Marijuana (Cannabis)

Related Information

Club Drugs

Scientific Name

Cannabis sativa

Impairment Potential Yes; Mean detection time for marijuana metabolites using a 100 ng/mL urinary cutoff by immunoassay is about 24 hours. Delta-9-THC blood levels as low as 2 ng/mL is consistent with recent usage and probably impairment. Studies have demonstrated that 94% of drivers with delta-9-THC levels over 25 ng/mL have failed standard roadside sobriety testing. Pilots exposed to marijuana demonstrated impaired flying skills as long as 24 hours postexposure.

Mechanism of Toxic Action Antiemetic for therapeutic uses/hallucinogen; derived from the hemp plant, *Cannabis sativa* (which contains 2% to 6% tetrahydrocannabinol and which is psychotropically active in the (-) enantiomeric form); affects serotonin release along with increasing catecholaminergic effect while inhibiting parasympathetic effects

Adverse Reactions

Cardiovascular: Dose-related tachycardia, sinus tachycardia

Central nervous system: Irritability, disorientation, euphoria, short-term memory disturbance, distortion of time and space, dysphoria, hyperthermia, synesthesia, hypothermia, psychosis

Dermatologic: Urticaria, pruritus, exanthem

Gastrointestinal: Constipation

Genitourinary: Urinary retention, impotence

Neuromuscular & skeletal: Trismus, fine tremor

Ocular: Lateral gaze nystagmus, mydriasis, injected conjunctival vessels

Respiratory: Bronchial irritation

Miscellaneous: Thirst

Signs and Symptoms of Overdose I.V. administration can cause diarrhea, nausea, vomiting, fevers and can progress in 12 hours to cyanosis, hypotension, renal failure, thrombocytopenia, rhabdomyolysis.

Mild cannabis intoxication (10 g/month): Fatigue, impaired recall, perceptual alterations, relaxation, sense of well being

Moderate intoxication (30 g/month): Depersonalization, memory deficits, mood swings

Excessive intoxication (60 g/month): Delusions, hallucinations, impaired coordination, paranoia, slurred speech

Admission Criteria/Prognosis Any patient who has injected a cannabinoid (need to monitor for azotemia, thrombocytopenia, and rhabdomyolysis), will require admission; severe psychotic episodes or hyperthermia will require admission

Toxicodynamics/Kinetics

Onset of action: Inhalation: 6-12 minutes; Oral: 30-120 minutes

Duration of acute effect: 0.5-3 hours

Absorption: Smoking: 18% to 50%; Ingestion: 5% to 20%

Distribution: V_d: 10 L/kg; increases with chronic use

Metabolism: Major metabolite is 11-hydroxy-tetrahydrocannabinol

Protein binding: 97% to 99%

Half-life: 28 hours (first-time users); 56 hours (chronic users)

Elimination: Feces (30% to 35%); renal (15% to 20%)

Reference Range Plasma levels >10 ng/mL associated with impairment (can result from ingestion of 20 mg of THC); urinary immunoassays will be positive for about one week with one time use or about one month with chronic use; one puff of marijuana cigarette yields a blood THC concentration of 7.0 ng/mL (1.75% THC cigarette) to 18.1 ng/mL (3.55% THC cigarette); mean peak salivary levels correspond to 864 ng/mL (1.75% THC) to 4167 ng/mL (3.55% THC); bleach may cause a 14% to 45% decrease in THC concentration in urine immunoassay results; THC blood levels of 7-29 ng/mL can result in production of 50% of maximal subjective high effect

Overdosage/Treatment

Decontamination: Ingestion: Lavage oral ingestion (within 1 hour)/activated charcoal with cathartic

Supportive therapy: Benzodiazepines for agitation; hypotension can be treated with Trendelenburg/crystalloid infusion; tachycardia can be treated with beta-blockers

Test Interactions Alkaline/acidic urine (or dilute urine) may cause false-negative urinary immunoassay tests; Visine® adulteration may also cause false-negative tests; bleach may cause a 14% to 45% decrease in THC concentration in urine immunoassays; urine drug screen is positive for 6 days with one-time use; may be positive for weeks with chronic use. When Pyridium® chlorochromate ("Urine Luck") adulterant is added to urine (at pH of 5-7), ~ 58% to 100% of THC-acid is lost, resulting in a possible false-negative assay. There have been reports of false-positive urine immunoassay screening tests for tetrahydrocannabinol (THC) in patients receiving pantoprazole.

Drug Interactions Attenuation of drowsiness can occur with concomitant administration of CNS depressants; pretreatment with indomethacin may cause attenuation of the euphoria with decreased cardiac effects; cocaine, atropine along with tricyclic antidepressants may cause additive increase in heart rate; disulfiram may produce hypomanic state; may cause additive increase in blood pressure when given with amphetamines

Pregnancy Issues C; increased incidence of protracted labor, fetal distress, stillbirths, low birth rate, small for gestational age infants; no associated congenital abnormalities

Additional Information Lethal dose: 30 mg/kg.

