

Urine Drug Screening: A Valuable Office Procedure

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Urine drug screening can enhance workplace safety, monitor medication compliance, and detect drug abuse. Ordering and interpreting these tests requires an understanding of testing modalities, detection times for specific drugs, and common explanations for false-positive and false-negative results. Employment screening, federal regulations, unusual patient behavior, and risk patterns may prompt urine drug screening. Compliance testing may be necessary for patients taking controlled substances. Standard immunoassay testing is fast, inexpensive, and the preferred initial test for urine drug screening. This method reliably detects morphine, codeine, and heroin; however, it often does not detect other opioids such as hydrocodone, oxycodone, methadone, fentanyl, buprenorphine, and tramadol. Unexpected positive test results should be confirmed with gas chromatography/mass spectrometry or high-performance liquid chromatography. A positive test result reflects use of the drug within the previous one to three days, although marijuana can be detected in the system for a longer period of time. Careful attention to urine collection methods can identify some attempts by patients to produce false-negative test results. (*Am Fam Physician*. 2010;81(5):635-640. Copyright © 2010 American Academy of Family Physicians.)

Urine drug screening is an office procedure that can enhance workplace safety, monitor patients' medication compliance, and detect drug abuse. Because of the personal, occupational, and legal implications that accompany drug testing, family physicians who perform urine drug screenings must be confident in their ability to interpret screening results and respond appropriately to that interpretation. Ordering and interpreting urine drug screenings requires an understanding of the different testing modalities, the detection times for specific drugs, and the common reasons for false-positive and false-negative test results.

Who Should Be Screened?

Urine drug screening is commonly required as a workplace mandate (e.g., pre-employment screenings; returning to work after an unexplained absence; industrial accidents where damage, injury, or loss of life may have been caused by negligence or impairment; federal regulations; random testing for continued licensure or employment). Screening may be required in safety-sensitive occupations, such as the trucking, mass transit, rail, airline, marine, or oil and

gas pipeline sectors. It may also be required for military or sports participation; for legal or criminal situations (e.g., post-accident testing, parole); or for health reasons (e.g., rehabilitation testing, pain management, treatment compliance monitoring, determining a cause of death). In addition to mandates and regulations, patient behavior or risk patterns may suggest that urine drug screening is warranted.

There are often no reliable signs of drug abuse, dependency, or addiction; nor are there definitive signs of diversion or trafficking. Relying on observations of aberrant behavior detects less than 50 percent of patients who are misusing drugs.¹ Patients who should be screened because of suspicion of drug misuse or dependency are listed in *Table 1*.

Treating chronic pain in patients with a history of substance abuse can pose a clinical challenge.^{2,3} Patients, particularly young men, with a history of alcohol or drug abuse or criminal convictions are at a higher risk of opioid misuse. Unfortunately, there is no set of predictor variables to routinely identify patients with chronic pain who are at risk of drug misuse or abuse.⁴ Universal precautions in pain management involve risk stratification, a medication agreement or

SORT: KEY RECOMMENDATIONS FOR PRACTICE

<i>Clinical recommendation</i>	<i>Evidence rating</i>	<i>References</i>
Immunoassay tests are the preferred initial test for urine drug screening.	C	10
Positive results from an immunoassay test should be followed by gas chromatography/mass spectrometry or high-performance liquid chromatography.	C	10
An extended opiate panel is needed to detect commonly used narcotics, including fentanyl (Duragesic), hydrocodone (Hycodan), methadone, oxycodone (Roxicodone, Oxycontin), buprenorphine, and tramadol (Ultram).	C	10
Appropriate collection techniques and tests of specimen integrity can reduce the risk of tampering.	C	15-17

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to <http://www.aafp.org/afpsort.xml>.

pain contract, adherence monitoring, and urine drug screening. This will facilitate the appropriate use of opioids for chronic pain management²; mitigate the adverse public health effects of diversion (e.g., deflection of prescription drugs into the illegal market)⁵; and help reduce illicit drug use.⁶

When Should Screening Occur?

