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COCAINE TREATMENT

Early Results From Various Approaches



**Health, Education, and
Human Services Division**

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Chairman
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Ranking Minority Member
Committee on Government Reform and Oversight
House of Representatives

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Cocaine use in the United States remains a serious and costly epidemic. In 1994, the National Household Survey on Drug Abuse conservatively estimated that more than three-quarters of a million people had used cocaine at least once a week within the past year. In 1993, cocaine was associated with almost 4,000 deaths.¹ Today, an estimated \$10 billion per year is lost in cocaine-related crimes and productivity.²

Although cocaine admissions to state-supported drug abuse treatment programs between 1985 and 1990 increased dramatically—from almost 39,000 people to more than 200,000—we found in 1991 that an effective treatment for cocaine addiction had not yet been identified.³ Today, public/private expenditures on cocaine-related treatment total about \$1 billion per year.

Because of cocaine's serious health, economic, and criminal justice implications for the nation, we have provided a status report on recent progress made in finding an effective treatment for cocaine users.⁴ Specifically, we reviewed the various types of federally funded treatment approaches evaluated over the past 5 years (1991 through 1995) to (1) determine the extent to which these therapies have proven successful and (2) identify additional research initiatives necessary to increase our knowledge of cocaine treatment effectiveness.

¹Drug Abuse Warning Network, *Annual Medical Examiner Data 1993*, Statistical Series 1, No. 13-B (Rockville, Md.: Substance Abuse and Mental Health Services Administration, 1995), p. 21.

²RAND, "Treatment: Effective (But Unpopular) Weapon Against Drugs," *RAND Research Review*, Vol. XIX, No. 1 (Spring 1995), p. 4.

³Drug Abuse: *The Crack Cocaine Epidemic: Health Consequences and Treatment* (GAO/HRD-91-55FS, Jan. 30, 1991), p. 24.

⁴"Treatment" does not refer to a singular therapeutic approach. Treatment approaches for individuals primarily using crack or cocaine, for example, may not be most appropriate for methadone clients who use cocaine as a secondary drug of choice.

To conduct our work, we reviewed the literature on cocaine treatment published from 1991 through 1995, examined records from the National Institute on Drug Abuse and the Center for Substance Abuse Treatment, synthesized the latest cocaine treatment research findings related to drug use and client retention in treatment programs, and assessed the utility of the various types of treatment approaches. In addition, we interviewed 20 cocaine treatment experts to determine important next steps in the development of an effective cocaine treatment strategy. (See app. I for further detail on our methodology.) We did our work from March 1995 to March 1996 in accordance with generally accepted government auditing standards.

Results in Brief

Given the relative recency of the epidemic, cocaine treatment research is still in the early stages of development. Attempts to treat cocaine users with approaches initially developed for other drugs had limited success. As a result, the federal government began to fund more cocaine-related treatment studies. Preliminary results of these studies show that three cognitive/behavioral treatment approaches—relapse prevention, community reinforcement/contingency management, and neurobehavioral therapy—have shown early promise with cocaine-abusing and cocaine-dependent clients, many of whom are classified as “hardcore” users. Clients treated with these approaches have demonstrated prolonged periods of cocaine abstinence and high rates of retention in treatment programs. For example, more than 60 percent of the cocaine-addicted clients who attended a relapse prevention program in New York were continuously abstinent from cocaine during the 6- to 24-month follow-up period; more than 70 percent completed the relapse prevention program. About half the cocaine-dependent clients receiving community reinforcement/contingency management in a Vermont outpatient program remained continuously abstinent through 4 months of treatment; 58 percent completed the entire 6-month course of therapy. And 36 percent of the cocaine-using clients enrolled in a California neurobehavioral therapy program were abstinent from cocaine 6 months after entering treatment; the average length of stay in the program was 18 weeks.

Research results on the effectiveness of pharmacological agents have been less favorable. Twenty major medications for the treatment of cocaine addiction have been studied by the National Institute on Drug Abuse (NIDA). While some medications have yielded favorable results in one or more clinical trials, no medication has demonstrated consistent

effectiveness in treating cocaine users. Further, no medication has yet been submitted to the Food and Drug Administration (FDA) for approval for cocaine treatment.

Cocaine treatment experts emphasized the importance of conducting more rigorous treatment evaluation studies, including identifying the important components of treatment, determining appropriate intensities and durations of treatment, and developing better assessments of clients' readiness and motivation for treatment.

Background

Cocaine addiction has been associated with a variety of serious health consequences: cardiovascular and respiratory problems, psychiatric disorders, acquired immunodeficiency syndrome (AIDS), sexually transmitted diseases, early child development abnormalities, and death. Because cocaine use became epidemic in the early 1980s, research opportunities have been limited, and a standard cocaine treatment has not yet been found. Many substance abuse centers have provided cocaine users with the same treatment approaches provided to opiate and other drug users. But these treatments have not been as successful for cocaine users, who have demonstrated high relapse and dropout rates. The large-scale Treatment Outcome Prospective Study (TOPS)⁵ showed that about one-third of the clients who reported returning to cocaine use in the year after treatment began to do so as early as the first week following treatment termination. Another 25 percent began using the drug within 2 to 4 weeks following treatment termination, for a cumulative first-month relapse rate of 57 percent. Studies of crack cocaine users found that 47 percent dropped out of therapy between the initial clinic visit and the first session; three-quarters dropped out by the fifth session.

Because of this lack of treatment success, in the late 1980s and early 1990s the federal government began playing a more active role in sponsoring cocaine-related treatment research, principally through NIDA⁶ and the Center for Substance Abuse Treatment (CSAT).⁷ NIDA is the largest federal sponsor of substance abuse-related research, conducting work in treatment and prevention research, epidemiology, neuroscience, behavioral research, health services research, and AIDS. Since 1991, NIDA

⁵TOPS, a national research study of community treatment programs, was initiated in the late 1970s. The study was conducted by the Research Triangle Institute and supported by NIDA.

⁶NIDA is a part of the Department of Health and Human Services' National Institutes of Health.