One "joint" weighs 0.5-1 g with an average THC content of 1% to 2% (5-20 mg); hash oil contains 30% to 50% THC; hashish is 3% to 6% THC; toxic dose is 15 mg/kg THC;

Decreases intraocular pressure; can cause bronchodilatation; therapeutic uses include prevention of nausea (oral THC dose of 5-15 mg/m²), and appetite suppression; higher THC levels are associated with higher puff amount and higher potency; levels are not associated with how long puffs are held. THC levels can range from 33 ng/mL (with a 30

mL puff, 1.75% THC) to 167 ng/mL (90 mL puff, 3.55% THC concentration). Potential for medicinal uses of cannabinoids include to alleviate chemotherapy-induced nausea and vomiting, lowering intraocular pressure, antiseizure medication, muscle relaxation in spastic disorders, appetite stimulation, relief of phantom limb pain, menstrual cramps, and migraine therapy.

First-time use of cannabis can precipitate an acute psychotic episode persisting for several months, with no previous psychiatric history. Decreases intraocular pressure; can cause bronchodilatation; therapeutic uses include prevention of nausea (oral THC dose of 5-15 mg/m²), and appetite suppression; higher THC levels are associated with higher puff amount and higher potency; levels are not associated with how long puffs are held. THC levels can range from 33 ng/mL (with a 30 mL puff, 1.75% THC) to 167 ng/mL (90 mL puff, 3.55% THC concentration). Potential for medicinal uses of cannabinoids include to alleviate chemotherapy-induced nausea and vomiting, lowering intraocular pressure, antiseizure medication, muscle relaxation in spastic disorders, appetite stimulation, relief of phantom limb pain, menstrual cramps, and migraine therapy.

Mid-Year 2000 Preliminary Emergency Department Drug Abuse Warning Network (DAWN) Data: **Note:** Marijuana/hashish is likely to be mentioned in combination with other substances, particularly alcohol and cocaine; therefore, one Emergency Department (ED) episode can include mentions of one or more drugs.

 • There were 47,535 marijuana/hashish mentions during the first half of 2000, which was statistically unchanged since the first half of 1999 (43,109 mentions).

 • There were no significant changes in marijuana/hashish mentions by age or gender, between the first halves of 1999 and 2000. By race, marijuana/hashish mentions changed only for patients reported as Hispanic, with an increase of 44% (from 3799 to 5465 mentions), from the first half of 1999 to the first half of 2000.

 • Marijuana/hashish mentions remained stable nationwide between the first half of 1999 and the first half of 2000 (from 43,109 to 47,535). For this period, marijuana/hashish mentions increased in 5 of the 21 metropolitan areas oversampled in DAWN and decreased in 3. The increases were found in San Francisco (121%), Seattle (60%), Miami-Hialeah (45%), Denver (33%), and San Diego (26%). A decrease of 20% was found in Phoenix; decreases of 17% were found in Newark and Philadelphia.

U.S. retail price per bulk gram in 2000: $9; U.S. spending on illicit marijuana in 2000: 10 billion dollars.

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Clinical Interpretation of Drug Testing

Jerrold B. Leikin, MD, FACP, FACEP, FACMT, FAACT, FACOEM

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Dr. Leikin is director of Medical Toxicology at NorthShore University HealthSystem - OMEGA at Glenbrook Hospital in Glenview, Illinois.

Disclosure: Dr. Leikin reports no affiliation with or financial interest in any organization that may pose a conflict of interest.

Please direct all correspondence to: Jerrold B. Leikin, MD, Director of Medical Toxicology, NorthShore University HealthSystem - OMEGA, Glenbrook Hospital, 2150 Pfingsten Rd, Suite 3000, Glenview, IL 60026; Tel: 847-657-1700; Fax: 847-657-1711; E-mail: jleikin@northshore.org.

Abstract

The clinical interpretation of urine drug screens (UDS) and its confirmatory process is a complicated, multi-step process that involves comprehensive knowledge of the analytic testing procedure, along with its rationale. While the

historic basis of the UDS is predicated on occupational drug testing regulations, the clinician must navigate through a maze of analytic procedures to properly verify and correlate psychiatric symptoms to drug use through information derived by urine drug analysis.

Introduction

"A large number of people at a small risk may give rise to more cases of disease than the small number who are at high risk," is an essential public health tenet.[1] Nowhere is this demonstrated as conclusively as with drug testing for occupational purposes. By following a very specific protocol, drug testing has certainly identified the large number of individuals at risk for impairment in safety-sensitive employment duties.[2] The Health and Human Services mandatory guidelines have been established and revised since President Reagan signed the Executive Order 12564 on September 15, 1986, establishing the goal of a Drug-Free Federal Workplace. The drug testing components follow a simple algorithm: screen, confirm, and verify. The first two modalities are laboratory based: screen is an immunoassay procedure and confirmation entails a more extensive analytic modality. Verification is performed with physician input, usually correlating the donor's (employee's) response to the laboratory data.

