Clinical Urine Drug Testing During Opioid Therapy: A Case-Based Approach to Patient Monitoring

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Needs Statement
Each year, chronic pain affects more than 50 million Americans. Chronic pain is debilitating and often becomes the defining factor in a patient’s life. Opioids are the most potent and effective class of analgesics available for the treatment of chronic pain. Complicating the effective use of opioids is the risk for misuse, abuse, and drug diversion, as confirmed by a 4.5% prevalence for nonmedical use of prescription opioids. While most patients on long-term opioid therapy will not develop opioid-use disorders and will not divert their prescription medications to others, the emergence of aberrant drug-related behaviors and the ability to detect such behaviors remain a significant concern for physicians. Yet, it is critical for clinicians to ensure that the benefits of a particular opioid analgesic outweigh its potential risks.

According to the recent recommendations from the American Pain Society and American Academy of Pain Medicine, implementing a risk management strategy with opioid therapy will allow the physician to take the patient’s history and physical examination into account when administering opioids, while frequently monitoring outcomes using strategies such as urine drug testing (UDT). Given the complexities associated with drug screening, physicians need to have an understanding of how to interpret test results. This activity provides pain-treating physicians with up-to-date information and practical case examples to illustrate the implementation and utility of UDT and monitoring in patients with chronic noncancer pain (CNCP) who are receiving long-term opioid therapy.

Accreditation Statement
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Learning Objectives
After completing this activity, participants should be better able to:

1. Summarize the American Pain Society/American Academy of Pain Medicine guideline recommendations for the use of urine drug testing (UDT) in patients with CNCP who are receiving long-term opioid therapy.
2. Describe the 2-step urine screen process (immunoassay and gas chromatography/mass spectrometry) and other UDT methodologies that aid in opioid risk management.
3. Implement a routine urine-screening program as part of a comprehensive risk management strategy for patients receiving opioid therapy for CNCP.
4. Determine appropriate next steps in a treatment plan while considering result interpretation and limitations of UDT.
5. Educate patients on the importance of adherence to their opioid treatment plan and the implications of irregular UDT results.

Target Audience
This activity is intended for physicians prescribing opioid therapy to patients with noncancer chronic pain.

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Estimated Time of Completion
Approximately 1 hour.

Method of Participation
There are no fees for participating in and receiving credit for this activity. The participant should, in order, read the objectives and monograph and answer the multiple-choice post-test. Participation is available online at www.CMEZone.com (availability may be delayed from original print date). Enter the project number “SR0960” in the keyword field to directly access this activity and receive instantaneous participation. Or, complete the answer sheet with registration and evaluation on page 8 and mail to: AKH Inc., PO Box 2187, Orange Park, FL 32067-2187; or fax to (904) 215-0534. Statements of participation will be mailed/e-mailed in approximately 4 weeks after receipt of the mailed or faxed submissions. A score of at least 70% is required to successfully complete this program. One retake is allowed. The corrected answer sheet will be provided for comparison with course information. Credit is available through January 31, 2011.

Financial Disclosures
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Dr. Wimbish has no relevant financial relationships to disclose.

Dr. Traub has no relevant financial relationships to disclose.

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Introduction

Advances in medical therapies and longer life spans for US adults have resulted in an increased prevalence of chronic diseases, including chronic pain syndromes, in the general population. Chronic pain affects more than 50 million people in the United States and has considerable impact on psychological health, ability to maintain interpersonal relationships, ability to perform activities of daily living, ability to work or attend school, and overall quality of life.2

If used responsibly, chronic opioid therapy is an effective strategy for the treatment of moderate to severe chronic noncancer pain (CNCP) that is not responsive to other measures. However, opioids also are associated with potentially serious adverse effects, as well as outcomes related to their potential for abuse and addiction. As a result, some providers avoid prescribing opioid therapy, leading to the undertreatment of patients in pain. In fact, several studies have investigated the reasons why health care providers are reluctant to prescribe chronic opioid therapy for patients with CNCP and have reported that concerns regarding aberrant drug-related behaviors (ADRBs), including misuse, abuse, or drug diversion, are paramount.3

