UVM ECHO Chronic Pain: Urine Drug Testing

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CME disclosures

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Objectives

• Review & context
• Identify the “why, who, when, what and how” of urine drug monitoring in chronic pain
• Emerging strategies/advancements
• Summary & take-aways
Review & Context
Chronic Disease Model

Category 1: Healthy/well (44%)
Category 2: Early Onset/ Stable Chronic illness (40%)
Category 3: Chronic illness & Rising Risk (10%)
Category 4: Complex/High cost care (6%)
Chronic Disease Model for OUD

**Category 1**
Healthy/well

**Category 2**
Early Onset/ Stable Chronic illness
Aberrant behavior/Misuse

**Category 3**
Chronic illness & Rising Risk
Opioid Use Disorder

**Category 4**
Complex/High cost care
Overdose/sequelae

**Unexposed**

**Exposed**
At risk

At risk

Exposed
OUD Disease Progression Risks

Category 1
Healthy/well

Category 2
Early Onset/Stable Chronic illness

Category 3
Chronic illness & Rising Risk
Opioid Use Disorder

Category 4
Complex/High cost care
Overdose/sequelae

Unexposed
At risk
Exposed

25%
10%

Focus of today

Category 1
Healthy/well
Unexposed
At risk
Exposed

Category 2
Early Onset/
Stable Chronic illness

Category 3
Chronic illness & Rising Risk
Opioid Use Disorder

Category 4
Complex/High cost care
Overdose/sequelae

Risk Mitigation Strategies

Tools in a toolbox

- Treatment agreements
- Frequent office visits
- Prescription Drug Monitoring Programs (PDMPs)
- Current Opioid Misuse Measure (COMM)
- Pill counts (optional)
- Urine drug monitoring

Adapted from R. Pinckney, Project ECHO 2018
Evidence Basis

“No study evaluated the effectiveness of risk mitigation strategies ... for improving outcomes related to overdose, addiction, abuse, or misuse.”

-CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016

Increasing but inconsistent use of risk mitigation strategies

- Cumbersome (e.g., use of PDMPs)
- Testing is difficult to interpret
- Resource allocation: Combined lab-based screening and confirmation testing ~ $175 for VT Medicaid
Increased Use of Risk Mitigation Strategies

Due to:

1. Prominent guidelines including:
   - CDC
   - AACC
   - APS

2. Provider-directed educational initiatives
3. State regulations
4. Adoption of “universal precautions” for pain patients
Rule Governing The Prescribing of Opioids for Pain
Final Adopted Rule 3/19
UDT as Risk Mitigation Strategy

1) At initiation of Opioids
   • “[Treatment agreement] shall include other requirements as determined by the prescriber, such as directly observed urine drug testing and pill counts”

2) Prior to prescribing >90 MME/day of Opioids
   • “Review of the patient’s Controlled Substance Treatment Agreement and Informed Consent, making any necessary revisions, including pill counts and directly observed urine testing to monitor adherence and possible use of other substances”

3) Prescribing Extended Release Formulations without Abuse Deterrents
   • “Agreement must include functional goals for treatment, dispensing pharmacy choice, safe storage and disposal of medication, and urine testing”
What guidelines do and don’t do

<table>
<thead>
<tr>
<th>What they agree on</th>
<th>What they don’t agree on</th>
</tr>
</thead>
<tbody>
<tr>
<td>The value of testing</td>
<td>Test frequency</td>
</tr>
<tr>
<td>The utility of urine</td>
<td>Testing strategy vs. another</td>
</tr>
<tr>
<td>Utility of randomization</td>
<td>Test menu</td>
</tr>
</tbody>
</table>

General value | The Specifics
The why, who, when, what and how of testing

A summation of guidelines and consensus opinions*

* Field in flux
Why: Unexpected test findings in chronic pain

- Self-report of drug use in chronic pain may be a unreliable predictor
- Clinician predictions of testing is not always accurate
- Rate of aberrant testing may be high

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients with chronic pain who are taking opioid medications with aberrant UDT results.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cook RF, 1995 (36)</td>
<td>50%</td>
</tr>
<tr>
<td>Fishbain DA, 1999 (37)</td>
<td>46.5%</td>
</tr>
<tr>
<td>Hariharin J, 2007 (38)</td>
<td>38%</td>
</tr>
<tr>
<td>Ives TJ, 2006 (39)</td>
<td>32%</td>
</tr>
<tr>
<td>Berndt S, 1993 (35)</td>
<td>32%</td>
</tr>
<tr>
<td>Katz NP, 2003 (12)</td>
<td>29%</td>
</tr>
<tr>
<td>Michna E, 2007 (8)</td>
<td>45%</td>
</tr>
<tr>
<td>West R, 2010 (40)</td>
<td>9-33%</td>
</tr>
<tr>
<td>Manchikanti L, 2006 (18)</td>
<td>16%</td>
</tr>
</tbody>
</table>
Why testing?

