Disulfiram Shows Promise for Cocaine Addiction

BY CARL SHERMAN
Contributing Writer

New York — Disulfiram, a drug that has long been used for alcohol dependence, appears promising for the treatment of cocaine addiction. Thomas Kosten, M.D., said at the annual conference of the Association for Research in Nervous and Mental Disease. A variety of medications, most developed for other indications, may ameliorate problems associated with cocaine and other stimulants by addressing diverse points of the complex neurobiological processes involved, said Dr. Kosten, professor of psychiatry at Yale University School of Medicine.

Increased release of dopamine, particularly in the nucleus accumbens, is the signature of drug reward; addiction, however, is hypodopaminergic, he said by downregulating dopamine receptors. Treatment that addresses this neural substrate should reverse the stimulant-induced dopamine secretion. D2 receptor agonists, such as bromocriptine, have proved ineffective in this regard, but indirect dopamine agonists also have fallen short of their promise. Most prominent among these is disulfiram, which inhibits the conversion of dopamine to norepinephrine. The compound has been shown to attenuate the craving induced by administration of cocaine and to reduce withdrawal. Another mechanism by which disulfiram facilitates reduction in cocaine use appears to be tied to the acceleration and accentuation of the nervousness and dysphoria that often follow ingestion of the drug. Dr. Kosten said at the meeting, cosponsored by the New York Academy of Medicine.

A metaanalysis of a series of studies involving 337 people given disulfiram or one of several control medications (naltrexone, bupropion, or methadone, for example) found that drug-free urines were significantly more frequent in those receiving disulfiram than controls (35% vs. 40%).

Another study suggested a genetic explanation for the superior efficacy of disulfiram in some patients. In half of the subjects, the drug did not increase nervousness and paranoia after cocaine intake, which could be attributed to differences in levels of dopamine b half-life (DH). In this case, the target of disulfiram: Low en
dogenous levels of DHJ should predict the cocaine-induced dysphoria that is linked to treatment response. In fact, disulfiram was associated with significantly more cocaine-free urines in those patients with one or two alleles that contributed to low DHJ content.

A number of side effects can substantially reduce the effectiveness of disulfiram for patients who suffer severe withdrawal symptoms in patients with high but low withdrawal severity, said Dr.

The drug, which inhibits the conversion of dopamine to norepinephrine, has been shown to attenuate the craving induced by administration of cocaine.

PRECAUTIONS (continued)

In a postmarketing report, one patient who had been taking 4 mg of galantamine daily for a week developed incontinence; the urines of all alcoholics were analyzed for the presence of cocaine metabolites.