⁷CSAT is part of the Substance Abuse and Mental Health Services Administration of the Department of Health and Human Services.

has funded about 100 cocaine treatment grants and conducted in-house research through its laboratory facilities. CSAT's mission includes developing treatment services, evaluating the effectiveness of these services, and providing technical assistance to providers and states. Since 1991, CSAT has funded approximately 65 substance abuse research projects with implications for cocaine addiction treatment.

CSAT cocaine-related data were not yet available at the time this report was published. Results therefore derive from a literature review of studies published from 1991 through 1995 and ongoing NIDA-supported cocaine studies, for which some outcome data were available.

During the 5-year period, two broad types of cocaine treatment approaches received research emphasis: cognitive/behavioral therapy and pharmacotherapy. Additionally, acupuncture has emerged as a potential therapy in the treatment of cocaine. Much of this research has been conducted in outpatient treatment settings, with a focus on "cocaine-dependent"⁸ clients—many of whom are considered to be "hardcore" drug users.⁹

Cognitive/Behavioral Therapies

Cognitive/behavioral therapies aim to modify the ways clients think, act, and relate to others, thereby facilitating initial abstinence and a continued drug-free lifestyle. These therapies include the psychotherapies, behavior therapies, skills training, and other counseling approaches. Three types of cognitive/behavioral therapies have received recent attention: relapse prevention, community reinforcement/contingency management, and neurobehavioral therapy.

Relapse prevention focuses on helping clients to identify high-risk, or "trigger," situations that contribute to drug relapse and to develop appropriate behaviors for avoiding, or better managing, these situations. For example, Yale University's Substance Abuse Treatment Unit has three principal elements in its 12-week relapse prevention program. First, clients identify personal triggers by keeping a daily log of the situations in which they crave the drug. Second, they work with therapists to learn more effective ways of coping with and avoiding these and other commonly

⁸Cocaine dependence is the most serious of all the cocaine diagnoses. Clients diagnosed as "cocaine-dependent" demonstrate myriad symptoms, including continual cocaine use and withdrawal symptoms; frequent intoxication; social and occupational problems; and physical, psychological, and emotional maladies.

⁹Treatment of Hardcore Cocaine Users (GAO/HEHS-95-179R, July 31, 1995).

perceived triggers. And third, therapists help clients extinguish the drug-craving reactions to these triggers. Clients are taught that relapse is a process, that social pressures to use drugs can be formidable, and that lifestyle changes are necessary to discourage future substance abuse.

Community reinforcement/contingency management aims to help the client achieve initial abstinence as well as an extended drug-free lifestyle. The therapy consists of several key community-oriented components, including the participation of a client's significant other (family member or friend) in the treatment process; providing management incentives or rewards¹⁰ for drug abstinence; providing employment counseling when needed; and encouraging client participation in recreational activities as pleasurable, healthy alternatives to drug use. If clients remain abstinent, they receive vouchers from the program and earn the right to participate in desired activities with their significant other. If clients test positive for drug use, or do not submit to urine testing, negative sanctions are applied (for example, their vouchers are rescinded). In this manner, community reinforcement therapy teaches clients about the consequences of their actions and strengthens family and social ties.

Neurobehavioral treatment is a comprehensive, 12-month outpatient treatment approach that includes individual therapy, drug education, client stabilization, and self-help groups. Relapse prevention techniques are included but constitute only a subset of neurobehavioral treatment.¹¹ Five major stages of recovery are distinguished during the treatment process—withdrawal, “honeymoon,” “the wall,” adjustment, and resolution—with emphasis on addressing the client's behavioral, emotional, cognitive, and relational problems at each stage of recovery. For example, in the withdrawal stage, depression, anxiety, self-doubt, and shame (emotional problems) and concentration difficulties, cocaine cravings, and short-term memory disruption (cognitive problems) are addressed. In the first 6 months, individual counseling is emphasized; in the second 6 months, weekly group counseling is provided, with optional individual and couple therapy sessions.

¹⁰The incentive or reward programs are typically referred to as “contingency management” or “voucher incentive” programs because vouchers for material goods are provided on a contingency basis (that is, when tests show that the client has not been using drugs).

¹¹Rewards for remaining abstinent are less emphasized in neurobehavioral therapy, as compared with community reinforcement.

Pharmacotherapy

Pharmacotherapy involves the use of medications to combat cocaine abuse and addiction. Recently, NIDA's pharmacotherapy research has focused on two objectives: facilitating initial abstinence and supporting an extended, drug-free lifestyle. To facilitate initial abstinence, research has focused on medications that treat the withdrawal symptoms of cocaine addiction and block the euphoric high induced by the drug. To help maintain an extended drug-free lifestyle, research has focused on blocking the client's craving for cocaine, treating the underlying psychopathologies, and treating the toxic effects of cocaine on the brain.

Acupuncture

The use of acupuncture in drug abuse treatment has not been limited to cocaine addiction. It has also been used during the past 20 years to treat addictions to opiates, tobacco, and alcohol. A Yale University acupuncture treatment program for cocaine abuse involved the insertion of needles into each ear at five strategic points, for a period of 50 minutes per session, over an 8-week period. Through the first 6 weeks, clients received the acupuncture therapy 5 days a week; in weeks 7 and 8, treatment was reduced to 3 days a week. Treatment was provided in a group context.

Three Cognitive/Behavioral Therapies Appear Favorable, but No Pharmacological Therapy Has Been Consistently Effective

The results from NIDA's cocaine treatment grants are only now becoming available. Because cocaine therapies are still in their early stages of development, treatment outcome results cannot be generalized to all cocaine users. However, early results from a review of the literature and ongoing NIDA studies reveal the promise of three cognitive/behavioral approaches to treatment. Moreover, while a pharmacological treatment has not yet been consistently demonstrated, NIDA is continuing to actively pursue the biology of cocaine addiction. Further, few well-designed methodological studies of acupuncture exist, but the limited research in this area demonstrates at least some positive findings.

Three Cognitive/Behavioral Treatments Appear Effective in Outpatient Settings

Early research indicates relapse prevention, community reinforcement/contingency management, and neurobehavioral therapy are potentially promising cocaine-addiction treatment approaches for promoting extended periods of client abstinence and treatment retention in outpatient treatment settings.¹² Table 1 provides an overview of cognitive/behavioral study methodologies and results.