Perceived value in:

- Risk mitigation strategies
- Occasional disconnect of subjective assessment with objective measure

<table>
<thead>
<tr>
<th>Primary Indications</th>
<th>Secondary Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Confirm prescriptions</td>
<td>1. Improve patient safety</td>
</tr>
<tr>
<td>2. Support SUD treatment referral</td>
<td>2. Support tapering or discontinuation of opioids</td>
</tr>
<tr>
<td>3. Indicate need for increased visits/evaluation</td>
<td>3. Guide use of naloxone</td>
</tr>
<tr>
<td>4. Identify other substances:</td>
<td></td>
</tr>
<tr>
<td>a) Co-use of respiratory depressants</td>
<td></td>
</tr>
<tr>
<td>b) Illicit/nonprescribed psychoactive meds</td>
<td></td>
</tr>
</tbody>
</table>

*Fundamentally, it is to identify disease progression in an exposed population.*
Who and when of testing?

- Baseline at initiation of any opioid therapy
- At least annually for all patients on opioids
- Higher risk patients will likely require more testing

Risk stratification:

<table>
<thead>
<tr>
<th>Level</th>
<th># Tests/Year</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>0.5 to 2</td>
<td>1, 2, 3, 4</td>
</tr>
<tr>
<td>Medium</td>
<td>1 to 3</td>
<td>2, 3, 4</td>
</tr>
<tr>
<td>High</td>
<td>2 to 4 or every month, office visit or every drug refill</td>
<td>2, 3, 4</td>
</tr>
<tr>
<td>Aberrant behavior</td>
<td>At each visit</td>
<td>3</td>
</tr>
</tbody>
</table>

References:
1. CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016;
4. Pain Physician Opioid Special Issue 2017; 20:S3-S92
## What testing?

<table>
<thead>
<tr>
<th>Opioids</th>
<th>Benzodiazepines</th>
<th>Stimulants</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine(^1,2)</td>
<td>Nordiazepam(^1,2)</td>
<td>Amphetamine(^1,2)</td>
<td>Ethanol (EtG) (^1,2)</td>
</tr>
<tr>
<td>Codeine(^1,2)</td>
<td>Oxazepam(^1,2)</td>
<td>Methamphetamine(^1,2)</td>
<td>Carisoprodol(^1)</td>
</tr>
<tr>
<td>Fentanyl(^1,2)</td>
<td>Temazepam(^1,2)</td>
<td>Methylphenidate(^1)</td>
<td>THC(^1,2)</td>
</tr>
<tr>
<td>Oxycodone(^1,2)</td>
<td>Alprazolam(^1,2)</td>
<td>Cocaine(^1,2)</td>
<td>Gabapentin</td>
</tr>
<tr>
<td>Oxymorphone(^1,2)</td>
<td>Lorazepam(^1,2)</td>
<td>MDMA(^1)</td>
<td>Phencyclidine(^1)</td>
</tr>
<tr>
<td>Hydrocodone(^1,2)</td>
<td>Clonazepam(^1,2)</td>
<td></td>
<td>Barbiturates(^1,2)</td>
</tr>
<tr>
<td>Hydromorphone(^1,2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6-AM (heroin)(^1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tramadol(^1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tapentadol(^1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methadone(^1,2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Buprenorphine(^1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Propoxyphene(^1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meperidine(^1)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Prevalence argues against routine testing

Prevalence argues consideration

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(1) Pain Physician 2012; 15:ES119-ES133

How to test?

