intervention to be engaging, thought-provoking, and useful with their goal of cocaine abstinence, as assessed by self-report. Although the

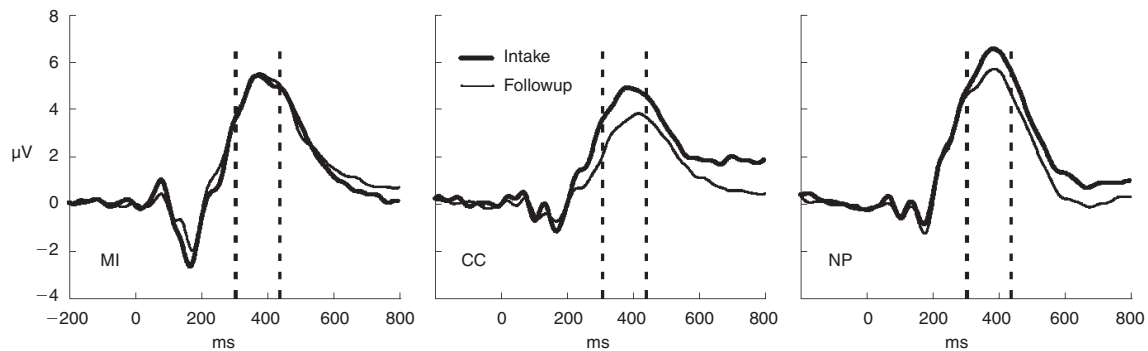
FIGURE 4. Group \times Session interaction plot showing the reduction in P300 amplitude at retest in the Cocaine Control (CC) and Non-Patient (NP) groups but not in the Motivational Interviewing (MI) group.



individual therapy was valued more highly, cocaine patients reported that the graphical ERP feedback was interesting and important, increased their thinking about quitting cocaine, and further helped in their attempts to quit. Therapists concurred with patient reports. Psychophysiological measures are complex and required significant simplification for feedback purposes. Nonetheless, this first attempt at simplification (colored graphical representation) appeared successful in that both therapists and clients indicated via rating scale and anecdotally that the ERP feedback was understandable and not confusing. Thus, the MI intervention incorporating psychophysiological feedback appears acceptable and feasible with treatment-seeking cocaine abusers.

In addition, cocaine patients who received the MI intervention appeared to use cocaine less frequently during and immediately post-treatment than the cocaine control group, according to biological samples. MI participants also significantly increased their use of behavioral change processes and slightly increased their endorsement of the negative aspects of cocaine use while the cocaine control group members decreased their endorsement of cocaine's negative aspects. Notably, brief MI interventions in other populations have resulted in similar findings.^{14,41} For example, at post-treatment, pregnant smokers who received MI reported slightly higher importance of the cons of smoking, but the level of cons for women in the

FIGURE 5. P300 waveforms for the Motivational Interviewing (MI), Cocaine Control (CC), and Non-Patient control (NP) groups with the P300 analysis window marked, showing the lack of P300 amplitude reduction at retest in the MI group.



control group decreased significantly. This suggests in the absence of active treatment, motivation for abstinence may decrease across time as less importance is placed on the negative aspects of substance use.⁴¹ Low endorsement of cons has been associated with no or low intention for behavior change (i.e., precontemplation stage⁴²).

The psychophysiological data, in addition to providing novel feedback, revealed interesting differences among the groups. On average, cocaine abusers (MI plus CC) had smaller P300 amplitudes than the non-drug-using controls (NP), supporting its utility as a feedback instrument. Additionally, group differences emerged in P300 change from pre- to post-treatment. When attending to visual stimuli, both the non-patient and cocaine control groups showed smaller P300s at retest indicating habituation or lowered engagement in the attention task on the second exposure. This is usual and has been documented in both early to late trials within a session,³⁹ and initial to later recording sessions separated by days or weeks.⁴⁰ Cocaine patients who received the MI intervention, however, responded differently, not showing the usual retest P300 reduction. Brief MI therapy with feedback about potential neural processing abnormalities may have led cocaine patients to pay more attention and be more engaged in the attention task during their second exposure. This finding suggests higher importance placed on ERP task performance by the MI participants, and may represent an indirect measure of motivation to change. Of course, it is not clear

how increased task engagement or increased motivation to enhance performance on a laboratory task relates to cocaine use, if at all. However, the MI with ERP feedback did have an impact on P300 amplitude at re-test, indicating that cocaine users who received this brief intervention were motivated to do something differently. Future studies need to replicate and explore this finding to understand its potential relationship to drug use and/or to determine how these feedback procedures might be used to affect behavior change.

Taken together, results indicate that the intervention concept is feasible, acceptable and has potential for impact on cocaine abuse. The concept can be extended and improved upon in several ways. The ERP feedback can be viewed as a “prototype” for physiologic feedback, although there are a number of advantages to using this particular instrument. Namely, ERP assessment: (1) is considerably more cost-effective than PET, CT, or MRI scans; (2) is less invasive than some alternative imaging methods (e.g., PET and CT require radiation exposure); and (3) provides immediate and graphical output. However, other brain imaging instruments and techniques may offer equally or perhaps more powerful possibilities for feedback interventions. Substantial interest and increased prevalence of imaging studies in recent years will expand our knowledge of acute and chronic drug effects on neurobiological systems, which will offer more precise and meaningful data for feedback. In particular, identifying measures of brain functioning that are

sensitive to changes in use or related to abstinence patterns would potentially allow for more influential “change feedback,”⁴ particularly if positive changes related to abstinence could be demonstrated.

Although brief interventions have been found to impact alcohol and smoking cessation, their efficacy and appropriate use in cocaine use disorders is unclear. Low intensity interventions may be insufficient for fairly severe cocaine dependent individuals such as those in the current sample. It could be that the appropriate role of MI and feedback for cocaine abuse is that of a preparatory treatment for patients of higher severity, to increase motivation for treatment participation. Findings supporting this role have been documented in the few studies of MI with cocaine abusers,^{13,14} as well as studies of other substances.⁴³ However, of note is a recent report by Bernstein et al.,⁴⁴ documenting positive effects of a brief, one-session MI intervention for cocaine users screened at a routine medical visit. It is likely, though, that interventions for chronic and severe cocaine abuse will need to be comprehensive in nature with multiple components. Results from the current study and others suggest that MI should be considered a promising component.

Results from this pilot study must be interpreted with caution as its primary purpose was to assess feasibility, acceptability and preliminary promise of effect. Weaknesses include: (1) small sample size; (2) short follow-up period; (3) lack of evaluation of the MI without physiological feedback and physiological feedback without MI to independently assess those components; and (4) lack of complete balance between the non-patient and cocaine-using groups (e.g., the cocaine users were all male while the non-patients included three females). With regard to ERP procedures, an audio-visual selective attention design was used to elicit a P300, which is an unnecessarily complex design. A simple visual selection or oddball design would reliably elicit a P300. Additionally, the data acquired here used a 128-channel neuroscience research ERP system with more electrodes (and thus higher cost) than a much less expensive 20-30 channel system needed to create P300 topographic maps. Further study with a larger number of participants, including women, and fully separated control conditions

is needed before firm conclusions can be made regarding the efficacy of MI and ERP feedback for cocaine abusers. Overall, however, the intervention concept is interesting, feasible, and acceptable to cocaine abusing patients, and preliminary data support further research of MI with personalized biological feedback in cocaine-using populations.

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Inhalant Use and Risky Behavior Correlates in a Sample of Rural Middle School Students

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ABSTRACT. This study found 20.4% of children attending a middle school located in rural Mississippi had used inhalants to “get high,” a figure that is much larger than the national average. Many (3.4%) students reported they had used inhalants on 10 or more occasions. Inhalant use was most associated with being younger, ever smoking, riding with a driver who had been drinking, and being involved in a fight. Nearly twice as many younger students reported usage in our sample compared to other studies. Longitudinal studies need to be conducted to investigate whether use of inhalants is a precursor to other risky behaviors, and subsequent progression to alcohol abuse or illicit drug use. doi:10.1300/J465v27n04_03 [Article copies available for a fee from The Haworth Document Delivery Service: 1-800-HAWORTH. E-mail address: <docdelivery@haworthpress.com> Website: <http://www.HaworthPress.com> © 2006 by The Haworth Press, Inc. All rights reserved.]

KEYWORDS. Inhalants, adolescents, drug use, middle school students, rural health

INTRODUCTION

Inhalant abuse can lead to a number of consequences ranging from short term confusion, to cognitive abnormalities, and even death.¹ Reports show that 12.1 percent of high school students had ever sniffed glue, breathed the contents of aerosol spray cans, or inhaled any paints or sprays to get high.² Inhalant use among middle school adolescents is slightly higher, with reported usage ranging from 11.7 percent for 6th graders to 16.9 percent for 8th graders.³ Of special interest is the apparent sudden rise in inhalant use, and other risky behaviors that might be a warning sign for the dangerous activity.

The purpose of this study was to determine the prevalence of a history of using inhalants

and investigate other risk factors that may be associated with inhalant use in a sample of rural adolescents. The school we studied is located in an area comparable to the entire population of the Mississippi Delta region—high poverty rate, low high school graduation rate, and a general lack of resources. It is in a county where 42.9 percent of the children live in poverty, the high school graduation rate is only 65.0 percent, and the unemployment rate is 8.0 percent.⁴

METHODS

Sampling Method

Questionnaires were administered to 290 students in the 7th and 8th grades at a Missis-

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Mississippi Delta area middle school during a school-wide designated classroom period in January, 2005. Participation was completely voluntary and no identifying information was gathered. All 290 students completed and returned their questionnaires. Most of the respondents were 13 or 14 years of age, but their ages ranged from 12 to 16 years.

Administrative Procedures

The school principal granted permission to conduct the study and the Institutional Review Board of the University of Mississippi Medical Center approved the project. Letters were sent to the homes informing parents of the study. No parents requested their child not participate in the study; however, if a student did not wish to participate, he/she simply did not fill out the questionnaire. There was no refusal to participate in the study. The students completed a pencil-and-paper self-administered questionnaire during a designated class period. The questionnaire took approximately 30 minutes to complete. Students dropped their completed questionnaires into large boxes at designated areas, thus ensuring anonymity.

Instrument/Measures

The questionnaire was based on the instrument used in the Centers for Disease Control and Prevention Middle School Youth Risk Behavior Survey (5). For the purpose of this study, we investigated inhalant use and its relationship to use of cigarettes, alcohol, and marijuana, as well as to a history of the student's having ever been suspended, been in a physical fight during the past year, driven after drinking alcohol, or ridden with a drinking driver. Inhalant use was determined from the survey item: "During your life, how many times have you sniffed glue, breathed the contents of aerosol spray cans, or inhaled any paints or sprays to get high?" The question had the following choices for response: 0 times; 1 or 2 times; 3 to 9 times; 10 to 19 times; 20 to 39 times; 40 or more times. For the purpose of this study, those who responded they had ever sniffed glue, breathed the contents of aerosol spray cans, or inhaled any paints or sprays to get high were considered "ever huffers."

Analysis Plan

We used SPSS version 12.0 for Windows to create contingency tables to identify associations between variables of interest and huffing behaviors. The significance of the associations between huffing practices and the independent variables was examined using the chi-square test, with a p -value ≤ 0.05 considered statistically significant. Unadjusted odds ratios and their 95% confidence limits were then used to estimate the level of the association between using inhalants and the variables of interest. Significant variables, as well as all demographic variables, were then incorporated into a backward stepwise logistic regression to determine the variables that were most associated with inhalant use when each variable was adjusted for all other variables in the model.

RESULTS

Females and males were almost evenly represented in the sample. The majority of the research participants described themselves as African-American (56.6%). Over two-thirds were either 13 or 14 years of age (74.4%), followed by 12 (11.8%) and 15 (10.7%), with only 3.1 percent reporting they were 16 years or age. Approximately one-fifth (20.4%) reported they had ever sniffed glue, breathed the contents of aerosol spray cans, or inhaled any paints or sprays to get high. Of those who had used inhalants, 55.9% reported using on 1 or 2 occasions (11.4% of total sample), 27.1% reported using on 3 to 9 occasions (5.5% of total sample), with the smallest percentage (17.0%) of students using on 10 or more occasions (3.4% of the total sample).

Table 1 shows those variables associated with ever using inhalants. Although one-fifth of 12 year-olds and 25.9 percent of 13-year-olds reported ever using inhalants, the rate steadily falls in ages 14-16. These age differences, however, were not statistically significant. The differences in inhalant use between genders and between races were small and not statistically significant. On the other hand, students who had ever tried smoking (OR = 3.0 [CI = 1.5, 8.6], $p = 0.001$), had ever consumed alcohol (OR = 2.5 [1.3, 4.8], $p = 0.006$), had

TABLE 1. Prevalence and odds ratios of middle school students who responded they had ever sniffed glue, breathed the contents of aerosol spray cans, or inhaled any paints or sprays to get high.

Variables	Used inhalants at least once in life			
	%	Odds Ratio	(95% CI)	p-Value ^a
Gender				
Male	20.4	1.0	0.57, 1.8	0.99
Female	20.4			
Race				
African American	19.6	0.95	0.53, 1.7	0.86
White	20.5			
Age				
12	20.6			
13	25.9			
14	18.9			0.30
15	9.7			
16	11.1			
Has ever tried smoking				
Yes	27.3	3.0	1.5, 5.6	0.001
No	11.3			
Has had more than a few sips of alcohol				
Yes	25.7	2.5	1.3, 4.8	0.006
No	12.3			
Has tried marijuana				
Yes	34.9	2.8	1.5, 5.3	0.001
No	16.0			
Have you ever been suspended or expelled from school				
Yes	26.2	1.9	1.1, 3.4	0.029
No	15.7			
Have you been in a physical fight in the past 12 months				
Yes	29.4	3.2	1.7, 5.9	< 0.001
No	11.6			
Has driven after drinking alcohol in the past 30 days . . .				
At least once	34.7	2.5	1.3, 4.9	0.007
Not at all	17.5			
Has ridden with a driver who had been drinking in the past 30 days . . .				
At least once	31.3	3.5	1.9, 6.5	< 0.001
Not at all	11.5			

^a Based on chi-square tests

ever tried marijuana (OR = 2.8 [CI = 1.5, 5.3], p=0.001), had ever been suspended or expelled (OR = 1.9 [CI= 1.1, 3.4], p=0.029), had been in a fight in the past 12 months (OR = 3.2 [CI= 1.7, 6.9], p < 0.001), had driven after consuming alcohol (OR = 2.5 [CI = 1.2, 4.9], p = 0.007) and had ridden with a driver who had been drinking (OR = 3.5 [CI = 1.9, 6.5], p < 0.001) were more likely to have ever used inhalants. All of the variables that were significant (p ≤ 0.05) were included in the final regression model. Gender, race, and age, which were not significant, were also included in the model as control variables.

