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TESTS FOR DRUGS OF ABUSE

Testing for drug use has become increasingly common, not only in health care, but also in drug rehabilitation, in the military, at the workplace, after accidents and in the criminal justice system. Performance-enhancing drugs such as anabolic steroids, growth hormone (*Genotropin*, and others) and erythropoietin *(Procrit, Epogen)* are not discussed here.

ASSAYS — Assays can be categorized as preliminary (initial) or confirmatory tests. Preliminary tests include immunological assays such as radioimmunoassay (RIA), homogenous enzyme immunoassay (EMIT), fluorescence polarization immunoassay (FPIA) and enzyme-linked immunoassay (ELISA). These assays tend to be highly sensitive, but they may be less specific than confirmatory tests. Confirmatory tests include high performance liquid chromatography (HPLC) gas chromatography and mass spectrometry; a combination of chromatography and mass spectrometry is considered the "gold standard" for confirmatory testing.

SPECIMENS – **Urine** is used most often to test for drugs because it is obtained easily and concentrations of drugs in urine are relatively high (K Wolff et al, Addiction 1999; 94:1279). Ingesting large quantities of liquids, taking diuretics or adding water or household bleach to a urine specimen can mask illicit drug use. **Blood** is useful for quantitative determinations, but many abused substances leave the blood relatively quickly. Where there is a well-accepted relationship between blood concentrations and pharmacological effect, as with ethanol, blood testing can be helpful. **Saliva** may be particularly useful for assessing drugs taken too recently to be detectable in urine. Testing procedures may affect saliva concentrations; saliva is usually slightly more acidic than plasma, but when stimulated to collect sufficient volume for a sample, it may become more basic, which can alter the saliva-to-plasma (S/P) ratio. Smoking or eating can contaminate a saliva sample. **Breath** testing is useful for volatile substances, especially alcohol, because urine alcohol levels do not correlate well with blood alcohol levels, while breath alcohol does. **Sweat** patches worn for 7 days have been used to monitor patients in the criminal justice system or in drug treatment facilities. Environmental contamination can lead to false-positive results (DA Kidwell and FP Smith, Forensic Sci Int 2001; 116:89). **Hair** gives a better long-term measure (1-6 months) of substance abuse than urine because drugs stored in hair remain there as the hair grows out. The concentration of drugs in hair varies with hair color, hair structure and growth rates. Shampoos, bleaches or dyes can alter drug concentrations in hair. Volatile drugs like marijuana may adhere to hair and give false-positive results (R Wennig, Forensic Sci Int 2000; 107:5).

FEDERAL DRUG TESTS — Federal drug testing programs require testing all specimens for marijuana metabolites, cocaine metabolites, opiate metabolites, amphetamines and phencyclidine. Many multidrug screening assays also detect barbiturates and benzodiazepines in urine. The US Department of Health and Human Services (DHHS) specifies urine testing in their current Mandatory Guidelines for Federal Workplace Drug Testing Programs, but drafts of new guidelines include use of hair, sweat and oral fluid (http://workplace.samhsa.gov). The DHHS has established specific threshold concentrations for a positive finding in urine for the drugs listed in the table. These concentrations were chosen for optimal sensitivity and specificity. The thresholds for other drugs, such as benzodiazepines, vary with the laboratory and the assay. The length of time someone will test positive following drug ingestion depends on the drug, the dose, its elimination half-life, and the source of the specimen.

FEDERALLY MANDATED URINE TESTS FOR DRUGS OF ABUSE

Test drug	Positive preliminary test	Duration of detectability	Some drugs that can cause false-positive preliminary urine tests
Amphetamines	1000 ng/ml[1]	2-3 days	Ephedrine, pseudoephedrine, phenylephrine, amphetamines, dextroamphetamine, methamphetamine, selegiline, chlorpromazine, trazodone, bupropion, desipramine, amantadine, ranitidine
Cocaine metabolites	300 ng/ml[2]	2-3 days; up to 8 days with heavy use	Topical anesthetics containing cocaine
Marijuana metabolites	50 ng/ml	1-7 days (light use); 1 month with chronic moderate to heavy use	Ibuprofen, naproxyn, dronabinol, efavirenz, hemp seed oil
Opiate metabolites	2000 ng/ml	1-3 days	Codeine, morphine, rifampin, fluoroquinolones, poppy seeds, quinine in tonic water
Phencyclidine	25 ng/ml	7-14 days	Ketamine; dextromethorphan

1. DHHS proposed new guidelines: 500 ng/ml
2. DHHS proposed new guidelines: 150 ng/ml

DRUGS — Blood and breath concentrations of **alcohol** correlate more closely than urine concentrations with central-nervous-system impairment.

False-positive determinations are especially common with **amphetamines**. Using a second immunoassay to double-check positive results can reduce the number of false positives. The exact substance present can be determined by confirmation testing.

Marijuana is converted into several metabolites; among these, Δ-9-tetrahydrocannabinol-9-carboxylic acid can be found in urine in high concentrations for the longest duration of time. Positive tests from passive inhalation of marijuana smoke or from consumption of hemp-containing foods found in health-food stores (such as nut butters or cold-pressed cooking oil) are unlikely (G Leson et al, J Anal Toxicol 2001; 25:691).

Cocaine has a short half-life (about 1 hour); it is largely metabolized to benzoylecgonine, which has an elimination half-life of about 7½ hours and is excreted in urine (RT Jones, NIDA Res Monogr 1997; 175:221).

Benzodiazepine immunoassays are standardized to a single benzodiazepine, such as nordiazepam (a diazepam metabolite), and cross-reactivity to other benzodiazepines is variable. If cross-reactivity to a benzodiazepine with a relatively short half-life, such as lorazepam (*Ativan*, and others), is low, and only a small dose of drug was taken, then the duration of a positive urine finding will be short compared to a longer half-life benzodiazepine with higher cross-reactivity, such as diazepam (*Valium*, and others).

Opiate immunoassays are highly sensitive for compounds showing structural similarity to morphine, such as codeine, 6-acetylmorphine, and dihydrocodeine, but less sensitive to more structurally dissimilar opioids such as oxycodone (*Oxycontin*, and others) or meperidine (*Demerol*, and others).

CONCLUSION — The reliability of tests for drugs of abuse depends on the timing and the assay. Use of confirmatory tests can reduce the number of false-positive results. Assays of hair can detect drugs used weeks before. Testing saliva, sweat and hair for abused drugs may circumvent the tampering that has weakened the reliability of urine specimens, but none of these sources are standardized as well as urine.

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