Urine Drug Testing – Interpreting Results

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INTRODUCTION

Urine drug testing is used to support treatment decisions in a variety of clinical situations, including monitoring compliance and/or to detect the use of prescribed, undisclosed, or illicit substances in patients who require controlled medication therapy. When used appropriately and as part of a patient-centred care approach, urine drug testing is more than just a "tool of verification" and can help promote safe medication use. Ordering and interpreting test results requires an understanding of the available testing modalities, test benefits and limitations, detection times for specific drugs, and common explanations for false positive or negative test results.

OBJECTIVES

This module will enable the clinician to:

- Use urine drug testing to improve patient management including monitoring, adherence to controlled prescription drugs and detection of illicit drug use.
- Order the most appropriate urine test and accurately interpret results, given the patient and the clinical setting.
- Develop a framework for having a conversation with patients about drug safety and the response to an unexpected urine drug test result.

CONTENTS

The use of urine drug testing in this module will focus on therapeutic monitoring of adherence to a controlled substance as part of treatment and patient management (e.g., chronic pain, palliative care, ADHD etc.). Urine drug screening for other purposes such as forensics, occupational, sport or legal issues is beyond the scope of this module.

This module will not address the use of opioids in the treatment of chronic pain. Please refer to the PBSG module Opioids – Challenges in Prescribing and Management (February 2011).

CASES

Case 1: Jenny, female, age 51

Jenny comes to you from another province where she has been followed by the same family doctor for several years. She has type 2 diabetes, chronic renal failure, diabetic neuropathy, chronic pain (low back and legs), hyperlipidemia, and hypertension.

Her records indicate that she is on multiple medications including diazepam 5 mg BID and oxycodone/acetaminophen 2 tabs PO QID.

Other daily medications include:
Humalog 20 U TID
Pantoprazole 40 mg
Glargine 65 U BID
Rosuvastatin 10 mg
Metformin 500 mg bid
Gabapentin 600 mg TID
Nifedipine XL 90 mg
Amitriptyline 10 mg HS
HCTZ 25 mg
Olmesartan 40 mg

A recent HbA1C was 9.8%.

You review a treatment agreement with her and advise her that part of her care will include urine drug tests. She is cooperative about this but a bit surprised. She asks, "so, is this because you think I am an addict?"

How would you respond to Jenny's question?

What additional history would you like to know about her?

How would you order her urine drug screen and what would you expect to find?

Case 2: Rod, male, age 32

Rod has chronic mechanical low back pain and severe degenerative disc disease. He has been on several different opioids over the years for his pain. He has been told he is not eligible for surgery because he does not have any neurological deficits. He also has a history of mild developmental delay, anxiety, and ADHD.

He takes the following medications: clonazepam 0.5 mg TID; Concerta (methylphenidate) 54 mg once daily; Hydromorphone Contin 8 mg TID; and Cesamet (nabilone) 1 mg TID. He has a signed treatment agreement on his chart.

You see Rod today and review results of a simple immunoassay urine test completed last week. His urine report is negative for all substances tested including opioids and benzodiazepines.

What explanation might there be for the urine drug screen result?

How will this result affect your conversation with Rod and what other questions might you ask?

How might it change the new prescription you write for him?

Case 3: Dave, male, age 36

Dave is new to your practice and you are waiting for clinical records from his retired family physician. You have some hospital records that corroborate a pelvic crush injury 20 years ago. His pain appears to be a combination of neuropathic and nociceptive. He is on duloxetine 60 mg and gabapentin 2700 mg daily. Your assessment of his pain suggests that it is having a significant negative impact on his function.

He has had interventional pain management in the past and says he has had partial relief from this. Today he is asking for some oxycodone for prn pain management while he waits for his referral to a pain specialist in your region, made by his previous physician.

Dave admits that he has been taking some Tylenol No. 1's from the pharmacy for his pain. He denies any other substance use other than cigarettes. You discuss and sign a treatment agreement with him that includes the use of urine drug testing.

How would you manage Dave?

Practice Reflection

- Would there be any benefit to having point of care testing available in your practice?
- Would you prescribe pain medication before obtaining urine drug test results?

Part Two – one week later

Based on his presentation, self-report and previous imaging reports of the pelvic and thoracic injuries in the hospital EMR system, a decision is made to prescribe a two-week prescription of oxycocet 1 to 2 tabs QID PRN to a maximum of six daily, dispensed at weekly intervals, while waiting for medication records and the urine drug screen to be obtained.

Prior to this visit, the results of the broad spectrum toxicology screen comes back and is positive for, norcodeine, morphine, amphetamine/methamphetamine, and cotinine (a nicotine metabolite).

When you see Dave and present the results he tells you that "yeah, I use crystal meth, that's none of your business… I'm here for you to treat my pain."

How would you respond and manage Dave at this second visit?

INFORMATION SECTION

1. The urine drug test is one of several medical management tools used to improve safety for patients who will, or are being treated over the long-term with controlled substances (e.g., opioids for chronic pain); are at increased risk for substance-use disorders; or have other relevant medical conditions or diagnoses.[1] Routine urine drug testing can help support a patient's adherence to drug therapy; monitor and differentiate prescribed versus illicit drug use; and help to diagnose drug misuse, diversion and/or a substance use disorder.[2]

2. In clinical practice some examples of specific situations that might warrant use of a urine drug test include:
   - Part of risk stratification for all patients when deciding to prescribe a controlled substance.
   - Ongoing monitoring when refilling a prescription for a longer term controlled substance.
   - Before increasing a patients' dose of analgesic.
   - Before referring to pain or addiction specialty services.[2]
   - Assessing ambiguous drug-related behaviours (double doctoring, running out early, etc.).

   Along with other information, such as reviewing old records or obtaining collateral information from significant others, urine test results can also confirm a patient's self-reported substance use.

3. There is no strong published evidence to help determine which patients with chronic non-cancer pain should have a urine drug test, or how often. A systematic review examining the effectiveness and harms of long-term (> 3 months) opioid therapy for chronic pain in adults reported no studies that adequately evaluated and demonstrated the benefit of risk reduction strategies (e.g., treatment agreements, pain scales, pill counts and urine drug testing) on clinical outcomes (overdose, addiction, abuse or misuse).[3] However, the use of these strategies *may* help clinicians' address some of their concerns and barriers to prescribing opioids safely for chronic pain management – particularly in patients at elevated risk [Low Evidence].[1,3,4] They may also assist the clinician in the earlier identification of people who are getting into difficulty with either the prescribed or illicit drugs.

