The Role of the Laboratory in the Diagnosis of LSD and Ecstasy Psychosis

LSD and Ecstasy and other hallucinogenic drugs (especially psilocybin mescaline) are in an anomalous position as frequently abused, widely available illicit drugs that are rarely identified in drug tests.

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Laboratory diagnosis of recent drug use has been the foundation of the medical management of drug use for more than four decades.[1,2] Drug tests, using serum and urine, continue to be the basis for hospital and emergency room drug identification.[3] Urine and, more recently, hair tests have been the basis for drug abuse prevention efforts following treatment in the criminal justice system, in the workplace, and in other settings for the past two decades.[4,5]

In 1988 the US Department of Health and Human Services (DHHS) issued guidelines for drug testing for five drugs: opiates, marijuana, cocaine, amphetamines, and PCP.[6] Since that time, drug testing often has come to mean testing for those drugs alone. This has placed LSD and Ecstasy (MDMA) and other hallucinogenic drugs (especially psilocybin mescaline) in an anomalous position as frequently abused, widely available illicit drugs that are rarely identified in drug tests. Because LSD and Ecstasy are relatively easily synthesized, cheap, and easily concealed, there are strong market forces promoting wider use of these drugs.

Although it is now possible to test for these drugs using widely available laboratory methods, these tests are relatively seldom requested. It is important that everyone involved in addiction know that these tests are available so that they become a routine part of all diagnostic and preventive programs. The major factor keeping costs of tests for LSD and Ecstasy relatively high is their infrequent use.

LYSERGIC ACID DIETHYLAMIDE (LSD)

LSD detection in urine and blood is technically difficult because the psychologically and pharmacologically effective doses of LSD are in the low microgram (μg) range. The usual LSD doses are 1 to 3 μg/kg, administered orally, but psychoactivity has been observed at a single dose of 25 μg. After administration, the small dose is extensively metabolized and distributed into total body mass. Therefore, very low concentrations are present in all body fluids, and the analytical sensitivity must be in the very low nanogram (ng) and/or picogram (pg) range to be diagnostically effective.[3]

The first analytical procedures for LSD identification and quantitation were fluorescence spectroscopy and chromatography (see Table). Some of the early methods had >1.0

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ng/ml sensitivity, which was only useful for the detection of LSD in bulk street preparations and, at best, identification of LSD in the body fluids for one to two hours after ingestion.

The fluorescence detection of LSD in body fluids had a major problem. The fluorescence spectrum of LSD was indistinguishable from other ergot alkaloids. Thus, the fluorescence assay was not specific. This technology was greatly improved when high pressure liquid chromatography (HPLC) was used for separation and fluorescence spectroscopy for quantitation.[7]

Greater sensitivity for LSD detection was achieved by radioimmunoassay (RIA). The increased sensitivity was partly due to detection of cross-reactive metabolites, since only a small percentage of the LSD dose is excreted into the urine unchanged. In this respect, the nonspecificity of the RIA benefits diagnosis of LSD use by identifying users for a longer time after drug ingestion.[8]

LSD plasma level peaked at 9 ng/ml after a 160-μg dose. In another study, after 140-μg dose (2 μg/kg), the peak plasma level was 5 ng/ml declining to 1 ng/ml in eight hours.[3]

Gas chromatography/mass spectrometry (GC/MS) technology added to the increased specificity and quantitation of LSD in biofluids. However, the sensitivity achievable by RIA was not increased by GC/MS utilization.[9]

Urine analysis detects LSD for a longer period than does blood analysis. The bio-fluid must be screened first by a sensitive RIA methodology and later confirmed by GC/MS. Since LSD decomposes at elevated temperatures and light, samples should be kept cool and in the dark. Under such conditions, the LSD in the samples remains stable for many months.[9] Although the LSD analytical methods have improved sensitivity and specificity, the cost of RIA and GC/MS remains high because LSD testing is still considered esoteric and is infrequent.

ECSTASY (MDMA)

MDMA (methylenedioxymethamphetamine), also known as Ecstasy or XTC, is a close structural congener of methamphetamine. Ecstasy is usually taken in oral doses of 100 to 150 mg. Analysis of Ecstasy in biological samples is performed by the same methods used for the analysis of amphetamines.[10] Throughout the years, a great number of methods for identifying the amphetamine class of drugs have been developed and published. Among routine screening procedures for amphetamines, MDMA cross-reacts best with the following immunoassay reagents: DPC/M (289%), EMIT/mono (33%), Abuscreen/HSM (109%), and Abbott A/M (84%). Other immunoassays are more specific for amphetamine and methamphetamine and, therefore, are not sensitive to MDMA.

TABLE
Procedures for Detecting LSD

	HPLC/ Fluor	RIA	GC/MS
Sensitivity (ng/ml)	0.5	0.1	0.05
Time of detection (day)	0.5	2.5	3.5
Volume of urine needed (ml)	40.0	0.2	1.0
List cost of analysis ($)	45.00	57.00	53.00

A positive immunoassay screening test must be confirmed by a specific chromatographic assay. Gas chromatography determination of plasma levels of MDMA and its metabolite MDA ranged from 105 to 5.1 ng/ml and 28.4 to 2.4 ng/ml, respectively, for the 24-hour period following ingestion of 50 μg MDMA.[11] Amphetamine assays are used routinely in drug testing laboratories; therefore, testing for MDMA is not nearly as expensive as for LSD.

The standard DHHS amphetamine cutoff of 1000 ng/ml, established in the DHHS guidelines, is so high that much recent Ecstasy use will be missed on screening. Once the screened urine is found negative, of course, it is not tested on GC/MS, so the Ecstasy use is missed. A lower cutoff, such as 300 ng/ml, or the use of a specific Ecstasy immunoassay reagent would be helpful in improving sensitivity for detecting Ecstasy use.

SUMMARY

Although drug testing conducted under the requirements of the Department of Transportation (DOT) and the Department of Health and Human Services is limited to the standard five-drug screen, it is important that other drug testing routinely include the hallucinogenic drugs, especially LSD and Ecstasy. Most drug testing is not bound by the DOT and DHHS restrictions. Both LSD and Ecstasy can be detected by using immunoassay screens followed by GC/MS confirmations. At higher doses, Ecstasy cross-reacts with most immunoassay screens for amphetamines. However, to identify Ecstasy use, the laboratory confirmation must test specifically for Ecstasy; otherwise, the screened positive test will go undetected, and will be reported as a negative result.

Laboratory testing for LSD and Ecstasy is especially important today for two reasons: because of the increasing importance of these

drugs in the overall addiction problem, and because one of the major forces pushing the drug market toward hallucinogens is the claim by drug sellers that these potent illicit drugs will not be detected by drug tests. The drug market's movement toward lower doses of LSD and Ecstasy, to reduce the likelihood of bad trips, tends to reassure novice users and to promote the wider use of these drugs. This lower dose pattern poses additional challenges to laboratory detection, especially when tests are done more than 12 hours after the use of the drug.

Earlier technical barriers to testing for these drugs in urine and serum have been removed. Today the need is for wider recognition that testing for these drugs is relatively easy and affordable, so that the testing becomes routine.

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