Urine Drug Screening in Long-term Opioid Therapy

While the place of Urine Drug Screening (UDS) in opioid dependence programs is established, its use and utility in the setting of long-term opioid use are not as clearly defined. As the use of opioids for chronic pain has increased over the past decades, so have the issues of prescription drug abuse.[1] Compliance monitoring with tools such as the urine drug screen, assists with the important balancing act between appropriate indicated use and drug abuse or diversion risk when it comes to long-term opioid prescribing. However, the benefits of UDS are not limited to these but extend to benefits for the patient by possibly promoting appropriate use and motivating behavior change while helping to strengthen the patient-physician relationship. Other benefits of UDS may be preserving access to the therapy and promotion of safe and effective use while protecting the community and society at large.[2] Clinical guidelines continue to recommend use of UDS for patients on chronic opioid therapy. [3, 4]

Non-compliance is common within patients with various diagnoses and it is known that many patients with chronic pain modulate their regimen or therapy based on their pain experience.[5,6] Patients often do not share these modifications with the prescriber and as such it is crucial to make use of available tools like the UDT to ensure patient safety and to provide the best medical care. There is a need to destigmatize the UDS and using this tool frequently in practice, not as a punitive exercise but rather as part of a conscientious patient-centered practice, could be beneficial in this regard.

It would be remiss to not acknowledge the limitations of the UDS. By far, it is not a perfect test and there is no one test that fits all. Interpretation can be a challenge and is a barrier to wider use.[7] UDS methodology has been discussed before in the Prescribing Corner of the Messenger *(May 2011 issue)*. Knowledge of the strengths and weaknesses of the different tests as well as a collaborative relationship with lab personnel are important for appropriate use and interpretation of the test. Excerpts from the NOUGG guidelines are appended to this document and provide an overview and comparison of the available lab tests. Point of Care testing is also available commercially to help expedite treatment decisions by offering a quick convenient test but this may be at the expense of accuracy.[8]

Various factors need to be considered when interpreting results for UDS including detection window of different drug classes in the urine, cross-reactivity with other drugs, metabolites of parent drug, test thresholds as well as indicators of sample tampering. UDS should not be interpreted in isolation and the holistic clinical picture including patient self-report and information from other sources such as pill counts should be considered. Table 1 below shows some compounds that can cross-react to give a false positive.

Interfering compound	Immunoassay Impacted
Quinolones	Opiates
Trazodone	Fentanyl; MDMA
Quetiapine	Methadone
Tramadol	Phenylcyclidine
Venlafaxine	Phenylcyclidine
Bupropion	Amphetamine
Dextromethorphan	Phenylcyclidine
Proton Pump Inhibitors	THCA
Poppy Seeds	Opiates

Table 1. Examples of Interacting Compounds in urine toxicology immunoassay.

An unexpected screening result can be verified with a confirmatory test before using it for discussion and treatment decisions. Alternatively, based on clinician judgement, a discussion may be carried out with the patient that may help explain unexpected findings and rule out the need for confirmatory testing. A test result that is in line with patient self-report may be used to support the patient in reflecting on and discontinuing inappropriate use. On the other end of the spectrum, results conflicting with patient self-report may be indicative of inappropriate drug use or aberrant behavior such as diversion. In these cases, appropriate clinical action should be taken. It should be borne in mind when making these decisions that, as the source of prescriptions, prescribers have a significant

responsibility towards countering the current societal crisis of prescription drug misuse[7] while adequately caring for their patients.

There is no consensus across guidelines for who should receive screening with the UDS and who should be excluded. The CDC guideline advocates for a uniform approach with recommendations to use urine drug testing in all patient being started on opioids for chronic pain and to repeat this at least once a year.[4] The Canadian guidelines defer to clinician judgement in deciding who should be screened, when and how often.[3] In general, UDS may be of particular value in caring for patients who are not well known to the prescriber such as those new to the practice, patients who request and are partial to a specific drug, patients who display problematic drug-related behavior and those in recovery from a substance-use disorder.

When ordering a UDS, clinicians should be as specific as possible with indicating the drug(s) being screened for. In addition, consideration should be made to the costs associated with testing. Screening tests are generally inexpensive while confirmatory tests are more expensive and should be ordered more judiciously. Before ordering the test, a discussion with the patient should be carried out to explain the usefulness of the test as a means of ensuring patient safety, promoting the prescriber-patient alliance and satisfying the treatment agreement. The patient should also be invited at this point to describe recent drug use, including over-the-counter drugs, and be asked to advise the prescriber if there may be an unexpected finding. The prescriber should be supportive of the patient and encourage the patient with a no-judgement approach. Results from the test should impact the patient's therapy whenever indicated and the frequency of testing may be increased in the context of the need to support clinical decision making.