4. Despite the lack of published evidence, several guidelines include recommendations for routine urine drug testing to manage chronic pain and opioid use.[5,6] However, guidelines *do not* provide clear instruction on how to use the test effectively, nor do they adequately clarify timing and interpretation of urine test results relevant to clinical practice.[1]
   a) In Canada, when utilizing a urine drug test to establish a baseline measure of risk or to monitor compliance, clinicians need to have an understanding about: the benefits and limitations; appropriate ordering; interpretation of tests; and how to use results to optimize pain management strategies [Low Evidence].[5]
   b) Guideline recommendations in the United States suggest that clinicians should use urine drug testing before starting opioid therapy and consider urine drug testing at least annually to assess for prescribed medications, as well as other controlled prescription and illicit drugs [Low Evidence].[6]

5. The decision to order a baseline urine drug test and how frequently to screen and monitor patients takes into consideration the individual's risk for opioid misuse and addiction; presence of any ambiguous drug-related behaviours; access to medications by other people in the living environment; and the local availability of urine drug testing.[1,5] Consider more frequent monitoring in those at higher baseline risk or exhibiting drug-related behavioural issues (e.g., every 2 to 4 weeks); others less frequently (e.g., random, 1 to 4 times per year) [Very Low Evidence, Expert Opinion].[7]

6. Universal Precautions in opioid prescribing includes baseline risk stratification, utilizing a signed treatment agreement as part of informed consent, adherence monitoring and urine drug screening.[2,8]
   a) The Opioid Risk Tool is one example of a screening tool to help with risk stratification (Table 1).[5,9]
   b) A urine drug test is commonly included as part of a treatment agreement outlining both the patient's and health care professional's responsibilities for safe medication use.[1,7] Sample opioid treatment agreements can be found online at:
      - National Pain Centre, Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-Cancer Pain. 2010: http://nationalpaincentre.mcmaster.ca/opioid/cgop_b_app_b05.html
      - Rx Files (adapted from above): http://www.rxfiles.ca/rxfiles/uploads/documents/Pain-CNMP-Opioid-TreatmentAGREEMENT.pdf

7. Ultimately, it is the clinician's judgment, along with the patient's clinical status, that determines whether to utilize a urine drug test and the testing schedule.[10] The frequency of urine testing generally increases with the patient's level of risk (Info point 5). Urine drug tests for all patients who are either candidates for or taking opioids is reasonable, and should be presented to patients as "routine" practice or an expectation of professional oversight. Normalizing the clinical context of using the urine drug test will help to avoid the test being viewed as "punitive" and may promote both clinician and patient acceptance. An unexpected urine drug test result should not be seen as an opportunity to discharge patients from practice.[1,2,5] Rather it should be seen as a clue to another potential diagnosis (substance use disorder) which requires treatment.

Table 1. Opioid Risk Tool

Factor	Mark each box that applies	Item score (if female)	Item score (if male)
1. Family History of Substance Abuse:			
Alcohol	[ ]	1	3
Illegal Drugs	[ ]	2	3
Prescription Drugs	[ ]	4	4
2. Personal History of Substance Abuse:			
Alcohol	[ ]	3	3
Illegal Drugs	[ ]	4	4
Prescription Drugs	[ ]	5	5
3. Age (if 16-45 years)	[ ]	1	1
4. History of Preadolescent Sexual Abuse	[ ]	3	**0***
5. Psychological Disease:			
Attention Deficit Disorder, Obsessive-Compulsive Disorder, or Bipolar, Schizophrenia	[ ]	2	2
Depression	[ ]	1	1
TOTAL POINTS		—	—
Total Risk Score Risk Category: Low Risk = 0 to 3; Moderate Risk = 4 to 7; High Risk = 8 and above			

Attribution: By Lynn R. Webster, MD: Medical Director of Lifetree Medical, Inc., Salt Lake City, UT 84106.
Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-Cancer Pain. Canada: National Opioid Use Guideline Group (NOUGG); 2010 [2017 January 13]. Available from: http://nationalpaincentre.mcmaster.ca/opioid/

***Reviewer Comment**: this scoring is 0 only because there was insufficient literature to validate it. Clinically, one would reasonably expect the impact of sexual abuse on males to be comparable to females as a risk factor.

URINE DRUG TESTING METHODS

8. Prior to ordering a urine drug test, a careful history of the patients' prescription, over-the-counter, supplement, and herbal medication use should be obtained.[2] This includes a detailed history of the patient's drug use for the preceding seven days.[5] It is also important to inquire about personal safety and safe storage.

PRACTICE TIP 1: Consulting with Pharmacists

Consulting with pharmacists to access or obtain a patient's past pharmacy record may be of benefit (e.g. past renewals, early releases, history of treatment etc.). Some provinces offer a provincial database maintained for controlled medication prescriptions; this type of network may be especially helpful for managing new patient prescriptions (e.g. PharmaNet access in British Columbia, see Table 4).

Table 2. Types of Urine Drug Testing Methods[1,2,5,7]

Urine Test	Benefits	Limitations/Comments	Cost
Point of Care (POC) Enzyme Immunoassay (EIA, ELISA®, EMIT®)	• Collected at practice setting • Portable (test strips/cups) • Immediate results for drug classes	• Some are less sensitive/specific tests • Will identify only substances or drug classes that have been pre-selected on the test panel • Does not identify specific drug or metabolites • Lacks quality assurance and control (integrity of test reagents following transport/storage, error rates) leading to misinterpretation	**$5–12** depending on number of panels and whether purchased in bulk

Immunoassay (Laboratory)
 	