Table 2 represents the reduced model results from the logistic regression that shows the variables most predictive of ever using inhalants for adolescents in our study. The factors that best predicted an adolescent ever using inhalants were: being younger (OR = 0.56 [CI = 0.39, 0.81], p = 0.002), ever smoking (OR = 2.6 [CI = 1.3, 5.5], p < 0.01), riding with a driver who had been drinking in the past 30 days (OR = 2.9 [CI = 1.5, 5.7], p = 0.003), and being involved in a fight in the past 12 months (OR = 2.7 [CI = 1.4, 5.3], p = .003).

DISCUSSION

We found the prevalence of a history of inhalant use among adolescents in our sample to

TABLE 2. Reduced model of logistic regression for adolescents who responded they had ever sniffed glue, breathed the contents of aerosol spray cans, or inhaled any paints or sprays to get high.

Variables	Odds Ratio	95% CI	p-Value
Age	0.56	0.39, 0.81	0.002
Has ever tried smoking			
Yes	2.6	1.3, 5.5	0.01
No	1.00		
Has ridden with a driver who had been drinking in the past 30 days . . .			
At least once	2.9	1.5, 5.7	0.002
Not at all	1.00		
Has been in a fight in the past 12 months			
Yes	2.7	1.4, 5.3	0.003
No	1.00		

be much higher than previously reported prevalence at the national level.^{2,3,6} The high usage among 12-14 year-olds is especially alarming. The decrease of inhalant use as age increases among the respondents suggests a potential rise in experimental huffing among younger adolescents. However, caution must be exercised in making this inference because students who participate in risky behaviors may be prematurely dropping out of school, leading to underreporting in older adolescents.⁷ Other studies have found that inhalant abuse was associated with early first use, use of multiple inhalants, and frequent use, as well as problems with other drugs and problem behaviors.⁸

A potential limitation of our study is that the sample is from a single school in a southern community and care must be exercised in extrapolating conclusions to other populations. Further, the results are based on self-report information, and some students may provide false and misleading information. For instance, we cannot discern the differences in those students who had admittedly used inhalants, and those who may have falsely replied they had not. However, even though the reliability and the validity has not been formally conducted on the MSYRBS,³ the Youth Risk Behavior Survey instrument has been shown to have good test-retest reliability among high school students.⁹ Because of the nature of cross-sectional studies, the true impact of antecedent inhalant use on risky behaviors cannot truly be ascertained. There is also a limitation in dichotomizing the responses of the inhalant variable. We recognize that those who have experimented a greater number of times with inhalants could also have a higher rate of risky behaviors.

This study calls attention to the early experimentation with inhalants, and underscores the importance of recognition of groups who have a higher propensity using. Because of the associations between other risky behaviors and inhalant use, studies on the development of inhalant use in adolescents and how this use impacts future behaviors need to be conducted. The potential impact of living in an impoverished rural area may have on huffing initiation is of special interest because inhalants are inexpensive and readily accessible. Studies have shown that social-economic level may play a part in inhalant use and abuse, perhaps because of the low cost

and easy access to inhalants. Other studies have found that those who live in areas with lower income levels may have a higher use of inhalants.¹⁰ Education and prevention efforts must increase, or the number of adolescents participating in this dangerous practice may continue to rise. Not only should prevention programs be geared toward younger students,⁸ but also toward parents.¹¹ Moreover, specific training should be provided for physicians who may be able to identify inhalant abuse in adolescent populations.¹² A more comprehensive approach to prevention of inhalants, including parental monitoring, early education in schools, and physician training is imperative to the deterrence of this easily available, inexpensive drug.

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Inhalant Use in Florida Youth

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ABSTRACT. *Purpose:* To determine (1) the prevalence of use, (2) risk and protective factors for use of inhalants in Florida youth.

Methods: The Florida Youth Substance Abuse Survey 2004 is a comprehensive assessment of youth substance abuse attitudes and practices obtained by sampling youth from sixty-five counties.

Results: The sample consisted of 60,345 students from 6th to 12th grade; ages 10 to 19 + years (mean 14.5 years \pm 4), 53% were female with 59% White, 19% African-American, 16% Hispanic, 5% Native American, 2% Asian and 7% other. Lifetime use was highest among 14 year olds (16.5%), and current use among 13 year olds (16.7%). Females had significantly ($p < .000$) higher rates than males for lifetime (14.2% vs. 12.7%) and current use (5.1% vs. 4.1%). Native Americans had the highest rates of lifetime use (17%) followed by Whites (15%), mixed/other (15%), Hispanics (14%), Asians (13%), and Blacks (9%). The younger the age of first use of alcohol, cigarettes and marijuana, the higher the lifetime and current prevalence of use of inhalants. Inhalant users were more likely to be depressed, acknowledge deviant behavior and skipping school, have lower grades, have siblings and friends who used illegal substances and parents with a history of antisocial behavior ($p < .000$).

Conclusion: Inhalant use may be a marker for adolescents with a high-risk profile for subsequent illegal drug use. Prevention efforts should be directed to these students at an early age. doi:10.1300/J465v27n04_04 [Article copies available for a fee from The Haworth Document Delivery Service: 1-800-HAWORTH. E-mail address: <docdelivery@haworthpress.com> Website: <http://www.HaworthPress.com> © 2006 by The Haworth Press, Inc. All rights reserved.]

KEYWORDS. Adolescents, inhalant use, risk and protective factors

Inhalants are a class of drugs defined by their mode of administration (inhalation) and by the form of the substance being administered (fumes), rather than by their chemical or psychoactive properties.¹ They include a range of substances as diverse as glues, aerosols, butane, paint thinner, and nail polish remover. School-based surveys indicate that the use of inhalants has consistently been highest among 8th graders.^{2,3} This is most likely related to the

fact that these products are inexpensive, legal, and easy to obtain, making them more attractive to younger adolescents who have less access to illicit drugs. While the proportion of high school students using any illicit drug continues to decline, the use of inhalants in this group continues to rise, according to one of the latest national surveys.² This rebound in use over the last few years is believed to be related to 'generational forgetting' as the proportion of young

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people who believe it is dangerous to use inhalants has declined.³

While inhalant use may go unnoticed, even a single session of repeated inhalations can lead to death from cardiac arrest or asphyxiation.¹ Chronic inhalant abuse can lead to cardiac, renal, hepatic, and neurological complications. Users may suffer serious injuries (e.g., falls, burns, frostbite) while intoxicated. Inhalant use may also be a marker for later use of other illicit drugs.⁴ A review of the effects of inhalants is beyond the scope of this manuscript and the reader is referred to excellent information available on the National Institute of Drug Abuse website and other literature reviews.^{1,5,6}

Twelve percent of high school students surveyed nationwide had used an inhalant during their lifetime.² Approximately 3.9% of high school students reported inhalant use within the 30 days preceding the survey (i.e., current inhalant use). Overall, the prevalence of current inhalant use was higher among 9th grade (5.4%) than 10th grade (3.5%), 11th grade (3.1%), and 12th grade (2.7%) students. While the prevalence of use may be higher at younger ages, use is not limited to early adolescence and unfortunately this is not a transitory behavior.⁷ Male students (12.6%) were more likely than female students (11.4%) to report lifetime inhalant use. In addition to age and gender, a difference in lifetime use by race or ethnic group has been noted in previous studies. The highest rates of use have been in Native American youth and the lowest rates in Asians, with Hispanics having higher rates of use than non-Hispanic white and African Americans.^{3,7-9} These ethnic disparities have been partially attributed to socioeconomic status with lower income adolescents being more likely to use inhalants.¹⁰ These surveys have also noted the increase in use by females and the decline in use by Native Americans over the decade of the 1990s.⁹

A few studies have evaluated risk factors for use. School failure has been found to be a major risk factor for inhalant use.^{8,11} The drop out rate among those not doing well academically may account for the lower prevalence of use of inhalants among older adolescents noted in school-based studies.¹¹ One study, evaluating the role of peers noted that peer drug use was a predictor of alcohol and marijuana use but not

of inhalant use.⁸ However, another study found that peer items were a significant predictor of involvement with inhalants but was stronger for current than lifetime use and stronger in the non-Hispanic white adolescents than among other minority groups.⁹ In the family domain, it has been noted that inhalant abusers are also more likely to grow up in families with parental alcoholism and drug abuse and to have a higher rate of delinquent behavior and psychopathology.^{8,11,12} A recent study, using data from the 2000 and 2001 National Household Survey on Drug Abuse, found that lifetime inhalant use among 12 to 17 year olds was higher among those who admitted to delinquent behavior, a history of mental health treatment and other drug and alcohol use.¹³

The purpose of this study was to determine the prevalence and risk factors for use of inhalants in Florida youth. This study uses data from the 2004 Florida Youth Substance Abuse Survey (FYSAS).¹⁴ The Communities that Care Youth Survey (CTCYS) serves as the basis for the Florida Youth Substance Abuse Survey.^{15,16} The Social Development Strategy is the theoretical framework on which the CTCYS is based and it informs and organizes the risk and protective factor framework of adolescent problem behavior that families, schools and communities can use to help children develop healthy behaviors.¹⁷ Research indicates that adolescents' exposure to a greater number of risk factors is associated with more drug use and delinquency.¹⁸

Florida is one of the few states in the country that collects such data biannually from the sixty seven counties in the state. The 2000 US Census indicates that Florida is more ethnically diverse than the rest of the nation, with a large percentage of its population composed of minorities. Thus, there is a wealth of data available from which to examine substance use and delinquent behaviors and trend differences between the sexes.

METHODS

Details on the population sample and data collection methods for the FYSAS have been published previously.¹⁴ The survey effort is sponsored by the Florida Department of Chil-

dren and Families (DCF), and directed by a multi-agency workgroup consisting of members from four Florida State agencies—(1) the Departments of Children and Families, (2) Health, (3) Education, and (4) Juvenile Justice—under the leadership of the Governor’s Office of Drug Control. The 2004 survey was the fifth wave of data collected and was based on a stratified, two-stage cluster sample of students attending public middle and high schools in Florida. The sampling plan targeted 56,344 middle school students (6th-8th graders) and 58,310 high school students (9th-12th graders) from all 67 of the state’s counties. After invalid responses were removed, the final sample of 60,345 students included 55.7% of the targeted middle school sample and 48.9% of the targeted high school sample. The sample was weighted in order to generate drug use prevalence estimates and risk and protective factor scale scores that accurately reflected the state as a whole.

Variables

Our *dependent* variable, inhalant use, was assessed by asking the following question: On how many occasions (if any) have you sniffed glue, breathed the contents of an aerosol spray can, or inhaled other gases or sprays, in order to get high . . . in your lifetime? . . . during the past 30 days? The responses were assessed on an ordinal scale as follows: none, 1-2 occasions, 3-5, 6-9, 10-19, 20-39 and 40 or more occasions. We dichotomized the scale to non-use = ‘0’ and use = ‘1’ for any use, in some analyses.

Independent variables: The risk and protective factors evaluated in the FYSAS survey were in four domains: (1) community, (2) family, (3) peer/individual and (4) school domains. The variables in these domains are listed in Appendix A. Examples of questions for the constructs in each domain are listed in Appendix A.

Analyses: SPSS 10.1 for windows was used to conduct all statistical procedures (19). We initially conducted frequency analyses on the demographic variables. We used chi-square analyses to evaluate differences in demographics between inhalant and non-inhalant users. Using lifetime inhalant use as a dichotomous outcome variable, we used logistic regression analyses to construct the most parsimonious model from the various risk and protective fac-

tors. The independent variables were added in a stepwise forward fashion. Statistical significance was calculated at the 0.05% alpha level. The first regression was run with the risk and protective factors in all domains, with age, gender, ethnicity and SES as covariates. We then repeated the procedure for each gender.

RESULTS

The demographic data for the entire sample is shown in Table 1. Use of inhalants at some point in their lives was acknowledged by 13.5% ($n = 7,638$) of these students. Lifetime use was highest among 14 year olds (16.5%) with the prevalence dropping to 10% by age 18 years. Among current users, use was highest among 13 year olds (6.7%), with 1.8% of 18 year olds reporting current use. When evaluating the prevalence of use by grade, as in previous studies, we noted that the highest prevalence of lifetime use was among 8th graders (17.2%), while current use was highest among 7th graders (6.9%). Both lifetime and current use were higher among females than males (14.2% vs. 12.7% and 5.1% vs. 4.1% respectively, $p < .000$). The highest rate of both lifetime (17.4%) and current use (6.3%) was among Native American youth, followed by white, mixed/other, Hispanic, Asian and African-American youth (Table 2). There were no significant differences among the Hispanic subgroups in lifetime or current inhalant use. However we did find a difference in lifetime but not current use by language spoken at home. Among those who spoke English, 86.3% were non-users while 88.4% of those who spoke Spanish were non-users ($\chi^2 = 30.462$, $p = .002$). There was no difference in use by place of residence (urban, town or rural) but there was a difference in both lifetime and current use by SES as measured by father’s level of education. Those with lower SES were more likely to be users ($\chi^2 = 459.65$, $p < .000$).

School: Use of inhalants was significantly associated with performance at school. Those whose grades were mostly Fs were more likely to use inhalants than those whose grades were mostly As (22.4% vs. 1.8%, $\chi^2 = 447.749$ $p < .000$) and use them more frequently (2.9% used

TABLE 1. Demographic Data on the Entire 2004 FYSAS Student Sample (N = 60,345)

	N	Valid %
Gender		
Male	27,126	45.0
Female	31,076	51.5
Race/Ethnicity		
White, non-Hispanic	25,443	42.2
African-American	11,358	18.8
Hispanic/Latino	12,820	21.2
American Indian	889	2.0
Asian	1,212	1.5
Native Hawaiian/Pacific Islander	260	0.4
Other/multiple	7,861	13.0
Age		
10	65	0.1
11	2,690	3.9
12	9,094	12.9
13	10,350	15.2
14	10,425	15.9
15	9,897	17.2
16	7,937	14.4
17	6,099	12.4
18	3,243	7.0
19 or older	340	0.7
Grade		
6th	8,939	14.8
7th	9,082	15.0
8th	8,885	14.7
9th	11,137	18.5
10th	8,391	13.9
11th	7,197	11.9
12th	6,283	10.4

Note: The totals do not add up to 60,345 as there are missing values in some categories (e.g., not all survey questions were answered). In addition, rounding can produce totals that do not equal 100%.

