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Drug testing conversations: Finding the right words
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Is it time to drug test your chronic pain patient?

Many physicians forego urine testing when treating patients with chronic pain. But is that wise? This review details whom to test—and when.

PRACTICE RECOMMENDATIONS

› *When you initiate opioid therapy for chronic pain, inform the patient that routine monitoring includes random urine drug testing (UDT).* C

› *Consider UDT not only for patients at high risk for abuse of prescription opioids, but for lower-risk individuals receiving opioid therapy, as well.* C

› *Use caution in interpreting the results of UDT; testing cannot reliably detect some opioids, and a negative result is not necessarily an indication of noncompliance.* C

Strength of recommendation (SOR)

A Good-quality patient-oriented evidence
B Inconsistent or limited-quality patient-oriented evidence
C Consensus, usual practice, opinion, disease-oriented evidence, case series

CASE 1► Marilyn H, a 54-year-old woman with multiple chronic conditions, visits a "new" primary care physician to establish care following the retirement of her previous physician. She has poorly controlled diabetes, hypertension, and a lung nodule recently noted on a chest radiograph. Marilyn requests prescriptions for hydrocodone and alprazolam, stating that she has taken both drugs for years for chronic back pain and anxiety.

CASE 2► Don F, 38, has been on oxycodone/acetaminophen (Percocet) for 3 years for back pain resulting from a car accident. He has a remote history of amphetamine abuse, but reports that he has been clean for 10 years. Since the initiation of his pain medication, there have been no problems, and no "lost" prescriptions or requests for early refills.

If you were Marilyn and Don's physician, would you order urine drug testing (UDT)?

Management of opioid therapy is a challenge for many family physicians, particularly when treating noncancer pain. Seemingly contradictory messages from various medical associations are part of the problem. Organizations such as the Joint Commission on Accreditation of Healthcare Organizations and the American Medical Association emphasize the importance of appropriate pain management, while regulatory bodies like the US Drug Enforcement Agency and many state medical boards warn of inappropriate prescribing and diversion of controlled substances.[1-4]

In the realm of opioid management guidelines, however, patient monitoring is a common theme. It's not hard to understand why. The Centers for Disease Control and Prevention reports that, between 1999 and 2005, the incidence of unintentional drug overdose more than doubled—a consequence of increasing abuse of prescription opioid analge-

Prescription medications account for more cases of abuse than heroin, cocaine, and hallucinogens combined.

sics.[5] Prescription medications are now the second most commonly abused drug category (marijuana is first[6]), accounting for more cases of abuse than heroin, cocaine, and hallucinogens combined.[7] In primary care and pain management settings, estimates are that more than 1 in 4 chronic pain patients misuse opioids or illicit drugs.[8]

Thus, physicians who prescribe controlled substances face increasing pressure to prevent opioid diversion. That pressure is reflected in the US Federation of State Medical Boards (FSMB)'s Model Policy for the Use of Controlled Substances for the Treatment of Pain, which was updated in 2004.[4] This policy underscores physicians' responsibility to closely monitor patients being treated with opioids for chronic pain.

Inexpensive and noninvasive. To this end, UDT can be a valuable tool. It is the most widely used and acceptable form of drug testing, because it is inexpensive and noninvasive, and because most drugs can be detected in urine for 1 to 3 days.[9,10] But many primary care physicians are unfamiliar with the complexities of UDT, and often fail to use it.[11] One study found that only 8% of family physicians employed UDT for patients on chronic opioid therapy.[12]

When introduced and used appropriately, UDT can not only help detect misuse of controlled substances, but may strengthen the doctor-patient relationship, as well. For that to happen, however, the physician who orders urine testing must know which patients to test, when to test, and what urine testing can (and cannot) reveal.