May be called "drugs of abuse screen"
	• Preferred test for initial screen
	• Antibody-based, enzyme mediated, to detect presence of drugs
	• Detects drugs for longer time (2–5 days), ability to detect will vary depending drug's concentration in urine and cutoff concentration
	• "Drugs of abuse" screen generally detects commonly abused substances:
	  • opiates*
	  • benzodiazepines
	  • methadone metabolite (EDDP)
	  • cocaine metabolite
	  • oxycodone
	  • amphetamines
		• Only identifies drug class not the specific drug (e.g., does not distinguish different types of opioids)
		• Often miss semi-synthetic or synthetic opioids (e.g., fentanyl, hydropmorphone, oxycodone, meperidine and methadone) and certain benzodiazepines
		• Cross reactivity/false positives (e.g. poppy seeds, quinolone antibiotics)
		• Must clarify which substances are included in the panel with the local laboratory (e.g., there is inconsistent inclusion of delta-9-tetrahydrocannabinol (THC) metabolite or phencyclidine (PCP))
			$20–$25

"Broad Urine Toxicology" Chromatography (gas or liquid) +/- Mass Spectrometry	• Confirmation of specific drug and/or its metabolites • Detects most drugs for 1–2 days • Identify drugs not included on immunoassay test, when result contested • More accurate to detect semi-synthetic / synthetic opioids • Differentiates all opiates, benzodiazepines and amphetamines • Does **not** react to poppy seeds	• May take longer for results • Must understand metabolism of certain drugs in order to correctly interpret (e.g., codeine metabolized to morphine, high dose morphine metabolized to hydromorphone) **NOTE:** some labs report qualitatively, either positive or negative, based on international toxicology standards. Drug levels below the standard toxicology threshold will be reported as negative.	**~ $40** per specimen

NOTES: ELISA = enzyme linked immunosorbent assay; EMIT= enzyme multiplied immunoassay; *most opiate immunoassays detect natural opiates (e.g., morphine and codeine), but do not reliably detect synthetic (e.g., methadone or fentanyl) or semi-synthetic opioids (e.g., oxycodone or hydromorphone), unless specifically requested.[1]
Mass spectrometry gives better specificity as opposed to chromatography. Combination and tandem testing also used when more specific detection and quantification needed (e.g., gas or liquid chromatography + mass spectrometry, or tandem mass spectrometry).[7]

9. Ordering the correct urine test and understanding the differences between laboratory and point-of-care (POC) testing is important when interpreting an unexpected result.[2] Ideally, the urine drug test method chosen needs to be a "function of the questions that need to be answered for the individual patient."[1]

10. The two main types of urine drug tests available are immunoassay (laboratory based or POC) and broad spectrum toxicology using chromatography (gas or liquid)/mass spectrometry.

11. Immunoassay is the preferred test for an initial urine drug screen. It is a less costly test designed to rapidly detect substances as being present, or not.[1]
    a) Point-of-care and "drugs of abuse" laboratory tests are limited immunoassays. Urine specimens with drug concentrations below threshold levels for tests are reported as negative, even if they are detected in very small amounts on their assay.[2]
    b) Unexpected results from an immunoassay test can be followed by a subsequent confirmatory test using gas chromatography/mass spectrometry or high performance liquid chromatography (see Info Point 14).

    Properties, benefits and limitations for each type of test are outlined in Table 2.

12. Definitive identification of a specific drug and/or its metabolites requires more sophisticated and costly tests such as the following:
    - gas chromatography/mass spectrometry (GC/MS)
    - liquid chromatography/mass spectrometry (LC/MS)
    - liquid chromatography-tandem mass spectrometry (LC-MS/MS).[1,7]

Note: Use of one combination or another depends on local laboratory facilities. It is always helpful to contact your local laboratory with technical questions and to understand any difference in cut-off levels between a POC and a laboratory immunoassay-based test (e.g., lower cut off levels will increase the sensitivity of this test but will also increase the risk of false positives).

PRACTICE TIP 2: Ordering A Urine Drug Screen[1]

- To get the most out of a urine drug test report, provide sufficient information to the laboratory on the requisition (e.g., under "notes and instructions") about the patient's current prescribed medications, including over-the-counter and herbal, in order to receive relevant laboratory interpretation based on drugs/metabolites that are expected to be identified.
- Include information about drugs that might be of particular concern (e.g., past history of fentanyl abuse, alerting lab to look for the drug or its metabolites).
- Use the appropriate test name. Different labs have different test names (e.g., broad spectrum, drugs of abuse screen, random urine, toxicology screen etc.).
- Consider consulting with your local lab resource (director, toxicologist) for clarification to review results and options for follow-up testing, especially when an unexpected result is reported.

Patient Urine Sample Collection

13. Urine sample collection may require: patients to remove bulky clothing and leave bags with staff; and have specimen temperature tested before POC testing or being sent to lab for an appropriately ordered test.
    a) Characteristics of a "normal" urine specimen are outlined in Table 3.
    b) If tampering is suspected, check urine temperature, pH, and creatinine concentration. A digital thermometer can quickly assess temperature. If the specimen does not meet temperature requirements, the patient should be requested to produce another specimen and consider sending both for analysis. If urine is unusually pale, a notation should be made or specific gravity checked.[1]

Table 3. Characteristics of a normal urine specimen, based on 30 mL or more[1,2]

Temperature within 4 mins of voiding	90˚F to 100˚F (32˚C to 38˚C)*
pH	4.5 to 8.0**
Urinary creatinine	> 2.0 mol/L
Specific gravity	> 1.003

Note: * if sufficient volume (30 mL) and patient is normothermic; ** sample degradation, due to improper storage or prolonged transportation, even in the absence of sample adulteration, can result in sample pH in excess of 8.0

INTERPRETING URINE DRUG TEST RESULTS

14. It is important to interpret urine drug test results in the context of the overall patient behaviours and not rely exclusively on the test results.[1]

15. Many factors can affect whether a drug is detected in a urine sample.[1,2] An immunoassay test's ability to detect drugs will vary according to the drug's concentration in the urine and the assay's cut off concentration.[1,5,7]
    a) A drug taken in low dose as recently as one to two days prior to a test may not show up if levels are below the test cut-off, due to normal metabolism.
    b) Urine dilution, either deliberate or due to excess fluid intake or diuretic use, can bring a drug level to below the cut-off.
    c) Agents that change the pH of the urine can also affect binding to the immunoassay panel.