There are several situations when performing urine drug screening may be appropriate. For example, writing a new prescription for a controlled substance would require evaluating the patient for a history of abuse or addiction, and may include screening. A history of substance misuse does not preclude opioid analgesia; however, patients in recovery may require boundary setting, clear delineation of the rules, and participation in an active recovery program. Urine drug screening is also useful before increasing patients' dosages of analgesics or referring patients to a pain or addiction specialist.

A negative urine drug screening result does not exclude occasional or even daily drug use. Because infrequent drug use is difficult to detect regardless of testing frequency, the benefits of frequent drug testing are greatest in patients who engage in moderate drug use.⁷ Random urine screening in patients taking opioids for pain management may reveal abnormal findings, including absence of the opioid, presence of additional nonprescribed substances, detection of illicit substances, and adulterated urine samples.⁸

Testing Methods

Before the screening, physicians should obtain a history of patients' prescription, over-the-counter, and herbal medication

Table 1. Behaviors that Raise Suspicion of Drug Misuse or Dependency

- Taking a controlled substance for a long period of time (new patients)
- Refusing to grant permission to obtain old records or communicate with previous physicians
- Demonstrating reluctance to undergo a comprehensive history, physical examination, or diagnostic testing (especially urine drug screening)
- Requesting a specific drug (often because of the higher resale value of a brand name)
- Professing multiple allergies to recommended medications
- Resisting other treatment options
- Other aberrant behavior:
 - Issuing threats or displaying anger
 - Targeting appointments at the end of the day or during off hours (nights or weekends)
 - Giving excessive flattery
 - Calling and visiting a physician's associates
 - Repeatedly losing a prescription
 - Requesting a dose escalation
 - Demonstrating noncompliance with prescription instructions
 - Demonstrating other evidence of alcohol or illicit drug misuse

use. This may raise suspicion of drug abuse or dependency.

There are two main types of urine drug screening: immunoassay testing and chromatography (i.e., gas chromatography/mass spectrometry [GC/MS] or high-performance liquid chromatography). Improper procedures may increase the risk of laboratory or on-site testing errors.⁹ To correctly interpret test results, physicians must understand the differences between the tests and the differences between laboratories and on-site testing. On-site instant drug testing is becoming more widely used because of its convenience and cost efficiency. The accuracy of on-site tests depends on the manufacturer, but some testing kits are extremely accurate, similar to the GC/MS laboratory tests.

Immunoassay tests use antibodies to detect the presence of drugs. These tests can be processed rapidly, are inexpensive, and are the preferred initial test for screening.¹⁰ The most commonly ordered drug screens are for cocaine metabolites, amphetamines, phencyclidine, marijuana metabolites, and opiate metabolites. The U.S. Department of Transportation requires testing for these five substances when conducting urine drug screenings for transportation employees. The accuracy of immunoassay testing varies, with a high predictive value for marijuana and cocaine, and a lower predictive value for opiates and amphetamines.¹⁰ A number of commonly prescribed medications can cause positive immunoassay tests (*Table 2*¹⁰⁻¹³).

The federal government sets threshold levels for these tests. Urine specimens with drug concentrations below the threshold are reported as negative. In clinical use, ordering tests without a threshold can increase the detection of drug compliance or abuse but may produce more false-positive results.¹¹

Positive results from an immunoassay test should be followed by confirmatory testing using GC/MS or high-performance liquid chromatography. These tests are more expensive and time consuming, but are more accurate than immunoassay tests.¹⁰ In these tests, the molecules are separated by the gas chromatograph and analyzed by the mass spectrometer. Each molecule is broken down

into ionized fragments and identified by its mass-to-charge ratio. The accuracy of this method makes GC/MS the forensic criterion standard.