What is evident, however, is that exactly the same laboratory testing methodology is utilized for other divergent clinical purposes—especially in emergent situations for the evaluation of psychiatric patients.[3] A recent Australian study[4] noted that urine drug screens (UDS) were most often requested in toxic ingestion situations followed by acute psychosis and impaired consciousness presentations. It is also commonly used by physicians who regularly provide care for adolescents; oftentimes, these physicians are not aware of the modalities of the UDS.[5] This may lead to differences in interpretation, depending on the clinical situation. The approach articulated in this article promotes that the above simple diagnostic algorithm (screen, confirm, and verify), which has been successfully utilized in employment drug testing, can also apply to psychiatric patient evaluations.

Testing Modalities

The primary drug test utilized in clinical inpatient and outpatient psychiatric encounters is typically the immunoassay-based UDS. The immunoassay technique utilizes drug-specific antibodies in order to detect the presence of that drug (or its metabolites) in the urine at a predetermined threshold. This qualitative assessment gives little information on administration route, timing, or chronicity of drug use. The five-panel UDS is probably the most commonly utilized brand of UDS used in the clinical setting. This form of UDS provides analysis of amphetamines, cocaine metabolite, opiates, marijuana metabolite, and phencyclidine.[2,6] Occasionally, barbiturates and benzodiazepines' analysis may also be provided on a clinical UDS.

These analytes may be enzyme labeled (enzyme immunoassay [EIA]) or radioactive labeled (radioimmunoassay [RIA]) which competes with the targeted drug/metabolite with the antibodies. A positive result occurs when the measuring tool (ie, light for EIA; radioactivity for RIA) is equal or greater than that of a positive control sample. Variations of this procedure exist in some reference laboratories (such as fluorescence polarization immunoassay; particle immunoassay). Enzyme immunoassays or particle immunoassays are used in most clinical hospital laboratories for drug screens. The immunoassay testing cutoffs have been standardized over the past 2 decades with drug detection times being relatively well established (Table 1; see Addendum for recent revisions[7]).

TABLE 1
URINARY IMMUNOASSAY CUTOFF FOR DRUGS OF ABUSE

Drug	Immunoassay Cutoff (ng/ml)	Usual Detection Time
Cocaine (metabolite)*	300	4–6 days
Phencyclidine	25	1–2 weeks
Amphetamines	1,000	1–2 weeks
Opiates	2,000	1 week
Marijuana (metabolite)†	50	5 days–3 weeks

* Benzoylecgonine.
† Δ-9-tetrahydrocannabinol-9-carboxylic acid.

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ADDENDUM
REVISED CONFIRMATORY TEST CUTOFF CONCENTRATIONS*

Initial Test Analyte	Initial Test Cutoff Concentration	Confirmatory Test Analyte	Confirmatory Test Cutoff Concentration
Marijuana metabolites	50 ng/mL	THCA	15 ng/ml
Cocaine metabolites	150 ng/mL	Benzoylecgonine	100 ng/ml
Opiate metabolites:			
Codeine/morphine†	2,000 ng/mL	Codeine	2,000 ng/ml
		Morphine	2,000 ng/ml
6-acetylmorphine	10 ng/mL	6-acetylmorphine	10 ng/ml
Phencyclidine	25 ng/mL	Phencyclidine	25 ng/ml
Amphetamines:‡			
AMP/MAMP§	500 ng/mL	AMP	250 ng/ml
		MAMP‖	250 ng/ml
MDMA	500 ng/mL	MDMA	250 ng/ml
		MDA	250 ng/ml
		MDEA	250 ng/ml

* The new guidelines effective at the end of 2010 encompass the above initial and confirmatory analyts and cutoffs conventrations.

† Morphine is the target analyte for codeine/morphine testing.

‡ Either a single initial test kit or multiple initial test kits may be used provided the single test kit detects each target analyte independently at the specified cutoff.

§ Methamphetamine is the target analyte for AMP/MAMP testing.

‖ To be reported positive for methamphetamine, a specimen must also contain amphetamine at a concentration equal to or greater than 100 ng/mL.

THCA=Δ-9-tetrahydrocannabinol-9-carboxylic acid; AMP/MAMP=amphetamine/methamphetamine; MDMA=methylenedioxymethamphetamine; MDA=methylenedioxyamphetamine; MDEA=methylenedioxyethylamphetamine.

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In occupational drug testing procedures, presumptive positive immunoassay screens are then confirmed by gas chromatography/mass spectrometry techniques.[6] The gas chromatography is used to separate the drug components from the urine while the mass spectrometry is utilized to identify and quantify the target analyte through either electron impact ionization or chemical ionization. The concentration of the drug is determined by the ratio of the drug to an internal standard. This complex procedure is not usually performed in hospital-based clinical chemistry laboratories due to the need for specialized equipment and personnel. However, the clinician can request such a technique be performed on a drug screen by a reference lab; the results can usually be obtained within 5 days. Confirmation cutoff concentrations have been established for occupational drug testing[6] (Table 2; see Addendum for recent revisions[7]).