16. Although variable, most drugs can be detected by immunoassay within about 2 to 5 days of use and within 1 to 2 days of use by chromatography/mass spectroscopy.
    - Long term use of lipid soluble drugs (e.g., marijuana, diazepam, ketamine or phenycyclidine) may extend detection to a week or more.
    - Chronic use of marijuana may result in detection for over 30 days. **Note:** Passive inhalation is unlikely to be detected in any urine drug screen.
    - Detection times will vary from patient to patient depending on the drug, the dose and the individual's metabolism, whether innate or acquired through tolerance.

Careful Interpretation - Metabolites

17. Broad spectrum toxicology typically detects the parent drug and/or metabolite(s), which helps to indicate recent use of prescription drugs, non-prescribed drugs, and illegal substances.[1] In general, the concentration of the parent drug in urine exceeds that of its metabolite(s).[1]
    - Of note, the metabolite may persist after the parent drug is no longer detectable. Hence codeine use may result in a report of codeine only, codeine and morphine, or morphine only depending upon the detection window.[1]
    - See Appendix 1 – Benzodiazepine, Opiate and Stimulant metabolites.

Positive Results

Note: see Appendix 2. Selected common challenges in interpretation are presented below.

18. Positive urine drug testing results do not typically provide enough information to determine the exposure time, dose or frequency of use. There is currently no validated relationship between the concentrations reported in the urine and the doses taken of any drug.[1] For example, a urine drug test positive for the opioid prescribed could mean that the patient took one dose of the prescribed opioid on the day of their office visit and diverted the rest of their supply.

19. For those patients who have not been prescribed morphine, the presence of morphine in the urine on immunoassay may be indicative of heroin use, although a morphine positive test result may also be due to codeine and opiate derivatives consumed in food (e.g., poppy seeds).[1]
    a) A positive test for morphine with the presence of 6-monoacetylmorphine (6-MAM), a heroin metabolite, is indicative of heroin use (Appendices 1, 2).
    b) Codeine is metabolized into morphine (but the reverse does not occur), so both may be present in urine following codeine use (see Info point 17).[1]
    c) With codeine ingestion, the concentration of the codeine/norcodeine (the parent molecule) should be greater than the metabolite (morphine) on broad spectrum testing (generally codeine/morphine ratio > 2). This specific testing may require the practitioner to contact the laboratory.

20. A positive urine test for oxymorphone (for a patient prescribed oxycodone) should confirm that the relative concentration of oxycodone is greater than oxymorphone, indicating that oxymorphone is a metabolite rather than a parent compound.[1] As with codeine/morphine above, this may require a specific request to your laboratory.
    Note: Although oxymorphone is approved by Health Canada, it is not marketed in Canada.

21. Interpretation of positive amphetamine and methamphetamine results can be challenging due to the biochemical similarities to many prescription and over the counter products (e.g., diet agents, decongestants, and selegiline for Parkinson's disease, beta-blockers).[1] A GC/MS report that is positive for methamphetamine is consistent with the ingestion of the street drug of abuse, "crystal meth". [1]

22. Although many benzodiazepines are detected by immunoassay, there is variable cross-reactivity for some agents. For instance, immunoassay and POC testing will frequently be negative for lorazepam, clonazepam, and alprazolam, but their presence could be confirmed by the broad spectrum toxicology screen which includes mass spectrometry (see Appendix 2). False-negative rates are reported to range from of 20 to 35% and up to 75%, compared with LC-MS/MS.[1]

Negative Results

23. "A negative test result may only mean that at the time of specimen collection, concentrations of those substances for which the test was performed (or can detect) were below the threshold limits required to report a positive result."[1] Additional, specific testing may be required. Assuming that the urine tested is an unaltered specimen from the patient, and the correct test has been ordered, a negative result may occur for any of the following reasons:
    - Patient not taking the drug, due to cost/lack of coverage.
    - Patient taking the drug at a low dose, below the toxicology reporting threshold.
    - Running out of drug early due to bingeing.
    - Diversion.[1]

False Positive and False Negative Results

24. Although urine testing is typically done with class-specific immunoassay drug panels (designed to classify substances as either present or absent according to predetermined cutoff thresholds), all positive immunoassay screens that cannot be explained by the patient's history should be confirmed by Broad Spectrum Toxicology Screens to rule out false positives.[11]
    - False positive immunoassay results are frequent due to cross-reactivity with other structurally related drugs (Appendix 2).
    - The concern for false-negative urine test results is of importance when testing for adherence to a prescribed therapeutic regimen.[2]

PATIENT CENTRED CARE APPROACH

25. In a patient-centred model of care, any testing should provide information that is clinically useful.[1] It is important to consider and document the following when considering urine drug testing:
    - Why was the test ordered?
    - What results were obtained?
    - Could it be a false positive or false negative?
    - What changes in treatment were made (if any) as a result of test results?[12]

Talking with Patients

26. Prior to ordering a urine drug test it is important to discuss the following with patients:[5,7]
    a) Inform them about the "routine" nature of the test (e.g., "I do this routinely for all of my patients on opioids…"). The test is not meant to "catch or punish" patients but to improve the safety and effectiveness of the treatment and would be an expected professional standard for anyone prescribing controlled substances.
    b) Take a careful history of medication use in the past week. Consider asking "what should I expect to see in the results?" This gives the patient the opportunity to inform the clinician about changes in their use of the prescribed drug or illicit use.[5]
    c) If using a treatment agreement, include the requirement for urine drug testing if not done so already.
    d) Collect the sample in the physician office and ensure proper labeling. Consider who will be using the test result information and follow up to be taken.

Unexpected Results – What to Do?[7]

27. Unexpected urine drug test results should be confirmed and viewed as an opportunity to initiate discussion with a patient about the possible reasons for the result(s).[2,5] Guiding principles for management following an unexpected urine drug test result include:[1,12]
    a) Considering the possibility that a test result could be false.
    b) An opportunity to improve communication, rather than "policing".
    c) Allowing an opportunity for the patient to address the report (explain circumstances, or not).
    d) Being willing to change a treatment plan if an abuse/diversion issue arises, this may mean:
        - Tightening boundaries with more frequent dispensing, more urine drug tests, blister packing meds.
        - Increased emphasis on non-drug treatments.
        - Referral to addiction services for an opinion.
        - Discontinuing the drug with or without a taper, and framing it as "firing the molecule" which differs from "firing the patient."[7]
        - Exploring patient safety, especially if they are older or frail and may be the victim of threats or theft.