These concerns are valid—the abuse of opioid analgesics has risen steadily over the past decade. According to the National Survey on Drug Use and Health (NSDUH), the number of individuals in the United States over the age of 12 reporting the use of one or more psychotherapeutic drugs (stimulants, sedatives, tranquilizers, and analgesics available through prescription) for nonmedical purposes at some time in their lives increased from 1.6 million in 2000 to 3.5 million in 2001 and to 6.2 million in 2002.4 More recently, an analysis of the 2007 NSDUH data found a prevalence of past-year nonmedical use of prescription opioids of 4.5%, which corresponds to approximately 10 million people.5

Significant consequences result from this dramatic rise in nonmedical prescription drug use. The number of emergency department (ED) contacts for psychic effects, dependence, or suicide attempts related to nonmedical use of single and combination opioid analgesics increased from 69,011 in 1999 to 119,185 in 2002.4

In an effort to optimize the benefits of chronic opioid therapy, the American Pain Society and the American Academy of Pain Medicine (APS/AAPM) recently released evidence-based guidelines6 to provide clinicians with strategies on responsible prescribing and dosing of opioid treatment. Additionally, medical societies and government agencies have recommended the institution of risk management programs, both at the industry and at the health practitioner levels.6 The goals of these programs are to help identify appropriate candidates for chronic opioid therapy, assure the safe and informed use of the product by both practitioners and patients, and ensure patients are being monitored for adverse outcomes.

Urine drug testing (UDT) has emerged as a critical aspect of comprehensive risk management and monitoring programs, and can help identify potential misuse, abuse, or drug diversion.2 This activity discusses the advantages and limitations of UDT, as well as case studies outlining practical clinical issues surrounding its use in patients undergoing chronic opioid therapy.

Urine Drug Testing: Initiating a Comprehensive Risk Management Strategy

Approach

ADRBs are associated with worsening medical and psychological outcomes, declining functional capacity, compromised interpersonal relationships and physician–patient rapport, and increased societal and health care costs.7,8 Thus, prevention or early detection of ADRBs is a key goal when considering initiation of chronic opioid therapy or maintaining patients on such treatment.

Several strategies can be employed to prevent ADRBs. Recently, the APS and the AAPM published guidelines that recommend extensive counseling before initiating chronic opioid therapy.2 Counseling should include discussions on mutually agreed-on practical treatment goals (eg, alleviation of pain to

Table 1. Opioid Risk Tool for Risk Stratification

<table>
<thead>
<tr>
<th>Item</th>
<th>Mark each box that applies</th>
<th>Item score if female</th>
<th>Item score if male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family history of substance abuse</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td>1</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Illegal drugs</td>
<td>2</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Prescription</td>
<td>4</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Personal history of substance abuse</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td>3</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Illegal drugs</td>
<td>4</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Prescription</td>
<td>5</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Age (mark box if 16-45)</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>History of preadolescent sexual abuse</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychological disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Attention-deficit disorder, obsessive-compulsive disorder, bipolar disorder, schizophrenia</td>
<td>2</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total score risk category:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low risk: 0 to 3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate risk: 4 to 7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High risk: 8 and above</td>
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</tbody>
</table>

promote functioning, but not the elimination of pain), benefits and risks associated with therapy, and responsibilities associated with such therapy, including intensive monitoring, personal responsibility for management of opioid medications, and the risk for and consequences of misuse. Additionally, the APS/AAPM guidelines recommend the use of written opioid treatment agreements to clearly outline these issues.

The APS/AAPM guidelines also suggest risk stratification to identify patients at high risk for an ADRB who may benefit from further consideration of nonopioid therapy, referral to a pain specialist, or more intensive monitoring if appropriate.2 Examples of validated screening instruments for risk stratification include the Screener and Opioid Assessment for Patients with Pain-Revised and the Opioid Risk Tool (ORT).2 In the ORT, each factor is assigned a point indicative of the patient’s overall risk (Table 1).9

Therapeutic risks and benefits do not remain static and can be affected by changes in the underlying pain condition, presence of coexisting disease, or changes in psychological or social circumstances. Thus, patients who are maintained on chronic opioid therapy require ongoing monitoring for ADRBs. Because patient self-reporting may be unreliable for determining the amount of opioid use, functionality, or ADRBs, the APS/AAPM guidelines recommend the use of alternate strategies, such as pill counts or family member or caregiver interviews.7 In some cases, prescription monitoring programs (PMPs) function in 38 states providing information on prescribers of Schedule II, III, and IV medications.10 By checking this database, a provider can track a patient’s source of scheduled medications.2