TABLE 2. Inhalant Use by Race (p < .001)

Racial Category	Lifetime Use	Current Use
Native Am*	17.4%	6.3%
White*	15.4%	5.4%
Other/mixed	14.5%	4.5%
Hispanic	13.5%	5.0%
Asian	12.5%	4.0%
African-Am*	8.7%	3.4%

it on 40 or more occasions versus 0.6% of those with mostly As). Similar findings were noted for current use. The prevalence and frequency of lifetime and current use also increased with the number of school days missed. Among those who had no missed days, the lifetime use of inhalants was 11.3% while among those who had skipped 11 or more days, the lifetime use rose to 22.5% ($\chi^2 = 803.3$, $p < .000$).

Peers: The prevalence and frequency of inhalant use increased as the number of best friends who used alcohol, cigarettes, marijuana and hard drugs increased.

Family: Inhalant users were more likely to have family members with alcohol problems (49.9% versus 31.2%, $\chi^2 = 943.8$, $p < .000$).

Mental Health: Current and lifetime users of inhalants were significantly more likely to acknowledge symptoms of depression and acknowledge deviant behavior (Tables 3 and 4).

The first regression model (Table 5) indicates that in the family domain, poor family supervision and increased family conflict are risk factors. An individual with a sensation seeking and rebellious personality, who perceives that his peers will reward him for engaging in delinquent behavior and has a favorable attitude towards alcohol and other drugs, is more likely to be an inhalant user, i.e., the predicted odds of

TABLE 3. Inhalant Use and Depression (p < .001)

	Lifetime Use		Current Use	
	YES	NO	YES	NO
Life not worth it	28.3%	10.1%	9.8%	2.9%
I think I am no good	21.6%	9.8%	8.6%	3.0%
I am a failure	24.5%	11.5%	10.4%	3.7%
Depressed most days	19.1%	9.3%	7.3%	2.6%

TABLE 4. Inhalant Use and Risky Behavior (p < .001)

'Doing crazy things'	Lifetime use	Current Use
never	6.5%	1.5%
not in the past year	16.3%	3.3%
once a month	27.3%	6.9%
≥ 1 x week	31.8 %	12.9%

use are significantly greater than 1.0. None of the school or community variables (see Appendix B) was significant in the final model. There was only one protective factor that was significant. Those with higher levels of social skills were less likely to use inhalants. We also noted, that one risk factor ‘having friends with delinquent behavior,’ served as a protective factor.

When the regression was repeated by gender we noted similarities and some differences between the genders (Tables 6 and 7). Males had

one protective and two risk factors that were significantly different. Community rewards for pro-social involvement served as a protective factor for males and poor family discipline and a family history of antisocial behavior were risk factors for males. Among females, one protective factor and four risk factors were significantly different. The protective factor that was significantly different was religiosity. The four risk factors were an increase in perceived availability of drugs and firearms and personal transi-

TABLE 5. Risk and Protective Factors for Inhalant Use

	Sig.	Predicted Odds	95.0% C.I. for Odds	
			Lower	Upper
Poor family supervision	.001	1.186	1.073	1.310
Family conflict	.000	1.309	1.222	1.403
Early initiation (of drug use and antisocial behavior)	.000	1.170	1.116	1.226
Sensation seeking	.000	1.332	1.271	1.395
Rebelliousness	.000	1.492	1.357	1.641
Friend’s delinquent behavior	.015	.884	.801	.976
Peer rewards for antisocial behavior	.000	1.193	1.130	1.260
Favorable attitudes toward ATOD use	.000	1.298	1.171	1.439
Social skills	.005	.866	.783	.956
Age	.000	.678	.652	.704
Gender	.000	.642	.570	.723

TABLE 6. Risk and Protective Factors for Inhalant Use Among Females

	Sig.	Predicted Odds	95.0% C.I. for Odds	
			Lower	Upper
Age	.000	.758	.734	.782
Belief in the moral order	.001	.835	.749	.932
Personal transitions and mobility	.002	1.069	1.026	1.115
Perceived availability of drugs and firearms	.032	1.077	1.006	1.153
Family conflict	.000	1.163	1.094	1.235
Parental attitudes favorable towards ATOD use	.013	1.053	1.011	1.097
Early initiation (of drug use and antisocial behavior)	.000	1.282	1.225	1.342
Sensation seeking	.000	1.271	1.220	1.324
Religiosity	.017	.893	.814	.980
Rebelliousness	.000	1.245	1.148	1.350
Friend’s use of drugs	.000	1.210	1.139	1.286
Peer rewards for antisocial behavior	.000	1.116	1.062	1.172
Favorable attitudes toward antisocial behavior	.053	1.117	.998	1.251
Favorable attitudes toward ATOD use	.000	1.254	1.144	1.375

TABLE 7. Risk and Protective Factors for Inhalant Use Among Males

	Sig.	Predicted Odds	95.0% C.I. for Odds	
			Lower	Upper
Age	.000	.782	.754	.810
Community rewards for pro-social involvement	.028	.924	.861	.992
Belief in the moral order	.000	.774	.682	.878
Family conflict	.000	1.245	1.161	1.334
Family history of antisocial behavior	.000	1.141	1.071	1.215
Early initiation (of drug use and antisocial behavior)	.000	1.232	1.180	1.287
Sensation seeking	.000	1.188	1.139	1.239
Rebelliousness	.000	1.269	1.156	1.392
Friend's delinquent behavior	.000	.717	.650	.792
Friend's use of drugs	.000	1.243	1.161	1.331
Peer rewards for antisocial behavior	.000	1.172	1.109	1.238
Favorable attitudes toward ATOD use	.000	1.286	1.166	1.417

tions and mobility, parental attitudes favorable toward alcohol and other drugs, and the subject having favorable attitudes towards antisocial behavior themselves.

DISCUSSION

The prevalence of current inhalant use ranges from 2.4% to 5.5% across state surveys (median: 3.8%) and from 1.4% to 5.0% across local surveys (median: 3.6%).³ In this survey of youth in Florida we note relatively high rates of current inhalant use (4.6%). We also found that both lifetime and current use was higher in females than males, a trend that has been noted by others. Like other surveys, the highest lifetime use was among 8th graders but the highest current use was among 7th graders indicating that there may be a trend downwards in age of use in Florida youth. As in other studies the highest rate of use was among Native Americans. Of particular note among current users was the finding that White and Hispanic youth had the same prevalence and frequency of use indicating an increase in use among Hispanic youth in the current decade. We did not find any differences among the various Hispanic subgroups surveyed.

When we employed a multivariate logistic regression model to evaluate the relative salience of risk and protective factors, the com-

munity and school variables did not reach significance even though our initial analyses indicated that inhalant users were more likely to get lower grades in school and skip more days. When the regression was repeated by gender we did find that some community variables became significant. For males, being rewarded for pro-social community involvement was protective. Consideration therefore, should be given to encouraging this type of activity in young males. Some such activities include scouting, 4H clubs and church groups. Discussion with parents about the importance of participation in such groups and the need for positive feedback should go a long way towards building positive self-esteem and possibly preventing early experimentation and involvement in high-risk behaviors. Among females, there were no community protective factors. The significant community risk factor, 'personal transitions and mobility' is more reflective of the family situation.

In the family domain, none of the protective factors studied played a role in decreasing inhalant use in either gender. We found that those who came from families with increased conflict, a history of substance use and were poorly supervised were more likely to be inhalant users. Parental attitudes were more of a risk for females while family behavior was more of a risk for males. Thus, multiple problem families put their children at risk for early problem behaviors.

In the peer domain, one risk factor 'having friends with delinquent behavior' served as a protective factor in males. One possible explanation for this is that parents who note this type of friendship may be more inclined to closely supervise their child.

In the individual domain, belief in the moral order in both genders and religiosity in females were protective factors. These factors indicate a more conventional or conservative upbringing which served to protect these youth. Risk factors for inhalant use in this domain, both in the initial model and with each gender, included unconventional behaviors. Many previous studies have noted this as a risk factor for use of other drugs like alcohol, cigarettes and marijuana.²⁰ We also noted that those with a sensation seeking personality and rebelliousness and those who admitted to depression had significantly higher rates of use of inhalants. These factors too, have been associated with substance use.²¹

Inhalant users with this constellation of family and individual risk factors are probably also those adolescents who go on to use other substances later in life as these risk factors have been found to be associated with use of other substances in older adolescents. Inhalant use may thus serve as a marker for those adolescents at risk for continued substance use in the future.

Since inhalant use begins at such a young age it is important to intervene early. Preventive programs will need to begin in elementary school as first use of inhalants is documented to occur at 6th grade in this data set. These results are also consistent with the notion of an 'indicated' prevention program.²² Indicated prevention approaches are used for individuals who may not be abusing substances but have risk factors that increase their chances of developing a drug abuse problem. Indicated prevention programs address factors associated with the individual such as conduct disorder and alienation from parents, school and positive peer groups. Less emphasis is placed on assessing or addressing environmental influences such as community values. The aim of 'indicated prevention programs' is not only the reduction in first-time substance abuse but also reduction in the length of time of continued substance abuse

and/or reduction in the severity of substance use.

Some limitations of this study are that it is cross-sectional and that it relies on individual reports of both substance use and the acknowledgement of risk and protective factors. However, self-reports have been widely used in youth and have been shown to be reliable.²³

In summary, young adolescents, growing up in families with internal conflict and poor supervision, who are rebellious, depressed or have sensation seeking personalities are more likely to develop positive attitudes towards drug use and be at risk for experimenting with inhalants. They are more likely to have friends who use drugs and get positive feedback from these friends for their behavior. Inhalant use may serve as a marker for those adolescents at risk for continued substance use in the future.

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APPENDIX A. Examples of Questions in the Constructs That Make Up the Four Domains

PROTECTIVE FACTORS

A. Community Domain: Community Rewards for Pro-Social Involvement (5 Items)

"There are people in my neighborhood who are proud of me when I do something well."

B. Family Domain: Family Rewards for Pro-Social Involvement (4 Items)

"How often do your parents tell you they're proud of you for something you've done?"

C. School Domain: School Opportunities for Pro-Social Involvement (5 Items)

"In my school, students have lots of chances to help decide things like class activities and rules."

D. Individual Domain: Social Skills (4 Items): The following is one scenario on the survey: "You are visiting another part of town, and you don't know any of the people your age there. You are walking down the street, and some teenager you don't know is walking toward you. He is about your size, and as he is about to pass you, he deliberately bumps into you and you almost lose your balance. What would you say or do?"

RISK FACTORS

A. Community Domain: Low Neighborhood Attachment (3 Items)

"I'd like to get out of my neighborhood" and "If I had to move, I would miss the neighborhood I now live in."

B. Family Domain: Parental Attitudes Favorable toward ATOD Use and Antisocial Behavior (6 Items)

"How wrong do your parents feel it would be for you to smoke marijuana?" and "How wrong do your parents feel it would be for you to pick a fight with someone?"

C. Individual Domain: Lack of Commitment to School (9 Items)

“How important do you think the things you are learning in school are going to be for your later life?” and
 “Now, thinking back over the past year in school, how often did you enjoy being in school?”

D. School Domain: Low Perceived Risks of Drug Use (4 Items)

“How much do you think people risk harming themselves if they try marijuana once or twice?”

APPENDIX B. Variables in Each Domain in the Florida Youth Survey

CP1	RPF: Community Opportunities for Prosocial Involvement
CP2	RPF: Community Rewards for Prosocial Involvement
CR3	RPF: Low Neighborhood Attachment
CR4	RPF: Community Disorganization
CR5	RPF: Personal Transitions and Mobility
CR7	RPF: Laws and Norms Favorable to Drug Use and Firearms
CR8	RPF: <u>Perceived Availability of Drugs and Firearms</u>
FP1	RPF: Family Attachment
FP2	RPF: Family Opportunities for Prosocial Involvement
FP3	RPF: Family Rewards for Prosocial Involvement
FR4	RPF: Poor Family Supervision
FR5	RPF: Poor Family Discipline
FR6	RPF: Family Conflict
FR7	RPF: Family History of Antisocial Behavior
FR8	RPF: Parental Attitudes Favorable Toward ATOD Use
FR9	RPF: <u>Parental Attitudes Favorable Toward Antisocial Behavior</u>
IP1	RPF: Religiosity
IP2	RPF: Social Skills
IP3	RPF: Belief in the Moral Order
IP4	RPF: Rebelliousness
IP5	RPF: Friend’s Delinquent Behavior
IP6	RPF: Friend’s Use of Drugs
IP7	RPF: Peer Rewards for Antisocial Behavior
IP8	RPF: Favorable Attitudes Toward Antisocial Behavior
IP9	RPF: Favorable Attitudes Toward ATOD Use
IP10	RPF: Low Perceived Risks of Drug Use
IP11	RPF: Early Initiation (of Drug Use and Antisocial Behavior)
IP13	RPF: Sensation Seeking
IP14	RPF: <u>Gang Involvement</u>
SP1	RPF: School Opportunities for Prosocial Involvement
SP2	RPF: School Rewards for Prosocial Involvement
SR3	RPF: Poor Academic Performance
SR4	RPF: Low School Commitment

Alcohol and Risks for HIV/AIDS Among Sexually Transmitted Infection Clinic Patients in Cape Town, South Africa

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ABSTRACT. Alcohol use is prevalent in South Africa and alcohol use may be associated with higher risk for HIV transmission. This paper reports a study of the association between alcohol use and HIV risk-related behavior among 134 men and 92 women receiving sexually transmitted infection (STI) clinic services in Cape Town, South Africa. Participants completed anonymous surveys of demographic information, substance use, and sexual risk behaviors. Results showed that problem drinking was common among STI clinic patients; 58% of men and 28% of women scored above a cut-off of 9 on the Alcohol Use Disorders Identification Test (AUDIT) suggesting possible problem drinking and 46% of men and 19% of women scored above 12 on the AUDIT indicating probable drinking problems. For men, heavier alcohol use was associated with having multiple sex partners in the past month, less condom use, and having a history of sexually assaulting women. Among women, higher scores on the AUDIT were also related to having multiple sex partners as well as a history of exchanging sex for money or materials. The association between alcohol use and sexual risk behaviors in a population at high-risk for HIV transmission demonstrates the need for integrating alcohol risk reduction counseling with HIV prevention counseling among STI clinic patients in South Africa. doi:10.1300/J465v27n04_05 [Article copies available for a fee from The Haworth Document Delivery Service: 1-800-HAWORTH. E-mail address: <docdelivery@haworthpress.com> Website: <<http://www.HaworthPress.com>> © 2006 by The Haworth Press, Inc. All rights reserved.]