RESOURCES for CLINICIANS — Urine Drug Testing

28. The online resources in Table 4 may be helpful to review and assist with ordering the right test, consultation and interpretation.

Table 4. Online Resources – Urine Drug Testing

Urine Drug Testing in Clinical Practice. The Art and Science of Patient Care. 2015. Edition 6.	A detailed discussion of urine drug testing, including interpretation and reasons for false positives and negatives. http://paindr.com/wp-content/uploads/2015/10/Urine-Drug-Testing-in-Clinical-Practice-Ed6_2015-08.pdf
Rx Files: Q& A Summary. 2011 Urine Drug Screening (UDS)	Frequently Asked Questions. "I do this routinely for all my patients when prescribing opioids for chronic pain." http://www.rxfiles.ca/rxfiles/uploads/documents/urine-drug-screening-uds-qanda.pdf
myTOPCARE. 2016 Transforming Opioid Prescribing in Primary Care (TOPCARE)	Urine Drug Testing for Prescribers/Training Resources **Urine Drug Testing** http://mytopcare.org/prescribers/ Resources for Prescribers – **Urine Drug Testing Interactive Vignettes** http://mytopcare.org/resources/resources-for-prescribers/
Gamma Dyna Care Labs®	Health Care Providers and Hospitals https://www.dynacare.ca/healthcare-providers-and-hospitals/continuing-medical-education/interpretation-guides.aspx
LifeLabs®	Test Information Directory.Drugs of Abuse Screen (Urine), enter "Drugs of abuse screen (urine)"; then click on "forms" http://tests.lifelabs.com/Laboratory_Test_Information/Search.aspx
Pharmacy Health Record Networks (PharmaNet) British Columbia	Province-wide network linking all BC pharmacies to a central set of data systems. http://www2.gov.bc.ca/gov/content/health/health-drug-coverage/pharmacare-for-bc-residents/pharmanet
Prescription Monitoring Programs in Canada: Best Practice and Program Review **Canadian Center on Substance Abuse. 2015**	Most provinces are currently operating some form of prescription monitoring program (BC, AB, SK, MB, ON, NS, NL), with two provinces having programs in development (NB, PEI), and one territory (Yukon, linked with AB program). http://www.ccsa.ca/Resource%20Library/CCSA-Prescription-Monitoring-Programs-in-Canada-Report-2015-en.pdf

THE BOTTOM LINE

- Urine drug testing is a tool used to improve safe patient care. What shows up in a urine drug test is important; however what does "not" show up can be equally important.
- Consult with local laboratories as needed (when unsure about the best test to order, or regarding unexpected results).
- Positive (or unexpectedly negative) test results provide an opportunity for a conversation with patients — test results can be false.

CASE COMMENTARIES

Case 1: Jenny, female, age 51

How would you respond to Jenny's question?

Reassure Jenny that the urine drug test is not used as a punitive tool to determine whether she is abusing drugs or medications; rather it is a universal test used in your practice for all patients to help monitor the safe use of many different types of drug treatments. Explain that an unexpected result will not result in her being dismissed from the practice, but would require discussion and possible prescription changes (Info point 7).

Explain to Jenny that she does not have to agree to testing; however she does need to understand that this decision may limit the options that you can safely offer to her in terms of managing her pain with certain drugs/medications. Emphasize, that the medications she is taking can be harmful to patients or to others when not taken properly, or when taken by someone other than the patient they are prescribed for (Info point 26).

What additional history would you like to know about her?

Obtain a history from Jenny's records and assess her baseline risk using the Opioid Risk Tool and other history (Info point 6, Table 1).

Ask Jenny how she is taking her current medications (e.g., timing, with food, extra doses on some days and none on others, etc.); and what other over-the-counter medications, supplements or herbal remedies might she also be taking? Inquire how she stores her medications – are they safe in her care? Does anyone else have access to them in her home? (Info point 8). Obtaining a pharmacy record may also be helpful to determine patterns of medication prescribing and use (Practice Tip 1).

Check whether there is any other supplemental history, consultants' reports, operative reports, investigations, etc., and assess her overall function to support the long-term opioid prescriptions.

Discuss the increased risk of adverse effects, including death, from using opioids and benzodiazepines together.

To help interpret results that may come back, consider asking Jenny "is there anything else you expect I might find in your urine test results?"(Info point 26).

How would you order her urine drug screen and what would you expect to find?

Since this is Jenny's initial visit, a "broad spectrum screen urine toxicology screen" is reasonable, although the test name may vary in your respective practice community (Info point 10; Practice Tip 2).

A "urine for drugs of abuse" immunoassay will miss some specific results unless specific drugs are requested (Table 2). Because Jenny is on diazepam, you might expect to find oxazepam and temazepam on the report along with both oxycodone/noroxycodone (Info point 22; Appendices 1,2).

Case 2: Rod, male, age 32

What explanation might there be for the urine drug screen result?

Urine test results are negative; ask Rod whether he is in fact taking his prescribed drugs.

Consider whether he might not be filling his prescription, may be taking his medication in a manner other than prescribed (altering frequency or method of ingestion), or diverting/selling them. Rod may be vulnerable due to his cognitive status, resulting in him giving away or trading his drugs, or having them stolen by others (Info point 23).

If a simple immunoassay is ordered, methylphenidate would not be detected unless it was specifically requested; similarly, clonazepam often does not show up as positive for benzodiazepines due to the metabolic pathway (Info point 22; Appendix 1 – Benzodiazepine Pathway; Appendix 2). Hydromorphone may not show up in a sample even though it was taken. If it was not taken close enough to the sampling time or if a long-acting form was injected, snorted or crushed, it will be metabolized faster and therefore may be eliminated before it can be detected in a urine sample.

Also consider if in fact the urine tested is Rod's or has been tampered with in some way (Info point 16). As tampering is a possibility, check the urine sample for temperature, pH, and specific gravity for dilution (this can be done with a "dip" in your practice setting). Point of care tests should also include a creatinine to ensure that the sample is compatible with actual urine (Info point 13; Table 3).

Assess Rod's risk for opioid misuse (Info points 5–6; Table 1). Consider whether he is at high risk for misuse or abuse of any of his medications, regardless of whether he is treated appropriately for any one of his diagnoses.