TABLE 2
CUTOFF CONCENTRATION FOR GC/MS CONFIRMATION TESTS IN OCCUPATIONAL DRUG TESTING

Drug	ng/ml
Marijuana metabolite	15
Cocaine metabolite	150
Phencyclidine	25
Amphetamine	500
Methamphetamine*	500
Codeine or morphine	2,000
6-acetylmorphine	10

* Amphetamine urine assay must also be ≥200 ng/mL.

GC/MS=gas chromatography/mass spectrometry.

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However, the confirmation rates from gas chromatography/mass spectrometry are so uneven across the five drugs

usually evaluated that the clinician must be aware of the methodology to achieve proper clinical interpretation (Table 3).[8]

TABLE 3
MEAN IMMUNOASSAY CONFIRMATION RATES[8]

Amphetamines	52%
Cocaine	98%
Opiates	30%
Phencyclidine	70%
Marijuana	91%

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It should be noted (as demonstrated by Table 3) that while false positive results may occur by the immunoassay techniques, false negative results rarely occur.

Individual Drug Testing Characteristics

Each of these drug categories must be evaluated individually rather than as an entire panel. The purpose of this section is to discuss the emergent clinical evaluation of these drug testing categories in the context of psychiatric illness presentation.

Amphetamine toxicity can present as mania or delirium in hyperadrenergic crisis due to central nervous system stimulation. Visual hallucinations, mydriasis, tachycardia, and tremor are usually encountered in acute intoxication. The immunoassay will detect both illicit and therapeutic amphetamine derivatives and, as noted, can often lead to improper determination. For example, several substances can cross react with immunoassay (especially polyclonal based). These substances may include ephedrine, psuedoephedrine, or even chloroquine. Newer monoclonal immunoassays reduce the possibility of cross-reactions, although interference can occur with certain antipsychotics (chlorpromazine, fluspirilene, or pipothrazin).[9] It should also be noted that the rate of amphetamine urinary excretion is determined by urinary pH: the lower the pH, the larger the amount of amphetamine is excreted. Thus, the detection time may be significantly lowered in an acidic urine environment. The clinician can request gas chromatography/mass spectrometry to determine the amount of amphetamine or methamphetamine in the urine sample. Due to its metabolism, both methamphetamine and amphetamine concentrations have to be known in order to determine the substance ingested. Illicit methamphetamine will usually result in a urinary methamphetamine level >500 ng/ml and a urinary amphetamine level >100 ng/ml. Furthermore, isomer analysis can give additional information regarding the type of amphetamine ingested. Typically, d-isomer (dextro) is indicative of illicit methamphetamine or some prescription amphetamines, whereas L-isomer (levo) implies that a medicinal agent was identified. All these types of analyses can usually be performed within 48 hours by a typical, clinical reference laboratory. Some hallucinogenic amphetamines (such as 2,5-dimethoxy-4-bromoamphetamine) may not elicit a positive amphetamine urinary immunoassay result.[10] Future incarnations of hospital-based UDS will probably include[3,4] methylene dioxy methamphetamine ("ecstasy") analysis.

Cocaine also exhibits a typical stimulant pattern similar to amphetamines in an acute state of intoxication. The stimulant symptoms usually last for a few hours, unlike most amphetamines (which have a longer half-life and therefore can last for several hours). Furthermore, unlike amphetamine immunoassays, it is the metabolite (benzoylecgonine) that is analyzed rather than the parent drug. Thus, the determination of acute use by qualitative assay alone can be futile—only with gas-chromatography/mass spectrometry quantitative analysis can recent use be determined and only then when the urinary benzoylecgonine level is exceedingly high (usually >10,000 ng/ml) following a 50 mg dose. A urinary ratio of the metabolite benzoylecgonine to parent compound cocaine of >100 may indicate that exposure occurred >10 hours prior to time of collection.[11] It should be noted that due to its unique structure, benzoylecgonine does not resemble any other topical anesthetic and therefore, immunoassay confirmation rates are higher than any other drug (Table 3).[8]

Phencyclidine has no current therapeutic application in the United States (and very little worldwide). Its use as an anesthetic has been discontinued for decades due to reports of psychotic reactions. Chemically related to ketamine, a

relatively low dose of phencyclidine (5 mg) can result in psychoactive effects.

As with amphetamines and cocaine, phencyclidine results in a stimulant pattern of intoxication with acute paranoid psychosis (associated with elevated pulse and blood pressure) that can last for several hours.[12] As a weak base, excretion is also pH dependent with an increased amount of drug being excreted in acidic urine. Substances that can cross react with the immunoassay include antihistamines (usually doxylamine or diphenhydramine), venlafaxine, or the cough suppressant dextromethorphan.[13] Ketamine can also result in a positive PCP screen.