¹²Since journals frequently do not publish studies with nonsignificant findings, we cannot determine how many attempted cognitive/behavioral studies have proven unsuccessful. This report is based only on available findings.

Table 1: Methodology and Results of Illustrative Cognitive/Behavioral Studies

Study group/publication date/affiliation	Sample design/size	Client diagnosis/demographics	Treatment outcomes	Study period
Relapse prevention				
Carroll and others (1994); Yale University, New Haven, Conn.	Random; N=121	<p>Clients met criteria for cocaine dependence</p> <p>average age: 29 male: 79% white: about 50% unemployed: about 40% single/divorced: about 70% at least high school graduate: about 80%</p>	Cocaine-abstinent at least 70% of the time in treatment	12 wks.
Carroll and others (1991); Yale University, New Haven, Conn.	Random; N=42	<p>Clients met criteria for both cocaine abuse and dependence</p> <p>average age: 27 male: 67% white: 67% average years of education: 13</p>	54% of high-severity cocaine users were able to attain at least 3 weeks of continuous abstinence; only 9% of high-severity cocaine users receiving standard psychotherapy could achieve this	12 wks.
Washton and Stone-Washton (1993); Washton Institute, New York	Consecutive admissions; N=60	<p>Clients met criteria for severe psychoactive drug dependence (85% were cocaine addicts)</p> <p>average age: about 35 male: about 80% white: about 70% employed: about 90%</p>	More than 60% abstinent from cocaine during 6- to 24-month follow-up period	About 28 wks.
Wells and others (1994); University of Washington, Seattle	Alternative assignment; N=110	<p>Cocaine was primary drug of choice</p> <p>average age: 29 male: 64% white: 84% employed full time for past 3 years: 68% average years of education: 13</p>	Average number of days of cocaine use cut by 71% within 6 months	24 wks.
Community reinforcement/contingency management				
Higgins and others (1991); University of Vermont, Burlington	Consecutive admissions; N=25	<p>Clients met criteria for cocaine dependence</p> <p>average age: 29 education ≥12 years: 46% employed: 62% single: 54%</p>	46% were continuously abstinent from cocaine for 8 treatment weeks	12 wks.

(continued)

Study group/publication date/affiliation	Sample design/size	Client diagnosis/ demographics	Treatment outcomes	Study period
Higgins and others (1993); University of Vermont, Burlington	Random; N=38	Clients met criteria for cocaine dependence average age: 29 male: 89% white: 100% unmarried: 89% completed high school: 63% employed: 42%	42% were continuously abstinent from cocaine for 16 treatment weeks	24 wks.
Contingency management only				
Silverman and others (1994, 1995); Johns Hopkins University, Baltimore	Frequency of cocaine-positive urines during initial 5 weeks of methadone therapy; N=37	Clients met criteria for heroin and cocaine dependence average age: 36 black: 26% married: 16% completed at least high school: 74% employed full time: 47%	Nearly 50% of the clients receiving vouchers for cocaine-free urines remained continuously abstinent from cocaine for 7 to 12 weeks	12 wks.
Neurobehavioral therapy				
Shoptaw and others (1994); Matrix Institute, Los Angeles	Random; N=146	Clients met criteria for stimulant abuse or dependence average age: 31 male: 84% white: 63% Hispanic: 25% average years of education: 13 unmarried: 78%	36% remained continuously abstinent from cocaine for at least 8 treatment weeks; 38% were abstinent from cocaine at 6-month follow-up	12 mos.
Rawson and others (1993); Matrix Institute, Los Angeles	Open trial; N=486	Cocaine-using clients average age: 30 male: 74% white: 76% average years of education: 14 single: 54%	At least 40% at two treatment sites remained continuously abstinent from cocaine through 6 months of treatment	6 mos.
Rosenblum and others (1994); National Development and Research Institutes, Inc., New York	Random; N=77	Methadone clients who met criteria for cocaine dependence age 24 to 43: 87% Hispanic: 64% black: 31% unemployed: 77% married/common law: 38% completed at least high school: 42%	Clients attending 3 to 19 sessions reduced past-month cocaine use by 5%; those attending 85 to 133 sessions reduced past-month cocaine use by 60%	6 mos.

(continued)

Study group/publication date/affiliation	Sample design/size	Client diagnosis/demographics	Treatment outcomes	Study period
Magura and others (1994); National Development and Research Institutes, Inc., New York	Random; N=62	Methadone clients who met criteria for cocaine dependence average age: 36 male: 56% Hispanic: 72% black: 23% married/common law: 49% completed at least high school: 38%	Group demonstrated significant decrease in cocaine use between entering treatment and 6-month follow-up; clients not receiving neurobehavioral therapy showed no significant decrease	6 mos.

Relapse Prevention

Clients who received relapse prevention treatment have demonstrated favorable abstinence rates not only during the period of treatment, but during follow-up periods as well. Client treatment retention results also appear to be favorable. For example, cocaine-dependent clients participating in a 12-week Yale University program focusing on relapse prevention were able to remain cocaine abstinent at least 70 percent of the time while in treatment.¹³ A year after treatment, gains were still evident: clients receiving relapse prevention treatment and a placebo medication were reported to have used cocaine on average fewer than 3 days in the past month.¹⁴

Positive outcome results were also found in two other programs: more than 60 percent of the primarily middle-class, cocaine-addicted clients attending a relapse prevention program at the Washton Institute in New York were abstinent from cocaine during the 6-to 24-month follow-up period.¹⁵ Similarly, in the Seattle area, cocaine-using clients cut their average number of days of cocaine use by 71 percent within 6 months.¹⁶

¹³Kathleen Carroll, Bruce Rounsaville, Lynn Gordon, Charla Nich, Peter Jatlow, Roseann Bisighini, and Frank Gawin, "Psychotherapy and Pharmacotherapy for Ambulatory Cocaine Abusers," *Archives of General Psychiatry*, Vol. 51 (1994), pp. 177-187.

¹⁴Unpublished 12-month data provided by Kathleen Carroll and Charla Nich, Oct. 19, 1995.

¹⁵Arnold Washton and Nannette Stone-Washton, "Outpatient Treatment of Cocaine and Crack Addiction: A Clinical Perspective," *National Institute on Drug Abuse Research Monograph #135* (Rockville, Md.: National Institute on Drug Abuse, 1993), pp. 15-30.

