

Urine drug screens: When might a test result be false-positive?

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Mr. L, age 35, has an appointment at a mental health clinic for ongoing treatment of depression. His medication list includes atorvastatin, bupropion, lisinopril, and cranberry capsules for non-descriptive urinary issues. He has been treated for some time at a different outpatient facility; however he recently moved and changed clinics.

At this visit, his first, Mr. L receives a full physical exam, including a urine drug screen point-of-care (POC) test. He informs the nurse that he has an extensive history of drug abuse: “You name it, I’ve done it.” Although he experimented with many illicit substances, he acknowledges that “downers” were his favorite. He believes that his drug abuse could have caused his depression, but is proud to declare that he has been “clean” for 12 months and his depression is approaching remission.

However, the urine drug screen is positive for amphetamines. Mr. L vehemently swears that the test must be wrong, restating that he has been clean for 12 months. “Besides, I don’t even like ‘uppers!’” Because of Mr. L’s insistence, the clinician does a brief literature search about false-positive results in urine drug screening, which shows that, rarely, bupropion can trigger a false positive in the amphetamine immunoassay.

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Disclosures

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Could this be a false-positive result? Or is Mr. L not telling the truth?

Because no clinical lab test is perfect, any clinician who runs urine drug screens will encounter a false-positive result. (See the *Box*,¹⁻³ page 22, for discussion of false negatives.) Understanding how each test works—and potential sources of error—can help you evaluate test results and determine the best course of action.

There are 2 main methods involved in urine drug testing: in-office (POC) urine testing and laboratory-based testing. This article describes the differences between these tests and summarizes the potential for false-positive results.


continued on page 22



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Practice Points

- Most clinicians who order urine drug screens eventually **will encounter a false-positive or false-negative result.**
- False positives in immunoassays are rare; however, **amphetamine and opiate false positives are more common** than cocaine metabolite and cannabinoid false positives.
- The **gas chromatography–mass spectrometry method is a good tool** to confirm initial positive or negative screens.
- **Familiarize yourself with the type of kit you are using** and ask the manufacturer for a list of possible interfering substances.
- **Understanding the limitations of urine drug screening kits is critical** for monitoring your patient’s use of illicit substance as well as chronic opioids.

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continued from page 17

Box

False negatives: A concern with opioids

Although this article focuses on false-positive results with urine drug screening, the occurrence of false negatives is equally important. For patients with conditions such as chronic pain, prescription opioid adherence could be monitored with urine drugs screens. Additionally, these drug screens could be used to determine abuse of prescription pain medication or illicit substances.¹

Depending on the urine drug screen kit being used, some substances, such as synthetic opioid products, might not be measured. Therefore, understanding the type of substances detected by the test you are using is critical to reduce the incidence of false negatives and the necessity of secondary testing.²

Because most urine drugs screen tests are designed to detect a drug class, such as benzodiazepines, opioids, or stimulants, a positive result with a patient prescribed an opioid will not indicate which specific opioid he (she) is using. This could be a problem because

some patients prescribed an opioid for pain might misuse additional non-prescribed, prescription opioids. Therefore, a positive result for such a patient would not be surprising; however, it will not indicate which drug was detected in the urine. In cases in which abuse is suspected, secondary testing is necessary to determine the specific medications found in the urine.¹

With point of care tests used in the clinic, synthetic opioids might only react at higher dosages because the test is designed to detect common chemical structures related to morphine. Therefore, patients using a lower dosage of medications such as hydromorphone or oxycodone could produce a false-negative result even if they adhered to their prescribed medication.³ Therefore, similar to all of the aforementioned situations, secondary testing using the more sensitive gas chromatography-mass spectrometry method is critical when a patient's report contradicts test results.¹

Clinical Point

Consider identifying which type of test you are using, and ask the manufacturer or lab to provide a list of known possible false positives

In-office urine testing

POC tests in urine drug screens use a technique called "immunoassay," which is quantitative and generally will detect the agent in urine for only 3 to 7 days after ingestion.⁴ This test relies on the principle of competitive binding: If a parent drug or metabolite is present in urine, it will bind to a specific antibody site on the test strip and produce a positive result.⁵ Other compounds that are similarly "shaped" on a molecular level also can bind to these antibody sites when present in sufficient quantity, producing a "cross reaction," also called a "false-positive" result. The *Table*⁶ lists agents that can cross-react with immunoassay tests. In addition to the cross-reaction, false positives also can occur because of technician or clerical error—making it important to review the process by which the specimen was obtained and tested if a false-positive result is suspected, as in the case described here.⁷

Different POC tests can have varying cross-reactivity patterns, based on

the antibody used.⁸ In general, false positives in immunoassays are rare, but amphetamine and opiate false positives are more common than cocaine metabolite and cannabinoid false positives.⁹ The odds of a false positive vary, depending on the specificity of the immunoassay used and the substance under detection.⁶

A study that analyzed 10,000 POC urine drug screens found that 362 specimens tested positive for amphetamines, but that 128 of those did not test positive for amphetamines using more sensitive tests.¹⁰ Of these 128 false positives reported, 53 patients were taking bupropion at the time of the test.¹⁰ Therefore, clinicians should do a thorough patient medication review at the time of POC urine drug testing. In addition, consider identifying which type of test you are using at your practice site, and ask the manufacturer or lab to provide a list of known possible false positives.