Consider testing all patients treated for chronic pain

The FSMB urges physicians to consider a written agreement with any patient receiving chronic opioid therapy who has a history of, or is at high risk for, substance abuse.[4] (Red flags are listed in **TABLE 1**.[13-15]) The document should state that the patient is responsible for providing urine and serum specimens for drug monitoring upon request. The 2009 guidelines from the American Pain Society

TABLE 1

Aberrant drug-related behavior: Red flags[13-15]

Use of opioids for non-analgesic indications
Lack of control (related to drug use or to patient behavior)
Compulsive use of medications
Continued use of drugs despite harm/lack of benefit
Cravings
Escalation of drug use
Selling/altering prescriptions
Theft or diversion
Request for early refills
Claims of "lost" prescriptions
Reluctance to try nonpharmacologic options
Use of multiple prescribers or pharmacies
Odd stories regarding need for medication
Reporting vague medical history or textbook symptoms
Unwillingness to name regular physician
No interest in a physical exam, diagnostic testing, or providing past records
Request for specific drug(s)
Extensive (or very limited) understanding of medications
Calling or arriving after hours or when regular doctor is unavailable
Insistence on being seen urgently (eg, because of being late for another appointment)

Ask laboratory personnel which drugs are included in their facility's urine test panel and what the lower limits are; both vary from 1 facility to another.

and the American Academy of Pain Medicine also address the role of drug monitoring, strongly recommending periodic urine screens for high-risk patients on chronic opioid therapy.[16]

Evidence suggests that predictors of aberrant behavior are not completely reliable, however, and that a substantial number of individuals using illicit substances will be missed if clinicians restrict urine testing to those they deem to be at high risk.[17] Thus, UDT may be a valuable tool for low-risk patients on chronic opioid therapy, as well. Written agreements governing opioid therapy may also be useful for low-risk patients.

When to test, what to test for

No guidelines specify when to test, but testing upon initiation of chronic opioid treatment, followed by random testing, is the most widely used strategy. Unobserved specimen collection is generally acceptable,[13] provided the specimens are requested at random rather than routinely at every visit.

Initial testing is done using an immunoassay drug panel.[13,18] **TABLE 2** lists the drugs most commonly included in a standard urine test. However, the drug panel can vary from 1 laboratory to another, as can the lower limits of drug detection. No-threshold testing is mentioned in pain management literature, but is not often available in clinical practice.

Before initiating UDT, it is important to know which drugs the laboratory you use routinely tests for and what its lower limits are. The simplest way to find out is to ask lab personnel.

CASE 1 ▶ At her first visit, Marilyn H's new physician focuses on controlling her blood sugar and blood pressure, ordering follow-up testing of the lung nodule, and refilling her hydrocodone and alprazolam prescriptions. The physician requests the patient's medical

TABLE 2

A standard urine drug test panel[13,18]

Amphetamines
Cocaine
Marijuana (THC)
Opiates (morphine and codeine)
Phencyclidine

THC, tetrahydrocannabinol.

records and orders a urine drug screen per clinic protocol, testing for benzodiazepines as well as for opioids. He gives his patient prescriptions for a 1-month supply of both drugs while the UDT results are pending.

The lab report comes in the following day, and indicates that Marilyn tested positive for cocaine but negative for other substances, including narcotics and benzodiazepines. The clinic immediately notifies the pharmacy to confiscate the patient's new prescriptions when she presents them and calls Marilyn, advising her that she will not be given any further prescriptions for controlled substances.

The physician refers the patient to a pain clinic, gives her the number of a substance abuse treatment center, and encourages her to follow up at the clinic for other medical issues. Marilyn fails to keep her appointment at the pain clinic and does not respond to a subsequent call.

Talking to patients about drug testing

Physicians are often concerned about patients' feelings about drug testing—worrying that patients may not feel trusted or respected by a doctor who asks them to submit to UDT. Others may fear that the mere mention of urine testing will encourage patients to misuse prescription opioids, that patients will view UDT as a punitive measure, or that those being tested will believe that the physician is more concerned with self-protection than with providing optimal care to the patient.

Making UDT routine. One way to circumvent such possibilities is to implement a systematic approach to drug testing. We recommend that physicians discuss the role of UDT in the initial education session with patients being started on a course of opiates. Describing UDT as simply another routine monitoring parameter—akin to the measure of microalbuminuria for patients with diabetes—can decrease or eliminate the stigma associated with drug testing.

CASE 2 ▶ A new policy encouraging UDT for all patients on chronic controlled substances has just been implemented at the clinic where Don F is being treated. His physician tells him about the policy, and a urine test is ordered at his next visit. The test comes back negative for all substances, including opioids.

When presented with the results over the phone, Don insists that he regularly takes his prescription medication, and makes a same-day appointment to discuss the results with his physician.