¹⁶Elizabeth Wells, Peggy Peterson, Randy Gainey, J. David Hawkins, and Richard Catalano, "Outpatient Treatment for Cocaine Abuse: A Controlled Comparison of Relapse Prevention and Twelve-Step Approaches," *American Journal of Drug and Alcohol Abuse*, Vol. 20, No. 1 (1994), pp. 1-17.

Community
Reinforcement/Contingency
Management

Among high-severity¹⁷ cocaine addicts participating in another Yale program, it was also found that 54 percent receiving relapse prevention therapy were able to attain at least 3 weeks of continuous abstinence, while only 9 percent of those receiving the interpersonal psychotherapy could remain abstinent for that period of time.¹⁸

Retention rates were also favorable: 67 percent of the relapse prevention clients completed the entire 12-week Yale program and more than 70 percent completed the Washton program.

Community reinforcement/contingency management programs have also appeared promising in fostering abstinence and retaining clients in treatment. Almost one-half (46 percent) of the cocaine-dependent clients participating in a 12-week community reinforcement/contingency management program at the University of Vermont were able to remain continuously abstinent from cocaine through 2 months of treatment;¹⁹ when the program was extended to 24 weeks, 42 percent of the participating cocaine-dependent subjects were able to achieve 4 months of continuous abstinence.²⁰ By comparison, only 5 percent of those in the control group receiving drug abuse counseling alone could remain continuously abstinent for the entire 4 months.

A year after clients began treatment, community reinforcement/contingency management treatment effects were still evident:²¹ 65 to 74 percent²² of those in the community reinforcement group reported 2 or

¹⁷“Severity” is defined in terms of median splits on the drug use subscale of the Addiction Severity Index. Subjects in the high-severity group demonstrated high weekly use of cocaine (4.9 grams/week); were chronic drug users (43.2 months of regular use); and had high levels of family/social, occupational, and legal problems.

¹⁸Kathleen Carroll, Bruce Rounsaville, and Frank Gawin, “A Comparative Trial of Psychotherapies for Ambulatory Cocaine Abusers: Relapse Prevention and Interpersonal Psychotherapy,” American Journal of Drug and Alcohol Abuse, Vol. 17, No. 3 (1991), pp. 229-47.

¹⁹Stephen Higgins, Dawn Delaney, Alan Budney, Warren Bickel, John Hughes, Florian Foerg, and James Fenwick, “A Behavioral Approach to Achieving Initial Cocaine Abstinence,” American Journal of Psychiatry, Vol. 148, No. 9 (1991), pp. 1218-24. To test the accuracy of self-reported client data, researchers at the University of Vermont compared self-reports to urine test results. In 98 percent of the cases in which a client indicated nonuse, urinalysis data confirmed the report.

²⁰Stephen Higgins, Alan Budney, Warren Bickel, John Hughes, Florian Foerg, and Gary Badger, “Achieving Cocaine Abstinence With a Behavioral Approach,” American Journal of Psychiatry, Vol. 150, No. 5 (1993), pp. 763-69.

²¹Unpublished 12-month data provided by Stephen Higgins, June 6, 1995.

²²The percentage range represents outcome results across two clinical trials.

fewer days of cocaine use in the past month. Only 45 percent of those in the counseling control group achieved such gains.²³

Contingency management was also studied independently in an inner-city Baltimore program.^{24,25} Positive results were found when tying the 12-week voucher reward system to cocaine drug testing. Nearly half of the cocaine-abusing and cocaine-dependent clients (who were also heroin users) given vouchers for cocaine-free urine test results were able to remain continuously abstinent for 7 to 12 weeks. Among clients receiving vouchers unpredictably—not tied to urine test results—only 1 client achieved abstinence for more than 2 weeks.

Client treatment retention was also high. Within the Vermont community reinforcement/contingency management group, 85 percent of the clients completed the 12-week program, compared with only 42 percent of those in the 12-step drug counseling control group. The 24-week program was completed by about five times as many clients in the community reinforcement group as those receiving drug counseling therapy (58 percent versus 11 percent).

Neurobehavioral Therapy

Several programs have demonstrated that a neurobehavioral therapeutic approach can also be effective in promoting cocaine abstinence and treatment retention. Thirty-six percent of the cocaine-abusing and cocaine-dependent clients participating in a neurobehavioral therapy program through the Matrix Institute in California succeeded in remaining continuously abstinent from cocaine for at least 8 consecutive weeks while in treatment.²⁶ Follow-up results obtained 6 months after treatment

²³Since not every client was using cocaine the same number of times per month at the point of treatment entry, Higgins calculated a magnitude-of-change score between treatment entry and 12-month follow-up for each group. At intake, 10 to 21 percent of community reinforcement clients reported ≤ 2 days of cocaine use in the past month; 12 months after treatment entry, 65 to 74 percent were using ≤ 2 days in the past month, for a positive gain of 53 to 55 percent. This gain was higher than that experienced by the drug counseling control group (29 percent).

²⁴K. Silverman, R.K. Brooner, I.D. Montoya, C.R. Schuster, and K.L. Preston, "Differential Reinforcement of Sustained Cocaine Abstinence in Intravenous Polydrug Abusers." In L.S. Harris (ed.), Problems of Drug Dependence 1994: Proceedings of the 56th Annual Scientific Meeting, The College on Problems of Drug Dependence. National Institute on Drug Abuse Research Monograph #153 (Rockville, Md.: National Institute on Drug Abuse Research, 1995), p. 212.

²⁵K. Silverman, C.J. Wong, A. Umbricht-Schneiter, I.D. Montoya, C. R. Schuster, and K.L. Preston, "Voucher-Based Reinforcement of Cocaine Abstinence: Effects of Reinforcement Schedule." In L.S. Harris (ed.), Problems of Drug Dependence 1995: Proceedings of the 57th Annual Scientific Meeting, The College on Problems of Drug Dependence. National Institute on Drug Abuse Research Monograph, in press. Also cited in NIDA Notes, Vol. 10, No. 5 (Sept./Oct. 1995), pp. 10, 14.

