Understanding and Interpreting Unexpected Urine Drug Screens

Jeffrey Fudin, B.S., Pharm.D., FCCP, FASHP
Diplomate, American Academy of Pain Management
Clinical Pharmacy Specialist & PGY2 Pain Residency Director;
Stratton VA Medical Center
East Tennessee State University, Common Misconceptions in Prescribing for Chronic Pain
Friday the 13th (November)
Adjunct Affiliations;
UCONN School of Pharmacy, Albany College of Pharmacy & Health Sciences,
SUNY/University at Buffalo, Western New England University

Disclosure Statement

- Astra Zeneca (Speakers Bureau, Advisory Board)
- DepoMed (Advisory Board)
- Endo (Consultant)
- Kaléo (Speakers Bureau, Advisory Board)
- KemPharm (Consultant)
- Millennium Health, LLC (Speakers Bureau, Advisory Board, Expert Witness)
- Practical Pain Management Development of Online Opioid Conversion Calculator
- Remitigate, LLC (Founder, Owner)
- Scilex Pharmaceuticals (Consultant)
- Zogenix (Consultant)
- Faculty (PainWeek; PainWeekEnds)

Learning Objectives

1) Differentiate between In-Office Qualitative Testing & Laboratory Quantitative Testing
2) Interpret unexpected UDT results
3) Integrate UDT results into ongoing clinical assessment and decision making
4) Communicate with patients about unexpected results in a positive, therapeutic manner
Street Value Perspective

120 Percocet 5/325 (brand name)  
$600.00  
120 Lortab 10/500 (any brand)  
$600.00  
60 Oxycontin 80mg  
$1500.00  
120 Actiq Lollipop 200mcg  
$3240.00  
Knowing when your patient is diverting drug...  
PRICELESS!

[Link: http://streetrx.com/]

The Clean Whiz Kit

In keeping with the theme...

• Common Misconceptions in Prescribing Opioids for Chronic Pain  
  – There is an agreed upon morphine daily equivalent  
  – An opioid is an opioid is an opioid  
  – Dialysis & Cancer patients earned a free pass  
  – Anuric patients can’t (or shouldn’t be) monitored  
  – Results of all urine drug tests are gospel  
  • Results of certain UDT ARE gospel
Variability in Opioid Equivalence Survey

- Sept 13 thru Dec 31, 2013, 411 Respondents
- RPhs, MD/DOs, NPs, PAs
- Convert to Daily MEQ:
  - Hydrocodone 80mg; Fentanyl 75mcg/hr;
  - Methadone 40mg; Oxycodone 120mg;
  - Hydromorphone 48mg

What do you think were the most outrageous conversions?

<table>
<thead>
<tr>
<th>Medication</th>
<th>Fentanyl</th>
<th>Hydromorphone</th>
<th>Methadone</th>
<th>Oxycodone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Late dose</td>
<td>130.37 mg</td>
<td>8.8 x 17.0 mg</td>
<td>308.37 mg</td>
<td>203.04 mg</td>
</tr>
<tr>
<td>Early dose</td>
<td>160.37 mg</td>
<td>10.8 x 18.0 mg</td>
<td>338.37 mg</td>
<td>228.04 mg</td>
</tr>
</tbody>
</table>

Urine Drug Testing (UDT) Rationale

- Guidelines recommend UDT as standard of care when prescribing chronic opioid therapy, especially for CNCP
- Helps to ensure compliance and mitigate risk
- Detects presence of illicit substances
- Detects absence of prescribed medication
- Helps to justify continual prescriptions
- Supports clinician decision to discontinue controlled substance medication

Urine Drug Testing (UDT) Rationale

- Supports justification for closer monitoring (more frequent visits / lab monitoring)
- Supports behavior modification and referral to psychologist

Potential Pitfalls

- Patient reliability to report compliance, use and misuse is dubious and often poor
- Behavior alone is unreliable for identifying patients at risk non-compliance, abuse, misuse, and diversion