The evaluation of marijuana positive urine drug screens can be quite problematic in an emergency situation. Due to its fat solubility, metabolism, and essentially unknown dosage ingested, the detection time for cannabinoid use can be quite variable. Generally, assuming social use of low concentration of D-9-tetrahydrocannabinol-9-carboxylic acid (THC; <4%), the detection time from smoking one joint may be as short as ~33 hours.[14,15] Furthermore, it is possible that passive exposure to cannabinoid can give a positive assay, although the urinary cannabinoid metabolite concentration is usually <35 ng/ml.[16]

Acute marijuana toxicity is taking on a new prominence as the concentration of the active ingredient increases. Over the past 20 years, the concentration of THC has more than tripled in recreational use approaching 10% concentration in a joint.[17] Thus, toxicity (particularly neurotoxicity) can be increasingly expected to be encountered after smoking cannabinoid substances. Psychosis (usually reversible) in adolescents has been noted to be a dose-related effect in Europe and India with an estimated risk for developing psychosis due to cannabis estimated to be ~2.8.[18,19] A urine marijuana metabolite amount >100 ng/ml on presentation may be a biomarker for such neurotoxicity.

Opiate use interpretation can be even more complicated. Generally, an opiate assay only will give a positive result following ingestion of morphine, or codeine. Synthetic opioid (ie, hydrocodone, oxycodone, methadone, and fentanyl) use usually will not result in a positive urine assay. The opiate antagonist naloxone also will not interfere with the opiate immunoassay. Codeine ingestion is metabolized to morphine—morphine cannot be metabolized to codeine.[6] Quantitative urinary morphine or codeine concentrations >15,000 ng/ml are indicative of recent (within 1 day) of use. Since poppy seeds contain a trace amount of morphine, ingestion of poppy seeds can result in a positive opiate urine immunoassay (usually within 48 hours of ingestion) while the quantitative urinary opiate analysis will usually be <1,000 ng/ml. Poppy seed ingestion should not interfere with methadone or other synthetic opioid immunoassay analysis. Furthermore, subsequent analysis for six-monoacetylmorphine metabolite (6-MAM) is distinctive for recent heroin use (if urinary concentration is <10 ng/ml). This heroin-specific metabolite will become a standard analyte in future incarnations of UDS.

Oftentimes, benzodiazepine, barbiturate, and tricyclic antidepressent (TCA) screens are included in the usual UDS obtained in the emergency department. The practitioner should be alerted to the fact that most benzodiazepine urine screens test only for oxazepam (a metabolite of temazepam, alpralozam, halazepam, and diazepam). It will usually not give a positive test for benzodiazepines excreted primarily as glucuronide conjugates (ie, clonazepam, lorazepam) and may not be sensitive at low dose (<10 mg) ingestion of benzodiazepines. Furthermore, oxaprozin or sertraline use can result in a false positive urinary benzodiazepine screen.[20] Flumazenil will not interfere with benzodiazepine immunoassays.[21]

The practitioner should also be aware of the potential consequences in the setting of an asymptomatic individual with a positive barbiturate urine assay; this should alert the clinician to the possibility of barbiturate withdrawal upon sustained abstinence. Barbiturate withdrawal is one of the more lethal withdrawal subtypes and often requires critical care management. Thus, a positive urinary screen must be explained in terms of duration and frequency of use in order to assess withdrawal risk. Barbiturate urinary detection times range from a few days for the shorter-acting barbiturate agents (such as secobarbital) to >1 week for long-acting barbiturates (such as phenobarbital).

TCA immunoassay screens are increasingly being utilized in clinical settings. Detection times for TCA substances may be as long as several days. The practioner should be aware that several medications have similar three-ring nucleus chemical structures as TCA and thus may cross-react with TCA immunoassays. These medications include cyproheptadine, carbamazepine, thioridazine, chlorpromazine, cyclobenzaprine, and quetiapine.[3] Structurally dissimilar antihistamines, such as diphenhydramine, promethazine, hydroxyzine, and cetirizine, may interfere with the TCA immunoassay.[22,23] Since virtually all of the above agents can result in lethargy, mydriasis and tachycardia, confusion can occur that such symptoms may be due to TCA toxicity (with the presence of a positive immunoassay) as opposed to

antihistamine, carbamazepine, cycloheptadine, or quetiapine toxicity.

