Breaking the Cycle of Addiction

A mix of drug therapy, behavioral therapy, and psychotherapy may prove to be most effective as researchers examine clinical data on how to treat cocaine addiction

This is the seventh in a series on addiction. Next: The legalization debate.

A DOCTOR WHO TREATS PEOPLE for drug addiction tells this story. "A woman was doing very well in treatment. Then one day she was changing her baby's diaper. She used baby powder and the sight of the white powder induced a tremendous craving for cocaine."

Charles O'Brien of the University of Pennsylvania in Philadelphia and the Philadelphia Veterans Administration Medical Center is the doctor. "The greatest clinical problem [in treating patients for drug addiction] is relapse," he says. Common, sometimes unexpected reminders of drug use can lure a chronic user to take cocaine again.

Faced with this intractable cycle of drug-taking behavior, those who treat cocaine addicts have been handicapped because until recently no one knew whether one method of treatment was any more effective than another. Now, physicians who are testing various methods in clinical trials are coming to believe that a combination of drug therapy, behavioral therapy, and psychotherapy is most likely to be effective. As yet, however, they are still in the early stages of evaluating these and other components of a more comprehensive treatment program.

The emerging treatment strategies represent a radical departure from the conventional wisdom that a person's addiction to cocaine was purely a psychological problem. People have used cocaine since the late 1800s, but not until 7 or 8 years ago did researchers recognize that it is a powerfully addictive drug. The delay helps to explain why efforts to identify specific programs for treating cocaine addiction are still in their infancy.

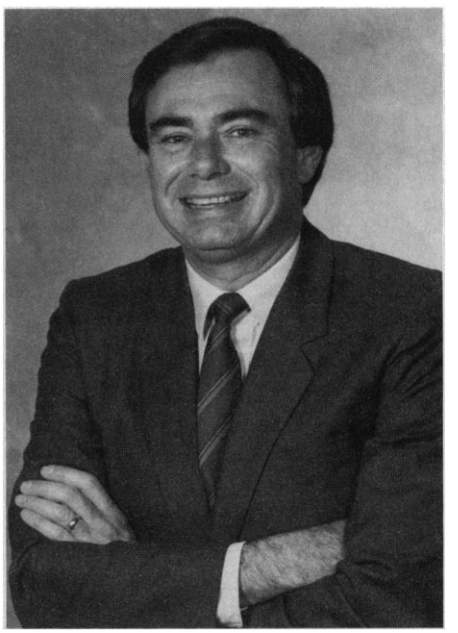
Many of the responses a person has to cocaine stem from neurochemical actions of the drug itself. For instance, several researchers think that one reason why cocaine initially causes such intense euphoria and pleasure is that it directly stimulates a so-called reward system in the brain that uses dopamine as a neurotransmitter (*Science*, 22 July, p. 416). Over time, however, the brain system behaves as if it is depleted and chronic users take cocaine to feel any pleasure at all. Habitually snorting cocaine powder or smoking "crack," a free-base form of the powdered salt, produces these effects, although many physicians think that people who smoke crack are more likely to become addicted and that they do so more quickly.

At the recent American Psychiatric Association meeting,* Frank Gawin and Herbert Kleber of Yale University School of Medicine in New Haven, Connecticut, discussed results of a controlled clinical trial in which they tested desipramine, a widely used antidepressant, in a group of chronic cocaine abusers. Of the 72 people enrolled in their 3-year study, one-third received desipramine, another third got lithium, and the rest were given placebo, each for 6 weeks. Sixty percent of those receiving desipramine were able to stop taking cocaine for 3 weeks or more, in contrast to 23% on lithium and 17% on placebo.

The Yale researchers view desipramine therapy as only one part of a treatment program that will ultimately include other therapies. "Desipramine is not being used as a cure for cocaine addiction, but as an adjunct to initiate abstinence," says Gawin. "It is somewhat like ameliorating the early withdrawal symptoms associated with opiate and alcohol withdrawal." Unlike the alcohol-related DTs or the muscle spasms, sweating, and nausea of heroin withdrawal, few physical symptoms result from cocaine withdrawal. Instead, users who stop repeatedly bingeing on cocaine go through three distinct stages.