Periodic UDT is another essential tool for monitoring patients on chronic opioid therapy. Indeed, investigators have reported that UDT identifies more nonadherent patients when compared with the use of behavior monitoring or self-reporting alone.11 Simply setting the expectation that UDT will be conducted may act as a deterrent to illicit drug use.12,13

The use of UDT is of higher yield in patients with risk factors for drug abuse or diversion. However, targeted nonuniversal UDT will miss some patients who engage in ADRBs. As a result, the APS/AAPM guidelines recommend the universal use of UDT in all patients receiving chronic opioid therapy.2 Although the optimal interval for recommended testing remains uncertain, the guidelines suggest using risk stratification as a guide to determine frequency of testing (strong recommendation, low-quality evidence).2 For example, they state that, in patients at low risk for adverse outcomes and on stable doses of opioids, monitoring at least once every 3 to 6 months may be sufficient. Patients who may require more frequent or intense monitoring, at least for a period of time after initiation of therapy or changes in opioid doses, include those with a prior history of an addictive disorder, those in an occupation demanding mental acuity, older adults, patients with an unstable or dysfunctional social environment, and those with comorbid psychiatric or medical conditions. Furthermore, monitoring on a weekly basis may be a reasonable strategy for patients at very high risk for adverse outcomes. The APS/AAPM guidelines also suggest that random urine drug screens may be more informative than scheduled or routine testing, as patients may change behaviors when they expect to be tested.

Despite its benefit in the clinical management of patients undergoing chronic opioid therapy, UDT remains underutilized. For example, Bhamb and colleagues conducted a survey of primary care providers and reported that only 7% ordered UDT before prescribing opioids and only 15% had used UDT for patients receiving ongoing opioid therapy.14 This may be at least partly attributed to the fact that primary care providers often do not anticipate the need for chronic therapy or because they perceive screening of the entire patient population receiving opioids as unnecessary when only a minority ultimately will demonstrate ADRBs.

### Techniques for Urine Drug Testing

UDT is conducted by immunoassay, either at the point of care (POC) or at a local laboratory, or by the more sophisticated gas chromatography/mass spectrometry (GC/MS) technique at an in-house or off-site laboratory.15 Each technology has its particular advantages and limitations (Table 2).16-18

#### Immunoassay

Immunoassays use antibodies to detect the presence (or suggest the absence) of specific drugs or metabolites and are the most common method for the initial screening process. These assays can be conducted quickly at the POC through urine “dipsticks,” cups, or card tests, or they can be conducted at the local laboratory, which allows large-scale screening through automation. Advantages of the immunoassay include rapid results, ability to conduct the test at the POC via urine dipstick tests, and relatively low costs.16-18

Although immunoassay testing demonstrates adequate sensitivity, it only shows the presence or absence of broad classes of drugs or metabolites (eg, nonsynthetic opioids, amphetamines, or cannabinoids) without distinguishing between

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**Table 2. Advantages and Limitations of Urine Drug Testing Technology**

<table>
<thead>
<tr>
<th>Test</th>
<th>Advantages</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immunoassay</td>
<td>Sensitive</td>
<td>Subject to cross-reactivity</td>
</tr>
<tr>
<td></td>
<td>Relatively inexpensive</td>
<td>Sensitivity and specificity vary by manufacturer and devices/equipment</td>
</tr>
<tr>
<td></td>
<td>Requires a small sample of urine</td>
<td>Does not reliably detect semisynthetic/synthetic opioids</td>
</tr>
<tr>
<td></td>
<td>Conducted at the point of care</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Can handle a high volume of cases</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rapid turnaround</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Can be performed by minimally trained staff</td>
<td></td>
</tr>
<tr>
<td>Gas chromatography/mass spectrometry</td>
<td>Highly specific and sensitive</td>
<td>Results not immediately available</td>
</tr>
<tr>
<td></td>
<td>Few false-negatives or false-positives</td>
<td>Relatively expensive; insurance may not cover</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Limited by laboratory services/quality</td>
</tr>
</tbody>
</table>

specific drugs within those classes, and thus is not specific.\textsuperscript{16-18} Immunoassay testing generally is unable to demonstrate overuse of a specific drug (eg, duplicate prescriptions for or overuse of prescribed extended-release oral morphine). Furthermore, many commonly used immunoassays do not have the capacity to detect synthetic or semisynthetic opioids (eg, oxycodone, fentanyl, methadone), although newer immunoassays are capable of detecting some of these substances. Another drawback is that various medications or substances can cross-react with the immunoassay to produce a false-positive result (Table 3).