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Alcohol is the most prevalent substance used in South Africa, with an average of 20 liters of alcoholic beverages consumed per capita by South Africans each year.¹⁻³ Men drink heavier than women at all ages and the greatest amount of drinking occurs in impoverished urban areas.² Studies of adolescents in high school show substantial alcohol use with more than

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half of boys and one in four girls drinking during their school years.⁴ As many as 39% of male and 23% of female South Africans between ages 10 and 21 drink alcohol.² By contrast, the next most common psychoactive substance used in South Africa is dagga (cannabis) which is used by only 5% of the population.⁵

Although the link between alcohol use and sexual risks for HIV infection are well known in developed countries,⁶ there are few studies that have systematically examined the association between alcohol use and sexual risks for HIV infection in southern Africa. Recently, a national second-generation behavioural surveillance survey in South Africa was among the first studies of its kind to empirically show that the relationship between frequency of alcohol use and HIV status was positive and statistically significant.⁷ Most research on alcohol use in relation to HIV risk in Africa has focused on business establishments where alcohol is served. For example, in Zimbabwean beerhalls, the HIV prevalence is as high as 30% and there is a close association between drinking alcohol in sexual contexts and risks for HIV infection.⁸ Similarly, a recent sexual networking study conducted in Cape Town South Africa reported that 94% of places where people meet new sex partners are informal and formal alcohol-serving establishments.^{9,10}

A study recently reported on alcohol use among sexually transmitted infection (STI) clinic patients in Cape Town showed that 52% of men and 17% of women with a history of repeat STIs indicated high levels of alcohol use.¹¹ In addition, individuals who drank more often and drank more heavily demonstrated greater risks for HIV transmission. Alcohol use is therefore linked to HIV risks through multiple social systems, such as risk venues and social networks, as well as multiple cognitive processes, such as outcome expectancies. The current study was conducted to replicate and extend previous findings in an independent sample of men and women STI clinic patients. In the current study we included all STI clinic patients, not just those with repeat STI. We compared people who did and did not indicate heavy drinking within genders on measures of recent HIV risk behavior, history of sexual assault, and HIV testing history. Based on past research, we hypothesized that individuals who

had patterns of heavier alcohol use would demonstrate more frequent high-risk sexual behavior, thereby increasing risks for HIV transmission.

METHODS

Participants and Setting. Participants were 134 men and 92 women receiving STI diagnostic and treatment services from an STI clinic in Cape Town, South Africa. The median age of the sample was 26 years, 13% of participants were married, 65% had a high school education or less, and 55% were employed.

The urban health clinic that served as the site for the current research treats over 1800 patients with STI per month. The majority of patients seen at the clinic are indigenous Africans of Xhosa cultural heritage. This public clinic primarily serves inner-city impoverished communities in and around Cape Town. Approximately half of all patients seen at the clinic have previously received STI services. The estimated HIV prevalence of clinic patients is 25%.

Measures

Measures were adapted from previous research conducted in Cape Town¹⁰ and all measures were administered in English, Xhosa and Afrikaans, the three languages spoken by nearly all clinic patients. All of the measures were translated and back-translated to assure parallel forms. Measures included demographic characteristics, alcohol and other drug use, sexual behaviors practiced over the previous month, HIV risk history, and HIV testing history.

Demographic Characteristics. Participants reported the age, gender, race, years of formal education, whether they were employed and their marital status.

Alcohol and Other Drug Use. To assess quantity and frequency of alcohol use as well as alcohol-related problems, participants completed the Alcohol Use Disorder Identification Test (AUDIT; 12), a 10-item self-report instrument that includes quantity and frequency of alcohol use and was designed to identify individuals for whom the use of alcohol places them at risk for developing alcohol problems or who

are experiencing such problems.¹³ AUDIT scores range from 0-40, and scores of 9 or above have been used to identify individuals who are at possible risk for alcohol problems and scores of 13 or above indicate probable alcohol use problems.¹⁴ The AUDIT has been used extensively in research including research in South Africa¹⁵ and is reliable and valid.¹⁶ Participants were also asked whether they had used alcohol, dagga (marijuana), Mandrax, injection drugs, and other drugs in the previous month.

Sexual Behaviors and Condom Use. Participants responded to a series of items assessing their number of male and female sex partners and frequency of sexual events as well as vaginal intercourse with and without condom use in the previous month. Participants were instructed to think back over the past 30 days (one month) and estimate the number of occasions in which they practiced each behavior. A 30 day recall period was selected to maximize recall accuracy of higher frequency behaviors, such as vaginal intercourse. Measures similar to these have been found reliable and valid in past research.¹⁷ Responses represented rates of behaviors occurring over the previous month. The proportion of intercourse occasions protected by condoms was calculated by taking the ratio of protected intercourse over the total frequency of intercourse. Participants also reported whether they had ever experienced a condom break or tear during sex.

HIV Risk History and HIV Testing. Participants indicated whether they had ever given or received money or other material gain in exchange for sex. We also assessed whether participants had ever been forced to have sex when they did not want to and whether they had ever forced someone to have sex against their will. Finally, participants were asked if they had ever been tested for HIV and the result of their most recent HIV test.

Procedures

Patients receiving services at the STI clinic were referred by a nurse or physician in the clinic to participate in an anonymous health survey. The criterion for referral to the study was that the patient was being seen at the clinic for an STI. Patients who agreed to enroll in the study completed a self-administered anonymous

survey with assistance offered as needed (less than 10% of participants needed assistance). Participant's names were not taken at any time of the survey collection which occurred completely separate from clinic services. Informed consent was implied by voluntary completion by persons of majority age (18 in South Africa) and anonymous procedures. All referred patients were approached and all agreed to participate. Sampling occurred throughout all hours of clinic operation over a 3-month period. We limited participant enrollment to the first five individuals referred per day to assure a range of participants recruited over time. Participants received 15 South African Rand (ZAR15 or approximately US\$2.50) to compensate for their time.

Data Analyses

Analyses were first conducted to compare men and women on measures of alcohol and other drug use. Contingency table chi-square tests were first performed to analyze associations between participant gender and (a) responses to individual AUDIT indicators of problem drinking, (b) AUDIT scores above and below the cutoff for likely problem drinking (> 9), and (c) AUDIT scores indicating a high likelihood for problem drinking (AUDIT score > 13). Second, analyses compared persons who scored 9 or above on the AUDIT to those scoring 8 or below on the AUDIT on measures of sexual risk and sexual protective behaviors and HIV risk history factors using logistic regressions within genders controlling for participant age, education, and marital status. All analyses used $p < .05$ as the criterion for statistical significance.

RESULTS

Results indicated that 73% of men and 39% of women reported current use of alcohol (see Table 1). The quantity and frequency items on the AUDIT indicated that 62% of men and 34% of women reported drinking at least twice a month and that more than half of men and 35% of women typically drink at least 3 alcoholic beverages when they do drink. Monthly consumption of at least 5 drinks for men and 4

TABLE 1. Response frequencies to AUDIT items, AUDIT scores, and use of other substances.

		Men (N = 134)		Women (N = 92)		χ^2
		N	%	N	%	
How often do you drink alcohol?	Never	36	27	56	61	26.7 ^b
	Monthly	11	12	5	4	
	2-4 per month	54	40	22	24	
	2-3 per week	23	17	8	9	
	4+ times per week	6	5	1	1	
How many drinks containing alcohol do you have on a typical day when you are drinking?	1 or 2	59	44	59	64	12.2 ^a
	3 or 4	20	15	15	16	
	5 or 6	29	22	10	11	
	7 or 9	12	9	3	3	
	10 or more	14	6	5	5	
How often do you have (5 for men/4 for women) or more drinks on one occasion?	Never	48	36	61	66	23.1 ^b
	Less than monthly	16	12	9	10	
	Monthly	26	19	8	9	
	Weekly	38	28	14	15	
	Daily	6	5	0		
How often during the last year have you found that you were not able to stop drinking once you had started?	Never	53	40	65	71	26.1 ^b
	Less than monthly	20	15	13	14	
	Monthly	28	21	6	7	
	Weekly	27	21	8	9	
	Daily	5	4	0		
How often during the last year have you failed to do what was normally expected of you due to drinking?	Never	64	48	66	72	20.5 ^b
	Less than monthly	20	15	16	17	
	Monthly	22	16	3	3	
	Weekly	22	16	6	7	
	Daily	6	5	1	1	
How often during the last year have you needed a first drink in the morning to get yourself going after a heavy drinking session?	Never	68	51	68	74	21.0 ^b
	Less than monthly	17	13	15	16	
	Monthly	17	13	2	2	
	Weekly	29	22	6	7	
	Daily	3	2	1	1	
How often during the last year have you felt shame or guilt after drinking?	Never	70	52	67	73	13.6 ^b
	Less than monthly	18	13	12	13	
	Monthly	14	10	4	4	
	Weekly	22	16	4	4	
	Daily	10	8	5	5	
How often during the last year have you been unable to remember what happened the night before because you had been drinking?	Never	68	51	70	76	25.3 ^b
	Less than monthly	17	13	15	16	
	Monthly	16	12	2	2	
	Weekly	26	19	5	5	
	Daily	7	5	0		
Have you or someone else been injured as a result of your drinking?	No	105	78	84	91	n.s.
	Yes/not last year	12	9	5	5	
	Yes/last year	17	13	3	3	

		Men (N = 134)		Women (N = 92)		χ^2
		N	%	N	%	
Has someone been concerned about your drinking?	No	83	62	74	80	9.4 ^b
	Yes/not last year	23	17	6	7	
	Yes/last year	28	21	12	13	
Audit Score 9 or greater		77	58	26	28	18.7 ^b
Audit Score 13 or greater		61	46	17	19	17.6 ^b
Used Marijuana (Dagga)		37	28	11	12	7.9 ^b
Used Mandrax		7	5	3	3	n.s.
Used any injected drug		5	4	3	3	n.s.
Used any other drugs		6	5	2	2	n.s.

Note: ^a $p < .05$, ^b $p < .01$

drinks for women on any one occasion was reported by 52% of men and 24% of women drinkers. In terms of indicators of alcohol problems, we found that men were significantly more likely to report drinking problems than women. The most prevalent indicator of problem drinking was being unable to stop drinking once started, with 60% of men and 29% of women endorsing this item. In addition, 22% of men reported that someone had been injured as a result of their drinking, with 13% indicating this problem in the past year.

More than half of men and one in four women scored 9 or above on the AUDIT indicating likely problem drinking and 46% of men and 19% of women scored 13 and higher indicating probable alcohol abuse. AUDIT scores were not associated with participant age, education, current employment, or marital status. Men (28%) and women (12%) also reported using dagga, a significant gender difference, with use of other drugs being infrequent.

Alcohol and HIV-Related Risks

Men who indicated drinking problems on the AUDIT (scores ≥ 9) were significantly more likely to have multiple sex partners, used condoms less often, and were more likely to have sexually assaulted a person than were men who did not indicate problem drinking (see Table 2). For women, problem drinking was also related to multiple sex partners. Women who drank at higher levels were also more likely to have experienced condom failures and were more likely to have received money or material in exchange for sex.

DISCUSSION

Replicating and extending previous research we found that alcohol use and problem drinking were prevalent among Cape Town STI clinic patients. More than half of men and one in four women were at risk of or were engaged in problem drinking, and nearly as many participants demonstrated drinking at a level that indicated a strong likelihood of problem drinking. Among men, alcohol use was associated with having two or more sex partners in the previous month and a lower proportion of condom use. Men who drank more heavily were also more likely to report having forced someone to have sex. For women, greater alcohol use was also associated with having multiple sex partners in the past month. Women who drank more heavily were also more likely to have experienced condom breaks and were more likely to have exchanged sex for money or materials. These findings occur in a context where all of the participants were being examined for STI, as many as one in four people are HIV positive, and only about half have been tested for HIV.

The current study findings should be interpreted in light of their methodological limitations. Our study like others in the field of HIV/AIDS risk and prevention relied on self-report behavioral instruments. The sensitivity and private nature of sexual behavior may have been influenced by social desirability, privacy concerns, and potential embarrassment. These social factors can create response biases and may have lead to under-reporting of substance use and risk behaviors. Our measures of alcohol and other drug use were also constrained by the

TABLE 2. Sexual behaviors in the past month among men and women with lower (Score ≤ 8 on AUDIT) and higher (Score ≥ 9 on AUDIT) patterns of alcohol use.

	Men					Women				
	Pattern of less problem drinking (N = 55)		Pattern of likely problem drinking (N = 77)			Pattern of less problem drinking (N = 66)		Pattern of likely problem drinking (N = 26)		
	M	SD	M	SD	OR	M	SD	M	SD	OR
Number of sex partners	1.6	1.1	1.9	1.0	1.2	1.3	0.6	2.1	1.6	3.2 ^b
Unprotected vaginal intercourse	3.8	4.8	5.3	5.5	1.1	6.8	6.1	9.0	8.2	1.1
% of intercourse protected by condoms	54.8	39.1	34.0	31.9	0.2 ^b	29.4	32.0	33.9	28.7	1.8
	N	%	N	%		N	%	N	%	
Two or more sex partners	23	42	48	62	2.6 ^b	21	32	17	65	4.9 ^b
Experienced condom breaks	20	36	34	44	1.7	24	39	17	65	3.2 ^a
Received money in exchange for sex	2	4	2	3	0.9	4	6	6	23	4.8 ^a
Gave money in exchange for sex	2	4	8	10	3.1	1	1	1	1	2.8
Tested for HIV	30	55	40	52	1.0	43	65	14	54	0.6
Tested HIV+	4	11	6	13	1.0	1	2	1	5	1.6
Forced to have sex	2	4	4	5	1.2	35	53	15	57	1.2
Forced someone to have sex	2	4	13	17	6.5 ^b	1	1	1	5	2.7

Note: OR = odds ratio adjusted for age, education, and marital status; ^a $p < .05$, ^b $p < .01$

brevity of our survey, suggesting the need for more comprehensive assessments of substance use, including alcohol dependence, in relation to HIV risk in future South African research. The study findings are also based on a relatively small sample, suggesting the need for further studies to replicate the observed associations. Finally, we sampled participants from one public health clinic in Cape Town, cautioning against generalizing the results to primary care settings and across cultural groups in Cape Town as well as other populations in South Africa. Despite these limitations, the current findings offer new information regarding the implications of alcohol use and HIV prevention in South Africa.