The first, immediate phase is a crash, says Gawin, characterized in its early stages by a rapid descent of mood and physical activity, fatigue, and an intense craving for more drug. Although the person ultimately feels exhausted toward the end of this phase, sleep is often difficult and addicts may drink alcohol, take tranquilizers such as Valium, or inject heroin to relax, which can lead to dependence on other drugs.

*The annual American Psychiatric Association meeting was held 7 to 12 May in Montreal, Quebec.



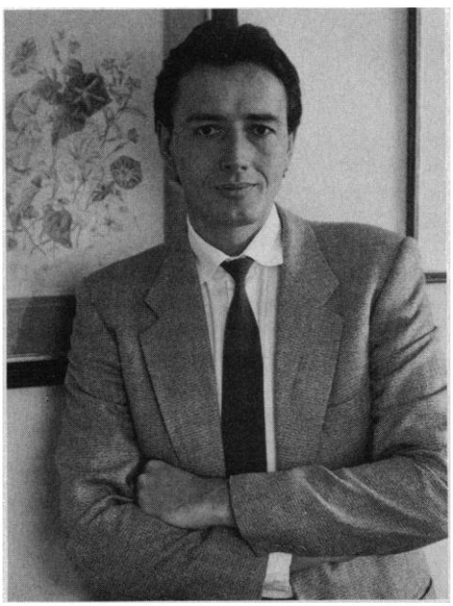
Charles O'Brien *finds that a combination of behavioral therapy and either psychotherapy or counseling helps addicts abstain from cocaine.*

The second phase of drug abstinence lasts for several weeks. It begins as sleep patterns become more normal, the person's mood improves, and craving for drug decreases. During the middle and late parts of this phase, however, the person becomes anxious, craves cocaine again, and is typically unable to experience normal pleasures from food or sex, for instance—a state called anhedonia. "The most common complaint of chronic cocaine users is boredom, since they don't know the word anhedonia" says Gawin. He sees anhedonia as a major force that drives habitual users to take cocaine again.

If the chronic user makes it to the third stage of withdrawal, the ability to experience pleasure can return along with a better mood. But the person may still feel episodic craving for cocaine. Treatment programs are geared to help addicts reach this stage and remain free from cocaine use.

The role of desipramine in a program to treat cocaine abusers is still being debated. No one is certain exactly how the drug relieves depression, and researchers are even further from understanding how it helps

some addicts stop taking cocaine for a while. The drug apparently blocks the reuptake of norepinephrine and serotonin into brain neurons. A prevalent theory is that the levels of these neurotransmitters are too low in depressed patients and that desipramine normalizes the levels. Gawin and Kleber speculate that in cocaine addicts desipramine relieves craving because it binds to a population of receptors in the brain reward pathway that regulate dopamine function.



Frank Gawin *reports that desipramine can help an addict initially to stop using cocaine.*

While desipramine may help an addict to break away from cocaine use for short periods of time, many researchers think that additional kinds of therapy will be needed to maintain long-term abstinence.

"No matter how many times you can get a person to stop smoking, drinking, or using cocaine, they often relapse," says O'Brien. "And this is where conditioned behavior is so important." He, Anna Rose Childress, A. Thomas McLellan, and George Woody, also of Philadelphia, and their colleagues, are testing a specific form of behavioral conditioning that is designed to disrupt patterns of behavior associated with repetitive drug taking. Alone it appears to be of little value, but in combination with psychotherapy or counseling it seems to help.

The Philadelphia researchers find that addicts are often not aware that the sight of drug paraphernalia or driving by the place where they used to buy drugs induces a tremendous craving for cocaine. For the addict, chronic cocaine use induces a kind of learning and memory much like the classical conditioning of Pavlov's dog in which the dog learned to salivate when he heard a bell that was previously associated with food.

