Urine Drug Testing
Key Concepts Toward Patient-Centered Risk Management

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**Introduction**

The use of urine drug testing (UDT) has increased over recent years. Testing has traditionally been conducted in forensic settings under supervision of a medical review officer. In this context, there is no doctor-patient relationship, and test results are often not used in the “donor’s” best interests. Healthcare professionals, however, can and should consider using UDT as an important part of a comprehensive care plan to assist in diagnostic and therapeutic decision making. By using UDT in a patient-centered fashion, the interests of both patient and healthcare professional are maintained.\(^1\)

Despite the paucity of high-quality evidence documenting the effectiveness of UDT, organizations such as the Federation of State Medical Boards have formally included UDT in their current guidelines for the treatment of chronic pain.\(^2-4\) The American Pain Society and American Academy of Pain Medicine recommend using UDT in high-risk patients receiving chronic opioid therapy to assist in assessing compliance with the treatment plan.\(^5\) These guidelines go further to suggest considering periodic UDT even for patients not at high risk or exhibiting any aberrant behaviors.\(^5\)

This guide introduces the reader to many of the key concepts of UDT. Integrating UDT, along with these specific key concepts, into clinical practice is essential to addressing the increasing incidence of prescription drug misuse and abuse while maintaining a patient-centered approach to risk management. In fact, UDT can offer valuable clinical information in a variety of clinical contexts regardless of the use of controlled substances, such as the opioid class of medications.\(^1,6\)

**Strategy for Urine Drug Testing: Explanation to Patient and Healthcare Professional**

- UDT should be considered a consensual diagnostic test to improve patient care\(^1\)
- Healthcare professionals should provide full explanation to the patient that UDT is being considered in order to:
  - Assist in objective documentation of adherence with the mutually agreed upon treatment plan\(^1\)
  - Aid in the diagnosis and treatment of the disease of addiction or drug misuse and abuse\(^1\)
  - Advocate for the patient in family, social, and third-party settings\(^1\)
- Urine may be “the best” biologic specimen for determining the presence or absence of certain drugs in a patient’s system due to its increased window of detection, typically 1-3 days for most drugs and/or their metabolites. UDT is a cost-effective and relatively noninvasive test\(^1\)
- Clinical UDT should be part of any comprehensive treatment agreement for chronic pain
  - Rarely is directly observed collection or formal forensic chain of custody appropriate for clinical care\(^1,6\)
  - A clinical chain of custody, however, will ensure that the result obtained applies to the patient for which the test was ordered
- An unexpected positive or negative result does not diagnose
  - Drug addiction
  - Physical dependence
  - Impairment
  - Criminal intent, such as diversion
- UDT should initially be applied consistently, for all patients, until actual individual risk can be determined\(^6\)

<table>
<thead>
<tr>
<th>Who to test: (^6)</th>
<th>When to test:</th>
</tr>
</thead>
<tbody>
<tr>
<td>All new patients</td>
<td>When starting treatment with a controlled substance</td>
</tr>
<tr>
<td>Patients who are resistant to full evaluation</td>
<td>When major changes in medication are necessary</td>
</tr>
<tr>
<td>Patients who display aberrant behavior</td>
<td>In support of a rational consultative referral</td>
</tr>
<tr>
<td>Consider periodically in all patients as clinically indicated</td>
<td>Periodically in all patients based on demonstrated risk</td>
</tr>
</tbody>
</table>
Ordering the Test: What Tests

- For initial testing, consider class-specific immunoassay drug panels (laboratory or point-of-care), although drug-specific immunoassay tests are now more commonly available.

- If the test results are contested or not consistent with the clinical picture, the original sample should be evaluated further to resolve the dispute (eg, discuss the result with the laboratory director/point-of-care vendor).
  - An unexpected positive result for opiates in itself is not sufficient to diagnose drug misuse, abuse, or addiction.

- “Opiate” immunoassay drug tests are better for detecting the presence of naturally occurring opium alkaloids (eg, codeine, morphine).
  - These tests have low or no sensitivity for semisynthetic or synthetic opioids (eg, hydrocodone, oxycodone, hydromorphone, methadone, fentanyl).
  - A negative test does not exclude these molecules unless the immunoassay is specific for that drug.

- GC/MS or similar tests identify specific molecules or their metabolites.
  - Removal of arbitrary reporting thresholds can increase test sensitivity without compromising reliability.

Panel Selection by Immunoassay

- For cases in which a sample is legitimately positive for a member of a class of drug being tested for (eg, “opiates”), it will be necessary to specifically identify the actual molecule causing the positive result because it may be another, unprescribed opioid that is actually being detected or a false positive.

- The following molecules should be considered for routine testing. Additional molecules may be added according to local patterns of drug misuse:
  - Cocaine*
  - Opiates*
  - Marijuana (THC)*
  - Amphetamines*
  - Phencyclidine (PCP)*
  - Oxycodone
  - Benzodiazepines
  - Methadone
  - Specific analytes as clinically indicated

*“Federal Five”/”NIDA Five” of regulated testing

Classification of Common Opioid Analgesics

<table>
<thead>
<tr>
<th>Naturally Occurring Alkaloids</th>
<th>Semisynthetics (derivatives of natural products)</th>
<th>Synthetic (completely man-made)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Codeine</td>
<td>Buprenorphine</td>
<td>Fentanyl</td>
</tr>
<tr>
<td>Morphine</td>
<td>Hydrocodone</td>
<td>Meperidine</td>
</tr>
<tr>
<td>Thebaine*</td>
<td>Hydromorphone</td>
<td>Methadone</td>
</tr>
<tr>
<td>Thebaine*</td>
<td>Oxycodone</td>
<td>Propoxyphene</td>
</tr>
<tr>
<td>Thebaine*</td>
<td>Oxymorphone</td>
<td>Tapentadol</td>
</tr>
<tr>
<td>Thebaine*</td>
<td></td>
<td>Tramadol</td>
</tr>
</tbody>
</table>

