Patient-Centered Urine Drug Testing

Douglas Gourlay, MD, MSc, FRCPC, FASAM
Declaration of Potential Conflict of Interest

- The content of this presentation is non-commercial and does not represent any conflict of interest.
Objectives

- Describe a patient-centered approach to urine drug testing (UDT)
  - Explain the differences between the clinical vs workplace/forensic test pool
- Express the importance of “testing strategy” in the clinical use of UDT
  - List common myths / misconceptions of urine drug testing analysis
- Summary
Why Do We Test?

- Forensics
- Treatment compliance / concurrent drug use
- Advocacy
  - With 3rd party, motivate/support behavioral change, identify abuse/addiction:
    Avoid “gotcha” syndrome
- Risk management
Non-Clinical vs Clinical Testing

- In non-clinical testing, the majority of donors are expected to be non-users
  - Thresholds are set based on donor characteristics NOT lab capabilities
  - “-ve test results *can* harm the donor”
- In pain practices this is NOT the case
  - Majority of donors *are* user of common drugs of misuse
    - Difference is they’re *legitimately* +ve
What’s Worse Than Not Doing UDT?

- Doing UDT inappropriately
  - Clinicians (and lab directors) must resist the urge to reach beyond the scientific AND clinical limits of the test
- Using ‘clinical’ test strategies for ‘forensic’ purposes
  - Agreeing to monitor for CPS / drug court
  - This is a dangerous practice
When to Test

- Consider urine drug testing (UDT) in all patients
  - Especially those starting opioid therapy
  - When making major changes in therapy
  - In response to aberrant behavior

- Testing frequency
  - Low risk: initially and yearly if no problems?
  - High risk: weekly? Monthly if stable?

- Medical Necessity

- Cheap, effective, and well tolerated by pts
  - Only patients ‘philosophically opposed’ to UDT are those patients with problems who don’t want help
How to Test

- There is no ‘right or wrong’ way to test
  - Laboratory testing
  - Point-of-care (‘test strips’)
- Never do a test you don’t know how to interpret the results
  - You must have a testing strategy
  - Need an action plan to deal with results
Testing Strategies

- Routine vs random testing
  - Random more reliable, more complex
  - Routine easier to ‘prepare’ for

- Reliability
  - Witnessed require same-sex observers
  - Can use temperature strips

- How to use the results
  - Avoid “gotcha” syndrome
Testing Techniques

- Screens
  - Immunoassay (EMIT)

- Confirmations (Identification)
  - GC/MS, LC/MS etc

- Point-of-care testing (’test strips’)
  - Immunoassay
Adulteration, Substitution, Volume Loading

- People do cheat!
- Witnessed vs unwitnessed collection
- Temperature monitoring
  - Min volume, time, within 1°C body temp
- pH, creatinine, “urine fingerprinting”
- Volume loading
  - Deliberately ingest H₂O to lower SG, Cr
    - Cr<1.8mmol/L AND SG<1.003 = suspicion
Drugs of Abuse

- NIDA-5 (aka “Federal Five”)
  - Cocaine
  - Opiates
  - THC
  - Amphetamines
  - PCP

- Benzodiazepines, barbiturates, methadone, etc
Cocaine

- Screen for metabolite, benzoylcegonine (BEG) NOT cocaine
- Metabolite $t_\frac{1}{2} >>$ parent $t_\frac{1}{2}$
- $H_2O$ soluble $\therefore$ does not accumulate
- Detectable at 300ng/mL for 3-5 day
- Cocaine (parent via HPLC) implies very recent drug use ie hours
Opiates

- Really codeine/morphine
  - Cross reacts with many other opioids
- Threshold varies – DOT 2000ng/mL; typically 300ng/mL (total opioids)
- Heroin use confirmed by 6-AM (6-MAM)
  - t½ short makes detection difficult
  - Never detect heroin parent*
  - Can’t distinguish morphine from heroin/morphine/codeine metabolism
# Opioids 101

<table>
<thead>
<tr>
<th>Natural</th>
<th>Semi-Synthetic</th>
<th>Synthetic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Codeine</td>
<td>Hydrocodone</td>
<td>Meperidine</td>
</tr>
<tr>
<td>Morphine</td>
<td>Hydromorphone</td>
<td>Fentanyl (Sufenta, Alfenta, Remifentanil)</td>
</tr>
<tr>
<td></td>
<td>Diacetyl Morphine</td>
<td></td>
</tr>
<tr>
<td>Thebaine</td>
<td>Oxycodone, Oxymorphone, Buprenorphine, Naltrexone, Naloxone</td>
<td>Methadone, Propoxyphene</td>
</tr>
</tbody>
</table>
THC

- Screen looks for all cannabinoids
- Variable cut-offs (50ng/mL / 15ng/mL)
- Fat soluble
- GC/MS looks only at THC-COOH
- Infrequent users detect for <3d
- Frequent, heavy users >7d (20ng/mL 77 days positive)
Amphetamines

- EMIT screens triggered with decongestants, antihistamines
- May react to MDMA (Ecstasy), MDA etc
- Many prescription and OTC drugs give false positive EMIT screens
- Cut-off 1000ng/mL, confirms 500ng/mL
- “Vicks Nasal Inhaler” dilemma (USA)
- Typically detectable for <3 d
PCP

- Phencyclidine (also reacts with ketamine)
- Low yield except with specific patient populations *in certain areas*
- Cut-off of 25ng/mL
- Detectable for < 7d
Other Drugs

- **Specific opioids**
  - Hydromorphone – may need to ask lab for assistance
  - Oxycodone – needs specific assay
  - Hydrocodone
  - Buprenorphine (immunoassay-expensive)
  - Methadone/fentanyl do NOT yield +ve ‘opiate’ screens