"We hook the patients up to a polygraph and show them videos of people using drugs or handling the paraphernalia," says O'Brien. "They get an increased heart rate, reduced skin temperature, and other dramatic indications of physiological arousal. They get upset and scared and say things like 'My God, I didn't know I still had this in me.' "

O'Brien and his co-workers use the videos and various cognitive methods to train their patients in a safe environment where no drugs are available. The overall process, which is called extinction of conditioned behavior, involves "repeatedly exposing a person to the stimuli that produce arousal," says O'Brien. With repetitive exposures, the arousal and craving for cocaine diminish. "We have tested extinction as a behavioral therapy and alone it is not effective," he says. "So then we ask if it adds to the benefit of other therapies." A clinical trial that is just ending indicates that it does.

"The best results seem to occur in the group of patients receiving psychotherapy from professionals plus extinction, and the second best combination is counseling—by experienced people who are not health professionals—plus extinction," says O'Brien. Less effective were counseling alone or psychotherapy alone.

"None of these people is cured," says O'Brien. "Obviously we'd like to get them to the point where they never relapse, but our best results are to have longer periods of remission. It is like having arthritis or diabetes; people learn to live in spite of their illness."

Kleber adds another dimension to the problem of relapse. "We [physicians] have a different goal than the patient," he says. "The patients want to go back to controlled use of cocaine, but I don't believe that once you have been addicted you can return to a controlled use pattern."

To date, no one's rules for treating chronic cocaine users are hard and fast. Kleber and Gawin are testing other drugs in addition to desipramine, including sertralene (which blocks serotonin reuptake), mazindol (an antiobesity drug), buspirone (an antianxiety drug not related to Valium), and chlorpromazine (an antipsychotic). They are also testing a combination of desipramine therapy with other forms of behavioral therapy. "We don't do formalized extinction training as O'Brien does," says Kleber. "Instead, we teach patients to avoid high risk situations and train them how to handle dangerous situations. We also try to reinforce how bad their addiction to cocaine was."

An issue that complicates any drug treatment program, including one for cocaine addiction, is that patients may have an underlying psychiatric problem in addition to their dependence on drugs. "There is no doubt that anecdotally, a significant percentage of people who go to mental health facilities have combined psychiatric disorders and substance abuse problems," says Lewis Judd of the National Institute of Mental Health in Rockville, Maryland. The problem is compounded because few treatment centers are equipped to handle these patients, he says.

No one is certain of the exact percentage, but several studies indicate that about half the people who take cocaine chronically have a history of affective (mood) disorder—about 30% have been depressed at some time in their lives and roughly 20% have had cyclothymia, a mild form of manic depressive disorder. A smaller percentage have a history of attentional deficit disorder and a few were at some time diagnosed with antisocial disorder.

Estimating the number of people with specific combinations of mental disorders and drug abuse problems is not easy, because of the lack of statistically valid surveys on large populations. As a result, most of the information about patients with a dual diagnoses of mental illness and substance abuse comes from interviews of people who enter treatment programs, who may not be a representative group.

Researchers also need to understand how a mental disorder may affect someone's ability to stop using drugs, says Jerome Jaffe of the Addiction Research Center in Baltimore, Maryland. "For instance, people who are depressed often find it more difficult to stop smoking, or stop taking opiates or cocaine," he says. "We are not sure if the depression precedes or follows the drug use, but how important is that? What is important is the person's state of mind at the time." Besides, he says, clinicians must deal with the drug abuse first before they can separate depression due to drug withdrawal from an underlying depression.

Physicians now have a drug and a mix of behavioral and psychotherapy that seem to help people stop using cocaine, at least initially. The next steps will be to test other forms of therapy alone and to combine them in various treatment programs to see which are most effective for different populations of patients. In the process researchers will continue to learn more about addiction and how to break its cycle.

■ **DEBORAH M. BARNES**

ADDITIONAL READING

C. P. O'Brien *et al.*, "Pharmacological and behavioral treatments of cocaine dependence: Controlled studies," *J. Clin. Psychiatry* **49**, 17 (1988).

F. H. Gawin and E. H. Ellinwood, "Cocaine and other stimulants: Actions, abuse, and treatment," *New Engl. J. Med.* **18**, 1173 (1988).