Interpreting test results—what UDT can (and can't) reveal

To avoid eroding trust by falsely accusing a patient of diversion or use of an illicit substance, it's important to familiarize yourself with testing limitations. Factors that can affect the results, and may interfere with the ability of UDT to provide a definitive picture, include:

Lab variability and technical limitations. Some urine drug panels may not have a lower limit sufficient to detect small quantities of opioids. Others may not detect certain

Avoid making patients feel stigmatized by explaining that urine drug testing is a standard monitoring protocol in your office.

TABLE 3

Classifying opioids[19]

Natural	Semisynthetic	Synthetic
Codeine Morphine	Hydrocodone Hydromorphone Oxycodone	Fentanyl Meperidine Methadone Propoxyphene

TABLE 4

Pharmacokinetics of common opioids: Time detectable in urine[9,21]

Drug (half-life)	Time detectable in urine	Comment
Codeine (2.5-3 h)	48 h	Pharmacogenetic-dependent effects may affect detection
Fentanyl Transdermal (17 h) Submucosal (7 h)	Not usually detected in urine (lack of metabolites)	Excretion of transdermal fentanyl can last days
Hydromorphone IR (2.3 h) ER (18.6 h)	2-4 d	Significant interpatient variability
Methadone (8-59 h)	3 d	
Morphine (1.5-2 h)	48-72 h	90% eliminated within 24 h
Oxycodone IR (3.2 h) ER (4.5 h)	Often not detected in urine	High-fat meals may increase serum concentrations of ER formulation
Propoxyphene Parent drug (6-12 h) Metabolite (30-36 h)	6-48 h	

ER, extended release; IR, immediate release.

Individual drugs within a class may not be identified on urine drug panels, so serum testing must be performed if confirmation of a particular agent is needed.

substances, notably the semisynthetic and synthetic opioids (TABLE 3).[19] Oxycodone is a prime example of a commonly prescribed semisynthetic opioid that does not appear on many urine test panels.[8]

In addition, individual drugs within a class may not be identified on UDT panels. When confirmation of a specific drug or metabolite is needed, serum testing must be performed.[8]

Differences in metabolism. Genetic differences in metabolism can also skew the results of UDT. Codeine, which relies on hepatic metabolism via cytochrome P450 2D6 for conversion to morphine, is the classic example; cytochrome P450 2D6 is a polymorphic enzyme, meaning that it manifests with different activity levels in different people. Patients who are poor metabolizers (an estimated 5%-10% of Caucasians, 1%-5% of Asians, 2%-7% of African Americans, and 2%-6% of Hispanics[20]) will convert very little codeine to morphine; conversely, those who are rapid metabolizers will convert extensive amounts. A rapid metabolizer taking codeine as prescribed may therefore have a negative UDT; in an average metabolizer taking the same dose, both codeine and morphine will be detected.[20]

Drugs' half-lives. Opioids with a short half-life (TABLE 4)[9,21] may not appear in the urine if the test is done several hours after the last dose. On the other hand, some opioids may have an extended half-life in patients with liver or kidney disease, and may appear in the urine longer than would be expected.[9]

False-positive results. Substances that may cause false positives for opioids on a urine test include dextromethorphan, papaverine, poppy seeds and oil, quinine, quinolones, rifampin, and verapamil.[10]

False-negative results. Many of the problems already discussed can lead to false-negative results, including the panel's failure to detect semisynthetic and synthetic opioids, rapid metabolism (most notably, of codeine), the timing of the test relative to the dose, and adulteration of the specimen. Thus, a negative test result in a patient on opioid therapy does not necessarily mean that he or she is noncompliant—and certainly is not proof of diversion.

Because of the variables that affect UDT outcomes, unanticipated results should be reviewed with the patient and possibly, with the lab, and viewed within the therapeutic context. When more definitive information is needed, serum testing may be performed as follow-up. While serum testing can detect drugs and their metabolites ingested within hours, it is not widely used on initial screening because it is a more invasive procedure with higher associated costs.[13]

CASE 2 ▶ Upon further discussion with Don F, the physician orders a serum oxycodone test, which shows a level of 10 ng/mL. The physician notes that serum testing is more appropriate than UDT for Don because of the inconsistent detection of oxycodone in urine. **JFP**

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Synthetic and semisynthetic opioids, such as fentanyl and oxycodone, may go undetected in urine drug testing.