For all of these reasons, the immunoassay is essentially a screening study, and all normal or abnormal results should be regarded as presumptive. Confirmatory testing is required in the face of an unexpected result, when there is strong clinical suspicion of opioid misuse despite a negative immunoassay test, or simply as periodic confirmation of an otherwise unremarkable immunoassay result.

**Table 3. Interpreting False-Positives and False-Negatives**

<table>
<thead>
<tr>
<th>Differential Diagnosis</th>
<th>False-Positive</th>
<th>False-Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cross-reaction</td>
<td>Drug levels fall below the cutoff level of the test</td>
<td></td>
</tr>
<tr>
<td>Technical or clerical</td>
<td>Intermittent dosing with short-acting drug (including binging)</td>
<td></td>
</tr>
<tr>
<td>error</td>
<td>Technical or clerical error</td>
<td></td>
</tr>
<tr>
<td>Urine adulteration</td>
<td>Test not designed to detect drug</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Urine adulteration</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Urine substitution</td>
<td></td>
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</table>

Recommended Action(s)

- Repeat testing and/or pursue confirmatory GC/MS if not already done
- Random testing or obtain urine sample under direct supervision
- Perform specimen validity testing
- Review patient’s medication profile
- Discuss with patient
- Consider cessation of opioid therapy and referral for counseling if evidence of ADRBs

ADRB, aberrant drug-related behaviors; GC/MS, gas chromatography/mass spectrometry

**Gas Chromatography/Mass Spectrometry**

GC/MS is considered the gold standard for confirmatory testing.\textsuperscript{16-18} The method is both sensitive and specific; it can detect small quantities of a substance and confirm the presence of a specific drug (eg, detect synthetic or semisynthetic opioids, distinguish between oxycodone and morphine in an opioid screen), and does not suffer from problems with cross-reacting substances.\textsuperscript{15}

This method, however, is time-consuming, requires a high level of expertise to perform, and is more costly than a urine dipstick test.\textsuperscript{16-18} Some GC/MS tests can fail to identify a positive specimen (eg, hydromorphone or fentanyl) if the column is designed to detect only certain substances (eg, morphine or codeine). For these reasons, GC/MS primarily is performed only after an abnormal or unexpected result is obtained from immunoassay or when there is strong suspicion of opioid misuse or diversion.

**Interpretation of Results From Urine Drug Testing**

An understanding of the drug pharmacokinetics, drug metabolism, strengths and limitations of the particular test, and a host of potential confounding factors will assist clinicians in recognizing false-positive and false-negative outcomes.\textsuperscript{7,16-18} Thus, the results of UDT should not be taken in isolation and require consideration of the individual patient and testing circumstances.

**Test Capabilities and Limitations**

It is important to be aware of the precise capabilities of the different types of tests in order to interpret UDT results accurately. For example, immunoassays are designed to detect broad classes of agents, including amphetamines, cocaine, non-opioid agonist/norepinephrine reuptake inhibitors, methadone—the latter 2 are available as separate tests. New liquid chromatography/MS protocols are capable of detecting novel analgesics, including the mixed opioid agonist/norepinephrine reuptake inhibitor, tapebndin.\textsuperscript{16-18} Thus, the provider should be aware of the “testing menu” associated with the laboratory performing the GC/MS tests and should consult with the laboratory technologist to determine if any additional tests should be ordered.

Although immunoassay results also can be confounded by the presence of cross-reacting substances (eg, prescription or over-the-counter medications, herbal agents, or food) that can result in false-positive outcomes (Table 3), GC/MS testing typically is not subject to issues of cross-reactivity.\textsuperscript{17}

The use of UDT in the workplace and the desire to reduce the rate of false-positive results from cross-reacting substances led to the institution of cutoff values for these assays, in which drug levels at or above this level are considered positive, whereas results below are considered negative.\textsuperscript{16-18} In the clinical setting, these cutoff values are less helpful because they may actually result in false-negative testing if drug levels fall below the defined cutoff values. Thus, providers should be aware of this phenomenon and consult with the laboratory technologist to determine whether cutoff values are used in the laboratory and whether the use of these values could affect UDT results, particularly if a false-negative test is suspected.