Types of Urine Drug Testing

<table>
<thead>
<tr>
<th>Immune Assay (IA)</th>
<th>Chromatography</th>
</tr>
</thead>
<tbody>
<tr>
<td>• In office or send out</td>
<td>• Usually send-out</td>
</tr>
<tr>
<td>• Inexpensive</td>
<td>• More expensive</td>
</tr>
<tr>
<td>• Results are quick (minutes)</td>
<td>• 24 hours to 1 week (per lab)</td>
</tr>
<tr>
<td>• Helps for initial detection</td>
<td>• Final result</td>
</tr>
<tr>
<td>• False negatives/positives</td>
<td>• Definitive testing</td>
</tr>
<tr>
<td>• False patient accusations</td>
<td>• Justifies RX decisions</td>
</tr>
<tr>
<td>• Easier for pts to manipulate low sensitivity, esp w/ synthetics</td>
<td>• 99.999 percent reliability high sensitivity</td>
</tr>
<tr>
<td>• Presence/absence of RX class only</td>
<td>• Presence/absence of RX metabolites</td>
</tr>
<tr>
<td>• No option for synthetics, designer drugs, and unique natural products</td>
<td>• Custom option for synthetics, designer drugs, and unique natural products</td>
</tr>
</tbody>
</table>
Opioid Chemistry and Cross-sensitivity

Phenyl-Propylamines

Benzodiazepines

http://www.remitigate.com/resources/
Addressing Unexpected Results

- False or Unexpected Positive
  - Discuss findings with patient
    - Confirm false positive (as a true negative) to support and document patient’s integrity and compliance
  - Confirm unexpected positive to justify
    - ADT products, and other RX adjustments
    - Substance abuse counseling
    - Alternative and other behavior health intervention
- False Negative
  - Confirm false negative (as a true positive) to support and document patient’s integrity and compliance

Select Opioid Analgesic Choices

- Extended Release Products:
  - Buprenorphine Transdermal Patch
  - Transdermal Fentanyl Patch
  - Hydromorphone-ER
  - Morphine-ER (several products available)
  - Oxycodeone-ER
  - Oxymorphone-ER
  - Zohydro-ER (Pernix Pharma)
  - Hysingla ER (Purdue Pharma)
- Synthetic Atypical:
  - Long Biological T1/2 & intermediate analgesic T1/2
    - Levorphanol
    - Methadone
Case Study 1 | Face Pain

- 43 year old Caucasian male
- TMJ and trigeminal neuralgia
- Failed NSAIDs, cartilage implants, nerve blocks, iontophoresis
- Past Medical History (PMH):
  + Hep C, but otherwise inconsequential
- Current pharmacologic regimen includes:
  - Gabapentin (Neurontin®) 1200mg PO TID
  - Hydrocodone ER (Hysingla®) 20mg PO QAM
  - Oxycodone tabs 5mg, 1 PO TID PRN

What do these results mean?

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opiate</td>
<td>Negative</td>
</tr>
<tr>
<td>Gabapentin (Neurontin®) 1200mg PO TID</td>
<td>Positive</td>
</tr>
<tr>
<td>Hydrocodone ER (Hysingla®) 20mg PO QAM</td>
<td>Negative</td>
</tr>
<tr>
<td>Oxycodone tabs 5mg, 1 PO TID PRN</td>
<td>Negative</td>
</tr>
</tbody>
</table>

Case Study 1 | Unexpected Results

Negative for Prescribed Medications
- Lack of oxycodone PRN use
- Pharmacokinetics (when was urine collected?)
- Noncompliance
- Test is not specific for the drug tested (opiate vs. synthetic)
- Drug-drug, drug-disease, drug-food/supplement interactions
- Genetic polymorphism
Case Study 1 | Face Pain

- Speak with patient
- Give patient an opportunity to explain
- Assessment: Document justification for plan
- Devise actionable medical plan based on lab findings
  - Change in drug therapy (Patch, ADF, no opioid)
  - Justification for f/u lab testing
  - Justification for alternative therapies
  - Justification for behavioral health

Case Study 2 | Chronic Back Pain

- 50 year old Caucasian female
- History of chronic low back pain with justifiable pathology
- Back surgery x 3 (failed back)
- PMH: chronic pain, depression, hypothyroidism
- Current pharmacologic regimen includes:
  - Duloxetine (Cymbalta®) 60mg PO QAM
  - Fentanyl (Duragesic®) 50mcg/hr changed Q72 hours
  - Hydrocodone + APAP (Lortab®) 5/325, 1 PO Q4H PRN

---

Case Study 2 | Chronic Back Pain

What do these results mean?