Methadone qualitative enzyme immunoassays are available in most clinical settings. These assays my not detect the long-acting methadone substances such as L-alpha-acetyl-methadol or its metabolites. False positive results with methadone immunoassays have occurred with verapamil, diphenhydramine, doxylamine, quetiapine, and certain psychotropic drugs (ie, cyamemazine, alimemazine, levomepromazine, chlorpromazine, clomipramine, and thioridazine).[24,25]

Clinical Use

Certainly, substance abuse plays a major role in the psychiatric evaluation. A retrospective review[26] from Cincinnati noted that ~36% of emergency psychiatric patients had a co-existing diagnosis of substance abuse. A more recent California study[27] noted that 44% of patients presenting to an urban psychiatric emergency service had a positive UDS with cocaine metabolite being present in 62% of these cases. Concurrent substance abuse in psychiatric patients presenting to an emergency department was more prevalent in non-psychotic individuals than psychotic ones.[28]

However, even with the realization that substance abuse is a significant risk factor to psychiatric patient presentation, it does not appear that a routine UDS affects disposition or even the subsequent length of inpatient stays in such a cohort.[29,30] Furthermore, clinical correlation by resident physicians or nurses can be achieved by physical examination relating to the drug's symptom complex (toxidrome) recognition in >80% of patient presentations.[31]

It thus appears that more information regarding substance abuse is required than can be elicited from a qualitative UDS alone. Obtaining the confirmatory gas chromatography/mass spectrometry quantitative analysis of specific analytes can give the clinician additional (although albeit somewhat united) forensic information that provides much more detailed information about a patient's recent drug use. For example, a urinary cannabinoid metabolite quantitation >100 ng/ml rules out passive exposure and is indicative of recent exposure. Opiate quantitative analysis also can reveal recent exposure (if >15,000 ng/ml), rules out poppy seed ingestion (if >2,000 ng/ml), and virtually is diagnostic of heroin exposure if 6-MAM is >10 ng/ml. Illicit methamphetamine use can be detected if urinary methamphetamine levels are >500 ng/ml and urinary amphetamine levels are >100 ng/ml. Recent amphetamine or methamphetamine use can be suspected if both levels are >1,000 ng/ml in urine with pH >7. Phencycline false positives can be ruled out by confirmatory analysis. Therefore, it is obvious from these few examples, that the UDS essentially tells an incomplete story with regards to substance abuse. It is therefore recommended that psychiatric practiners should routinely utilize confirmatory analysis techniques in the comprehensive evaluation of their patients in a similar fashion as is performed in employment drug testing.

Therefore, if any clinical drug correlation to laboratory results is required, gas chromatography/mass spectrometry quantitative analysis should be considered. UDS analysis alone in a psychiatric patient-centered fashion may be appropriate for monitoring pain management or ongoing addiction/chemical dependency issues; however, the acute psychiatric patient evaluation often requires more information than a simple UDS can provide.[32-34]

Conclusion

The analytic basis for the UDS is the immunoassay technique, which is a qualitative test with predetermined thresholds. A confirmatory test involving gas chromatography/mass spectrometry can literally give a "fingerprint" of a drug analyte, both in a structural and a quantitative analysis. Utilizing both of these techniques in a clinical setting, the clinician can obtain far more information regarding the specifics of drug usage and thus correlate these findings to the patient's history and symptom presentation. *PP*

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Medical Cannabis in Illinois

Although the medical-legal landscape is still evolving, a pilot program gives physicians important protections

By Jonathan Loiterman, JD, MBA

LAST AUGUST, Illinois passed the Compassionate Use of Medical Cannabis Pilot Program Act, joining 20 other states in recognizing some form of medical cannabis use even though federal laws criminalizing such activities remain in effect. Illinois' medical cannabis program, which is among the most tightly regulated in the nation, aims to provide a safe, controlled method for qualified patients who are being treated for defined diagnoses to possess and use limited quantities of cannabis subject to a variety of restrictions and fees.

Cannabis' status under federal law and the requirements of Illinois law necessitate that procedures for recommending and obtaining cannabis exist outside of the normal procedures used for traditional pharmaceuticals. As a result, physicians recommending cannabis and those with patients seeking cannabis recommendations must understand the basic mechanics of how the law works and what is expected of physicians.

Medical Cannabis Industry Overview

Illinois' law requires patients, distributors, and growers to each obtain a different type of license issued by a different agency: the Department of Public Health, the Department of Financial and Professional Regulation, and the Department of Agriculture, respectively. Because these agencies are still finalizing the regulations, no such licenses have been issued, and any activities involving cannabis, medical or otherwise, remain unlawful until licenses have been granted. As of this writing, each agency has published proposed rules for public comment at *http://mcpp. illinois.gov*. It is anticipated the rules will be finalized in late summer or early fall of 2014 before applications for patients, caregivers, dispensaries, and cultivation centers are accepted. It is likely that medical cannabis patients will first be able to obtain legal cannabis in early 2015.

The Illinois law is a pilot program with a fixed sunset date. This means that effective Dec. 31, 2017, the law will cease to provide any protection for medical cannabis activities unless and until the legislature takes action to extend the program. Given the time needed to ramp up licensing, production, and distribution, the current program actually contemplates just three years of practical access to legal cannabis.

Illinois' program is conceived as a two-tiered system for

cultivation and distribution of cannabis. Up to 22 cultivation centers—one for each Illinois State Police District—is authorized under the law. These licenses will be issued by the Department of Agriculture on a merit-based system. Cultivation centers have the exclusive privilege of growing cannabis and manufacturing cannabis-infused products in Illinois; patients and dispensaries are prohibited from growing cannabis on their own. Cultivation centers can only sell cannabis to licensed dispensaries and are expressly prohibited from selling directly to patients, registered or otherwise. Cultivation centers are also responsible for incorporating an electronic tracking system to track all cannabis products from seed to sale.