**Drug Metabolism and Clearance**

An understanding of drug metabolic pathways can be beneficial in interpreting UDT correctly, especially when opioids are the drug of interest.\textsuperscript{16-18} For example, a positive immunoassay for opiates relies on detection of morphine within the urine.
Case Study 1

A 34-year-old woman with a 2-year history of chronic low back pain that she attributes to work-related activities (eg, lifting boxes) presents to a local pain specialty clinic with intermittent worsening of her moderate to severe pain. Review of her past evaluation reveals degenerative joint disease of the spine and signs or symptoms of radiculopathy not amenable to surgical intervention.

The patient relates that because of increasing functional limitations, she has gained more than 40 lb over the past 2 years and is unable to sit and stand for more than 30 minutes.

Her family history is notable for low back pain in her father, mother, and both grandmothers, all of whom are on disability. She smokes 1.5 packs of cigarettes per day. Her ORT score is calculated as 6. She has a history of marijuana use and has no other medical problems.

The patient has been prescribed hydrocodone/acetaminophen (APAP) (5/500 mg) 1 tablet 4 times daily as needed, which decreases her pain intensity score from a baseline of 8 (on a 1-10 scale) to a 3.

Baseline UDT with immunoassay fails to show hydrocodone but does show a small amount of hydromorphone. Review of PMP data for this patient is consistent with only one prescribing physician and a prescription for hydrocodone/APAP (5/500 mg).

Interpretation

It is possible that this immunoassay test performed by the laboratory does not detect hydrocodone but can detect hydromorphone. Thus this scenario could still be consistent with treatment with hydrocodone/APAP, as about 10% of hydrocodone is metabolized to hydromorphone. GC/MS testing could be pursued to delineate the presence of hydrocodone and hydromorphone in this sample for confirmation.

Case Study 2

A 46-year-old man presents to a local pain specialty clinic to establish care. He has a history of complex regional pain syndrome (CRPS) manifesting with right lower extremity pain that developed after an injury to the right ankle. The patient has been discharged from 3 previous clinics secondary to noncompliance with the prescribed treatment regimen. The patient’s medical history is notable for obesity, diabetes mellitus type 2, anxiety, and a seizure disorder. His medical profile includes pregabalin (150 mg twice daily), duloxetine 60 mg in the morning, metformin (1,000 mg twice daily), and phenytoin (300 mg at bedtime). His previous prescribed pain regimen consists of both long- and short-acting oxycodone. He is unemployed and an active smoker.

The patient’s ORT score is calculated as 7 out of 10. Review of PMP data for this patient is consistent with only one prescribing physician and a prescription for oxycodone/APAP (5/500 mg 1 tablet 4 times daily as needed), lidocaine patch, paroxetine (20 mg daily), levothyroxine (125 mcg daily), and modafinil (200 mg daily). He is unemployed and an active smoker.

Interpretation

Phenytoin induces p450 isoenzymes and thereby leads to rapid metabolism of oxycodone to oxymorphine. Furthermore, this patient may be using marijuana for his untreated or undertreated anxiety disorder; it is up to the individual provider as to whether marijuana use in this context is therapeutic and is consistent with the overall care plan. Thus, the provider should be aware of the state’s laws on the use of medical marijuana.

Case Study 3

A 38-year-old woman with documented bilateral temporomandibular joint (TMJ) pain presents to a local pain specialty clinic to establish care. She states that the TMJ pain causes her to be unable to eat or sleep. Her review of systems is otherwise negative, and her family and social history are unremarkable.

She is started on monthly prescriptions of long-acting oxycodone at 10 mg twice daily and titrated up to 80 mg twice daily with good pain control. She is always on time for appointments and never calls for early refills. Random POC testing on one follow-up visit fails to detect any opioids. The sample is sent to a local laboratory for confirmatory testing, and, again, no opioids are detected.