²⁶Steven Shoptaw, Richard Rawson, Michael McCann, and Jeanne Obert, "The Matrix Model of Outpatient Stimulant Abuse Treatment: Evidence of Efficacy," Journal of Addictive Diseases, Vol. 13, No. 4 (1994), pp. 129-41.

entry showed that 38 percent of these clients still tested drug free. In a separate examination of two neurobehavioral outpatient treatment sites, at least 40 percent of the cocaine clients in each site remained continuously abstinent through the entire 6-month course of therapy.²⁷

Given the high rate of cocaine use among methadone clients,^{28,29,30} the neurobehavioral model was adapted in New York for use among methadone clients meeting the diagnostic criteria for cocaine dependence. In an intensive 6-month program, a strong relationship was found between the number of treatment sessions attended and cocaine use reduction.³¹ Clients attending 3 to 19 sessions experienced a 5-percent reduction in cocaine use during the previous month. Those attending 85 to 133 sessions experienced a 60-percent reduction in their past 30-day use of cocaine. In another New York study with cocaine-addicted methadone clients,³² those clients receiving neurobehavioral treatment demonstrated a significant decrease in cocaine use between entering treatment and 6-month follow-up; the control group showed no statistically significant decrease.³³

Neurobehavioral retention rates also proved favorable. In the California study of two treatment sites, clients were retained an average of about 5 months and 3 months, respectively; in the other California study, the average length of stay for cocaine users was about 4-1/2 months. For the first New York study, a total of 61 percent of the cocaine-dependent

²⁷Richard Rawson, Jeanne Obert, Michael McCann, and Walter Ling, "Neurobehavioral Treatment for Cocaine Dependency: A Preliminary Evaluation," *Cocaine Treatment: Research and Clinical Perspectives*. National Institute on Drug Abuse Research Monograph #135 (Rockville, Md.: National Institute on Drug Abuse, 1993), pp. 92-115.

²⁸Methadone Maintenance: Some Treatment Programs Are Not Effective; Greater Federal Oversight Needed (GAO/HRD-90-104, Mar. 22, 1990), p. 18.

²⁹S. Magura, Q. Siddiqi, R. Freeman, and D. Lipton, "Changes in Cocaine Use After Entry to Methadone Treatment," *Journal of Addictive Diseases*, Vol. 10, No. 4 (1991), pp. 31-45.

³⁰W. Condelli, J. Fairbank, M. Dennis, and J. V. Rachal, "Cocaine Use By Clients in Methadone Programs: Significance, Scope, and Behavioral Interventions," *Journal of Substance Abuse Treatment*, Vol. 8 (1991), pp. 203-12.

³¹Andrew Rosenblum, Stephen Magura, Jeffrey Foote, Michael Palij, Leonard Handelsman, Meg Lovejoy, and Barry Stimmel, "Treatment Intensity and Reduction in Drug Use for Cocaine-Dependent Methadone Patients: A Dose Response Relationship." Prior version of this paper was presented at the American Society of Addiction Medicine Annual Conference, New York, Apr. 1994.

³²Stephen Magura, Andrew Rosenblum, Meg Lovejoy, Leonard Handelsman, Jeffrey Foote, and Barry Stimmel, "Neurobehavioral Treatment for Cocaine-Using Methadone Patients: A Preliminary Report," *Journal of Addictive Diseases*, Vol. 13, No. 4 (1994), pp. 143-60.

³³At treatment entry, 100 percent of both the neurobehavioral and control groups were using cocaine. But at 6-month follow-up, only 64 percent of the former had used cocaine, compared with 84 percent of the control group.

methadone clients completed the initial 6-month cocaine treatment regimen.

No Effective Medication for Treating Cocaine Addiction Has Yet Been Found

Currently, there is no FDA-approved pharmacotherapy for cocaine addiction. While some medications have proven successful in one or more clinical trials, no medication has demonstrated “substantial efficacy” once subjected to several rigorously controlled trials.

Twenty major medications have been considered by NIDA’s Medications Development Division (MDD). Fourteen have been tested with humans, five are in the animal experimentation stage, and one is being tested on both humans and animals for different treatment effects. Table 2 provides a summary of the medications tested, their current phase of testing, and therapeutic uses.

Table 2: Medications Tested for the Treatment of Cocaine

Medication	Therapeutic use
Human trials	
Amantadine	Supports maintenance therapy
Bromocriptine	Supports maintenance therapy
Buprenorphine	Blocks euphoria
Bupropion	Helps achieve initial abstinence
Carbamazepine	Treats withdrawal
Desipramine	Treats withdrawal
Fluoxetine	Treats withdrawal
Flupenthixol	Treats withdrawal
Imipramine	Treats withdrawal
L-DOPA	Serves as replacement therapy
L-tryptophan	Serves as functional antagonist
Mazindol	Treats withdrawal
Methylphenidate	Supports maintenance therapy
Nifedipine	Blocks euphoria
Sertraline	Treats withdrawal
Animal trials	
Diltiazem	Blocks euphoria/treats cocaine cardiotoxicity
Nifedipine	Treats cocaine cardiotoxicity
Monoclonal antibodies	Serves as functional blocker
SCH23390	Blocks euphoria
Sulpiride	Blocks euphoria
Verapamil	Blocks euphoria/treats cocaine cardiotoxicity

Of the 20 medications tested, MDD has labeled 6 as “disappointing”: buprenorphine, carbamazepine, desipramine, imipramine, mazindol, and nifedipine. The remainder are still under investigation, but numerous clinical trials thus far have yielded mixed results. For example, a 1992 study by Ziedonis and Kosten indicated that amantadine was effective in reducing cocaine craving; yet a 1989 study by Gawin, Morgan, Kosten, and Kleber indicated that this medication was not as effective as a placebo in reducing cocaine craving.³⁴ Additional pharmacological studies are cited in the bibliography.

Thus, no pharmacotherapy for cocaine exists that compares with methadone, which reduces heroin craving, enables the client to stabilize psychological functioning, and eliminates or reduces the heroin withdrawal process. Nor has any medication proven effective as a supportive therapy, to be used in combination with one or more cognitive/behavioral therapies, to enhance cocaine abstinence.