Applying Test Results

Because false-positive and false-negative test results are possible (*Table 2*¹⁰⁻¹³), physicians should choose a test panel based on the substances they are seeking to detect. The routine opiate test is designed to detect morphine metabolites. An expanded opiate panel is needed to detect other commonly used narcotics, including fentanyl (Duragesic), hydrocodone (Hycodan), methadone, oxycodone (Roxicodone, Oxycontin), buprenorphine, and tramadol (Ultram).¹⁰ Unexpected results should be confirmed and discussed with the patient. Except for marijuana, which can be detected for weeks after heavy use, positive results reflect use of the drug within the previous one to three days. A test that is positive for morphine may be from morphine, codeine, or heroin use because of drug metabolism (morphine is a metabolite of heroin and codeine). Heroin use can be confirmed by the presence of the metabolite 6-monoacetylmorphine, but the window for detection is only a few hours after heroin use. Casual passive exposure to marijuana smoke is unlikely to give a positive test result.¹⁰

Hydrocodone is metabolized to hydromorphone in the liver; therefore, a patient taking hydrocodone as prescribed may test positive for hydromorphone.¹⁴ Similarly, the morphine metabolite in codeine may be the only drug detectable two or three days after ingestion.

The concern for false-negative results is most acute when testing for adherence to a prescribed therapeutic regimen. Adherence can be masked by dilute urine, time since ingestion, quantity ingested, or the laboratory's established threshold limits. Discussing adherence with the patient is helpful, but testing for a particular medication may be necessary to resolve issues of diverting the prescribed medication. Negative results in a

A negative urine drug screening result does not exclude occasional or even daily drug use.

Table 2. Drugs that May Cause False-Positive Results in Immunoassay Testing

<i>Test drug or drug category</i>	<i>Drugs that may cause false-positive results</i>	<i>Duration of detectability</i>
Amphetamines	Amantadine (Symmetrel), bupropion (Wellbutrin), chlorpromazine, desipramine (Norpramin), fluoxetine (Prozac), L-methamphetamine (in nasal decongestants*), labetalol (Normodyne), methylphenidate (Ritalin), phentermine, phenylephrine, phenylpropanolamine, promethazine (Phenergan), pseudoephedrine, ranitidine (Zantac), thioridazine, trazodone (Desyrel)	Two to three days
Benzodiazepines	Oxaprozin (Daypro), sertraline (Zoloft)	Three days for short-acting agents (e.g., lorazepam [Ativan]) Up to 30 days for long-acting agents (e.g., diazepam [Valium])
Cocaine	Topical anesthetics containing cocaine	Two to three days with occasional use Up to eight days with heavy use
Opiates	Dextromethorphan, diphenhydramine (Benadryl), fluoroquinolones†, poppy seeds, quinine, rifampin, verapamil‡	One to three days
Phencyclidine	Dextromethorphan, diphenhydramine, ibuprofen, imipramine (Tofranil), ketamine (Ketalar), meperidine (Demerol), thioridazine, tramadol (Ultram), venlafaxine (Effexor)	Seven to 14 days
Tetrahydrocannabinol	Dronabinol (Marinol), nonsteroidal anti-inflammatory drugs§, proton pump inhibitors (pantoprazole [Protonix])	Three days with single use Five to seven days with use around four times per week 10 to 15 days with daily use More than 30 days with long-term, heavy use

*—Current immunoassays have corrected the false-positive result for nasal decongestants containing L-methamphetamine.

†—Notably, ciprofloxacin (Cipro), levofloxacin (Levaquin), and ofloxacin (Floxin).

‡—In methadone assays only.

§—Notably, ibuprofen, naproxen (Naprosyn), and sulindac (Clinoril).

Information from references 10 through 13.

dilute urine specimen make interpretation problematic. The director or toxicologist of the reference laboratory can serve as a valuable resource if questions arise.