Interpretation

There are several possible explanations for this scenario. For example, it is possible that neither the POC nor the local laboratory immunoassay is designed to detect oxycodone. To help clarify the situation, the provider should contact the laboratory to confirm whether this is the case. If the local laboratory assay is capable of detecting oxycodone, then this scenario could be consistent with either misuse (eg, binging, in which the patient is consuming the entire course of oxycodone early in the month) or drug diversion. The provider should tighten control by scheduling more frequent follow-up visits and performing pill counts, and should remain suspicious of diversion.

Case Study 4

A 28-year-old woman undergoing chronic opioid therapy for fibromyalgia presents for a routine follow-up visit. She is obese and her history is notable for hypothyroidism, endometriosis, chronic fatigue syndrome, depression, pelvic pain, 3 previous cervical spine operations, and sexual abuse during adolescence. Her medication profile consists of hydrocodone/APAP (5/500 mg 1 tablet 4 times daily as needed), lidocaine patch, paroxetine (20 mg daily), levothyroxine (125 mcg daily), and modafinil (200 mg daily). She is married, has 2 children, and currently works as a cashier at a grocery store. Her family history is unknown as she was adopted.

Her ORT score is calculated as 9 out of 10. PMP data reveal that she has seen 2 other physicians in the past year, both of who prescribed hydrocodone/APAP that was filled at different pharmacies. Urine samples were obtained and sent to a local laboratory for testing. Hydrocodone was not detected on any tests.

Interpretation

This scenario suggests that the patient did not take hydrocodone/APAP in the 24 hours preceding testing. Again, these results may be the result of binging or drug diversion. The PMP and ORT scores suggest a high risk for overdose. This care requires closer monitoring before reaching a definitive conclusion.
Thus, immunoassays can only detect use of morphine or opioids that are metabolized to morphine (eg, codeine or heroin) and cannot detect synthetic or semisynthetic opioids that are not (Table 4).

Similarly, detection of the heroin metabolite, 6-monoacetyl morphine (6-MAM), on GC/MS is indicative of recent heroin use, but only if the test is performed before 6-MAM is metabolized to morphine. Additionally, because codeine is metabolized to morphine, the presence of both codeine and morphine on GC/MS testing should be expected in a patient receiving codeine as part of a pain control regimen or cough suppressant therapy.

Drug clearance and drug detection time is another factor that must be considered when interpreting UDT.16-18 For example, a negative UDT may not necessarily reflect abstinence from illicit drug use or nonadherence to prescribed therapy if the time interval between drug injection/ingestion and collection is sufficiently long. Of course, drug clearance itself can vary according to a whole host of factors, including urine pH, urine volume, body weight, malabsorption, drug dose and route of administration, duration of use, comorbid conditions, and altered metabolism due to hepatic or renal insufficiency or pharmacogenetic variations.

**Specimen Validity**

Adulterating, substituting, and diluting urine samples are common practices used to avoid detection of drug use.17 These may include in vivo adulteration (use of excessive water intake or “flushes” before urine collection), ex vivo adulteration (addition of water or other substances to the urine after collection), or substitution (use of urine from another source) (Table 4).

Understanding the specific characteristics of a urine specimen can help identify false-negative results. For example, specimen tampering should be suspected if samples have unusual color, excessive bubble formation, or abnormal temperature (<32°C or >38°C within 4 minutes of collection).17

Other laboratory testing can help determine if the specimen has been tampered with, but may not be performed until requested by the provider.17 Specific gravity less than 1.002 or greater than 1.020 and urine creatinine concentrations less than 20 mg/dL may be indicative of specimen tampering, although occasionally some lab abnormalities can result from medical illness (eg, diabetes insipidus).17 If specimen tampering or substitution is a concern, collection should be performed under direct observation.

**Laboratory Consultation**

Clinicians should consider UDT results in the context of all of the clinical information; in case of a discrepancy, the laboratory technologist should be asked to review the laboratory procedures that were used, clarify test results, and determine the need for further testing.

**Clinical Action Based on Abnormal Urine Drug Testing**

Clinicians should consider a differential diagnosis for abnormal UDT results, including drug abuse or addiction, self-treatment of poorly controlled pain, or psychological issues. Furthermore, absence of an expected drug on UDT may be due to testing methodology limitations, intermittent dosing by the patient of a short-acting opioid, or drug diversion.2,16-18

UDT results suggesting ADRBs may require cessation of chronic opioid therapy.2 Results should be discussed with the patient in person in a nonconfrontational manner. An abnormal UDT should be used as an objective piece of evidence to determine if underlying factors are affecting treatment.