<table>
<thead>
<tr>
<th>IA In-Office Results</th>
<th>Chromatography [send out] Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test</td>
<td>Result</td>
</tr>
<tr>
<td>Opiate</td>
<td>Negative</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>Positive</td>
</tr>
<tr>
<td>Benzoylecgonine (cocaine metabolite)</td>
<td>Positive</td>
</tr>
<tr>
<td>Benzoylecgonine</td>
<td>Positive</td>
</tr>
</tbody>
</table>

Duloxetine (Cymbalta®) 60mg PO QAM
Fentanyl (Duragesic®) 50mcg/hr changed Q72 hours
Hydrocodone + APAP (Lortab®) 5/325, 1 PO Q4H PRN
**Case Study 2 | Unexpected Results**

Negative for Prescribed Medications
Positive for unprescribed and illicits
- Lack of hydrocodone PRN use
- Pharmacokinetics (when was urine collected?)
- Noncompliance (illegally obtained drugs)
- Test is not specific for the drug tested (opiate vs. synthetic, in this case fentanyl)
- Drug-drug, drug-disease, drug-food/supplement interactions
- Genetic polymorphism

---

**Case Study 3 | Lower Chest & Abdominal Pain**

Negative for Prescribed Medications
False Positive for Unprescribed and Illicits
- 33 year old American Indian male
- Lung cancer, now free of disease
- Chronic upper abdominal & chest pain following his original tumor resection and radiation
- PMH: depression
- Current pharmacologic regimen includes:
  - Morphine (Avinza®) 90mg PO QAM
  - Venlafaxine (Effexor®) ER 225mg PO QAM

---

**Case Study 3 | Unexpected Results**

What do these results mean?

<table>
<thead>
<tr>
<th>In-Office Test Results</th>
<th>LC-MS/MS Laboratory Test Results</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Test</strong></td>
<td><strong>Result</strong></td>
</tr>
<tr>
<td>Opiate</td>
<td>Positive</td>
</tr>
<tr>
<td>Phencyclidine (PCP)</td>
<td>Positive</td>
</tr>
<tr>
<td>Morphin (Avinza®) 90mg PO QAM</td>
<td>Positive</td>
</tr>
<tr>
<td>Hydromorphone (PCP)</td>
<td>Positive</td>
</tr>
<tr>
<td>Venlafaxine (Effexor®) ER 225mg PO QAM</td>
<td>Positive</td>
</tr>
</tbody>
</table>
Knowledge of P-Kinetics is Essential

- Morphine Metabolism
  - Phase II Glucuronidation by UGT2B7
    - M3G (morphine-3-glucuronide)
    - M6G (morphine-6-glucuronide)
      - Less than 5% → hydromorphone

Case Study 3 | Unexpected Results

- Patient was compliant with
  - Morphine
  - Venlafaxine
- PCP was false positive because of venlafaxine
- Hydromorphone confirmation unexpected?
  - It is a rare metabolite of morphine
- Educate patient and clearly document in the chart

Case Study 4 | Icing on the Cake

Drugs:
- Butrans 15mg TD Patch, changed Qweek
- Quetiapine 50mg PO QHS
- Alprazolam 0.5mg PO TID
- Ibuprofen 600mg PO TID PRN
Case Study 4 | Unexpected Results

What do these results mean?

<table>
<thead>
<tr>
<th>In-Office Test Results</th>
<th>LC-MS/MS Laboratory Test Results</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Test</strong></td>
<td><strong>Buprenorphine, buprenorphine-</strong></td>
</tr>
<tr>
<td>Opiate</td>
<td><strong>norbuprenorphine, norbuprenorphine-</strong></td>
</tr>
<tr>
<td>Buprenorphine</td>
<td><strong>glucuronide, and norbuprenorphine-</strong></td>
</tr>
<tr>
<td>Benzodiazepine</td>
<td><strong>glucuronide</strong></td>
</tr>
<tr>
<td>Cannabinoid</td>
<td>Positive</td>
</tr>
<tr>
<td>Methadone</td>
<td>Positive</td>
</tr>
</tbody>
</table>

Butrans 15mg TD Patch, changed Q week
Quetiapine 50mg PO QHS
Alprazolam 0.5mg PO TID
Ibuprofen 600mg PO TID PRN

Case Study 4 | What does it mean?

- Buprenorphine is a POTENT synthetic opioid and will not test positive for IA opiate screen at most buprenorphine TD doses
- Positive “opiate” screen would indicate that the patient was using another unprescribed drug
- Alprazolam generally will not test positive on an IA test
- Alprazolam and buprenorphine were confirmed by definitive test results
- Quetiapine may cause false positive methadone
- Ibuprofen may cause false positive cannabinoid

SOFTWARE HELP TO INTERPRET UDT

11/27/2015
How does this affect you?

Accurately found taking...
- more drug than prescribed
- an old prescription drug
- someone else's prescription
- an illicit drug

Falsely accused of taking...
- unprescribed drug
- not taking prescribed drug
- taking illicit drugs

Definitive Chromatography test may be warranted

References