Most common body fluid used: Urine

**Pro's**
- Easy access
- Long window of detection
- Broad test menus

**Con’s**
- Difficult to establish time since last dose
- Tampering issues arise

- Hair
- Oral Fluids
- Blood
- Urine
Current state: Traditional methods of testing

Aka:
- Screening cups
- Presumptive testing
- Definitive testing

Technique:
- Immunoassay
- Immunoassay
- LCMSMS
## Method Considerations

<table>
<thead>
<tr>
<th>Method Considerations</th>
<th>POCT</th>
<th>EIA</th>
<th>LCMSMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost</td>
<td>🟢</td>
<td>🟠️</td>
<td>🟥</td>
</tr>
<tr>
<td>Speed</td>
<td>🟢</td>
<td>🟠️</td>
<td>🟥</td>
</tr>
<tr>
<td>Accessibility</td>
<td>🟢</td>
<td>🟠️</td>
<td>🟥</td>
</tr>
<tr>
<td>Test menu</td>
<td>🟥</td>
<td>🟠️</td>
<td>🟢</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>🟥</td>
<td>🟠️</td>
<td>🟢</td>
</tr>
<tr>
<td>Specificity</td>
<td>🟥</td>
<td>🟠️</td>
<td>🟢</td>
</tr>
</tbody>
</table>
Implicit access, cost vs. quality discussion

Favoring definitive testing

1: False negatives by immunoassay:
   • 50% for cocaine
   • 22% for benzodiazepines

2: False positives by immunoassay:
   • 14% for amphetamines
   • 34% for opioids

Limiting definitive testing

1. Payor limits:
   MassHealth: pays for 1 (screen vs. confirm)
   Inconsistent policies (some require screen)

2. Timeliness of POCT result

3. Cost: Debated: POCT cheaper but overall cost to system is not quantified

## How to test?

<table>
<thead>
<tr>
<th>First step</th>
<th>Next step</th>
<th>Support for strategy; some examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>POCT or EIA</td>
<td></td>
<td>Some payors</td>
</tr>
<tr>
<td>POCT or EIA</td>
<td>Confirmation testing, as needed</td>
<td>CDC, Manchikanti et al., 2011</td>
</tr>
<tr>
<td>Direct to confirmation</td>
<td>-</td>
<td>AAPM, AACC, Melanson et al., 2018</td>
</tr>
</tbody>
</table>

 Melanson JALM 2018 2: 587.
Emerging Strategies & Advancements
Changing the technological paradigm

• “More than 50% of laboratories have adjusted their toxicology testing in response to the opioid crisis”

• 9% laboratories use exclusively MS technology
  • Majority rely on direct to confirmation testing
  • Introduction of MS screening techniques

- 2018 Poll at AACC Annual meeting
<table>
<thead>
<tr>
<th>Method considerations</th>
<th>POCT</th>
<th>EIA</th>
<th>LCMSMS</th>
<th>MS Screen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost</td>
<td>![Green Circle]</td>
<td>![Yellow Circle]</td>
<td>![Red Circle]</td>
<td>![Green Circle]</td>
</tr>
<tr>
<td>Speed</td>
<td>![Green Circle]</td>
<td>![Yellow Circle]</td>
<td>![Red Circle]</td>
<td>![Yellow Circle]</td>
</tr>
<tr>
<td>Accessibility</td>
<td>![Green Circle]</td>
<td>![Yellow Circle]</td>
<td>![Red Circle]</td>
<td>![Red Circle]</td>
</tr>
<tr>
<td>Test menu</td>
<td>![Red Circle]</td>
<td>![Yellow Circle]</td>
<td>![Green Circle]</td>
<td>![Green Circle]</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>![Red Circle]</td>
<td>![Yellow Circle]</td>
<td>![Green Circle]</td>
<td>![Green Circle]</td>
</tr>
<tr>
<td>Specificity</td>
<td>![Red Circle]</td>
<td>![Yellow Circle]</td>
<td>![Green Circle]</td>
<td>![Green Circle]</td>
</tr>
</tbody>
</table>
Medication matching

- First introduced to private sector ~2012
- Now beginning to emerge in academic settings
- Rapidly becoming “standard of care” in pain management

Development of consistent/inconsistent reporting

<table>
<thead>
<tr>
<th>Prescription medications</th>
<th>Consistent with reported medications</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Drug B: ABSENT</td>
</tr>
<tr>
<td></td>
<td>Drug C: ABSENT</td>
</tr>
</tbody>
</table>
Specimen “spiking”

- Common for buprenorphine
- Recent anecdotal observations of spiking for opioid treatment

Not currently in literature; however, interested in providers who suspect this behavior. Consideration for future research study.
Summary & Key Take-aways
Summary

• Guidelines are predominantly expert opinion
• Consensus has not fully emerged
• Field is likely to continue to change over next 2-5 years
Other key take-aways

- Randomized collections are preferred
- UDT should be part of “Universal precautions” for Opioid Prescribing
- Office policy on testing should be in place
- Interpreting results is challenging and essential
- When in doubt, consult your laboratory
Sample Questions
Sample Questions

