Advantages & Disadvantages of Drug Testing in Alternative Matrices

Marilyn A. Huestis, Ph.D.
Chief, Chemistry & Drug Metabolism, IRP
National Institute on Drug Abuse
National Institutes of Health

OJP Offender Drug Abuse Monitoring Program
BJS-NIJ Expert Topic Meeting II
Washington, DC August 5, 2010
Chemistry & Drug Metabolism

- Employ chemical & toxicological tools to address human drug abuse
- Our clinical research focuses on behavioral & physiological toxicities of drug use
- Identify & quantify biomarkers of drug use in complex biological matrices
- Correlate with drug’s pharmacodynamic effects
- Provide framework for understanding mechanisms of drug action & toxicity, & for interpreting drug test results in individuals
Drug Effects & Detection Times

- Intoxication
- Impairment
- Under Influence
- Blood
- Oral Fluid
- Urine
- Sweat
- Hair

- Minutes
- Hours
- Days
- Weeks
- Months
- Years
Urine Drug Testing

Advantages

- Sufficient specimen volume
- Known testing accuracy/reliability
- Known analytes & cutoffs to measure
- Extensive clinical studies inform interpretation of results
- Choice of on-site technologies for rapid results
- Easily automated
- Less expensive
Urine Drug Testing

◆ Disadvantages
  ◆ Collection difficult
    ◆ Same gender collection
    ◆ Considered invasion of privacy
    ◆ Donors may be unable to provide specimen (Shy bladder)
  ◆ Ease of adulteration & dilution with chemicals or simply excess water
  ◆ Measure of exposure only
  ◆ Not correlated with pharmacodynamic effects
  ◆ Difficult to differentiate new drug exposure from residual drug excretion
Potential Advantages of Alternate Matrices

- Unique information
- Less invasive collection
- Multiple sampling
- Parent drug
- Greater stability
- Lower disease risk
- Longer detection window for some
- Easier collection, shipment & storage
Oral Fluid (Saliva)
Mean Plasma Methamphetamine & Amphetamine After Single Oral 10 or 20 mg Methamphetamine Dose (N = 5)
Mean Oral Fluid Methamphetamine & Amphetamine After Oral 10 or 20 mg Methamphetamine Dose (N = 5)
Methamphetamine Cmax in Oral Fluid & Plasma

ng/mL

Oral Fluid
Plasma

Low Dose
High Dose
Methamphetamine Detection Times in Oral Fluid & Urine After 10 & 20 mg MAMP

- **Oral fluid (cutoffs 50 Meth/2.5 Amp)**
- **Urine (cutoffs 500Meth/200 Amp)**

---

**Hours**

- **Low Dose**
- **High Dose**
Cocaine

Concentration (ng/mL)

Time (h)

Oral fluid COC - 150 mg/70 kg
Oral fluid COC - 75 mg/70 kg
Plasma COC - 150 mg/kg
Plasma COC - 75 mg/70 kg
Benzoylecgonine

Concentration (ng/mL) vs. Time (h)

- Oral fluid - 75 mg/70 kg BE
- Oral fluid - 150 mg/70 kg BE
- Plasma - 150 mg/70 kg BE
- Plasma - 75 mg/70 kg BE
Controlled Codeine Administration

- Plasma - 60 mg/70 kg (n=16)
- Plasma - 120 mg/70 kg (n=14)
- Oral fluid - 60 mg/70 kg (n=19)
- Oral fluid - 120 mg/70 kg (n=13)

citric acid candy collection
Opiates

- Presley et al FSI 2003
  - Tested 77,218 workplace oral fluid specimens
  - 66.7% of opiate positive tests positive for 6AM
  - 6AM stabilized in acidic pH oral fluid
  - Mean morphine 755 ± 201 ng/mL, 6AM 416 ± 148 ng/mL, codeine 196 ± 36 ng/mL
- Finding heroin, 6AM, &/or acetylcodine identifies heroin usage

- Rohrig & Moore JAT 2003
  - Eating poppy seeds & morphine-containing foodstuffs produced positive oral fluid morphine at 40 ng/mL for ~ 1 h
Oral Fluid & Plasma THC & Urine THCCOOH After Smoking a 3.55 % THC Cigarette

ng/mL or ng/mg

0 1 10 100 1000 10000

0.01 0.1 1 10 100

Oral Fluid
Plasma
THCCOOH/CR

Hours
0 1 10 100
Oral Fluid Testing

◆ Strengths:
  ◆ Observed, non-invasive collection
  ◆ More difficult to adulterate
  ◆ Gender neutral specimen collection
  ◆ Basic drugs concentrate in lower pH of oral fluid as compared to blood
  ◆ May correlate with plasma concentrations
  ◆ Reflects more recent drug use (cutoff dependent)
  ◆ On-site technology being developed
Oral Fluid Testing