The rates of alcohol use and the potential for problem drinking observed in this study indicate the need for HIV prevention interventions adapted for South African men and women who use alcohol. In South Africa, sexual partners are often met in drinking establishments, where alcohol can be used to barter for sex.⁹ Alcohol may also reduce the likelihood of using condoms and increase risk taking behaviors,¹⁸ al-

though these associations are only now being empirically verified in South Africa. Interventions that integrate both alcohol risk reduction and sexual risk reduction may be viable in South African STI clinics. Brief sexual risk reduction interventions delivered in conjunction with voluntary HIV counseling and testing (VCT) as well as risk reduction counseling delivered independent of VCT have shown promise in Southern Africa.^{20,21} In addition, there are well established brief alcohol risk reduction interventions used in Southern Africa that are also delivered in the context of a single motivational interviewing session.²² Brief counseling may be integrated in a unified HIV and alcohol abuse prevention intervention for use in South Africa. For example, people who evidence patterns of problem drinking on a screening instrument such as the AUDIT in an STI clinic may be counseled for both HIV risk reduction and alcohol reduction. Given the prevalence of alcohol use observed in the STI clinic in this study and the potential for alcohol use to increase HIV transmission risks are important factors to consider when designing HIV prevention interven-

tions for South African men and women. Implementing alcohol screening and integrating alcohol and sexual risk reduction counseling among STI patients should be a public health priority in South Africa.

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Illy: Clinical and Public Health Implications of a Street Drug

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ABSTRACT. We conducted a prospective, observational study of patients presenting to an emergency department with suspected use of a street drug known as “illy” to identify the active ingredient in illy and describe the clinical presentation and outcomes associated with its use. Vital signs, mental status, restraint use, and urine toxicology (UT) results were recorded. Patients were interviewed about drug use patterns and co-ingestants. Fifty-nine patients (89.9% males) with a mean age of 22 years ($SD \pm 4.37$) were enrolled over a 34-month period. UT was obtained in 61% of patients; of these 91.7% tested positive for phencyclidine (PCP). Seventy-eight percent of patients were discharged, (15.3%) required psychiatric evaluation; 3 were admitted, one died in the ED. Patients reported concurrent drug use (54%) and at-risk drinking (50%). PCP is likely the active component of illy. Most patients require observation and supportive care only, however major complications including death may occur. doi:10.1300/J465v27n04_06 [Article copies available for a fee from The Haworth Document Delivery Service: 1-800-HAWORTH. E-mail address: <docdelivery@haworthpress.com> Website: <<http://www.HaworthPress.com>> © 2006 by The Haworth Press, Inc. All rights reserved.]

KEYWORDS. Substance abuse, phencyclidine, street drug, urine toxicology

INTRODUCTION

An new street drug known as “illy,” “wet,” “fry,” “dip,” “dank,” “sherm” or “hydro” appeared on the streets in the beginning of the nineties.¹⁻³ It is described as marijuana soaked in “embalming fluid” (a mixture of formalde-

hyde and methanol) with the purpose of enhancing the euphoric effect of the marijuana.⁴⁻⁶ Patients present with dissociative symptoms, sometimes resembling schizophrenia. These symptoms range from disorganized speech and thoughts with mild agitation to acute psychosis with delirium and violent behaviors. The use of

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this drug has recently increased in popularity in the Northeast, Missouri, California, and Texas and has been documented in emergency departments and psychiatric clinics as a preferred drug of abuse for many patients.⁷⁻¹⁰

Concomitantly substantial increases in urine toxicology screens positive for PCP were noted to occur in the nineties in Connecticut and Missouri with a noticeable rise in PCP use in these areas.⁴ In 1997, the Connecticut state forensic laboratory reported as many as ten PCP-positive samples out of 3,000 samples per month with only five PCP-positive samples for the entire year in 1996.⁴ Analysis of patient's urine toxicology screens,^{8,11-13} as well as gas chromatography of the "embalming fluid"^{5,12} and studies on several purchased or confiscated samples of illy^{4,11} identified PCP and PCP-like substances as an active ingredient in this drug of abuse. Illy and other forms of adulterated marijuana are not reportable to national drug abuse databases and many users are unaware that PCP is in these drugs^{4,5,8,11-13} making trends difficult to elicit. However, the Drug Abuse Warning Network (DAWN) reported a near doubling in ED visits secondary to PCP use (or PCP in combination with another chemical) from 1991 to 1995 while the American Association of Poison Control Centers (AAPCC) showed an upward trend.⁴ There are many small case reports which correlate PCP-like behavior or clinical toxidrome to these drug^{6,14} or confirm the presence of PCP in patients who use them.^{8,12,13} To date, no one has studied a large cohort of patients with acute "illy" intoxication within a geographic region, accompanied by confirmatory urine toxicology screens and correlating clinical evaluations with treatment of the toxidrome. In fact, some suggest that the embalming fluid is the mind-altering drug.¹⁵ As many of these patients presenting to this urban center appeared to be clinically intoxicated with PCP, we sought to identify the active ingredient in Illy. In addition our objectives were to describe the clinical findings, management and patterns of use of a cohort of patients presenting to an urban emergency department with self-reported, witnessed or suspected illy intoxication.

MATERIALS AND METHODS

Study Design

This prospective clinical observational study was approved by the Human Investigation Committee. We chose this method in order to identify the demographic factors manifestations and outcomes associated with the reported use of illy.

Study Setting and Population

A convenience sample of fifty-nine adult patients was enrolled over a 34 month period, from December 1997 to October 2000 in the emergency department (ED) of a level-one trauma center with a census of 60,000 adult visits per year. Inclusion criteria were patients 18 years of age or older with a chief complaint related to witnessed, self-reported or suspected illy use. Suspected illy use was based on practitioner observation and assessment of patients who exhibited violent or bizarre behavior unexplained by acute psychiatric or other illness, trauma, co-ingestion of other substances or acute psychotic behavior without a previous history of psychiatric illness. Data were obtained by questionnaire and medical record review.

Data Collection/Study Protocol

Data collected prospectively from the patient medical record included patient demographics, vital signs, mode of transport to the ED, use of physical and/or chemical restraints in the ED, and ED course including initial behavioral response, mental status, and ED disposition. Urine toxicology screening was performed at the discretion of the treating physician as necessary for initiation of ED treatment and evaluation, using ED protocols for obtaining urine samples. Samples found to be positive for phencyclidine using the CEDIA immunoassay (sensitivity 25 ng/ml, Microgenics Corp.) were confirmed with gas chromatography and mass spectrometry (GC/MS) in the hospital clinical chemistry laboratory. Patients who reported illy use or exhibited symptoms of suspected illy use were approached by the treating emergency physician and asked to answer a se-

ries of questions about their drug and alcohol use. In patients who experienced transient altered mental status, the treating physician obtained verbal consent to administer the questionnaire once the patient was determined to be oriented to person, place and time, and able to provide informed consent.

The 11-item survey included open-ended and multiple choice questions regarding frequency of illy use, symptoms attributed to illy, price, brand name and suspected contents of the drug purchased as illy, concomitant and past use of alcohol and other drugs (AOD). During the course of the study the questionnaire was enhanced to assess alcohol use using the low risk guidelines developed by the National Institute of Alcoholism and Alcohol Abuse.¹⁶ These guidelines place low-risk consumption limits at 7 drinks/week or fewer than 4 drinks per occasion for females and anyone age 65 and over, and 14 drinks/week or fewer than 5 drinks per occasion for males under age 65. Quantity and frequency of alcohol use were asked and used the standard NIAAA questions for quantity and frequency of alcohol use. Data were entered into an Excel spreadsheet and analyzed using SPSS version 11.0.

Data Analysis

Data were analyzed using descriptive statistics, as this was an observational study. Continuous variables were analyzed using means and standard deviations; categorical variables were analyzed using frequencies.

RESULTS

Demographics

Fifty-nine patients were enrolled. Most were male (89.8%) with a median age of 23 years (SD \pm 4.38 yrs; range 18-39 yrs). Patients were referred to the ED by several sources; police referral (66%); self-referrals (14%); friend request (12%); family request (9%). A majority of patients (81.4%) were transported to the ED via ambulance. Patients came to the attention of law enforcement due to family or friend referral or various observed behaviors such as driving

down the wrong side of road, motor vehicle collisions or bizarre behaviors including screaming while standing naked on a store counter, rolling in mud, walking around naked in public, walking the median line on a busy street or simply acting strange, screaming, making random movements and grabbing people.

Signs and Symptoms

Vital signs were recorded in 58 patients, as one patient presented in full cardiopulmonary arrest (Table 1). At presentation, four categories of mental status with verbal response were observed; oriented and converses, but slow to respond (39.0%) oriented and converses normally (25.4%); disoriented and uses inappropriate words (23.7%); unresponsive (10.2%). Behavioral symptoms on presentation included: cooperative (47.4%); combative (27.6%); irritable (17.2%); chemically sedated (3.4%). Patients could present with more than one category of behavioral symptoms. The majority of patients required physical restraints (89.7%) and chemical restraints were used in 20.7% of patients. Restraints were used when the attending physician felt that the patient was at risk of harm because of altered mental status.

Urine Toxicology Results

Urine toxicology screens were obtained in 36 of the 59 study participants (61.0%); 91.7% (33/36) were positive for PCP. Two urine specimens were positive for drugs of abuse other than PCP; one each for cocaine and opiates.

Length of Stay and ED Disposition

Mean length of stay (LOS) in the ED was 4 hours and 20 minutes (268.1 minutes \pm 143.99 min; range 58-595 minutes).

TABLE 1. Vital Signs on Presentation to the Emergency Department (ED)

Vital Signs	Mean	SD
Systolic Blood Pressure	144.5 mm Hg	\pm 27.57
Pulse	88.0 bpm	\pm 23.84
Respiratory Rate	18.4 per min	\pm 3.90
Temperature	98.1°F	\pm 0.99

Four patients (6.8%) were seriously ill as a result of their illy use: Three required hospital admission and one died. The patient who died, a known illy user, died from cardiac arrest in the ED after being found in a car with illy paraphernalia. On postmortem examination and toxicology analysis, PCP was the only illicit drug detected.

Reasons for hospital admission included one each of the following: seizure, traumatic open globe injury, and persistent lethargy. Of the 55 remaining patients, 39 (71.0%) were discharged home, 9 (16.4%) were transferred to a Crisis Intervention Unit (CIU) or other psychiatric facility, 5 (9.1%) were transported to jail, and 2 (3.6%) patients left the ED before treatment was completed. One patient originally seen for acute illy intoxication was admitted days later to the psychiatric ward for persistent psychosis.

Alcohol and Other Drug Use

Forty-eight patients consented to complete the co-ingestant questionnaire. Patients were divided into 4 categories based upon the frequency of reported illy use. Twenty-six (54.2%) used it "often" (one or more times per week) while eight (16.7%) were first time users. Eight (16.7%) stated that they used illy "occasionally" (a few times a month), and six (12.5%) used "rarely" (once or twice). When asked to describe their preferred method of illy use, eighteen patients smoked illy stuffed into a hollowed out cigarette or "blunt" and 13 patients rolled it in cigarette paper themselves. Additional information was obtained on co-ingestants and past illicit drug use (Table 2). When it became evident that a significant proportion of illy users co-ingested alcohol, questions were added to determine their level of drinking. Data from thirty-two patients revealed that when asked about quantity and frequency of alcohol consumption, 50.0% (16/32) of patients interviewed exceeded the low risk guidelines developed by the National Institute of Alcoholism and Alcohol abuse.¹⁶ Eleven met criteria for binge drinking (5 or more drinks per occasion).

DISCUSSION

Based on clinical presentation and toxicology results, PCP appears to be the active com-

TABLE 2. Co-Ingestants and Past Use of Illicit Drugs

	Co-ingestants (N = 48)	Past illicit (N = 48)
Tobacco	52.1% (25)	—
Alcohol	52.1% (25)	—
Marijuana	39.6% (19)	83.3% (40)
PCP	12.5% (6)	27.1% (13)
Cocaine	6.3% (3)	20.8% (10)
Crack	2.1% (1)	12.5% (6)
Ecstasy	2.1% (1)	2.1% (1)
LSD	0.0% (0)	8.3% (4)
Heroin	0.0% (0)	6.3% (3)

ponent of illy as 92% of urines were positive for PCP. For the purposes of this discussion the term illy will be used synonymously with a PCP-laced substance whether it be marijuana or other smokable materials. Samples of illy in New Haven, Connecticut and elsewhere have been found to contain PCP with "embalming fluid" and mint leaves, parsley flakes, oregano, tobacco or cut up duct tape with no detectable marijuana confirming our suspicion that the real high from illy comes from PCP.^{4,5} The emergence of illy as a street drug may represent an unrecognized resurgence of PCP use and we recommend that patients who present to the emergency department with reported or suspected illy use be treated as one would patients who have ingested PCP.

The decision to obtain a urine toxicology screen was left to the discretion of the treating physician and there is no reason to suspect that this led to a selection bias in this observational study. In fact one may hypothesize that physicians were more likely not to order toxicology screens when the clinical presentation was indicative of illy use. Although some patients who reported illy use in Connecticut tested negative for PCP,¹⁷ urinalyses do not rule out PCP use.⁴ False negative results can occur from less than 25 ng/ml of PCP in the urine or the presence of other adulterating compounds in the specimen. Many designer drugs available on the streets that contain PCP analogs and result in PCP-like effects may not be detected by a

urine toxicology screen that is confirmed by GC/MS. Cases of false positive results with immunoassay alone have been documented with drugs such as diphenhydramine, dextromethorphan, methadone, PCP analogs, or chlorpromazine. However, confirmatory testing of these specimens for PCP by GC/MS analysis—as performed at our hospital—does not result in false positive findings. Only two urine specimens in our study had another drug of abuse present confirming patient reports that they were using illy alone for a high and not typically in combination with other drugs such as cocaine. Tetrahydrocannabinol (THC) is not routinely tested for in our urine toxicology screens as it provides an inaccurate picture of current marijuana use and may continue to be excreted in the urine for a few days with one time use to several weeks in chronic users.

Currently, “embalming fluid” is thought to act as a vehicle to aid in the uniform distribution of PCP and smoking the substance while it is still wet increases the length of time the drug can be smoked. This may explain one nickname for the concoction—“wet”—as in “getting wet.”^{4,8} Formaldehyde and methanol, components of embalming fluid, were originally thought to be responsible for the effects of adulterated marijuana,^{6,14,18} but currently are not thought to cause the predominant dissociative and violent symptoms, which are now attributed to PCP.^{4,5,7,19} Inhalation of formaldehyde and methanol in small doses is postulated to produce lung irritation and not the constellation of effects clearly displayed by our cohort. The concentration of formaldehyde, ethanol, and methanol in embalming fluid is low, and they do not produce agitation and hallucination.