• Opioid metabolites
• Fentanyl testing regulations
• THC second hand smoke
• Poppy seeds
• Benzodiazepine testing
Opioid testing

A 33 year old woman arrives at your office with long-standing back pain. She has been managed on OxyContin for the pain. She also reports taking trazadone regularly for depression. You perform a urine drug screen with the following results:

<table>
<thead>
<tr>
<th>Screening results</th>
<th>Cutoff</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphetamines</td>
<td>500 ng/ml</td>
<td>Negative</td>
</tr>
<tr>
<td>THC</td>
<td>50 ng/ml</td>
<td>Negative</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>100 ng/ml</td>
<td>Negative</td>
</tr>
<tr>
<td>Cocaine metabolite</td>
<td>150 ng/ml</td>
<td>Negative</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>25 ng/ml</td>
<td>Positive</td>
</tr>
<tr>
<td>Opiates</td>
<td>300 ng/ml</td>
<td>Positive</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>5 ng/ml</td>
<td>Positive</td>
</tr>
</tbody>
</table>

• Thoughts?
• What do you do next?
## Opioid testing continued

<table>
<thead>
<tr>
<th>Confirmation Result</th>
<th>Cutoff</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxycodone</td>
<td>25 ng/dl</td>
<td>80 ng/ml; Positive</td>
</tr>
<tr>
<td>Noroxycodone</td>
<td>25 ng/dl</td>
<td>30 ng/ml; Positive</td>
</tr>
<tr>
<td>Oxymorphone</td>
<td>100 ng/ml</td>
<td>70 ng/ml; Positive</td>
</tr>
<tr>
<td>Noroxymorphine</td>
<td>25 ng/ml</td>
<td>40 ng/ml; Positive</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>1 ng/ml</td>
<td>Negative</td>
</tr>
</tbody>
</table>

- Thoughts?
- Is she on more than one opioid?
- What do you think about the fentanyl?
Fentanyl testing regulations

Your office routinely runs point of care testing for “drugs of abuse” testing under a CLIA-waived certificate. You read a recent article in JSAT advocating for the cost-effective strategy of using fentanyl testing strips to support POCT-based fentanyl testing. Since your UDT cup does not contain fentanyl, you have recently acquired fentanyl testing strips.

This follows CLIA-waived standards: Yes or No?
Recent changes in Fentanyl testing

• Up until January 2019: no POCT-based Fentanyl testing

• Now, one POCT testing option is available; however, be aware that it requires a moderate complexity laboratory to run
THC second hand smoke

During your first appointment on Monday morning, a mother of a 17-year old boy brings her son to the clinic. She says her son has been “hanging around” with a “bunch of troublesome boys” for the past few months and she suspects they have been smoking marijuana (THC). Speaking privately to the son, you ask if he has been using THC. He insists that he had been routinely, but stopped about two weeks ago when his mother “got on his case”. He admits to hanging out with his friends Friday night. There were five friends in a car smoking but he promises he didn’t, as he knows his mother has been worried. He is insistent you take a urine sample to prove to his mother he hasn’t been using.

• Thoughts?
• What are likely urine test results?
• Would these differ if they were confirmation vs. immunoassay?
Conditions required for detection of second hand smoke

- POOR VENTILATION
- TESTING <24 HOURS
- HIGHLY SENSITIVE TESTING
Impact of THC retention over time

Select factors that influence THC levels

- **Body size and metabolic rate**
  - THC is lipophilic
  - Increased BMI (Body Mass Index) will prolong THC detection
  - Slow metabolic rate will reduce clearance

- **Amount and regularity of use**

- **Sensitivity of testing**
  - Immunoassay sensitivity: Usually set at 50 ng/ml
  - Confirmation sensitivity: Range 3-15 ng/ml

<table>
<thead>
<tr>
<th>Frequency of use</th>
<th>Detection window (days) at 3 ng/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single use</td>
<td>3 days</td>
</tr>
<tr>
<td>Moderate (4 x/week)</td>
<td>5 days</td>
</tr>
<tr>
<td>Heavy (daily)</td>
<td>10 days</td>
</tr>
<tr>
<td>Chronic heavy use</td>
<td>30 days</td>
</tr>
</tbody>
</table>

You perform a urine drug testing to assess treatment adherence in a 40-year-old female whom you have recently tapered off of chronic opioids. Her results are below. She insists she has been compliant with treatment and has not used heroin or other opioids. She has read that poppy seeds are a possible cause of a positive test and was wondering whether you felt that was possible.