In conclusion, UDS is a valuable tool to incorporate and utilize in practice for safer chronic pain prescribing. Excerpts from the National Opioid Use Guideline group are included with this document.

Suggested Resources:

1. Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-Cancer Pain (Recommendation 03) http://nationalpaincentre.mcmaster.ca/opioid/cgop_b01_r03.html

Physicians may inquire about ordering and interpretation of results by contacting the concerned laboratory services.

References:

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7. George S, Braithwaite RA. Use of on-site testing for drugs of abuse. *Clin Chem*. 2002;48:1639-1646.
8. National Advisory Committee on Prescription Drug Misuse. (2013). First do no harm: Responding to Canada's prescription drug crisis. Ottawa: Canadian Centre on Substance Abuse. http://www.ccsa.ca/Resource%20Library/Canada-Strategy-Prescription-Drug-Misuse-Report-en.pdf
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Appendix B-3: Urine Drug Screening (UDS)

Table B Appendix 3.1 Immunoassay versus Chromatography for Detection of Opioid Use

Immunoassay	Chromatography
• Does not differentiate between various opioids	Differentiates: codeine, morphine, oxycodone, hydrocodone, hydromorphone, heroin (monoacetylmorphine).
• Will show false positives: Poppy seeds, quinolone antibiotics.	Does not react to poppy seeds.
•Often misses semi-synthetic and synthetic opioids, e.g., oxycodone, methadone, fentanyl.	More accurate for semi-synthetic and synthetic opioids.

Table B Appendix 3.2 Detection Times for Immunoassay and Chromatography

	Number of days drug is detectable	
Drug	**Immunoassay**	**Chromatography**
Benzodiazepines (regular use)	• 20+ days for regular diazepam use. • Immunoassay does not distinguish different benzodiazepines. • Intermediate-acting benzodiazepines such as clonazepam are often undetected.	Not usually used for benzodiazepines.
Cannabis	20+	Not used for cannabis.
Cocaine + metabolite	3–7	1–2
Codeine	2–5	1–2 (Codeine metabolized to morphine.)
Hydrocodone	2–5	1–2
Hydromorphone	2–5	1–2
Meperidine	1 (often missed)	1
Morphine	2–5	1–2: Morphine can be metabolized to hydromorphone
Oxycodone	Often missed	1–2

Source: Adapted from Brands 1998.

R03 Discussion…continued

Table B-3.1 reviews some common unexpected results and provides a range of possible reasons and some potential actions. In some cases the physician may find it useful to review unexpected results with the laboratory or a physician experienced in interpreting UDS. Prescribers who are unfamiliar with using UDS should take steps to increase knowledge and skill by seeking out an appropriate educational resource or observership.

Table B-3.1 Interpreting Unexpected Results of Urine Drug Screens

	Unexpected Result	Possible Explanations	Actions for the Physician
1	UDS *negative* for prescribed opioid.	• False negative. • Non-compliance. • Diversion.	• Repeat test using chromatography; specify the drug of interest (e.g. oxycodone often missed by immunoassay). • Take a detailed history of the patient's medication use for the preceding 7 days (e.g., could learn that patient ran out several days prior to test) • Ask patient if they've given the drug to others. • Monitor compliance with pill counts.
2	UDS *positive* for non-prescribed opioid or benzodiazepines.	• False positive. • Patient acquired opioids from other sources (double-doctoring, "street").	• Repeat UDS regularly. • Ask the patient if they accessed opioids from other sources. • Assess for opioid misuse/addiction (See Recommendation 12). • Review/revise treatment agreement
3	UDS *positive* for illicit drugs (e.g., cocaine, cannabis).	• False positive. • Patient is occasional user or addicted to the illicit drug. • Cannabis is positive for patients taking dronabinol (Marinol®), THC:CBD (Sativex®) or using medical marijuana.	• Repeat UDS regularly. • Assess for abuse/addiction and refer for addiction treatment as appropriate • Ask about medical prescription of dronabinol, THC:CBD or medical marijuana access program.
4	Urine creatinine is lower than 2-3 mmol/liter.	• Patient added water to sample.	• Repeat UDS • Consider supervised collection or temperature testing • Take a detailed history of the patient's medication use for the preceding 7 days • Review/revise treatment agreement.
5	Urine sample is cold.	• Delay in handling sample (urine cools within minutes). • Patient added water to sample.	• Repeat UDS, consider supervised collection or temperature testing • Take a detailed history of the patient's medication use for the preceding 7 days • Review/revise treatment agreement.