But recent animal research³⁵ has demonstrated the positive effects of a new immunization procedure in protecting rats against the stimulant effects of cocaine. When vaccinated, rats produced antibodies that acted like biological “sponges” or blockers, diminishing by more than 70 percent the amount of cocaine reaching the brain. As a result, inoculated rats experienced significantly lower cocaine stimulation levels than noninoculated rats. Further research needs to be conducted before human clinical trials can be planned.

Few Well-Designed Acupuncture Outcome Research Studies Exist

Some treatment centers are now offering acupuncture as therapy for cocaine and other substance abuse. For example, in 1993, the Lincoln Hospital Substance Abuse Treatment Clinic treated about 250 clients per day with acupuncture therapy. To date, however, few well-designed evaluation studies have assessed the utility of acupuncture treatment.

But the limited research findings are somewhat favorable. Almost 90 percent of a group of inner-city, cocaine-dependent methadone clients who completed an 8-week course of acupuncture remained abstinent for

³⁴Tabular summaries of cocaine pharmacological studies provided by the Regulatory Affairs Branch, Medications Development Division, NIDA, Dec. 28, 1994.

³⁵“NIDA Media Advisory,” Dec. 14, 1995.

more than a month.³⁶ These individuals had been regular users of cocaine, on average, for 13 years. Fifty percent of the clients, however, did not complete the 2-month program. Inner-city, cocaine-dependent methadone clients participating in a second acupuncture research study decreased their frequency of cocaine use and craving for the drug after just 6 weeks of therapy.³⁷ These participants had been regular cocaine users, on average, for more than 10 years. And chronic crack cocaine users demonstrated a statistically significant tendency toward greater day-to-day reductions in cocaine use during a 4-week course of acupuncture therapy. But they did not differ from the control group in their overall percentage of drug-free test results.^{38,39}

More Research Is Needed to Formulate a Standard Cocaine Treatment Approach

Much has been learned about cocaine treatment in the 15-year period since the epidemic began. Studies show that client abstinence and retention rates can be positively affected through a number of promising treatment approaches.⁴⁰ However, according to cocaine treatment experts, additional research is needed before standard, generalizable cocaine treatment strategies can be formulated for cocaine addicts of varying demographic and clinical groups. (See app. II for a summary of the experts' suggestions.)

In the cognitive/behavioral area, for example, the experts indicated a need for additional clinical research aimed at identifying the important components of promising treatment practices, further development and testing of client reward systems (contingency contracting), additional study of the triggers that promote relapse, and identification of appropriate intensities and durations of treatment.

³⁶Arthur Margolin, S. Kelly Avants, Patrick Chang, and Thomas Kosten, "Acupuncture for the Treatment of Cocaine Dependence in Methadone-Maintained Patients," The American Journal on Addictions, Vol. 2, No. 3 (1993), pp. 194-201.

³⁷S. Kelly Avants, Arthur Margolin, Patrick Chang, Thomas Kosten, and Stephen Birch, "Acupuncture for the Treatment of Cocaine Addiction: Investigation of a Needle Puncture Control," Journal of Substance Abuse Treatment, Vol. 12, No. 3 (1995), pp. 195-205.

³⁸Vincent Brewington, Michael Smith, and Douglas Lipton, "Acupuncture as a Detoxification Treatment: An Analysis of Controlled Research," Journal of Substance Abuse Treatment, Vol. 11, No. 4, pp. 289-307.

³⁹Douglas Lipton, Vincent Brewington, and Michael Smith, "Acupuncture and Crack Addicts: A Single-Blind Placebo Test of Efficacy," Presentation at Advances in Cocaine Treatment, NIDA Technical Review Meeting, Aug. 1990.

⁴⁰In addition to investigation of these specific treatment approaches, research is also being conducted more globally in institutional settings (see app. III).

In the pharmacological area, the experts recommended further development and testing of medications to block the effects of cocaine and reduce craving, examining the human toxicity effects of pharmaceutical agents found useful in animal experiments, conducting outcome studies combining cognitive/behavioral and pharmacological therapies, developing maintenance medications, and conducting more longitudinal studies of medication treatment effectiveness.

The experts also highlighted the need for further research into client/treatment matching, client retention, client readiness and motivation for treatment, and long-term treatment outcomes.

Summary

Three cognitive/behavioral treatment approaches—relapse prevention, community reinforcement/contingency management, and neurobehavioral therapy—have demonstrated favorable results in the treatment of cocaine addiction. Preliminary findings show that clients exposed to these therapies were able to remain abstinent and in treatment for prolonged periods of time. These findings are particularly encouraging since initial treatment approaches of the early 1980s were not very successful. Although currently an insufficient number of studies within each treatment area exists to draw definitive conclusions about the utility or generalizability of any specific treatment approach, more study results should become available within the next few years. Research experts agreed that continued research and study are needed to enhance and confirm or deny these early results.

Agency Comments

NIDA reviewed a draft of this report and provided comments, which are included in appendix IV. NIDA officials generally agreed with our conclusions on the effectiveness of cognitive/behavioral and pharmacological therapies for cocaine treatment. However, they felt we were too positive about the early results of acupuncture treatment, particularly given the lack of well-designed outcome studies. We agreed with NIDA on this point and reworded our statements on acupuncture's use in treating cocaine addiction to clarify the preliminary nature of the results and the need for more well-controlled studies. Other technical and definitional changes were incorporated, as appropriate.

We are sending copies of this report to the Director of the National Institute on Drug Abuse, the Director of the Center for Substance Abuse Treatment, and other interested parties. We will also make copies available to others on request. If you have any questions about this report, please call me at (202) 512-7119 or Jared Hermalin, the Evaluator-in-Charge, at (202) 512-3551. Dwayne Simpson of Texas Christian University and George DeLeon of the National Development and Research Institutes served as independent reviewers. Mark Nadel and Karen Sloan also contributed to this report.

A handwritten signature in black ink that reads "Sarah F. Jaggar". The signature is written in a cursive style with a long, sweeping underline that extends to the left.