Send his next urine sample to a community laboratory, request a "broad spectrum urine toxicology screen" and list the medications he is currently taking in the requisition (Info points 10–11, 24; Practice Tip 2).

How will this result affect your conversation with Rod and what other questions might you ask?

Ask Rod about his current level of function and pain control.

Inquire about what supports Rod has in place to help him to take his medications and to also keep them secure. For example: "Is there anyone else who lives with you or has access to where you keep your medications?"; "Does anyone help you or remind you to take your medications?"; Do you ever give your drugs away? You could also ask what else Rod thinks you might find in his urine, and why (Info point 26).

How might it change the new prescription you write for him?

Safe prescribing interventions for Rod might include tightening prescription intervals, compliance packaging to help avoid any mix up, a change to his current dispensing routine (e.g., weekly) and emphasizing/promoting his safety to help support and reassure him about his care (Info point 27).

Random requests to bring in all unused medication can confirm that Rod is using his narcotics as prescribed and that they are not being diverted. A fentanyl patch with exchange at the pharmacy is another similar strategy.

Pharmacies can be requested to dispense controlled medications only when a lock box accompanies the patient and this can be added to the prescription.

Case 3: Dave, male, age 36

How would you manage Dave?

Ask and clarify how many Tylenol No. 1's Dave is currently taking. Obtaining a pharmacy health record to see what Dave has been prescribed in the past may be helpful (Info point 8; Practice Tip 1). It may also be useful to review Dave's current list of medications (prescribed, over -the-counter and herbal) looking for any cross reacting compounds (Info point 8; Appendix 2).

Review the role of urine drug testing in your practice with Dave and inform him that you are going to send his urine for laboratory testing. It may be helpful to mention to Dave ahead of time (before you send the urine drug test), that this test will pick up everything, and ask him "is there anything else you think I should know that I might anticipate finding in the results?" In doing so, emphasize that results won't change your decision to keep him as a patient in your practice (Info points 7, 26).

As the initial screen, ordering a "broad spectrum urine toxicology" will specify that you would like screening for a wide variety of substances (Table 2).

To manage Dave at this time, options include not prescribing oxycodone and offering an NSAID or alternatively prescribing a small number/amount of oxycodone with short dispensing intervals (e.g., weekly) until his next visit and when you have obtained more information.

Talking point (based on treatment decision)

"I understand that your pain is having a major impact on your life right now and we want to help you to deal with the current situation, but how we decide to manage your pain, including the ongoing use of any narcotic medication, will be based on my assessment over the next couple of weeks."

Part Two – one week later

How would you respond and manage Dave at this second visit?

Norcodeine and morphine would be expected given Dave's admitted use of over-the-counter Tylenol® with codeine (Appendices 1 and 2).

With this unexpected urine drug test result, allow Dave the opportunity to explain further, complete a more thorough dependence or addiction history, revisit the use of a written treatment agreement (if not already initiated), and state your concern about his safety using oxycodone and the recreational use of methamphetamines. Review what changes you would make in your current approach to prescribing and Dave's current needs for pain management (Info points 6, 27).

It is likely that Dave will not be happy about a decision not to continue prescribing oxycodone. Whether or not he admits to a problem with opioids or is using them as "currency" for the purchase of illicit drugs, the risk is high that ongoing opioid prescribing can cause harm. Discuss the potential role of non-pharmacological and non-opioid medication options and your desire to work with him to find other solutions for his pain management.

Talking Point

"I am concerned about your safety and the combination of drugs you are currently taking. I am not willing to put you at risk by prescribing opiate medication for your pain but would be willing to explore other options to help you."

Dave could be offered an assessment for a stimulant use disorder. Depending on your own comfort level and experience with addiction/substance abuse and chronic pain, you may wish to consider formal or informal consultation with a colleague (Info point 27).

We always welcome your input. If you would like to provide feedback on this module, the following link will take you to an electronic survey: **http://members.fmpe.org/modulefeedback**

Author: **Lori Regenstreif, MD, CCFP**
Family Physician
Hamilton, Ontario

Reviewers: **Peter Butt, MD, CCFP, FCFP**
Family Physician, Addiction Medicine
Saskatoon, Saskatchewan

Roman D Jovey, MD
Family Physician, Focussed Practice in Pain Management and Addiction
Mississauga, Ontario

Medical Editor: **Elizabeth Shaw, MD, CCFP, FCFP**
Family Physician
Hamilton, Ontario

Medical Writer/Module Development Coordinator: **Wendy Leadbetter, RN, BScN**
Hamilton, Ontario

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LEVELS OF EVIDENCE

Evidence Level	Type of Evidence Included
High	• Systematic reviews/meta-analyses that include a wide range of well-designed studies (few limitations/risk of bias, directly applicable to target population); summary estimate has a narrow confidence interval. • Large, well designed RCTs. Study conclusions are unlikely to be strongly affected by information from future studies.
Moderate	• Systematic reviews/meta-analyses of studies with more limitations/risk of bias (less well designed RCTs, cohort, case control studies), or when the summary estimate has a wide confidence interval. • Single, moderate sized, well-designed RCTs. • Well-designed, consistent, controlled but not randomized trials. • Large cohort studies. Study conclusions could change with additional information from future studies.
Low	• Small RCTs with a high risk of bias. • Controlled or cohort studies with significant limitations/risk of bias or significant variation between study results. Evidence from well-designed studies in representative populations is lacking or insufficient.
Very Low	• Expert Opinion • Individual case reports or series