Clinically, our cohort presented with varying degrees of dissociative behavior with vital signs and medical complications consistent with PCP intoxication. While most required a period of observation and/or chemical sedation, most patients were typically discharged to home. Similar dissociative behaviors have been noted by McCarron et al. in their prospective study of 1000 PCP intoxications.²⁰ Although the most common behavioral alterations are violence and agitation, other clinical findings may include mutism, staring, hallucinations, delusions, euphoria, sedation, lethargy and coma. Many of our patients presented ori-

ented and conversant but slow to respond (39.0%) or oriented and normal (25.4%), similar to subjects in the study by McCarron et al. who found that 45% were alert and oriented on presentation.²⁰ In this same study, 35% exhibited violent behaviors with 19 experiencing severe injuries. Though the majority of patients were ultimately cooperative and treated with observation alone, many were combative and irritable prior to and upon arrival in the ED requiring physical and chemical restraints for their safety. One patient had a traumatic injury requiring admission to the hospital and one patient dies, as previously described. Clinical values obtained from our cohort are consistent with prior studies.²⁰⁻²² Most patients who use PCP and illy are male with a mean age of 23 years.²⁰ In these studies, as in ours, severe disturbances of vital signs are rare. Elevations of blood pressure are neither severe nor persistent. Tachycardia was recorded in up to 30% of patients in one study. Respiratory rate was unchanged when compared to a nonintoxicated age-matched cohort in a study by Barton et al.²² Rarely, hyperthermia and hypertensive crisis have been documented in PCP users and McCarron et al. noted seizures (3.1%), cardiac arrest (0.3%) and apnea (2.8%),²¹ of which our patients experienced both seizure (n = 1) and cardiac arrest (n = 1). Although our cohort was too limited to assess rhabdomyolysis, it occurred commonly in one study²⁰ and was found to be the most common serious medical complication requiring hospitalization in another.²²

Clinical management of illy users is consistent with management of PCP intoxication. When clinically indicated, urine samples should be obtained in patients who present with acute psychosis in the absence of prior psychiatric or other disorders to rule out illy use. From our experience and related studies in the literature, benzodiazepines (diazepam, midazolam) are recommended over antipsychotics (phenothiazines, butyrophenones) to chemically restrain patients who are agitated and psychotic. Though we did not encounter any complications after phenothiazine use for chemical restraint in our patients, they may potentiate anticholinergic properties known to be present in PCP, cause significant hypotension, and worsen hyperthermia. Both phenothiazines and butyrophenones can cause acute dystonic

reactions and caution should be exercised with their use as they can also prolong the QT interval.²³ While we have no clear recommendations regarding the management of rhabdomyolysis based upon our cohort, it is important to hydrate patients orally or intravenously to avoid this complication. This visit may also be an opportunity to counsel patients about other high risk behaviors, including alcohol and tobacco use.

Law enforcement officers, prehospital personnel and psychiatric professionals play an important role in the management of the acutely intoxicated illy patient reflected in the high percentage of police and psychiatric referral and ambulance utilization for patient transport. The authors (GD, LD) were invited to brief law enforcement officers regarding the management of illy users in the field due to their violent and erratic behaviors. Educating these professionals may avoid costly and unnecessarily aggressive interventions for these patients. Illy users required additional resources including acute psychiatric assessment posing an unnecessary burden on the health care system as many EDs do not have acute psychiatric care immediately available and patients require admission or transfer for evaluation. PCP-induced psychosis may last for several days or more resulting in hospital admission.^{8,23}

Coordinated public health actions would help to inform illy users of the complications and risks associated with the use of this drug. Several users thought that they were being offered marijuana only. The state of Connecticut launched an education campaign related to illy that has been used in other states to increase awareness and combat its use (Figure 1). In a 2003 survey of 494 at-risk youth grades 7-12 in Houston, Texas, 11% reported lifetime use of adulterated marijuana ("fry") while 2% reported using within the past 30 days.²⁴ Most participants in a pilot study of 38 current fry users in Texas (ages 13-20) reported they used fry initially with friends or family members and indicated that their second fry event occurred during the same or next day after their initial use,¹⁰ suggesting public health initiatives should start at the middle school and high school grade levels. Twenty-seven percent of our study patients reported use of PCP in the past and 53% reported frequent use of illy, indicating a certain

FIGURE 1. Flyer from the Connecticut Department of Public Health



level of awareness of and preference for the effects of illy amongst users. In interviews of current users, illy was shown to have addictive properties¹⁰ and its use is highly correlated with a subgroup of patients who meet the NIAAA criteria for alcohol abuse. Because of this, we suggest screening these patients for alcohol and other drugs of abuse, and, as merited, a brief bedside intervention for alcohol. We recommend that illy intoxication be reported to the AAPCC (American Academy of Poison Control Centers) to better document a pattern of use and understand its epidemiology. As users were generally unaware that this drug contains PCP^{4,5,8,11-13} ongoing public dialogue may heighten awareness of the serious and possibly deadly consequences of this drug. It is speculated that with such knowledge, patients will be less likely to choose to use illy.

LIMITATIONS

Limitations of this study are inherent to its prospective, observational, convenience sample design. While the majority of patients had urine samples obtained which were overwhelmingly PCP-positive, our ability to confirm that the main active ingredient in illy is

PCP is limited in that all patients did not have a urine screen performed. Though we surveyed patients regarding patterns of alcohol use, we did not determine acute alcohol use at the time of the visit and its clinical contribution. Levels of formaldehyde, methanol were not tested as they are currently not thought to cause the dissociative and violent symptoms now attributed to PCP. Due to our small sample size and single site design, we have no recommendations regarding the treatment of rare PCP-related side-effects such as hyperthermia, rhabdomyolysis and myoglobinuria.^{23,25} We were unable to assess the chronic effects of illy use due to the study design. A percentage of patients did not respond or responded incompletely to the co-ingestant questionnaire potentially biasing this group.

CONCLUSIONS

PCP is most likely the active component of illy in our cohort and the explanation for the dissociative behavior exhibited by its users. The majority of patients who present after reported or suspected illy use require a period of observation and supportive care only, however some experience major complications including death. At-risk alcohol consumption as well as concurrent use of other drugs is common. Illy use may mask awareness of PCP resurgence.

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HIV Incidence, Retention, and Changes of High-Risk Behaviors Among Rural Injection Drug Users in Guangxi, China

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ABSTRACT. *Background:* A prospective observational study of HIV seroincidence among high-risk injection drug users (IDU) was carried out in Guangxi, China. The primary objectives of

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this study were (1) to estimate HIV seroincidence, (2) to estimate participant retention rate, and (3) to evaluate changes in drug use and sexual behavior over a one year period.

Methods: Five hundred HIV seronegative IDU were enrolled. HIV-1 incidence and retention rates were analyzed as a function of sociodemographic, behavioral, and recruitment variables. Changes in drug use and sexual behavior were analyzed at the baseline, 6-month and 12-month follow-up visits.

Results: At 12 months of follow-up, the HIV-1 incidence rate was 3.1 per 100 person years, [95% CI: (1.6%; 5.2%)] and participant retention rate was 87%. Reported changes in high-risk behaviors over 12-months included significant decreases in the frequency of heroin injection, in direct or indirect sharing of injection equipment, and in the number of sexual partners.

Conclusions: HIV incidence is high among IDU in Guangxi, China despite a self-reported decrease in some high risk behaviors over the course of the study. doi:10.1300/J465v27n04_07 [Article copies available for a fee from The Haworth Document Delivery Service: 1-800-HAWORTH. E-mail address: <docdelivery@haworthpress.com> Website: <http://www.HaworthPress.com> © 2006 by The Haworth Press, Inc. All rights reserved.]

KEYWORDS. IDU, HIV incidence, retention, Guangxi, China

INTRODUCTION

Since 1994, China has experienced a rapid increase in the number of HIV/AIDS cases. The cumulative number of HIV/AIDS cases reported between January 1985 and September 2004 is 89,067. According to the Chinese Ministry of Health, the number of people currently living with HIV/AIDS in China is 650,000.¹ The major transmission routes for HIV, based on reported cases, are injection drug use (44%), former unsafe blood collection (11%), heterosexual transmission (19%), and men who have sex with men (7%).¹ Experts estimate that there will be 10 million HIV infections by 2010 if effective countermeasures are not taken.²

The first HIV outbreak among injection drug users (IDU) in China was reported in Yunnan in 1989.³ By the end of 2002, all 31 of China's provinces, municipalities and autonomous regions reported HIV infection among this population.¹ The reported number of drug users in China in 2003 was 1.05 million, with an annual increase rate of 11% in the past years.⁴

The major spread of the initial drug related epidemic in China began in Yunnan province and took two major routes, northbound to Sichuan, Guizhou, Gansu, Ningxia, and Xinjiang and eastbound to Guangxi, Guangdong and Guizhou.⁵⁻¹⁰ Data from the Ministry of Public Security confirmed that epidemic routes coincided with the major drug trafficking roads from the golden triangle into China.

Among the 31 provinces and municipalities in China, Guangxi province has the 4th highest number of cumulative reported HIV cases. Located along the major drug (heroin) trafficking trade route linking Guangxi with Yunnan and also Vietnam, the epidemic is primarily fueled by injection drug use.^{11,12} The first case of HIV among local drug users in Guangxi was reported in 1996.¹² HIV infection among IDU accounted for 69% (5961/8602) of the cumulative reported cases of HIV in Guangxi with an estimated number of more than 40,000.¹³ According to the Guangxi Centers for Disease Control, HIV prevalence among IDU ranges between 11% and 60% in their sentinel sites.¹³

Currently, there are approximately 50,000 IDU registered with the Guangxi provincial public security department. Local security agencies estimate the actual number is several times higher. Provincial behavioral surveillance data reports that syringe sharing among IDU is higher than in other provinces, 54.5% vs. 45.9%, respectively.¹³ It is highly likely this will contribute to a rapid increase in HIV infection among IDU in the coming years, which could subsequently spread into the general population.

In the beginning years of the HIV epidemic in Guangxi, most IDU and most known HIV cases were among urban inhabitants. With the improvement in roads and transportation systems linking urban to rural areas, the drug trade,

drug use and subsequently HIV has also followed to these rural areas.

This prospective cohort study, called HIV Prevention Trials Network (HPTN) 033, was based in Heng County, Guangxi, which is primarily rural and has an estimated population of 1.1 million. The primary objectives of this study were to observe HIV sero-incidence, participant retention rate and changes in drug-using and sexual risk behaviors among IDU targeted for inclusion in future HIV prevention studies. This was the first study done in Heng County to collect risk behavior and sero-status on their injection drug using population.

METHODS

Inclusion criteria for the HPTN 033 study were the following: (1) HIV-1 antibody negative at enrollment; (2) injected drugs at least three times per week in the previous month or on at least three occasions in the previous three months used injection equipment after another person; (3) expressed willingness to participate for twelve months; (4) were able and willing to provide written informed consent and sufficient locator information; and (5) were at least 18 years old at time of enrollment. Potential participants who had an obvious psychological/psychiatric disorder or any other condition that, in the opinion of the investigator, would preclude provision of informed consent, make participation in the study unsafe, or otherwise interfere with achieving the study objectives were excluded from the study.

The Guangxi Zhuang Autonomous Region Institutional Review Board (IRB) and the Western IRB in Olympia, Washington, approved the study protocol prior to the July 2002 start date.

Participants Recruitment and Retention

Between July and November 2002, potential participants were recruited through street outreach, publicity, and respondent-driven sampling, where IDU who participate in screening were encouraged to bring their friends for a small monetary incentive. These referrals were limited to a maximum of 5 persons per participant in order to enroll/attract a more representa-

tive sample of the local injection drug user population. The sampling methodology was a convenience sample using chain-referral sampling. Participants were recruited and completed all study procedures in either Mandarin Chinese or the local language, *Tu Baihua*. All recruiters and interviewers are fluent in both languages. Prior to the initiation of the study we informed the local public security officials about the study. They were supportive of the study and agreed not to target or interfere with participants.

One of the main objectives of the study was to estimate the retention rate of high-risk IDU in a standardized HIV research study. High retention rate in longitudinal studies plays a crucial role in the ability to prevent potential biases induced by missing data. A written manual was used to facilitate high retention rate during follow-up visits. Preparation for follow-up visits began with obtaining sufficient locator information from a participant at the enrollment visit. Each participant was required to provide at least two different contact sources to qualify for this study. The data manager entered the locator information for all enrolled participants into the Participant Information File System (PIFS) software program.

Whenever possible, follow-up visits were scheduled on the "target date," which was exactly 6 and 12 months after the enrollment date. To be considered retained, participants needed to return to the clinic during a 6 week window period, which was 2 weeks before and 4 weeks after their target date. Appointment reminder procedures every 6 months included: sending reminder letters or making phone calls 2-3 weeks before their target date; having the outreach workers go to their homes and/or named locator areas to locate participants or their contact people and employing local village doctors to help with retention efforts. In addition, study subjects received 50 yuan (\$6.25) for each study visit to cover transportation costs and their time.

Data Collection

Screening and enrollment procedures included several steps. Prescreening occurred during recruitment in the field to establish if there was interest in participation, communi-

cate the research site location and determine if participant met the pre-screening requirements. Screening at the study site confirmed eligibility and obtained consent to perform HIV-1 antibody testing by EIA (Vironostika HIV Uni-form II plus O; Organon Teknika) with confirmatory Western Blot (HIV Blot 2.2; GeneLabs Diagnostics, Singapore). A socio-demographics and risk assessment questionnaire, focusing on drug use and sexual behavior, was also administered at screening in Mandarin or local dialect after translation and backtranslation of questionnaire from English to Mandarin. The questionnaire was designed to collect self-reported sociodemographic data and behavioral information concerning drug injection practices (types of drugs, frequency of use, sharing experience) and characteristics of sexual behavior with primary and casual partners. Evidence of drug injection sites was also sought at time of interview. Participants were instructed to return within 14 days for their test results. At the return visit, after HIV antibody results were given, participants who tested HIV seronegative were offered enrollment into the study. Those who gave written informed consent were enrolled. Those who tested HIV seropositive were counseled and referred to physicians and local services.

The design of the prospective HIV incidence cohort study required follow-up study visits both 6 and 12 months after participant enrollment. During these two visits, participants completed an HIV behavioral risk assessment, received HIV pre-test and risk reduction counseling, and underwent phlebotomy for HIV antibody testing. Risk reduction counseling included information on safe injection and safe sex practices. Participants were counseled on the importance of using clean injection equipment and told how to clean their injection equipment. Condoms were also offered to participants. As with screening, participants returned to the site within 14 days to receive their HIV test results and for post-test counseling. For participants who tested HIV seropositive, their blood was re-drawn and re-tested for confirmation. Participants who tested HIV seropositive during 6 month and 12 month follow up visits were counseled and referred to available medical and psychosocial services.