Sarah F. Jaggar
Director, Health Financing and
Public Health Issues

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Abbreviations

AIDS	acquired immunodeficiency syndrome
CSAT	Center for Substance Abuse Treatment
FDA	Food and Drug Administration
MDD	Medications Development Division
NIDA	National Institute on Drug Abuse
TOPS	Treatment Outcome Prospective Study

Methodology

To determine the extent to which cocaine therapies have proven successful, we identified studies with current reportable data on two outcome variables: drug abstinence and treatment retention. We reviewed the literature published between 1991 and 1995; examined Center for Substance Abuse Treatment (CSAT) and National Institute on Drug Abuse (NIDA) agency records of cocaine-related grants awarded during this time period; and, as necessary, contacted project investigators.

The approximately 65 cocaine-related grants supported by CSAT were still in progress at the time of this writing; neither abstinence nor retention data were available for inclusion in this report. Most of the approximately 100 NIDA longitudinal studies were also in progress. Our report was therefore based on articles published during the 5-year period, unpublished documents provided by federal drug agencies, and those available abstinence and retention findings from ongoing NIDA-supported studies.

We classified the studies from each of these sources into two treatment categories: cognitive/behavioral and pharmacological treatments. We then classified the cognitive/behavioral studies as either relapse prevention, community reinforcement/contingency management, or neurobehavioral therapy and the pharmacological studies by drug type.

We then reviewed those studies with reported abstinence and/or retention findings within each treatment area to determine the utility of each approach. In making determinations about treatment utility, we gave consideration to whether or not the studies had appropriate designs for determining treatment effectiveness.

The intent of this report was not to provide an exhaustive evaluation synthesis of the cocaine studies currently available (particularly given the limited number of studies available), nor to assess the qualitative methodology of each study. Rather, the objective was to determine whether particular treatment approaches appeared favorable or promising, and to provide examples of such favorable cocaine treatment approaches in the text. Given the relatively limited number of studies available, additional work is necessary before determinations can be made about the utility of any treatment approach for specific demographic and clinical groups.

To identify additional research initiatives necessary for increasing our knowledge of cocaine treatment effectiveness, we conducted telephone

interviews with 20 cocaine treatment experts. Each of the experts we selected was either a principal investigator or coinvestigator on a currently funded cocaine-related federal grant or contract, a member of a federal cocaine grant/contract review committee within the past 2 years, or an author of at least two cocaine peer-reviewed publications. The names and affiliations of the 20 experts who participated are listed below. (Two additional individuals chose not to participate.)

M. Douglas Anglin
University of California, Los Angeles
Neuropsychiatric Institute

Kathleen Carroll
Yale University

George DeLeon
National Development and Research Institutes

Frank Gawin
University of California, Los Angeles

Dean Gerstein
National Opinion Research Center

Edward Gottheil
Thomas Jefferson University

John Grabowski
University of Texas
Health Science Center

Barbara Havassy
University of California, San Francisco

Stephen Higgins
University of Vermont

Herbert Kleber
Columbia University

Thomas Kosten
Yale University

Appendix I
Methodology

William McAuliffe
Harvard University

Thomas McLellan
Philadelphia Veterans Administration Medical Center
University of Pennsylvania

Stephen Magura
National Development and Research Institutes

Jerome Platt
Medical College of Pennsylvania and Hahnemann University

Richard Rawson
Matrix Institute on Addictions

Harvey Siegel
Wright State University

Dwayne Simpson
Texas Christian University

Michael Thase
University of Pittsburgh

Arnold Washton
Washton Institute

Research Initiatives Necessary for Increasing Understanding of Cocaine Treatment Effectiveness

Following are the responses of the 20 treatment experts to the GAO question, “What important knowledge gaps remain in our understanding of cocaine treatment effectiveness in each of the following two areas: cognitive/behavioral and pharmacological interventions?” Relevant individual response items were placed into six clinical and methodological categories: cognitive/behavioral issues, pharmacological issues, the cognitive/behavioral and pharmacological synergy, clinical assessment/outcome issues, population subgroup treatment issues, and methodological issues. The frequency count for each category is also provided.

Cognitive/Behavioral Issues

Identifying important components of promising treatment practices, developing and testing contingency contracting strategies, recognizing the triggers of relapse, determining appropriate intensity and duration of treatment protocols, assessing the utility of low-intensity treatments, defining and increasing important aspects of social and community support, and codifying appropriate treatment practices.

Categorical frequency: 12.

Pharmacological Issues

Developing drugs to diminish the craving for cocaine; developing drugs to block the effects of cocaine; developing maintenance medication for continued relapse prevention; examining the utility of multiple untried drugs indicated in the Physician’s Desk Reference; longitudinally testing the effects of drugs; assessing human toxicity effects of drugs found useful in animal experiments; developing detoxification medication; and further investigating vaccines, agonists, and antagonists.

Categorical frequency: 14.

Cognitive/Behavioral and Pharmacological Synergy

Testing drugs as adjuncts to cognitive/behavioral therapies, determining the impact of combined drug and cognitive/behavioral therapies on the extension of relapse prevention, and assessing the combination of drugs and cognitive/behavioral therapies that works best for various subgroups.

Categorical frequency: 6.

**Appendix II
Research Initiatives Necessary for
Increasing Understanding of Cocaine
Treatment Effectiveness**

**Clinical
Assessment/Outcome
Issues**

Improving the effectiveness of recruitment and retention of clients in treatment, better assessing readiness and motivation for treatment, better assessing impact of dual disorders on treatment outcome, investigating unknown long-term drug treatment outcomes, developing information on long-term incentives for maintaining drug abstinence, increasing knowledge about “aftercare” treatment planning, increasing knowledge of treatment outcome for managed care/health maintenance organizations to plan client treatments, and improving the effectiveness of outpatient care.

Categorical frequency: 11.

**Population Subgroup
Treatment Issues**

Better matching client needs to treatment services as well as determining which clients do well with specific therapies, what groups can be effectively treated, who can become abstinent without use of drugs, what subgroups learn or do not learn about relapse risk factors in treatment settings, and what educational/IQ levels are necessary for making effective use of cognitive approaches.

Categorical frequency: 10.

Methodological Issues

Need for the following: more clinical trials to demonstrate the efficacy of basic treatment services; testing treatments on a wider population of cocaine users; more systematic data collection; improved technology for conducting randomized, longitudinal trials; evaluating the patient selection process (volunteers may represent a biased sample); and conducting cost-effectiveness studies.