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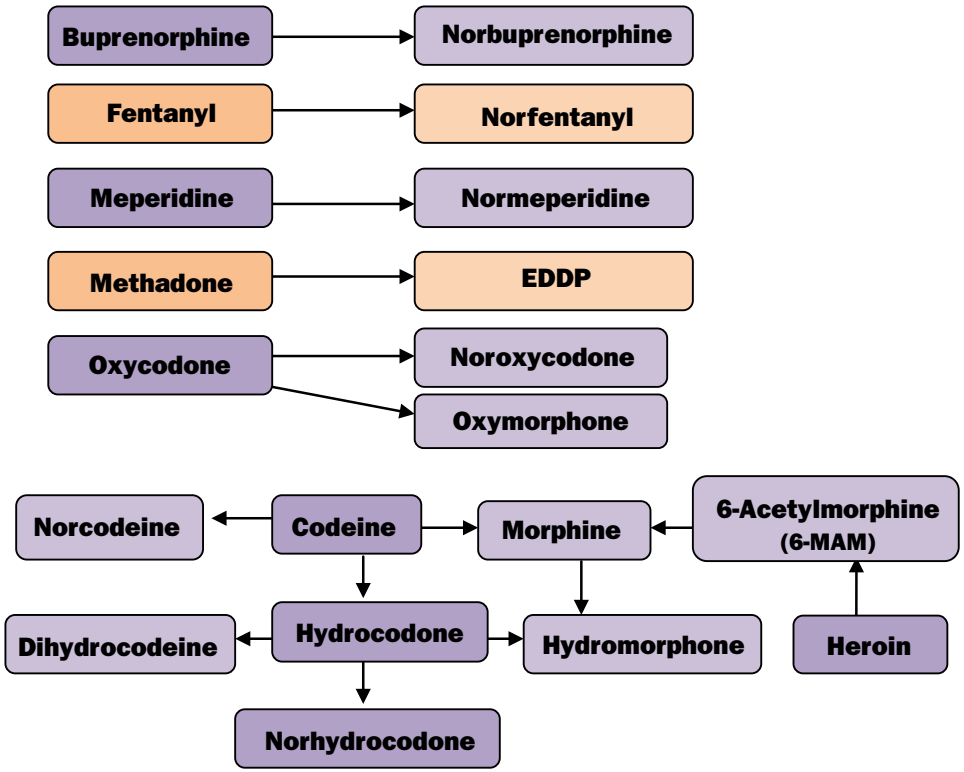
APPENDIX 1. Opioid, Benzodiazepine and Stimulant Drug Metabolites

Metabolism of Opioids

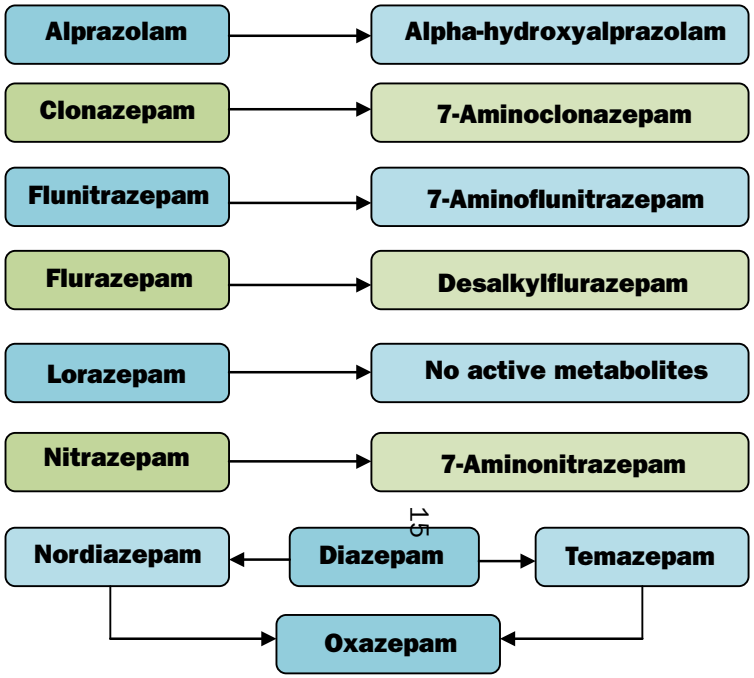


LEGEND

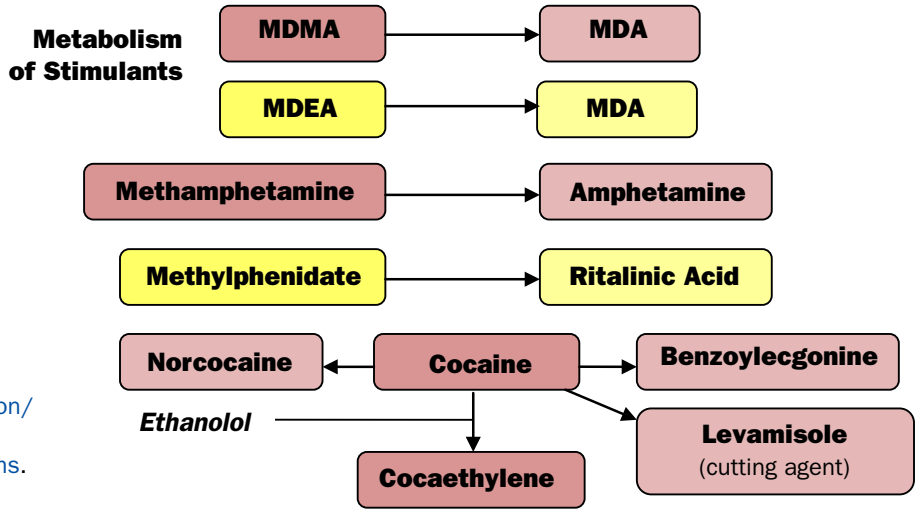
→ Known metabolites

EDDP: 2-ethylidene-1,5-dimethyl-2,2-diphenylpyrrolidine
MDA: Methylenedioxyamphetamine
MDEA: Methylenedioxyethylamphetamine
MDMA: Methylenedioxymethamphetamine

Metabolism of Benzodiazepines



Metabolism of Stimulants



Adapted from:
1) Gourlay DL, Heit, HA, Caplan, YH Urine Drug Testing in Clinical Practice. The Art and Science of Patient Care. Monograph. 2015; Edition 6. http://www.udtmonograph6.com/cme.html; **2)** Dynacare Labs Healthcare Providers; Toxicology Interpretations. 2016. https://www.dynacare.ca/healthcare-providers-and-hospitals/continuing-medical-education/interpretation-guides.aspx; **3)** LifeLabs. Drugs of Abuse – Metabolic Pathway-Reference Document. 2015. http://tests.lifelabs.com/test_information.aspx?id=25062&view=forms.

APPENDIX 2. Urine Drug Testing – Interpreting Results

Note: the following provides a generalized overview, and may vary dependent on the laboratory and testing available to you in your practice community. Detection windows for Immunoassay generally range from two to five days and Chromatography one to two days, although there may be variability due to drug, dose, testing time after last dose, frequency of use and individual patient metabolism.