Up to 60 dispensary licenses are authorized in Illinois. Dispensaries have the exclusive privilege of selling cannabis to patients in Illinois; even registered patients lawfully in possession of cannabis cannot sell it to one another. Although traditional pharmacies are not categorically excluded from functioning as dispensaries, pharmacies would have to apply for and receive a dispensing license in the same way as anyone else. Pharmacies are likely to find the mandated security and record-keeping practices a burdensome distraction to their existing business procedures. Cannabis sold to patients through a dispensary must include the same seed-to-sale tracking and labeling required by cultivation centers, allowing law enforcement and regulatory authorities to identify the dispensary, the cultivation center, and the registered patient to whom the cannabis was sold.

Considerations of Federal Law

Cannabis remains an illegal, Schedule I drug under federal law, conflicting with laws in Illinois that protect the activities described above. Both President Obama and Attorney General Eric Holder have made public statements that individuals operating in compliance with a state-mandated medical cannabis program are not an enforcement priority. Yet federal authorities have stopped short of de-criminalizing or re-scheduling cannabis or otherwise formally permitting these activities.

In August 2013, Deputy Attorney General James Cole published what has since been referred to as the "Cole Memorandum." This document provides guidance to federal prosecutors on high-level enforcement priorities. These include: preventing access by minors; prohibiting financial gain for organized crime; preventing the use of firearms in the cultivation and distribution of cannabis;

and other items. The Cole Memorandum, once again, stops short of providing assurances to patients, physicians, and medical cannabis businesses that they will be immune from federal enforcement by complying with state law.

As a result, physicians who are employed by the federal government, receive research grants, consulting fees, or otherwise have professional engagement with the federal government should proceed with caution before participating in medical cannabis activities, since nothing in the law, statements by high-ranking public officials, or the Cole Memorandum provide certainty on this front.

Patients and Caregivers

Each patient who wishes to use medical cannabis must submit an application to the Department of Public Health that meets a number of rigorous requirements, including a written certification from a physician diagnosing the patient with one of approximately 40 diagnoses approved by the legislature, proof of residency, proof of identify, a fingerprint-based background check, and an application fee (proposed at $150). A number of classes of patients are disqualified including minors, people with felony drug convictions, law enforcement officers, firefighters, EMTs, corrections officers, school bus drivers, CDL license-holders, and individuals operating dispensaries.

Approved Diagnoses

The several dozen authorized diagnoses tend to be serious illnesses with objective diagnostic criteria, such as AIDS, spinal cord injury, and ALS. Common symptoms often associated with medical cannabis, such as pain, anxiety, and depression, are not included. The law authorizes the Department of Public Health to accept petitions to include additional diagnoses. The Department has fairly wide latitude to set rules governing the petitions and to exercise discretion in adding more diagnoses.

Once a patient submits a qualifying application and receives approval from the Department of Public Health, that patient is issued a registration card, allowing the patient to purchase and use up to 2.5 oz. of cannabis every 14 days from a single dispensary registered with the Department of Public Health. Patients are not free to purchase from any dispensary, and any requests to use a different dispensary must be reviewed by the Department of Public Health. Patients may designate one

Qualifying Conditions

A PATIENT MUST obtain written certification from a physician in order to use medical cannabis. The physician will certify the patient has one of 40 possible conditions. The legislature has approved approximately 40 diagnoses, but the law authorizes the state to include additional ones.

- Cancer
- Glaucoma
- HIV/AIDS
- Hepatitis C
- ALS
- Crohn's Disease
- Alzheimer's Disease
- Cachexia/Wasting Disease
- Muscular Dystrophy
- Severe Fibromyalgia
- Spinal Cord Disease
- Tarlov Cysts
- Hydromyelia
- Syringomyelia
- Rheumatoid Arthritis
- Fibrous Dysplasia
- Spinal Cord Injury
- Traumatic Brain Injury
- Multiple Sclerosis
- Arnold-Chiari Malformation
- Spinocerebellar Ataxia
- Tourette's
- Myoclonus
- Dystonia
- Reflex Sympathetic Dystrophy
- Residual Limb Pain
- Causalgia
- CRPS
- Neurofibromatosis
- Chronic Inflammatory Demyelinating Polyneuropathy
- Sirogen's Syndrome
- Lupus
- Interstitial Cystitis
- Myasthenia Gravis
- Hydrocephalus
- Nail-Patella Syndrome
- Multiple Sclerosis

non-physician caregiver to assist them with purchasing and transporting cannabis products. Caregivers undergo a similar application and background check process as patients and are subject to similar prohibitions on individuals with criminal histories. Each caregiver may assist only one patient.