**Screening Results:**
- Opiates: POSITIVE
- 6-AM: NEGATIVE

**Confirmation Results:**
- Codeine: 90 ng/ml
- Morphine: 1000 ng/ml

- Thoughts?
- Is this poppy seed ingestion?
Poppy seeds background

- Poppy seeds develop bathed in opium-rich milky sap.
- Rigorous washing minimizes the presence of opium in the poppy seed.
- Naturally-occurring opiates (morphine and codeine) can therefore be detected with poppy seed consumption.
- Morphine and codeine levels from poppy seeds tend to be low (<2000 ng/ml) but variable.
### Poppy seed misconceptions

**SORT: KEY RECOMMENDATIONS FOR PRACTICE**

<table>
<thead>
<tr>
<th>Clinical recommendation</th>
<th>Evidence rating</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine drug testing can be used to monitor compliance with prescribed therapy and detect the use of nonprescribed and illicit substances, especially opioids, benzodiazepines, and heroin.</td>
<td>C</td>
<td>1</td>
</tr>
<tr>
<td>Immunoassays are subject to false-positive and false-negative results. All positive and any unexpected negative results must be verified by confirmatory testing.</td>
<td>C</td>
<td>9</td>
</tr>
<tr>
<td><strong>Casual dietary ingestion of poppy seeds does not cause a positive result for opioids on urine drug testing.</strong></td>
<td>C</td>
<td>22</td>
</tr>
<tr>
<td>Casual exposure to cannabis smoke does not cause a positive result on urine drug testing.</td>
<td>C</td>
<td>23</td>
</tr>
</tbody>
</table>

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afpsort.

---

#### Percentage of Morphin- and Codeine-Positive Urine and OF Specimens by Cutoff Level and Collection Time

<table>
<thead>
<tr>
<th>Urine</th>
<th>Morphine</th>
<th>Codeine</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>300 ng/mL cutoff</td>
<td>2,000 ng/mL cutoff</td>
</tr>
<tr>
<td>Time (h)</td>
<td>Roll</td>
<td>Seeds</td>
</tr>
<tr>
<td>2</td>
<td>83.3</td>
<td>100.0</td>
</tr>
<tr>
<td>4</td>
<td>91.6</td>
<td>100.0</td>
</tr>
<tr>
<td>6</td>
<td>75.0</td>
<td>91.6</td>
</tr>
<tr>
<td>20</td>
<td>50.0</td>
<td>100.0</td>
</tr>
</tbody>
</table>
Benzodiazepine screening

You are managing the care of a 42-year-old man who is being prescribed lorazepam. You perform a POCT in your office and his benzodiazepines are negative. The patient claims they are taking it regularly.

- Thoughts?
- What if this were a lab-based immunoassay screen?
Benzodiazepine immunoassay design

Benzodiazepine immunoassay screen

- Oxazepam
- Temazepam
- Nordiazepam
- Diazepam
- Chlorazepate
- Chlordiazepoxide

Antibody

OXAZEPAM → TEMAZEPAM → NORDIAZEPAM → DIAZEPAM → CHLORAZEPATE → CHLORDIAZEPoxide
Risk points for benzodiazepine immunoassays

Often undetected benzodiazepines by Immunoassay

Oxazepam

- Alprazolam
  - ALPRAZOLAM
  - ALPHA-HYDROXY-ALPRAZOLAM

- Clonazepam
  - 7-AMINO-CLONAZEPAM
  - LORAZEPAM GLUCURONIDE

- Lorazepam

Alprazolam is detected in some assays even though it has a different metabolic pathway.

Imunoassays are improving; POCT lags behind in recent advances.
Reference material
<table>
<thead>
<tr>
<th>Drugs/drug Class</th>
<th>Select examples of cross-reactivities</th>
</tr>
</thead>
</table>
| Cannabinoids     | Efavirenz  
Naproxen  
Ibuprofen  
Riboflavin  
Tolmetin        |
| Opioids          | Diphenhydramine  
Poppy seeds  
Dextromethorphan |
| Amphetamines     | Phenylpropanolamine  
Promethazine  
Thioridazine  
Trazodone  
Trimipramine  
Methylphenidate  
Pseudoephedrine, ephedrine  
Desipramine  
Bupropion  
Propanolol, Labetalol  
Selegline  
Amantadine  
Ranitidine  
Vick’s vapor spray |
| Benzodiazepines  | Oxaprozin  
Quetapine  
Sertraline |