*Thebaine is a precursor from which many of the semisynthetic analgesics are derived (eg, buprenorphine, oxycodone)
## Test Interpretation

<table>
<thead>
<tr>
<th>Drug</th>
<th>Approximate Retention Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphetamines</td>
<td>Up to 3 days</td>
</tr>
</tbody>
</table>
| Barbiturates (depending on the specific agent and quantity used) | Short acting (eg, secobarbital) 24 hours  
                                      | Long acting (eg, phenobarbital) 2-3 weeks                      |
| Benzodiazepines                           | Days to weeks                                                 |
| Cocaine Metabolite                        | 2-4 days (benzoyl ecgonine)                                     |
| Ethanol                                   | 2-4 hours                                                      |
| Methadone                                 | Up to 3 days                                                  |
| EDDP*                                     | Up to 6 days                                                  |
| Opioids                                   | 2-3 days                                                       |
| Propoxyphene                              | 6-48 hours                                                     |
| Cannabinoids                              | Moderate user (4 times/week) 5 days  
                                      | Heavy user (using daily) 10 days  
                                      | Retention time for chronic users may be 20-28 days |
| Phencyclidine                             | Up to 8 days                                                  
                                      | Up to 30 days in chronic users (mean value = 14 days)         |

*Note: Interpretation of retention time must take into account variability of urine specimens, drug metabolism and half-life, patient’s physical condition, fluid intake, and method and frequency of ingestion. These are general guidelines only.*

*EDDP (2-ethylidene–1, 5 dimethyl–3, 3–diphenylpyrrolidine, the metabolite of methadone)*

- Test reliability can be improved by paying attention to sample volume (≥30 mL), temperature (90-100°F <4 minutes from collection), and concentration (random urinary creatinine >20 mg/dL). Inexpensive sample cups with LCD temperature strips are available and recommended
  - As a general rule, concentrated samples provide more reliable information
- Understanding basic opioid metabolism will enhance UDT result interpretation

### Metabolism of Opioids

<table>
<thead>
<tr>
<th>Opioid Metabolism</th>
<th>Morphine</th>
<th>6-MAM*</th>
<th>Heroin†</th>
</tr>
</thead>
<tbody>
<tr>
<td>codeine</td>
<td>➞</td>
<td>➞</td>
<td></td>
</tr>
<tr>
<td>hydrocodone</td>
<td>➞</td>
<td></td>
<td></td>
</tr>
<tr>
<td>oxycodone</td>
<td>➞</td>
<td></td>
<td></td>
</tr>
<tr>
<td>morphine</td>
<td>➞</td>
<td>6-MAM*</td>
<td></td>
</tr>
<tr>
<td>hydromorphone</td>
<td>➞</td>
<td></td>
<td></td>
</tr>
<tr>
<td>oxymorphone</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*6-MAM = 6 – monoacetylmorphine (short-lived metabolite of heroin)
†heroin = diacetylmorphine
Clinical Pearls for Patient-Centered Urine Drug Testing

• It is not necessary to limit choice of therapeutic agents to those that can be readily detected in the urine; expectation of a reliable negative UDT result can be an asset in assessing treatment compliance.

• A positive UDT result for opiates in a patient using any fentanyl product should alert the clinician to the possibility of use of an unprescribed/illicit opioid.

• Identification of the specific agent causing a class-specific positive result can be useful, especially in monitoring therapeutic compliance or interpreting a contested result.

• Scientific personnel (laboratory or point-of-care representative) can provide a wealth of information to assist in the proper interpretation of UDT results; it is also important to periodically review testing strategies and laboratory practices to ensure that your testing needs are continuing to be met.

• It is important to caution any patient participating in UDT to avoid foodstuffs, such as poppy seed bagels, that might complicate the interpretation of test results.

• Prior to ordering a urine drug test, the healthcare professional should ask the patient to disclose any over-the-counter or prescription drug use from other sources; ideally the healthcare professional will list prescribed medications/expected analytes on the requisition.

• The interpretation of unexpectedly negative UDT results for a prescribed medication may be complex and should not be considered definitive evidence of drug diversion.

• Reasons for a negative UDT result for a prescribed opioid medication may include:
  - Inadequate treatment of pain (ie, pseudoaddiction)—medical
  - Bingeing on drug (ie, drug misuse or addiction)—medical
  - Diversion—criminal

• Use quantitative UDT results with caution, if at all. Although quantitative testing of UDT may be available, these values are of limited use in assessing treatment compliance. Quantified UDT results should be used cautiously and rarely to challenge patient compliance. Current software and laboratory products have not yet been shown to be scientifically valid to provide this information.

• Interpreting UDT beyond the current scientific knowledge may put clinicians and patients at medicolegal risk.

Conclusion

UDT should not be regarded as a matter of mistrust, but rather as one of many clinical tools available to improve patient care while assisting in the effective management of risk. While this document is necessarily brief, readers are encouraged to examine these issues in greater depth using the following resources:


• Pain and Addiction: Expert Practice Series at http://quantiamd.com/home/addiction

To learn more about how you can help improve patient safety and reduce the risks of prescription pain medications, call us at 1-800-233-8969 or visit our Web site:

www.caresalliance.org

C.A.R.E.S Alliance was created to help patients, healthcare professionals, nonprofit organizations, and people in the pharmaceutical industry work together to improve patient safety.