Exploration of other nonopioid pain control options may be considered for these patients. Additionally, patients who display ADRBs often require referral for chemical dependency and/or psychological counseling to address issues of addiction, as well as other factors that may lead to opioid misuse or abuse, including anxiety and depression.

**Conclusion**

Chronic opioid therapy is an effective strategy for the treatment of CNCP. Use of precounseling and risk stratification can help identify appropriate candidates for chronic opioid therapy, as well as guide intervals for appropriate monitoring.

The recent APS/AAPM guidelines stress that UDT is a valuable tool for detection of ADRBs, but successful use of UDT requires a comprehensive understanding of the testing technologies, their strengths and limitations, and drug metabolism and clearance. Interpretation of UDT also requires consideration of the differential diagnosis of false-positive and false-negative results.

Clinicians should be aware that preliminary tests performed by immunoassays are presumptive and that confirmatory testing (eg, GC/MS) is required before decisions can be made based on UDT. If a careful analysis and interpretation of UDT suggests ADRBs, chronic opioids therapy should be discontinued, and the patient should be referred for nonopioid pain control strategies, psychological counseling, and/or drug dependency counseling.
CME Post-Test

Select the single-letter response that best answers the question or completes the sentence.

1. Which of the following substances is reliably detected by point-of-care (POC) opioid immunoassays?
   a. Morphine
   b. Oxycodone
   c. Methadone
   d. Fentanyl

2. A false-positive result can be caused by which of the following factors?
   a. Presence of cross-reacting substances within the urine
   b. Overhydration before obtaining urine sample
   c. Dilution of urine sample with water
   d. High cutoff values

3. Which of the following measures is most appropriate in the context of an unexpected or abnormal result in a POC urine drug immunoassay?
   a. Terminate opioid therapy
   b. Notify the patient that he or she is in violation of the opioid treatment agreement
   c. Repeat the immunoassay on the next clinic visit
   d. Pursue confirmatory testing with gas chromatography/mass spectrometry (GC/MS)

4. Which of the following represents the chief advantage of GC/MS for urine drug testing (UDT)?
   a. Low cost
   b. High specificity
   c. Availability for POC testing
   d. Speed

5. Which of the following is the most reliable indicator of aberrant drug-related behavior (ADRB)?
   a. Patient report
   b. Clinical judgment
   c. Abnormal test on immunoassay urine drug screen
   d. Abnormal test on GC/MS spectrometry UDT

6. The properties of POC immunoassay for UDT make it well suited for which purpose?
   a. Confirmatory testing
   b. Definitive determination of ADRBs
   c. Screening
   d. All of the above

7. Use of which of the following substances might explain a urine drug immunoassay showing the presence of morphine?
   a. Use of cough suppressants containing codeine
   b. Use of oxycodone
   c. Use of fentanyl
   d. Use of meperidine

8. Which of the following could account for a false-negative urine test?
   a. High cutoff values
   b. Urine substitution or adulteration
   c. A “testing menu” does not detect certain drugs
   d. All of the above

9. Which of the following substances can be detected on urine drug immunoassay following use of heroin?
   a. Heroin
   b. Morphine
   c. Codeine
   d. Oxycodone

10. According to the Opioid Risk Tool, which of the following factors is a risk for ADRBs?
    a. Family history of substance abuse
    b. History of preadolescent sexual abuse
    c. Psychological disease
    d. All of the above

References

Post-Test Answer Section

Please circle the correct answer for each question. (A score of at least 70% is required to receive credit.)

1. a b c d
2. a b c d
3. a b c d
4. a b c d
5. a b c d
6. a b c d
7. a b c d
8. a b c d
9. a b c d
10. a b c d

7. The content was objective, current, scientifically based, and free of commercial bias.

Yes   No (please explain):

8. Based on information presented in this activity, I will:
   a. do nothing, as the content was not convincing.
   b. seek additional information on this topic.
   c. change my practice.
   d. do nothing, as current practice reflects the program’s recommendations.

9. The most important concept learned during this activity that may effect a change in patient care is:

10. What issue(s) related to the therapeutic area discussed in this activity, or other topics, would you like addressed in future continuing education?

11. Additional comments:

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