Viewing Addiction as a Syndrome Will Open Doors

BY KATE JOHNSON
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COLORADO SPRINGS — All addictions, whether chemical or behavioral, should be viewed as different manifestations of an underlying addiction syndrome—and addiction recovery programs will fail to achieve optimal outcomes until their protocols reflect this view, Howard J. Shaffer, Ph.D., said at a symposium on addictive disorders sponsored by Psychotherapy Associates.

"We need this different way of viewing and assessing the nature of addiction so that we can do better in treating it," he said in an interview.

Between 80% and 90% of individuals recovering from addiction will relapse within the first year, possibly because their treatment is too narrowly focused on a single substance or behavior, rather than on their general susceptibility to addiction, said Dr. Shaffer of Harvard Medical School and director of the division on addictions at the Cambridge (Massachusetts) Health Alliance. "The existing focus on addictive substances does not adequately capture the origin, nature and processes of addiction," he wrote in his initial description of the syndrome model of addiction (Harv. Rev. Psychiatry 2004;12:367-74).

"Genetic predisposition to addiction is not drug specific," he said, pointing to the phenomenon of addiction "hopping" as an example. This phenomenon is commonly seen in addiction recovery programs, when the addiction that is being treated—alcoholism, for example—is replaced by another previously unrecognized addiction, such as exercise or disordered eating, he said.

Indeed, in an ongoing study of 508 subjects with multiple drunk driving offenses, Dr. Shaffer has found a high rate of coexisting addictions. These include alcohol abuse/dependence in 98%, substance abuse/dependence in 42%, nicotine dependence in 17%, and pathological gambling in 2%.

In addition, he found comorbid mental disorders in the group, including alcohol/substance abuse/gambling disorder in 99%, generalized anxiety disorder/depression or dysthymia in 20%, conduct disorder in 22%, posttraumatic stress disorder in 14%, and mania in 9%.

"Most [comorbidities] are being missed, and so that's the next issue. We have to do a really rigorous evaluation," Dr. Shaffer said. ■

DRUG UPDATE

Alcohol Dependence

The medications approved to treat alcohol dependence are severely underused despite evidence of their efficacy. It's estimated that less than 1% of people with alcohol dependence and abuse receive medication as part of their treatment. That's despite a call by the National Institute on Alcohol Abuse and Alcoholism for both primary care and mental health physicians to screen for alcohol abuse and then intervene or refer when needed. The NIAAA publishes a clinician's guide for helping patients who drink too much (http://pubs.niaaa.nih.gov/publications/Practitioner/CliniciansGuide2005/guide.pdf).

Last December, the Food and Drug Administration gave "approvable" status to Vivitrol, a long-acting, once-monthly formulation of naltrexone. Marketing of the drug is expected to start this year following final FDA approval. Vivitrol and the other three agents already on the market are all effective and differ mainly by mechanism of action and recommended treatment regimens.

Potential compliance is a major factor when choosing a drug. The once-monthly formulation of naltrexone is expected to have excellent compliance. Compliance is a concern with acamprosate, prescribed as two tablets taken three times a day, for a total of six tablets daily. Conventional naltrexone and disulfiram are dosed as once-daily tablets.

There are few direct comparisons among agents in the literature. There was no statistical difference in efficacy between acamprosate and daily naltrexone for treatment of alcohol dependence in a metaanalysis. The researchers concluded that both agents were effective for reducing alcohol consumption in alcoholics.

Many physicians are awaiting results from the randomized, placebo-controlled Combining Medications and Behavioral Interventions (COMBINE) study sponsored by the NIAAA. The trial compares various combinations of acamprosate, naltrexone, and behavioral interventions. Results are expected in mid-2006. Another agent, topiramate, is being studied in phase III trials for treatment of alcohol dependence.