DRUG	Metabolite/Substances Detected in Broad Spectrum Toxicology	Cross reactants (False Positive) or False negatives
Anesthetic		
Ketamine	Ketamine	
Anticonvulsant		
Gabapentin	Gabapentin	
Antidepressants		
Bupropion	Bupropion	
Trazodone	MCPP (metabolite trazodone, designer drug)	
Benzodiazepines		
Broad Spectrum Toxicology ordered to differentiate different classes. EIA does not differentiate benzodiazepines, prone to false negatives; metabolism is complex. • Short acting: 1 to 2 days • Intermediate acting: 2 to 5 days, may not be detected (see next column) • Long acting: 7 to 10 days (some up to 20 to 30 days)		False negative: the following ***benzodiazepines*** are often undetected in immunoassay: • Clonazepam • Lorazepam • Flunitrazepam • Temazepam False Positive EIA screen for patients taking oxaprozin, gravol or sertraline at high concentrations.
Alprazolam	Metabolized to alpha-hydroxyalprazolam; both may be detected	
Clonazepam	7-aminoclonazepam metabolite detected primarily	
Diazepam	Metabolized to nordiazepam, temazepam and oxazepam; all may be detected after use	
Flunitrazepam	7-aminoflunitrazepam metabolite detected primarily	
Flurazepam	Desalkylflurazepam metabolite detected primarily	
Lorazepam	Lorazepam	
Nitrazepam	Metabolized to 7-aminoitrazepam, both may be detected after use	
Oxazepam	Oxazepam detected after use; nordiazepam and temazepam metabolite	
Temazepam	Metabolized to oxazepam; both may be detected after use; also a diazepam metabolite	

APPENDIX 2. Urine Drug Testing – Interpreting Results cont'd

DRUG	Metabolite/Substances Detected in Broad Spectrum Toxicology	Cross reactants (False Positive) or False negatives
Cannabinoids		
Cannabis	THC not detected in urine. THC-COOH metabolite detected.	• Cesamet does not contain THC, cannot be detected by EIA. • Synthetic cannabinoids not detected in EIA but can be in broad spectrum toxicology screen. • Following may cause False Positive EIA: baby wash/shampoo; NSAIDs, patients taking dronabinol (Marinol®), nabiximol (Sativex®), Pantoprazole, Efavirnez.
JWH-200; JWH-018	Synthetic Cannabinoids	
Narcotics		
OPIOIDS		**Prescribed (therapeutic) Opioids** False Negative on broad spectrum toxicology, consider: • Non-compliance • Binging • Diversion (especially if test repeatedly negative) **Non Prescribed (illicit) Opioids** Positive results (on EIA ONLY), consider: • False positive (e.g., poppy seeds) • Levofloxacin, some fluoroquinolones **Notes** • Heroin: rarely detected EIA (half-life = 3 to 5 mins). • 6-MAM difficult to detect (half-life = 25 to 30 mins), detected within few hours. • Remember that EIA/POC will often miss semi synthetic and synthetic opioids. • Fentanyl: if expected but not detected and/or using fentanyl patch, order broad spectrum toxicology screen & add "no lower limits" for lab to report results below cut-off but above limit of detection.
Buprenorphine	Buprenorphine, norbuprenorphine Suboxone and buprenorphine/naloxone preparations also include naloxone	
Codeine	Norcodeine, morphine and hydrocodone may all may be detected after use	
Fentanyl	Fentanyl and norfentanyl detected after use	
Heroin	6-MAM metabolite = definitive evidence of heroin use **Note**: some street heroin can be contaminated with other opiates (e.g., codeine)	
Hydrocodone	Hydrocodone, Norhydrocodone, Dihydrocodone	
Hydromorphone	Hydromorphone; also a hydrocodone and morphine metabolite	
Morphine	Morphine and hydromorphone may be detected; also a 6-MAM (heroin) and codeine metabolite	
Naloxone	Included in Targin®(oxycodone-naloxone) preparations of oxycodone; included in suboxone preparations of buprenorphine; naloxone	
Naltrexone	Naltrexone	
Meperidine	Metabolized to Normeperidine; both detected	
Methadone	Metabolized to EDDP; both detected	
Oxycodone	Metabolized to noroxycodone; both detected/ Targin® preparations also include naloxone	

APPENDIX 2. Urine Drug Testing – Interpreting Results cont'd

DRUG	Metabolite/Substances Detected in Broad Spectrum Toxicology	Cross reactants (False Positive) or False negatives
Stimulants		
Use Broad Spectrum Toxicology to differentiate classes of amphetamines.		False positive EIA screen for amphetamines with following interfering agents: buproprion, chlorpromazine, ephedrine, psudoephedrine, promethazine, ranitidine, selegiline, trazodone, lisdextroamphetaime.
Amphetamine	Methamphetamine metabolite; both may be detected	
MDEA	Metabolized to MDA; both detected	
MDMA	Ecstasy; metabolized to MDA; both may be detected MDEA and MDMA are MDA metabolites	
Cocaine	Metabolized to benzoylecgonine (BEG), norcocaine and cocaethylene (formed when cocaine used with alcohol), Levamisole may be found as it is used as a cutting agent	
Benzylpiperazine	Synthetic stimulant; designer drug	
MDPV	Synthetic amphetamines; designer cathinones drug ("bath salts")	
Mephedrone		
Methylphenidate	Metabolized to ritalinic acid; both detected	
Diphenhydramine	Diphenhydramine	
Ephedrine Pseudoephedrine	Ephedrine/Pseudoephedrine	
Nicotine	Cotinine	
NOTES: EIA = Enzyme Immunoassay; POC = Point of Care; EDDP = 2–ethylidene-1, 5–dimethyl-2, 2—diphenylpyrrolidine; MCPP = 1–(3-cholophenyl) piperazine; MDA = methylenedioxyamphetamine; MDEA = methylenedioxyethylamphetamine; MDMA = methylyenedioxymethamphetamine; MDPV = 3, 4–methylenedioxypyrovalerone; THC = 11-nor-9-carboxy-Δ9-tetrahydrocannabinol; 6-MAM = 6- mono- acetylmorphine.		

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