- **Benzodiazepines**
  - Difficult to reliably detect, especially clonazepam even when abused – check with lab regarding sensitivity
Poppy Seeds

- Poppy seeds don’t give false positives
  - They lead to TRUE positives
  - Can exceed DOT cutoffs for several hours
  - May show both morphine and codeine
  - NEVER accounts for 6-MAM

- People on UDT programs should not eat poppy seeds
Passive Marijuana

- ‘Incidental’ exposure does not lead to +ve UDT
- Depends on cut off concentration
- Can not easily distinguish prescribed oral THC from smoked marijuana
- Single use does not lead to persistent +ve results
Passive Cocaine

- Nasal cocaine (cocaine HCl) can not be put in cigarette to give positive result
  - Crack cocaine can lead to positive result
- Cocaine base sublimates when heated.
  - Found on many surfaces where crack cocaine is used
  - $20 bills frequently test positive for cocaine
- Medical uses result in positive results
  - ENT, ophthalmology, plastic surgery
Opioid Metabolism

- **Codeine** ➔ **Morphine** ➔ **6-MAM** ➔ **Heroin**
  - Morphine-X-Glucuronides (Not detected with HPLC but detected with GC/MS)
  - **(Detected <12h)**
  - **(Not detected)**
Drug Testing Traps

- **codeine**
  - >89%
- **morphine**
  - >97%
- **norhydrocodone**
- **hydrocodone**
- **Hydrocodone**
  - <11%
- **Hydromorphone**
  - <3%

Baselt RC. *Disposition of Toxic Drugs and Chemicals in Man.* 7th ed 2004

* Identification of Hydrocodone in Human Urine Following Controlled Codeine Administration, JM Oyler et al. *Journal of Analytical Toxicology* 24(7) 2000 p530-535

** Evidence of Morphine Metabolism to hydromorphone in pain patients chronically treated with morphine, E Cone et al, *Journal of Analytical Toxicology* 30(1) 2006 p1-5
# Test Interpretation (GC/MS)

<table>
<thead>
<tr>
<th>Test</th>
<th>Codeine</th>
<th>Morphine</th>
<th>6-MAM</th>
<th>Drug (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td>+</td>
<td></td>
<td>M/H&gt;12h</td>
</tr>
<tr>
<td>2</td>
<td>+</td>
<td>+</td>
<td></td>
<td>C/M+C/H&gt;12h</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>+</td>
<td>+</td>
<td>H&lt;12</td>
</tr>
<tr>
<td>4</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>H&lt;12h</td>
</tr>
</tbody>
</table>

M = Morphine  C = Codeine  H = Heroin
New Use?
(Consider Creatinine)

<table>
<thead>
<tr>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
<th>Day 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Test:
- Day 1: +
- Day 2: -
- Day 3: +
- Day 4: -
- Day 5: -

Result:
- Threshold (Cut-off)
- CR decrease
- CR increase

Graph:
- Drug levels from 301 to 298
- Test results at days 1 to 5
- Threshold line at 300
What to Do With Unexpected Results?

- First, call the lab
  - If unexpected +ve, check for legitimate reasons for true positives
    - ENT cocaine for epistaxis
    - Morphine in codeine user
    - Hydrocodone in codeine user (~11% or less)
  - If unexpected –ve, check for test sensitivity, subthreshold results, dilute sample, lab error

- Speak with patient
  - Ask about ALL drug use including OTC and time of last use
    - When truly negative, look for bingeing (ie running out)

- Never ignore an aberrant result!
Test Interpretation Traps
Urinary Levels

- Urinary drug and drug metabolite excretion are a function of many factors which may not be static
  - Volumes of distribution, urinary pH, state of hydration, time of last dose, GI absorption effects etc
  - It is unwise to draw any conclusions based solely or largely on urinary analyte concentrations
  - Drug testing is the beginning not the end of discussion – use ‘social engineering’ to solve the problem
Using the Results
(it’s all in the strategy)

- First, do the results “fit”?  
  - If yes, could they be ‘hiding’ an abnormal result? i.e. +ve opiates / +ve bzd  
    - Beware of the expected analyte

- Compliance testing  
  - What does the –ve mean?  
    - Have a diff Dx for the unexpected result

- Can you interpret the results?  
  - Ask before collecting sample  
    - New meds? New OTC drugs? Recreational use?
Approaching the Patient

- “Offer” drug testing to the patient
  - Majority of patients will have no problems with UDT
    - If patient is ‘philosophically opposed’ to UDT, bodes poorly for this patient
    - Remind patient that this will severely limit the pharmacologic choices for treating their pain
  - Reassure the patient that UDT is part of a comprehensive risk management strategy
Case Discussion

- **Case I**
  - “Opiate +ve, no opiate seen” with patient on Cipro
  - Is this a false positive d/t the antibiotic?
    - +/- sub threshold opioid use?

- **Case II**
  - “Cocaine +ve UDT in patient who recently had dental surgery”
  - Possible explanations?

- **Case III**
  - “Strongly +ve methadone parent, no EDDP seen”
  - Possible explanations?

- **Case IV**
  - “EDDP +ve, no parent seen” — possibilities?
Conclusions

- UDT, when done with respect and sensitivity can be an important part of a comprehensive care plan for all, not only high risk patients that
  - Reduces patient stigma
  - Improves patient care
  - And hopefully, reduces risk

- The clinical context is essential for proper UDT interpretation
  - Risk management is FOR the patient
Resources

- http://drug-interactions.com
- http://www.emergingsolutionsinpain.com
- http://www.quantiaMD.com
  — Pain and Addiction Series
  — For UDT monograph
- dgourlay@cogeco.ca