- Limitations:
  - Specimen volume
    - Generally low, especially after stimulant use
    - Many devices have Unknown volume collected
  - Drug adsorption to collection device
  - Elution buffer
    - Differential drug recovery
    - Dilutes oral fluid reducing sensitivity
    - May interfere with LCMS techniques
  - Potential for passive contamination from smoked & oral drugs
Sweat Testing
Cocaine Secretion in PharmChek Sweat Patches

N = 7

ng/patch ± SEM
cutoff

Days
0-6 6-13 13-20 20-28 28-34 34-42 42-48 48-55 55-62 62-68

75 mg/70 kg COC HCl 150 mg/70 kg COC HCl

No drug detected No drug detected No drug detected

0 20 40 60 80 100 120 140 160 180

34-42 42-48 28-34 0-6 6-13 13-20
Variable Cocaine Concentrations in Sweat

75 mg/70 kg cocaine (days 20, 22, 24)

150 mg/70 kg cocaine (days 48, 50, 52)
78% Opiate Positive Sweat Patches After Heroin Self-Administration Positive for Heroin &/or 6-AM

- Heroin (H)
- 6-Acetylmorphine (6-AM)
- Morphine (M)
- Codeine (C)

**N = 369**
Cannabinoids in Sweat

- **Sweat**
  - THC present at low ng/patch concentrations
  - Extraction efficiency low from patch
  - Unknown drug reabsorption through skin
  - Almost no controlled drug administration data
    - After oral 14.8 mg THC per day for 5 days, no positive sweat patches
THC sweat excretion in 11 heavy cannabis users during abstinence with 24 h monitoring

Dashed line indicates 1.0 ng/patch cutoff proposed by SAMHSA

* Negative sweat patch at LOQ of 0.4 ng/patch.
Sweat Testing

- Advantages
  - Convenient & less invasive method for monitoring drug use
  - Window of detection $\geq$ urine testing (dependent upon drug class)
  - Cumulative measure of exposure
  - Presence of parent drug (heroin, 6AM)
  - Difficult to adulterate specimen
Sweat Testing

- Disadvantages
  - Variation in sweat production
  - Low analyte concentrations
  - Occasional skin sensitivity
  - Dose-response relationships?
  - Residual excretion of drug?
  - Contamination during handling?
Hair
Multiple Sources of Drugs in Hair

External contamination

Skin
Sebum
Sweat
Blood
Unanswered Questions

- Color bias: melanin content affects drug deposition?
- Dose-concentration relationships?
- Minimum dose for drug detection?
- Are externally applied drugs removed by washing?
- Does segmental analysis reflect drug use history?
- Are there specific biomarkers that eliminate concern about external contamination of hair?
  - Cocaethylene, norcocaine, benzoylecgonine (BE), BE/cocaine ratio
  - Recent evidence that these biomarkers present in both US Pharmacopeia & street cocaine
# D5Cocaine Time Course in Human Hair

**Dose:** 749.5 mg IN

<table>
<thead>
<tr>
<th>Months post dose</th>
<th>Root</th>
<th>Hair shaft</th>
<th>Tip</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.7</td>
<td>0.18</td>
<td>0.54 0.16</td>
<td></td>
</tr>
<tr>
<td>3.5</td>
<td>0.17</td>
<td>0.92 0.11</td>
<td></td>
</tr>
<tr>
<td>4.7</td>
<td>0.34</td>
<td>0.18</td>
<td></td>
</tr>
<tr>
<td>5.7</td>
<td>0.22</td>
<td>0.22</td>
<td></td>
</tr>
<tr>
<td>6.7</td>
<td>0.25</td>
<td>0.44</td>
<td></td>
</tr>
</tbody>
</table>

*Months post dose (cm)*

*Courtesy: Henderson & Harkey, "Hair Analysis of Drugs of Abuse", Final Report, 1993*
In Vitro vs In Vivo
Codeine Incorporation Into Rat Hair

In Vitro
- SD White
- DA Brown
- LE Black

In Vivo
- SD White
- DA Brown
- LE Black

dpm/mg

ng/mg
Cannabinoids in Hair

- **Non-daily cannabis users (N = 33)**
  - (1 - 5 joints or blunts per week)
  - 30% cannabinoid screen pos ≥ 5 pg/mg
  - 72.7% THC ≥ 1 pg/mg
  - 80% THCCOOH ≥ 0.1 pg/mg

- **Daily cannabis users (N = 20)**
  - 65% cannabinoid screen pos ≥ 5 pg/mg
  - 60% THC ≥ 1 pg/mg
  - 80% THCCOOH ≥ 0.1 pg/mg
Cannabinoids in Hair

- Hair
  - Least sensitive matrix for cannabis detection
  - Almost no controlled drug administration data
  - Potential for contamination from cannabis smoke requires measurement of THCCOOH by tandem mass spectrometry
Advantages of Hair Testing