Preventing and Detecting Specimen Tampering

The concentration of a drug in urine depends on several factors, including time since use, amount and frequency of use, fluid intake, body fat percentage, and metabolic factors. There are many ways for patients to circumvent testing. These include adding adulterants to urine at the time of testing, urine dilution through excessive water ingestion, consumption of substances that interfere with testing, and substitution of a clean urine sample. Appropriate collection

techniques and tests of specimen integrity can reduce the risk of tampering.¹⁵⁻¹⁷

Several chemicals can be added to a urine sample to interfere with urine drug testing. Household chemicals, including over-the-counter eye drops containing tetrahydrozoline; bleach; vinegar; soap; ammonia; drain cleaner; and table salt, can produce a false-negative test. A variety of commercial products that are available online may also be used. These include glutaraldehyde, sodium or potassium nitrite, pyridinium chlorochromate, and peroxide/peroxidase. Some substances are detectable because of changes they produce in the appearance, specific gravity, or pH of the urine.¹⁰

Dilution of the urine through excessive water consumption or diuretics can decrease

the urine drug concentration and make a negative test result more likely. Therefore, excessively dilute samples should be rejected.

In situations where observed voiding is mandated, urinary substitution techniques and devices can be quite sophisticated and difficult to detect. An artificial penis with an electronic, temperature-controlled urine reservoir can be purchased online. Patients may attempt to evade detection by voiding before testing, then refilling their bladder with clean urine using a catheter.¹⁵

Federal testing procedures will catch some, but not all, tampering attempts. Summaries of the most important factors are listed in *Tables 3*¹⁶ and *4*.^{15,17} Excessively dilute, adulterated, or any other rejected urine is reported as positive.

Legal Issues for Drug Testing

Legally mandated drug testing requires the expertise of a Certified Medical Review Officer (CMRO). The CMRO is a physician who is responsible for receiving, reviewing, and evaluating results generated by employers' drug testing programs. The CMRO is also responsible for the accuracy and integrity of the drug testing process by determining whether there is a legitimate explanation for unexpected test results and protecting the confidentiality of the drug testing information.

When performing non-legally mandated tests, physicians should be familiar with the specific drug screening statutes and regulations in their own state. State regulations might address chain of custody requirements, patient privacy, which specimens may be screened, and how results may be used or shared. Reference laboratories routinely offer medical review officer services and telephone consultation with a laboratory toxicologist. When in doubt, the rules and best practices of the U.S. Department of Transportation provide a legally defensible framework for most jurisdictions.

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Table 3. Steps to Reduce Tampering in Urine Drug Screening

Request removal of any unnecessary outer clothing
Remove anything in the collection area that could be used to adulterate or substitute a urine specimen
Request the display and removal of any items in the patient's pockets, coat, hat, etc.
Require all other personal belongings (e.g., briefcase, purse) to remain with the outer clothing
Instruct the patient to wash and dry his or her hands (preferably with liquid soap) under direct observation and not to wash again until after delivering the specimen
Place a bluing agent in the commode and turn off the water supply to the testing site

Information from reference 16.

Table 4. Methods and Criteria for Urine Drug Screening

Collection methods and criteria

Collection of split samples in sealed tamper-resistant containers
Direct observation of specimen collection (when required)
Sample size of 30 mL or more
Temperature between 90°F (32.2°C) and 100°F (37.7°C)
Urine pH of 4.5 to 8.5
Use of an approved chain of custody form to track specimen handling

Findings suggestive of adulterated, diluted, or substituted specimens*

General

Temperature < 90°F or > 100°F
Unusual appearance (e.g., bubbly, cloudy, clear, dark)

Adulterated

Nitrite concentration > 500 mg per dL (4.2 mmol per L)
Urine pH < 3 or ≥ 11

Diluted

Creatinine concentration ≥ 2.0 mg per dL but < 20 mg per dL (176.8 mmol per L)
Specific gravity > 1.0010 but < 1.0030

Substituted

Creatinine concentration < 2.0 mg per dL (17.68 mmol per L)
Specific gravity ≤ 1.0010 or ≥ 1.0200

*—*Guidelines from the Substance Abuse and Mental Health Services Administration.*

Information from references 15 and 17.

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Author disclosure: Nothing to disclose.

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