Study staff made locator contacts with study participants at months 3 and 9. The locator contacts served the purpose of enhancing retention by providing a mechanism to confirm or update participants' locator information, confirming or re-scheduling the participant's next follow-up visit, reinforcing instructions for the participant to contact the study site to update locator information and, if needed, giving participants the option to request HIV counseling and/or testing between scheduled visits. In addition, any difficulties experienced in contacting participants at these time points served to trigger timely mobilization of outreach efforts to ensure that participants were located in time for the next scheduled follow-up visit. The contacts were conducted in-person at the study site, via telephone, or via street/home outreach.

During the course of the study follow-up and in a smaller separate follow-up study of participants, there was no evidence that subjects were harmed by public security officials as a consequence of being study participants.

Statistical Analysis

A sample size of 500 was set in order to achieve a half-width of about 2.5% for the 95% confidence interval for the HIV incidence (based on a 12-month retention rate of 90% and a true rate of 8% HIV seroincidence). Case report forms were faxed to the HPTN statistical and data management center (Statistical Center for HIV/AIDS Research and Prevention, Fred Hutchinson Cancer Research Center, Seattle, USA) where the data were entered into the study database. All analyses were performed using the SAS software (SAS, version 8.2). Descriptive statistics on sociodemographic and behavioral characteristics of screened participants were computed. HIV incidence density rate was calculated based on Poisson distribution, with person time of follow-up as the denominator. A proportional hazards model analysis was performed on discrete time scale of semi-annual visits to identify the baseline predictors (socio-demographic, drug use and sexual risk behaviors) of HIV incidence. A logistic regression was used to investigate the baseline factors contribution to the study retention rate. The generalized estimating equations regression method and McNemar's test of agreement

were used to analyze longitudinal trends in self reporting of drug use, sharing of injection equipment, and sexual behavior over time.

RESULTS

The recruitment, screening and enrollment of high-risk IDU occurred during a 5 month period beginning in July 2002 and ending in November 2002. More than 712 IDU were prescreened for eligibility and interest, and 172/702 (25%) tested positive for HIV-1 antibody. A total of 500 eligible high-risk IDU gave consent for this study. The ages of the participants ranged from 18 years to 51 years, with median of 26. The gender distribution was 96% males and 4% females. The majority of the participants were Han (94%). Most had no college education (99%). Sixty-two percent were single and 63% were unemployed. Most (66%) lived with their parents or relatives. All (100%) had injected drugs in the month prior to baseline and 93% reported injecting drugs at least 3 times per week in the three months prior to baseline.

Participants were considered retained at the 12-month visit if they completed the 12-month follow-up visit or if they had seroconverted prior to the 12-month visit. Under this definition, over-all retention rate was 87% (436/500) for the 12-month visit. Univariate logistic regression analysis did not identify any baseline predictors (socio-demographic, drug use and sexual risk behaviors) of retention. Of 64 participants lost to follow-up, two died, one withdrew from the study, and the remaining 61 were unable to be contacted.

During the 1-year follow-up period, 14 HIV antibody seroconversions were observed to have occurred within 450.5 person-years of risk. The observed HIV incidence rate was 3.1 per 100 person years [95% CI: 1.6%, 5.2%]. Univariate proportional hazard model analysis on discrete time scale of semi-annual visits did not identify any baseline predictors (socio-demographic, drug use and sexual risk behaviors) of HIV incidence.

Table 1 shows the self-reported changes in drug use behavior between baseline and 12-month follow-up. Injecting heroin alone at least once per week in the past three months sig-

nificantly decreased from 97% at baseline to 67% at 12-month follow-up ($P < 0.0001$). Injecting heroin mixed with another drug at least once per week in the past three months significantly decreased from 42% at baseline to 10% at 12-month follow-up ($P < 0.0001$). Injecting other drugs at least once per week in the past 3 months decreased from 8% at baseline to 2% ($P = 0.0002$). Among the participants who reported injecting heroin mixed with another drug and/or injecting other drugs, all reported the other drug was a benzodiazepine. The majority stated that that benzodiazepine was diazepam.

Table 2 shows the self-reported changes in sharing injection equipment over time. The percentage of participants who reported they had, at least once in the three months prior to the visit, shared a needle or used a needle after another person had used it significantly decreased from 68% at baseline to 9% at 12-month follow-up ($P < 0.0001$). Similarly, the percentages of those who reported they had, at least once during the three months prior to the visit, shared rinse water (75% to 8%), shared a cooker (34% to 2%), shared cotton (7% to 0%), or used front/back-loaded syringes (66% to 10%) all decreased significantly ($P < 0.0001$) from baseline to 12 months. Among those who injected after someone else, the percentage of participants who reported that they did not know the HIV status of the prior injector decreased from 68% at baseline to 17% at 12-month follow-up ($P < 0.0001$).

Table 3 shows the self-reported changes in sexual behavior, among male participants, between baseline and the 12-month follow-up. The time frame for all questions is six months prior to the visit at which they were asked. The mean number of different female sex partners decreased from 2.80 at baseline to 1.23 at 12-month ($P < 0.0001$). Among participants who had sex with a female partner(s) during the previous six months, the mean number of different sex partners decreased from 3.56 at baseline to 1.88 at 12-months ($P < 0.0001$). The percentage of participants who had sex with a non-primary female partner decreased from 51% at baseline to 28% at 12-months ($P < 0.0001$). There was a significant decrease in the mean number of new partners between baseline (1.55) and 12-months (0.66) ($P < 0.0001$).

TABLE 1. Changes in drug use behavior during the last 3 months at baseline, 6-months, and 12-months

Type of Drug	Pattern of Use	Timepoint			P-Value
		Baseline (BL)	Month 6	Month 12	BL vs. Month 12
Heroin alone	Never	3% 17/500	18% 63/360	33% 125/378	< 0.0001
	At least once	97% 483/500	83% 297/360	67% 253/378	
Cocaine	Never	99% 494/500	99% 356/360	100% 378/378	0.25
Heroin+ Cocaine	Never	100% 498/500	100% 360/360	100% 378/378	1.0000
Heroin + another drug	Never	58% 288/500	86% 310/360	90% 340/378	< 0.0001
	At least once	42% 212/500	14% 50/360	10% 38/378	
Opium	Never	> 99% 499/500	> 99% 359/360	100% 378/378	1.0000
Buprenorphine	Never	99% 496/500	100% 360/360	100% 378/378	0.25
Amphetamines	Never	100% 500/500	100% 360/360	100% 378/378	1.0000
Morphine	Never	100% 500/500	100% 360/360	100% 378/378	1.0000
Tranquilizers	Never	> 99% 498/500	100% 360/360	100% 378/378	1.0000
Other drug	Never	92% 460/500	97% 348/360	98% 370/378	0.0002
	At least once	8% 40/500	3% 12/360	2% 8/378	

Note: P-values computed using an exact McNemar's test for change in behavior between baseline and 12 months

Fewer participants reported they had new sex partners during the 6 months prior to the 12-month follow-up (25%) compared with the number who reported having new partners in the 6 months prior to the baseline visit (42%) ($P < 0.0001$). Among those who did report having new sex partners, the mean number of new sex partners decreased between baseline (3.70) and 12-months (2.69) ($P = 0.0123$).

DISCUSSION

This study found that the HIV seroincidence rate during this 12-month prospective cohort study among high-risk IDU in Guangxi was 3.1 per 100 person years [95% CI: 1.6%, 5.2%]. Previous smaller studies have reported HIV

seroincidence rates among other IDU populations in China. A 1998 study conducted in Pingxiang County in Guangxi province reported HIV incidence of 2.38 per 100 person-years among drug users at the first follow-up period and 6.86 per 100 person-years during the second follow-up visit.¹² A recent 12-month prospective cohort study in Xichang County of Sichuan province found that HIV incidence was 3.17 per 100 person-years [95% CI: 0.98%, 5.37%] at the 12 month follow-up visit (YM Shao, unpublished data). Both the above mentioned studies plus our results from this Guangxi study demonstrate that HIV is spreading rapidly among IDU in geographic areas other than Yunnan, the typical epicenter of the HIV/AIDS epidemic in China. At the time the above studies were conducted, neither drug

TABLE 2. Changes of injection equipment sharing behavior during the last 3 months at baseline, 6-months and 12-months

Sharing Injection Equipments		Timepoint			P-Value
		Baseline (BL)	Month 6	Month 12	BL vs. Month 12
Used needle after another has used it	Never	32% 159/500	79% 286/360	91% 343/378	< 0.0001
	At least once	68% 341/500	21% 75/360	9% 35/378	
Know HIV status of previous injector	Yes	32% 108/341	92% 69/75	83% 29/35	< 0.0001
	No	68% 233/341	8% 6/75	17% 6/35	
Used needle after HIV positive person has used it	Never	95% 103/108	94% 65/69	100% 29/29	
	At least once	5% 5/108	6% 4/69	0% 0/29	
Shared rinse water	Never	25% 125/500	69% 248/360	92% 347/378	< 0.0001
	At least once	75% 374/500	30% 109/360	8% 31/378	
	Do not know	< 1% 1/508	1% 3/360	0% 0/378	
Shared a cooker	Never	66% 331/500	95% 343/360	98% 369/378	< 0.0001
	At least once	34% 169/500	5% 17/360	2% 9/378	
Shared cotton	Never	93% 467/500	99% 358/360	100% 378/378	< 0.0001
	At least once	7% 33/500	1% 2/360	0% 0/378	
Used front or backloaded syringe*	Never	34% 172/500	74% 268/360	90% 341/378	< 0.0001
	At least once	66% 328/500	26% 92/360	10% 37/378	

Note: P-values computed using an exact McNemar's test for change in behavior between baseline and 12 months. P-values not presented could not be calculated using an exact McNemar's test.

* Preloading syringe through front or back of syringe with use of a previously used syringe or needle.

treatment nor needle and syringe exchange programs were readily available in the study areas.

The overall retention rate at the end of 12 months was 87%. Retention methods used in the study were designed by borrowing experiences from other international studies.^{14,15} Maintaining high retention rates is generally believed to be more difficult when working with IDU in prospective cohort studies. Some studies have reported that approximately 25% of the participants were lost to follow-up.^{16,17} Our results suggest that a well designed and thoroughly executed retention plan is key in achieving high retention rates even when work-

ing with an IDU population. No baseline behavioral characteristics were found to significantly affect retention in this study. Other studies have also found that HIV high-risk behaviors were not associated with cohort retention.^{14-16,18}

Our study identified self-reported changes of high risk behaviors over the 12 month follow-up period. Statistically significant decreases in reported behaviors were observed for injection of heroin alone, injection of heroin plus another drug, and direct sharing or indirect sharing of injection equipment. Statistically significant changes in male sexual behaviors

TABLE 3. Changes in male sexual behavior during the last 6 months at baseline, 6-months and 12-months

Sexual Behavior (last six months)		Timepoint			P-Value for Timepoint Difference		
		Baseline (BL)	Month 6	Month 12	BL vs. Month 6	BL vs. Month 12	Month 6 vs. 12
Number of different female partners	Mean (SE)	2.80 (0.19)	1.52 (0.13)	1.23 (0.10)	< 0.0001	< 0.0001	0.0120
	Median	1.0	1.0	1.0			
	Min-max	0.0-30.0	0.0-20.0	0.0-20.0			
	N	479	350	363			
Vaginal/anal sex with female	Yes	79% 377/479	66% 232/350	65% 237/363	< 0.0001	< 0.0001	0.8858
If yes—number of different female partners	Mean (SE)	3.56 (0.22)	2.29 (0.18)	1.88 (0.13)	< 0.0001	< 0.0001	0.0098
	Median	2.0	1.0	1.0			
	Min-max	1.0-30.0	1.0-20.0	1.0-20.0			
	N	377	232	237			
Primary female partner	Yes	49% 233/479	46% 162/350	46% 166/363	0.0560	0.1389	0.6803
Female partner inject drugs	Yes	8% 18/233	7% 11/162	5% 8/166	0.5299	0.0603	0.2760
	No	91% 212/233	93% 151/162	95% 158/166			
	Don't know	1% 3/233	0% 0/162	0% 0/166			
Sex with non- primary female	Yes	51% 245/479	30% 106/350	28% 100/363	< 0.0001	< 0.0001	0.3177
How many new partners did you have?	Mean (SE)	1.55 (0.15)	0.74 (0.10)	0.66 (0.09)	< 0.0001	< 0.0001	0.1905
	Median	0.0	0.0	0.0			
	Min-max	0.0-30.0	0.0-20.0	0.0-19.0			
	N	479	350	363			
Did you have new sex partners?	Yes	42% 201/479	27% 93/350	25% 89/363	< 0.0001	< 0.0001	0.4958
If yes—how many new partners?	Mean (SE)	3.70 (0.29)	2.77 (0.25)	2.69 (0.29)	0.0101	0.0123	0.6286
	Median	3.0	2.0	2.0			
	Min-max	1.0-30.0	1.0-20.0	1.0-19.0			
	N	201	93	89			

Note: P-values computed via GEE methodology required for correlated data.

included a decrease in the number of non-primary female partners and the number of new female partners. The reported reduction in drug injection risk behaviors is similar to other large cohort studies of IDU in developed countries.¹⁹⁻²³ Because there was no control group, however, it is difficult to attribute this observed reduction to the counseling and education participants received during their visits. Also, given the high HIV incidence and reliance on self-report data, we cannot be certain that the reported reduction in drug injecting and reduc-

tion in injection equipment sharing is accurate. It is very possible that high risk drug and/or sexual behaviors were under-reported which would have limited the detection of a significant association between behavioral risk variables and HIV incidence.

Limitations of this study also include a possible selection bias. Because this study was restricted to IDU within the inclusion criteria, these results may not be representative of the general IDU population in this region and should be used with caution when applied to

IDU in other regions. IDU who injected drugs and shared injection equipment less frequently than required by our inclusion criteria were not included in this study. It is possible that if these IDU were included in this study, characteristics of drug injection behavior (such as the frequency of injection and the frequency of sharing equipment) might be found to be statistically associated with HIV seroconversion.

Our data strongly demonstrate that HIV is spreading rapidly among high-risk IDU in Guangxi, China. The high seroincidence and retention rate in this study population offer the opportunity to conduct HIV vaccine and other intervention trials to prevent HIV transmission.