<table>
<thead>
<tr>
<th>Drugs/drug Class</th>
<th>Select examples of cross-reactivities</th>
</tr>
</thead>
</table>
| Buprenorphine    | Sulfamethazole-Trimethoprim  
Codeine  
Tramadol  
Quinine |
| MDMA (ecstasy)   | Bupropion |
| Fentanyl         | Metamphetamine  
Trazodone  
Illicit Fentanyl |
| Tapentadol       | Doxepin  
Imipramine  
Trimipramine  
Tramadol |

For a more complete list, work with your laboratory
Select parent-drug combinations

<table>
<thead>
<tr>
<th>Parent Drug</th>
<th>Metabolite</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heroin</td>
<td>6-AM</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>Norbuprenorphine</td>
</tr>
<tr>
<td>Methadone</td>
<td>EDDP</td>
</tr>
<tr>
<td>Ethanol</td>
<td>EtG/EtS</td>
</tr>
<tr>
<td>Cocaine</td>
<td>Benzoylecgonine</td>
</tr>
<tr>
<td>Methylphenidate</td>
<td>Ritalinic acid</td>
</tr>
</tbody>
</table>
Simplified metabolic pathways: Opioids

- HEROIN
- 6-AM
- CODEINE
- MORPHINE
- HYDRO-CODONE
- HYDRO-MORPHONE
Common metabolic pathways: Benzodiazepines
### Opioid metabolites – a more comprehensive list

<table>
<thead>
<tr>
<th>Opioids</th>
<th>Metabolites</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrocodone</td>
<td>Hydromorphone&lt;br&gt;Dihydrocodeine&lt;br&gt;Normorphine&lt;br&gt;Norhydrocodone&lt;br&gt;Hydrocodol&lt;br&gt;Hydromorphol</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>Oxymorphone&lt;br&gt;Noroxycodeine&lt;br&gt;Oxycodols and their oxides</td>
</tr>
<tr>
<td>Morphine</td>
<td>Hydromorphone (minor)&lt;br&gt;Morphine-3-glucuronide&lt;br&gt;Morphine-6-glucuronide&lt;br&gt;Normorphine</td>
</tr>
<tr>
<td>Methadone</td>
<td>2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine&lt;br&gt;Oxymorphone-3-glucuronide&lt;br&gt;Hydromorphine-3-glucuronide</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>Dihydromorphone&lt;br&gt;Hydromorphone-3-glucuronide</td>
</tr>
<tr>
<td>Oxymorphone</td>
<td>Oxymorphone-3-glucuronide&lt;br&gt;Oxymorphol</td>
</tr>
<tr>
<td>Codeine</td>
<td>Hydrocodone (minor)&lt;br&gt;Norcodeine&lt;br&gt;Morphine</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Opioids</th>
<th>Metabolites</th>
</tr>
</thead>
<tbody>
<tr>
<td>Propoxyphene</td>
<td>Norpropoxyphene</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>Norfentanyl</td>
</tr>
<tr>
<td>Tramadol</td>
<td>O-desmethyl-tramadol&lt;br&gt;Nortramadol</td>
</tr>
<tr>
<td>Butorphanol</td>
<td>Hydroxybutorphanol&lt;br&gt;Norbutorphanol</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>Norbuprenorphine&lt;br&gt;Norbuprenorphine-3-glucuronide&lt;br&gt;Buprenorphine 3-glucuronide</td>
</tr>
<tr>
<td>Heroin</td>
<td>Morphine&lt;br&gt;Codeine (contaminant)&lt;br&gt;6-monoacetylmorphine (6-AM)</td>
</tr>
</tbody>
</table>

Pain Physician 2011; 14:123-14
Why is interpretation so challenging?

Complicated by:

Tests
- False positives and negatives
- Technical language
- Complex metabolism

Patients
- Denied use
- Tampering
- Patient factors

Lack of standardization
- Variable cutoffs/methods

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Prim Care Companion CNS Disord. 2012; 14(4).

Texas study and CDC
Questions
ECHO Reminders

• Volunteers to present cases
  • Use the case presentation form template

• Please complete evaluation forms for each session
  • CME will be processed once session evaluation form is received at UVM

• UVM Project ECHO materials available at www.vtahec.org

• Please contact us with any questions/suggestions
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  • Elizabeth.Cote@uvm.edu
  • ahec@uvm.edu