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Table

Prescription drugs, over-the-counter products, and foods that could trigger a false-positive result in urine immunoassays

Amphetamines	Amantadine, brompheniramine, bupropion, chlorpromazine, desipramine, desoxyephedrine, ephedrine, isometheptene, isoxsuprine, labetalol, phentermine, phenylephrine, ^a phenylpropanolamine, promethazine, pseudoephedrine, ^a ranitidine, ^a selegiline, thioridazine, trazodone, trimethobenzamide, trimipramine
Barbiturates	Ibuprofen, ^a naproxen ^a
Benzodiazepines	Oxaprozin, sertraline
Cannabinoids	Dronabinol, efavirenz, hemp-containing foods, ^a ibuprofen, ^a ketoprofen, naproxen, ^a piroxicam, promethazine, ^a proton pump inhibitors, ^a sulindac, tolmetin
Cocaine	Coca leaf teas (de-cocainized) ^a
LSD	Amitriptyline, dicyclomine, ergotamine, promethazine, sumatriptan
Methadone	Chlorpromazine, clomipramine, diphenhydramine, ^a doxylamine, ibuprofen, ^a quetiapine, thioridazine, verapamil
Opiates	Dextromethorphan, ^a diphenhydramine, ^a fluoroquinolones, poppy seeds and oil, ^a rifampin
Phencyclidine	Dextroamphetamine, dextromethorphan, ^a diphenhydramine, ^a doxylamine, ^a ibuprofen, ^a imipramine, ketamine, meperidine, thioridazine, tramadol, venlafaxine
Tricyclic antidepressants	Carbamazepine, cyclobenzaprine, cyproheptadine, diphenhydramine, ^a ibuprofen, ^a hydroxyzine, quetiapine

^aCan be purchased over-the-counter in some states or through Internet sources

Source: Reference 6

Clinical Point

If a false positive is suspected, results can be confirmed using gas chromatography–mass spectrometry

Laboratory-based GC–MS testing

If a false positive is suspected on a POC immunoassay-based urine drug screen, results can be confirmed using gas chromatography–mass spectrometry (GC–MS). Although GC–MS is more accurate than an immunoassay, it also is more expensive and time-consuming.⁹

GC–MS breaks down a specimen into ionized fragments and separates them based on their mass–charge ratio. Because of this, GC–MS is able to identify the presence of a specific drug (eg, oxycodone) instead of a broad class (eg, opioid). The GC–MS method is a good tool to confirm initial positive screens when their integrity is in question because, unlike POC tests used during an office visit, GC–MS is not influenced by cross-reacting compounds.^{11–13}

GC–MS is not error-free, however. For example, heroin and hydrocodone are metabolized into morphine and hydro-

morphone, respectively. Depending on when the specimen was collected, the metabolites, not the parents, might be the compounds identified, which might produce confusing results.

Clinical recommendations

When a POC drug screen is positive, confirming the result with GC–MS is good clinical practice. False positives can strain the relationship between patient and provider, thus compromising care. Examining the procedures that were used to obtain the specimen, as well as double-checking POC test results, is, when appropriate, good medicine.

CASE CONTINUED

Because Mr. L is adamant about his sobriety and the fact that his drugs of choice were sedatives, not stimulants, the clinician orders a second drug screen by GC–MS. The second screen is negative for substances of abuse;

Clinical Point

False positives can strain the relationship between patient and provider, thus compromising care

Related Resources

- Saitman A, Park HD, Fitzgerald RL. False-positive interferences of common urine drug screen immunoassays: a review. *J Anal Toxicol.* 2014;38(7):387-396.
- Tenore PL. Advanced urine toxicology testing. *J Addict Dis.* 2010;29(4):436-448.

Drug Brand Names

Amantadine • Symdine, Symmetrel	Isoxsuprine • Vasodilan, Vasoprine
Amitriptyline • Elavil	Ketoprofen • Orudis, Oruvail
Atorvastatin • Lipitor	Labetalol • Normodyne, Trandate
Brompheniramine • Dimetane	Lisinopril • Prinivil, Zestril
Bupropion • Wellbutrin, Zyban	Meperidine • Demerol
Carbamazepine • Carbatrol, Tegretol	Naproxen • Aleve, Naprosyn
Chlorpromazine • Thorazine	Oxaprozin • Daypro
Clomipramine • Anafranil	Oxycodone • Oxycontin, Percocet, Percodan,
Cyclobenzaprine • Amrix, Flexeril	Roxicodone
Cyproheptadine • Periactin	Phentermine • Adipex, Phentrol
Desipramine • Nopramin	Phenylephrine • Sudafed PE, Neo-Synephrine
Desoxyephedrine • Desoxyn	Piroxicam • Feldene
Dextromethorphan • Delsym, Robitussin,	Promethazine • Phenergan
Dicyclomine • Bentyl, Dicyclot	Pseudoephedrine • Sudafed, Dimetapp
Diphenhydramine • Benadryl, Unisom	Quetiapine • Seroquel
Doxylamine • Robitussin, NyQuil	Ranitidine • Zantac
Dronabinol • Marinol	Rifampin • Rifadin, Rimactane
Efavirenz • Sustiva	Selegiline • EMSAM
Ephedrine • Mistol, Va-Tro-Nol	Sertraline • Zoloft
Ergotamine • Ergomar, Cafergot	Sulindac • Clinoril
Hydrocodone • Vicodin	Sumatriptan • Imitrex
Hydromorphone • Dilaudid, Palladone	Thioridazine • Mellaril
Hydroxyzine • Atarax, Vistaril	Tolmetin • Tolectin
Isometheptene • Amidrine, Migrend	Trazodone • Desyrel, Oleptro
	Trimethobenzamide • Benzacot, Tigan
	Trimipramine • Surmontil
	Verapamil • Calan, Isoptin

Mr. L's clinician concludes that bupropion produced a false-positive result on the POC urine drug screen, confirming Mr. L's assertions.

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