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Mothball Withdrawal Encephalopathy— Case Report and Review of Paradichlorobenzene Neurotoxicity

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ABSTRACT. Paradichlorobenzene (PDB) is a common household deodorant and pesticide found in room deodorizers, toilet bowl fresheners, and some mothballs. Although human exposure to the compound is generally limited and harmless, PDB in larger doses can produce neurotoxic effects, including a chemical “high” similar to that seen with inhalants such as toluene. Although rare, frank addiction to PDB has been reported, and, in such cases, has been associated with gait ataxia, tremor, dysarthria, limb weakness, and bradyphrenia, in various combinations. In such cases, the adverse neurologic consequences have been presumed to result from a direct toxic effect of this small, organic molecule. We report a case of chronic mothball ingestion where profound encephalopathy with cognitive, pyramidal, extrapyramidal, and cerebellar features appears to have been largely the result of PDB withdrawal, rather than direct toxicity. This case raises important questions about the mechanism of PDB neurotoxicity and possible treatment options for PDB-addicted patients. We propose that in cases with clear clinical deterioration after abstinence, readministration and gradual taper of PDB might be considered a therapeutic option. doi:10.1300/J465v27n04_08 [Article copies available for a fee from The Haworth Document Delivery Service: 1-800-HAWORTH. E-mail address: <docdelivery@haworthpress.com> Website: <http://www.HaworthPress.com> © 2006 by The Haworth Press, Inc. All rights reserved.]

KEYWORDS. 2-dichlorobenzene, neurotoxicity syndromes, substance-related disorders, substance withdrawal syndrome, basal ganglia diseases, catatonia

INTRODUCTION

Paradichlorobenzene (PDB) is a small organic molecule found in room deodorizers, toilet bowl fresheners, and some mothballs.

Accidental exposure to high levels of PDB may have adverse hepatic, renal, and hematological effects.¹ PDB also depresses the central nervous system, and can produce intoxicating effects similar to those of inhalants such as tolu-

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ene. Initial exposure to PDB may be followed by repeated voluntary exposures and even frank addiction.^{2,3} Although most reports of neurotoxicity suggest a direct effect of PDB, we report a case in which chronic mothball ingestion was associated with a PDB withdrawal syndrome characterized by bradyphrenia, akinesia, rigidity, mutism, dystonia, gait ataxia, and widespread denervation of limb muscles.

CASE REPORT

A healthy 42-year-old African-American woman with a remote history of major depression with psychotic features was admitted to the Neurology service at another hospital with four months of increasing gait unsteadiness. Initial assessment including brain MRI did not reveal a clear etiology. The patient had been eating mothballs and toilet-bowl fresheners for at least two years, but her presentation was deemed inconsistent with known naphthalene toxicity (the most common active ingredient of mothballs). She was transferred to Psychiatry for treatment of suspected conversion disorder.

Over three weeks, her neurologic status deteriorated. Her behavior was described as "increasingly bizarre." Speech became slow and hypophonic, with single-word answers; complete mutism ensued. She developed cogwheel rigidity and became unable to walk. EEG showed slow activity over the left occiput, but brain SPECT imaging was normal. Tests for hypothyroidism, syphilis, and Lyme disease were normal, as were urine toxicology, 24-hour urine for heavy metals, serum anti-Purkinje cell antibodies and CSF 14-3-3 protein. In total, three lumbar punctures revealed normal CSF glucose and white blood cell counts with negative bacterial and viral studies. Primary psychiatric catatonia was considered. Therapeutic trials of antidepressants, antipsychotics, and benzodiazepines produced no clinical improvement.

Four weeks after hospitalization, she was transferred to Neurology at Johns Hopkins Hospital. She was mute, severely bradykinetic, and moderately rigid with prominent torticollis and dystonic posturing of both hands, but able to follow simple commands intermittently such as "wiggle your toes." Multiple EEGs showed

diffuse slowing. MRI revealed scattered foci of T2 signal hyperintensity in the periventricular white matter, splenium of the corpus callosum, and deep cerebellar nuclei bilaterally, suggesting patchy demyelination (Figure 1). MR spectroscopy (MRS) showed changes consistent with combined demyelination and axonal loss. Electromyography revealed widespread denervation of limb muscles with intact sensory responses, suggesting an active polyradiculopathy or motor neuronopathy. Urine porphyrins and serum ceruloplasmin and thiamine levels were normal. A search for occult malignancy was unrevealing. A urinary organic acid assay sent to assess for possible mitochondrial disease disclosed the presence of 2,5-dichlorophenol (DCP, a PDB metabolite), more than two months after initial hospitalization. The assay revealed no other metabolic abnormalities, nor the presence of naphthalene, nor its metabolites.

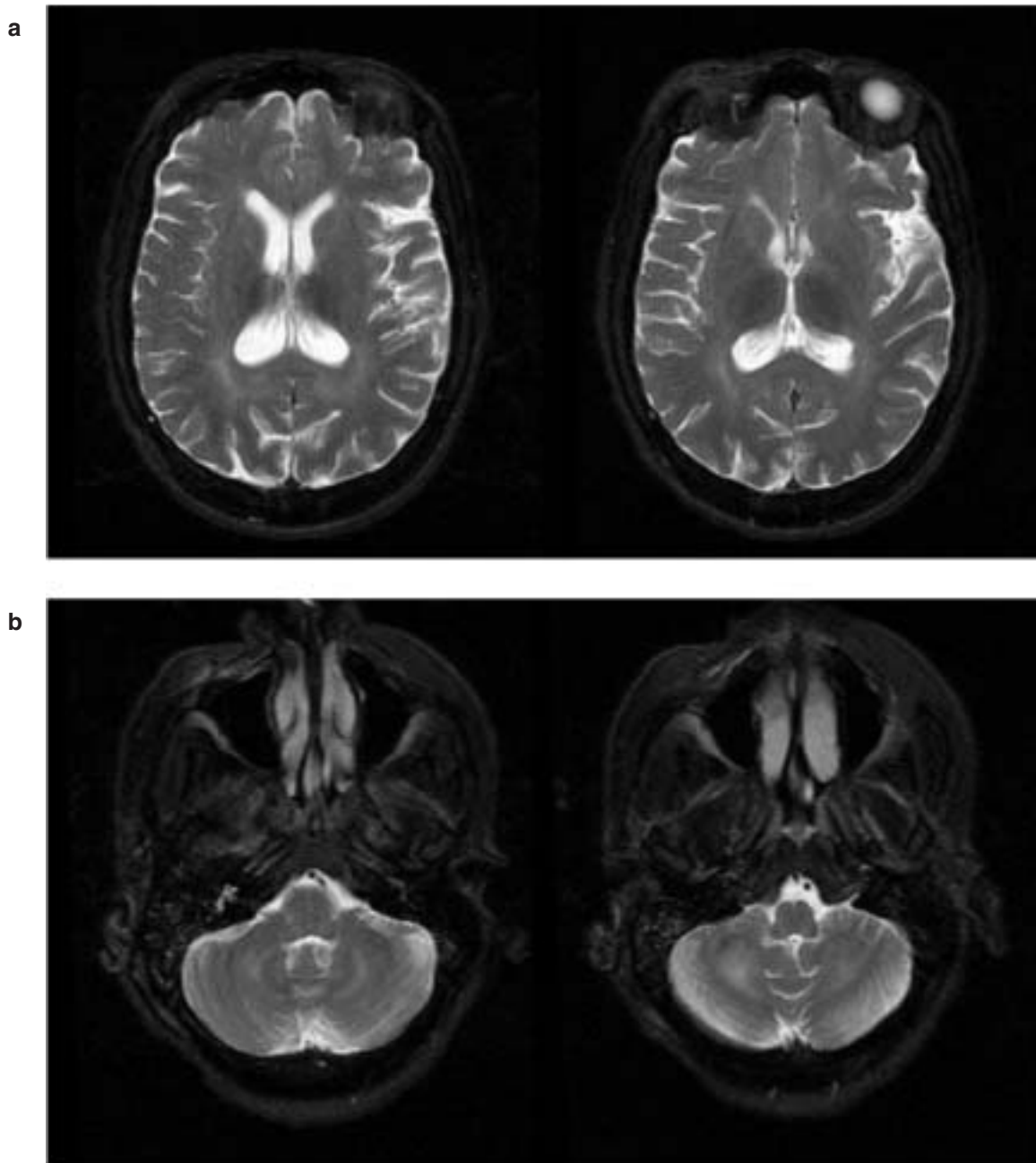
During her hospital stay, the patient remained nonverbal and minimally responsive. She often attended to examiners with her eyes, intermittently showed two fingers to command, and sporadically waved goodbye to the team exiting the room. Therapeutic trials of methylphenidate and carbidopa-levodopa produced no improvement. A gastrostomy tube was placed, and she was discharged to a rehabilitation facility.

Re-examination 6 months later revealed an alert, cooperative woman with normal language, naming, immediate recall, and attention but impaired calculation and abstract reasoning. Torticollis had resolved and increasing proximal strength allowed self-feeding despite bilateral hand contractures. She ambulated with assistance and a walker. She had no memory of events occurring during hospitalization. She recalled eating mothballs regularly, but could not explain how this habit began. One year after hospitalization, the patient could converse normally and eat independently, but remained in a nursing home due to impaired executive functioning and inability to walk more than short distances.

DISCUSSION

Our patient initially developed disturbed gait that began four months before hospitaliza-

FIGURE 1. MRI revealed patchy areas of T2 signal hyperintensity in the (a) periventricular white matter, splenium of the corpus callosum, and (b) deep cerebellar nuclei bilaterally, suggestive of demyelination.



tion. Because PDB abstinence might have begun either before or at initial hospitalization, the clinical symptoms may either have been due to direct toxic or withdrawal effects. However, the rapid neurologic decline weeks after hospital admission makes the overall clinical syndrome suspicious for PDB withdrawal.

Our patient's clinical profile included bradyphrenia, akinesia, rigidity, mutism, dystonia, gait ataxia, and widespread denervation of limb muscles. These signs point to diffuse central nervous system dysfunction with dominant frontal lobe, basal ganglia, cerebellar, and anterior horn cell involvement. The findings and

time course are strikingly similar to those described in five previously reported cases of PDB addiction (Table 1). Notably, in one case symptoms began shortly after hospitalization-imposed abstinence and became worse with time, suggesting withdrawal effects.⁴ In another case, symptoms developed soon after PDB ingestions stopped temporarily, lessened when ingestions resumed, recurred when ingestions stopped permanently, then gradually abated over 4 months.⁵ The effective PDB ‘challenge,’ ‘re-challenge,’ and recovery in that case provides compelling evidence of withdrawal toxicity.

If PDB withdrawal is the cause there must be a biologically plausible mechanism to produce the observed syndrome. PDB is lipophilic and can accumulate in adipose tissue,^{7,8} so it may accumulate in and damage myelin, possibly leading to secondary neuronal dysfunction. In our patient, MRI and MRS were indeed consistent with demyelination. However, this does not explain why symptoms developed (presumably) only after abstinence and why the clinical severity was out of proportion to the radiographic changes, contrasting sharply with other demyelinating diseases like multiple sclerosis. Instead, neuronal loss, as implied by MRS and widespread limb denervation by EMG, might explain the clinical severity. It is known that withdrawal can destroy neurons in animal models of abstinence after chronic exposure to ethanol.⁹ Likewise, ethanol withdrawal after chronic exposure produces life-threatening central nervous system dysfunction in humans. Although we could not find

similar evidence for PDB specifically, it is plausible that PDB withdrawal could lead to neuronal death and severe neurologic dysfunction.

Given the combination of biologic plausibility and clinical evidence in support of a withdrawal mechanism, we believe this to be a case of “mothball withdrawal encephalopathy.” Our case suggests withdrawal may be more destructive than exposure, and raises questions about this unusual clinical syndrome. First, how do PDB and its metabolite DCP relate to the patient’s clinical syndrome? Liver clearance of both substances is fast (days) but accumulation in adipose tissue and depletion of these stores is slow (weeks).^{7,8} So, although we found DCP and not PDB in our patient’s urine, this is pharmacologically consistent with either DCP or PDB adipose stores, depending on whether liver metabolism of the parent compound occurs before or after accumulation in fatty tissues. Which compound’s withdrawal was primarily responsible for nervous system damage remains unclear.

Second, what is the most appropriate treatment for chronic PDB addiction? To speed PDB/DCP depletion from adipose tissue in our patient, we considered serum dialysis, a ketogenic diet, and displacement by propofol, but we found no empiric data or clinical consensus to support using these methods. We also considered feeding the patient mothballs or administering PDB parenterally to treat the suspected withdrawal syndrome (similar to historical treatments for alcohol withdrawal syndrome, using parenteral ethanol), but this seemed im-

TABLE 1. Summary of clinical features in reported cases of PDB addiction-associated neurotoxicity.

Reference	Age/gender	Symptoms	Known timecourse
[2]	16 yo female	Decreased visual acuity, cerebellar ataxia	Inhalation of PDB for unknown duration, symptoms resolved a few months after final exposure
[3]	54 yo female	Progressive weakness, difficulty walking	Decades sniffing mothball/toilet deodorizers, no long term follow up
[5]	19 yo female	Dermatosis, unsteady gait, hand tremor, mental sluggishness	2.5 yr PDB mothball ingestion, symptoms resolved 4 months after final exposure
[6]	25 yo female	Cerebellar ataxia, dysarthria, generalized weakness, hypotonia	6 yr PDB powder exposure, symptoms resolved 6-8 months after final exposure
[4]	21 yo female	Acute cerebellar syndrome progressing to mutism and catatonia	7 mo PDB mothball ingestion, some recovery 2 months after final exposure

prudent given the severity and duration of her neurologic syndrome at the time of diagnosis. Furthermore, previous reports indicated that recovery would likely occur within 4-8 months, as it indeed did for our patient, though with significant neurologic residua.

Further scientific study might be beneficial in clarifying the underlying mechanisms of PDB neurotoxicity, and might help guide therapeutic decision making. However, without new scientific information, we encourage providers to at least consider early re-administration and gradual taper of PDB as a possible therapeutic option in cases of PDB addiction with clear clinical deterioration immediately following a period of abstinence.

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ADDENDUM

While this report was under review, another case of PDB mothball addiction was reported (Feuillet L, Mallet S, Spadari M. *Twin girls with neurocutaneous symptoms caused by mothball intoxication*. *N Engl J Med*, 2006; 355(4): 423-4.). Symptoms in the more heavily affected patient began after two months of abstinence and included dermatosis, unsteady gait, a cerebellar syndrome, and mental sluggishness, among others. A total recovery occurred after 6 months. This is consistent with the other cases in Table 1.



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