Because alcohol is a known toxin to embryos, fetuses, and nursing infants, any of the three agents listed below is preferable to continued alcohol intake in a pregnant or nursing woman. Avoid disulfiram in the first trimester if possible. The limited efficacy of disulfiram prompts some experts to say that its benefit does not outweigh its risk during pregnancy. Naltrexone appears to be a better choice in the first trimester. Because of naltrexone's potential to alter opioid receptors and other sites in the brain, acamprosate may be preferable after the first trimester. If treatment is deemed necessary for a nursing mother, acamprosate is the best choice of the three drugs because it appears to pose the least risk to infants. No systematic dosage adjustments are needed for patients older than 70 years, but dosages of acamprosate should be reduced for patients with renal dysfunction.

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Drug	Cost/Day*	Dosage	What the Experts Say**
acamprosate [Campral]	no generic [$4.20]	666 mg t.i.d.	Trade formulation only. A glutamate antagonist that maintains abstinence in alcohol-dependent patients. Establish abstinence before prescribing. Affects glutamate and α-aminobutyric acid (GABA) neurotransmitter systems, but exact mechanism of action regarding alcohol is unclear. Patients who are the best candidates for this agent are not yet known. A higher daily pill count than other options might compromise compliance. No clinically relevant drug-drug interactions are known, an advantage over the other agents. Contraindicated for patients with severe renal impairment. With moderate renal impairment, reduce dosage to one 333-mg tablet t.i.d.
disulfiram [Antabuse]	no generic [$1.40]	250 mg/day	Trade formulation only. Although taken daily, its effects can last up to 14 days. Poor compliance makes this agent ineffective. An aversive medication; when taken with alcohol, it causes a severe, uncomfortable reaction, including flushing, nausea, headaches, and hypotension. Approved by the FDA before proof of efficacy was required (only safety data were required). Literature on efficacy is not as strong as it is for the other agents. Can interact with any nonprescription drug containing alcohol, as well as with certain other drugs including amitriptyline, warfarin, and diazepam (but only alcohol produces an aversive reaction). Monitor patients periodically for liver function. Dosage listed is average. Actual dosage can range from 125 to 500 mg/day.
naltrexone [ReVia]	$4.04 [$6.83]	50 mg/day	Blocks opiate receptors, thus reducing craving for alcohol and dampening the primary dopamine reward system in response to drinking. Can reduce heavy drinking and relapse. In clinical trials, provided prolonged abstinence, compared with placebo. Opioids block its action, so assess patients for opioid use prior to prescribing. Naltrexone causes opiate withdrawal in people who are opiate dependent. Can interact with yohimbine. Monitor patients periodically for liver function.
naltrexone, long acting [Vivitrol]	no generic [not yet available]	380 mg, once monthly	Trade formulation only. Once-monthly, intramuscular injection by physician should boost compliance, at least among patients who return for care. (Compliance with daily medications is a problem for many alcoholics.) A good complement to counseling and self-help recovery programs. Also effective for patients with comorbid psychiatric illness. Good adverse-effect profile in phase III study (JAMA 2005;293:1617-25) of two dosages: 190 mg and 380 mg once per month. The 6-month compliance was 64%; the higher dosage was more effective but was linked with more discontinuation for adverse effects. The 190-mg/mo dosage is unlikely to get FDA approval.

* Cost/day is based on the average wholesale price of a 100-unit bottle, or closest size, in the 2005 Red Book. Cost/day for generic naltrexone is based on the federal upper limit for Medicaid reimbursement in the 2005 Red Book.
**Comments reflect the viewpoints and expertise of the following sources:
Henry R. Kranzler, M.D., professor of psychiatry and associate scientific director of the alcohol research center at the University of Connecticut, Farmington. Affiliations with Ortho-McNeil Inc., Bristol-Myers Squibb Co., Forest Pharmaceuticals Inc., Alkermes Inc., and DrugAbuse Sciences Inc.
Michael E. Scott, M.D., of the department of psychiatry at the University of Arizona, Tucson, and medical director of Sierra Tucson Inc. Reported no conflicts of interest.
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