Even though patients registered with the Department of Public Health are authorized to possess, and use cannabis, there are quite a few important restrictions on those activities. Patients are prohibited from possessing cannabis in schools or school busses, correctional facilities, or licensed childcare facilities.

Patients are prohibited from smoking cannabis in any place where patients could expect to be seen by other people, though this restriction is loosened when cannabis is ingested through oral, dermal, sublingual, or other non-smoking routes of administration. Cannabis may not be used in close proximity to a minor, and landlords are authorized to set their own rules about the smoking of cannabis on rental properties. While employers are prohibited from discriminating against medical cannabis patients based on their status as registered patients, the law expressly authorizes employers to continue any zero-tolerance policies.

Nevertheless, registered patients do receive some limited protections. Patients cannot be disqualified for organ transplants due to the use of medical cannabis authorized by law in Illinois. Moreover, individuals cannot be denied child custody or visitation solely for actions allowed by the law.

Registered patients are not authorized to drive while under the influence of cannabis or allowed to be intoxicated in the workplace, regardless of their status as registered patients. Finally, although prices for medical cannabis are likely to be on the order of several hundred dollars per ounce (based on market statistics from other states) the law does not require Medicaid or private insurance to cover medical cannabis.

Physician Responsibilities

Most important for Illinois physicians, the law places doctors in a trusted, gatekeeping role. Generally, a pre-condition for registration is a bona-fide physician-patient relationship where treatment for a qualifying diagnosis is provided on an ongoing basis. The only clear exception is that patients receiving care through the Veteran's Administration are exempted from certification, since VA physicians providing their care are prohibited from certifying patients due to cannabis' status under federal law. Physicians may not set up clinics on the premises of a dispensary; physicians making medical cannabis recommendations may not advertise or have financial interests in dispensaries or cultivation centers; physicians may not conduct the required physical examination through remote electronic means; and, generally, the law contemplates that the certifying physician's relationship with the patient reflects ongoing treatment for a qualifying diagnosis, including physical examination, detailed records, and overall responsibility to provide care for the qualifying diagnosis.

To preserve physicians' independent judgment on matters related to medical cannabis, the law prohibits physicians from receiving any kickback or remuneration from dispensaries. Dispensaries are prohibited from referring patients to a particular physician for certification, and physicians who make or intend to make medical cannabis recommendations are prohibited from having a financial interest in a cultivation center or dispensary.

The ongoing character of physician-patient relationships under the law is important since patients will need to re-certify annually. Moreover, physicians have the responsibility to report to the Department of Public Health when a patient the physician certifies no longer has the qualifying condition.

Physicians receive a number of important protections for providing medical cannabis certifications in compliance with Illinois law. They will not be subject to arrest, prosecution, or penalty, including discipline by the Medical Disciplinary Board solely for providing cannabis certifications under the law. Nothing in the law expressly prohibits physicians from becoming registered patients, provided that their use complies with standards of medical practice and does not constitute negligence.

Nothing about the law requires a physician to certify a patient to use medical cannabis. Rather, the law simply creates a means for physicians to recommend cannabis to patients who could benefit from it use, in the physician's medical judgment, without having to resort to black market solutions for fulfillment.

Evolving Medical Legal Landscape

The law is too new for allegations of medical negligence related to recommending, or failing to recommend, cannabis to have emerged, let alone be resolved. The law provides little guidance to physicians about when and under what circumstances cannabis recommendations should or should not be provided. Physicians searching the scientific and medical literature on the subject are likely to be met with frustrating limitations due to decades of outright criminalization of cannabis in the United States.

While the law contemplates certain educational programs designed to raise awareness about the medical uses of cannabis, disagreements over its medical utility and a narrowing knowledge gap among physicians never formally trained in the therapeutic role of medical cannabis are likely to continue in the foreseeable future.

Given that cannabis' status as a Schedule I drug is based on the FDA's finding that there is no accepted medical benefit to using cannabis, it is unlikely physicians will face substantial risk of litigation from simply declining to make recommendations. Physicians who refuse to participate are more likely to see their patients shop for another provider who is willing to consider making a cannabis recommendation.

On the other hand, physicians who make cannabis recommendations must be concerned about possible adverse reactions with other drugs, behavioral and social changes brought about by cannabis use, drug dependence and abuse, malingering, and the lack of formal training to assist physicians facing these issues.

State Seeking Physician Input

Illinois' medical cannabis legislation is the result of difficult, political negotiations informed by successes and failures in other jurisdictions. Although the law has been passed, medical cannabis policy at the state and federal levels is far from settled.

[Editor's comment: At press time for this article, Illinois published new draft rules, including changes, with a 45-day public comment period. Please check the Medical Cannabis Pilot Program website or www.mcpp.illinois.gov. In addition, *Chicago Medicine* will report on the proposed rules next month.]

Mr. Loiterman is senior associate in the law firm of Lowis & Gellen, LLP. He focuses on health care litigation, including medical malpractice, and pharmaceutical and medical device product liability cases involving catastrophic injuries and death.