Categorical frequency: 7.

Cocaine Outcomes by Treatment Setting

In addition to the study of particular treatment approaches (such as relapse prevention, community reinforcement/contingency management, and neurobehavioral therapy), researchers are also beginning to examine the results of cocaine treatment in different types of settings (that is, outpatient, inpatient, day-hospital, and therapeutic communities). In general, outpatient and day-hospital stays tend to be less costly than extended inpatient stays. Results of recent studies suggest that cocaine treatment can be effective in these less costly settings, but further replication is necessary before any firm conclusions can be drawn.

Clients attending a California-based Veterans Administration intensive outpatient program with a self-help component were able to remain cocaine abstinent 73 percent of the time, when followed up 24 months after treatment admission.⁴¹ This result was comparable to that found among clients attending a more costly program consisting of both an inpatient stay and a highly intensive outpatient/self-help program. The California-based program results also surpassed those achieved by clients who participated in both an inpatient and a low-intensity outpatient/self-help program (56 percent). These results point to the conclusion that clients with a cocaine problem may be able to do quite well in an intensive outpatient setting that consists of at least four visits per month for at least 6 months.

In a second California study, cocaine-dependent inpatients fared better than outpatients at both 6 and 12 months following treatment entry, although both groups fared well.⁴² Allowing for up to two slips (or brief episodes of use), at the 6-month period the inpatient abstinence rate was 79 percent, whereas the outpatient rate was 67 percent. At the 12-month period, the abstinence rates were 72 percent and 50 percent, respectively.

The effects of day-hospital versus inpatient treatment were assessed in Philadelphia.⁴³ About one-half (53 percent) of those cocaine-dependent clients attending a day-hospital program were able to remain continuously abstinent throughout the 6 months following treatment completion. This rate was comparable to that of inpatients: 47 percent.

⁴¹M. Elena Khalsa, Alfonso Paredes, and M. Douglas Anglin, "A Natural History Assessment of Cocaine Dependence: Pre- and Post-Treatment Behavioral Patterns," unpublished manuscript.

⁴²Unpublished inpatient-outpatient data provided by Barbara Havassy, Sept. 25, 1995.

⁴³Arthur L. Alterman, Charles P. O'Brien, A. Thomas McLellan, Donna S. August, Edward C. Snider, Marian Droba, James W. Cornish, Charles P. Hall, Arnold H. Raphaelson, and Francis X. Schrade, "Effectiveness and Costs of Inpatient Versus Outpatient Hospital Cocaine Rehabilitation," *The Journal of Nervous and Mental Disease*, Vol. 182, No. 3 (1994), pp. 157-63.

And finally, the impact of a day-treatment program (using therapeutic community techniques) was compared with standard methadone maintenance treatment in New York.⁴⁴ At 6-month follow-up, only 19.1 percent of those remaining in the day-treatment program had used cocaine during the past 30 days. These results were substantially better than those of participants in the standard methadone maintenance treatment program, where 41.8 percent were using cocaine at 6-month follow-up. The day-treatment therapeutic community group also demonstrated significantly greater reductions in heroin use, needle use, criminal activity, and psychological dysfunction scores.

⁴⁴George DeLeon, Graham Staines, Theresa Perlis, Stanley Sacks, Karen McKendrick, Robert Hilton, and Ronald Brady, "Therapeutic Community Methods in Methadone Maintenance (Passages): An Open Clinical Trial," *Drug and Alcohol Dependence*, Vol. 37 (1995), pp. 45-57.

Comments From the National Institute on Drug Abuse



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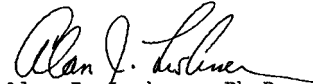
Ms. Sarah F. Jaggar
Director
Health Financing and Public
Health Issues
U.S. General Accounting Office
441 G Street, N.W.
Washington, D.C. 20548

Dear Ms. Jaggar:

This is in response to your February 22 letter requesting comments on a draft report Cocaine Treatment: Early Results From Various Treatment Approaches. Enclosed are the National Institute on Drug Abuse's (NIDA) comments.

If you have any questions, please contact Dr. Lisa Onken, Division of Clinical and Services Research, NIDA, at (301) 443-0107.

Sincerely,


Alan I. Leshner, Ph.D.
Director

Enclosure

cc: Dr. Wendy Baldwin
Ms. Diane S. Wax
Ms. Patricia L. Abell

Appendix IV
Comments From the National Institute on
Drug Abuse

COMMENTS OF NIDA ON THE GENERAL ACCOUNTING OFFICE'S DRAFT REPORT
"Cocaine Treatment: Early Results From Various Treatment
Approaches."

Report Number: GAO/HEHS-96-80

General Comments

Overall, NIDA believes this report to be a fair and reasonable summary of the effectiveness of behavioral therapies and pharmacotherapies for cocaine dependence. We concur with the conclusions about behavioral therapy and pharmacotherapy reached in this report. However, we had some concerns about the section on acupuncture. We have the following comments to offer:

1. The section on acupuncture research as a treatment for drug abuse appears overly positive. The studies cited do not describe the design of the studies, nor report complete results. Furthermore, though it is suggested that few well-designed studies exist to date, and the number of controlled evaluations should be increased to assess the utility of acupuncture treatment for drug abuse, the report neglects to cite a NIDA review article that proposes directions for future studies (McLellan, T., Grossman, D., Blaine, J., and Haverkos, H. Acupuncture Treatment for Drug Abuse: A Technical Review. Journal of Substance Abuse Treatment, 10, 569-576.) This review states that, based upon commonly accepted empirical testing standards, such as those used in the evaluation of new medications or new devices by the Food and Drug Administration, there is not adequate scientific evidence from well-controlled trials to prove conclusively that acupuncture is effective in the treatment of most of the common substance dependence disorders including cocaine and heroin addiction.
2. In the background section, acupuncture was given more "attention" than pharmacotherapy. This might project the incorrect impression that acupuncture is equally "mainstream" as the behavioral and pharmacological treatment approaches.
3. We feel that it is important to point out in the report that by statute the effectiveness of pharmacotherapy needs to be reviewed, confirmed and approved by the FDA, a process that sets it apart from the development of behavioral and other treatments.

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