- Large window of drug detection
- Brief periods of abstinence will not alter test outcome
- Hair is easy to collect, handle & store
- Collection less invasive than urine collection
- Retesting can be accomplished
- Adulteration of hair test may be more difficult or more apparent
Disadvantages of Hair Testing

- Hair melanin concentration affects drug incorporation of basic drugs (color bias?)
- Poor incorporation of neutral & acidic drugs: low concentrations (pg/mg)
- Possibility of environmental contamination from smoked drugs
- Recent drug use not detected
- Expensive, frequently requires tandem mass spectrometry, highly trained analysts
- Few controlled studies to guide interpretation
Quest Diagnostics Drug Testing Index
Data To Be Released After August 20
Represent >500,000 tests in 2009
## % Positive Opiates Workplace Testing
### Pre-employment

<table>
<thead>
<tr>
<th></th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
</tr>
</thead>
<tbody>
<tr>
<td>COD</td>
<td>0.22</td>
<td>0.19</td>
<td>0.16</td>
<td>0.19</td>
<td>0.18</td>
</tr>
<tr>
<td>MOR</td>
<td>0.34</td>
<td>0.30</td>
<td>0.29</td>
<td>0.31</td>
<td>0.32</td>
</tr>
<tr>
<td>HC</td>
<td>0.69</td>
<td>0.70</td>
<td>0.79</td>
<td>0.78</td>
<td>0.78</td>
</tr>
<tr>
<td>HM</td>
<td>0.37</td>
<td>0.38</td>
<td>0.48</td>
<td>0.50</td>
<td>0.47</td>
</tr>
<tr>
<td>OXYC</td>
<td>0.56</td>
<td>0.64</td>
<td>0.88</td>
<td>0.83</td>
<td>1.00</td>
</tr>
<tr>
<td></td>
<td>2005</td>
<td>2006</td>
<td>2007</td>
<td>2008</td>
<td>2009</td>
</tr>
<tr>
<td>--------</td>
<td>-------</td>
<td>-------</td>
<td>-------</td>
<td>-------</td>
<td>-------</td>
</tr>
<tr>
<td>COD</td>
<td>0.36</td>
<td>0.31</td>
<td>0.30</td>
<td>0.34</td>
<td>0.46</td>
</tr>
<tr>
<td>MOR</td>
<td>1.0</td>
<td>0.90</td>
<td>1.0</td>
<td>1.2</td>
<td>1.2</td>
</tr>
<tr>
<td>HC</td>
<td>2.3</td>
<td>2.1</td>
<td>2.9</td>
<td>3.2</td>
<td>3.7</td>
</tr>
<tr>
<td>HM</td>
<td>1.2</td>
<td>1.2</td>
<td>1.8</td>
<td>2.2</td>
<td>2.3</td>
</tr>
</tbody>
</table>
Acknowledgements

- Participants & their families
- Clinical staff
- CDM Staff
  - Karl Scheidweiler, PhD
  - Allan Barnes, BS
  - Dave Darwin, BS
  - Tsadik Abraham, MS
  - Robert Goodwin OD, PhD
Acknowledgements

◆ Post Doctoral & Visiting Fellows

◆ Ana de Castro, Ph.D.      Tamsin Kelly, Ph.D.
◆ Takeshi Saito, Ph.D.     Won Kyong Yang, Ph.D.
◆ Stephane Pirnay, Ph.D.   Bruno de Martinis, Ph.D.
◆ Garry Milman, Ph.D.     Marta Concheiro, Ph.D.

◆ Past & Current Doctoral Students

◆ Rich Gustafson, Ph.D.   Riet Dams, Ph.D.
◆ Robin Choo, Ph.D.       Erin Kolbrich Spargo, Ph.D.
◆ Sherri Kacinko, Ph.D.   Gene Schwilke
◆ Erin Karschner          Teresa Gray, M.S.
◆ David Schwope, M.S.     Dayong Lee, M.S.
Acknowledgements

◆ Post Doctoral & Visiting Fellows
  ◆ Ana de Castro, Ph.D.  Tamsin Kelly, Ph.D.
  ◆ Takeshi Saito, Ph.D.  Won Kyong Yang, Ph.D.
  ◆ Stephane Pirnay, Ph.D.  Bruno de Martinis, Ph.D.
  ◆ Garry Milman, Ph.D.  Marta Concheiro, Ph.D.

◆ Doctoral Students
  ◆ Rich Gustafson, Ph.D.  Riet Dams, Ph.D.
  ◆ Robin Choo, Ph.D.  Erin Kolbrich Spargo, Ph.D.
  ◆ Sherri Kacinko, Ph.D.  Gene Schwilke
  ◆ Erin Karschner
  ◆ David Schwope, M.S.  Teresa Gray, M.S.
  ◆ Dayong Lee, M.S.