ORAL FLUID DRUG TESTING

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TESTING FOR DRUGS OF ABUSE

- Tests for impairment/drug-induced effect
  - Blood
  - Saliva
  - Performance

- Tests for recent drug exposure
  - Urine
  - Saliva

- Tests for historical drug exposure
  - Hair
  - Sweat
Why Test Saliva?

- Easily and rapidly obtained
- Minimal invasion of privacy
- Difficult to adulterate
- Short drug detection time provides evidence of recent drug exposure
- Presence of active drug indicates potential for ongoing drug effect at time of testing
Three Glands: Parotid, Submandibular, and Sublingual

Two Types of Secreting Cells:
- Serous cells secrete water fluid containing electrolytes and amylase
- Mucous cells secrete mucins (mucoproteins and mucopolysaccharides)
Phy si ology of oral fluid production

- Saliva flow varies from 0.5 to 1.5 L/day
- Resting flow: 0.1 to 1 mL/min
- Can be stimulated to peak flow of approximately 10 mL/min
ORAL FLUID COLLECTION

- Spitting/swabbing
- Flow stimulated collection
- Saliva collection devices
- Pure parotid saliva collection (aspiration)
DRUG TRANSPORT INTO SALIVA

- Passive diffusion (most drugs)
  - Physiochemical (pKa, liposolubility, molecular weight)
  - Plasma protein binding
  - pH (increases with stimulation)
    Normal pH 5.6 – 7 (up to 7.8)
- Filtration through pores in membrane
INFLUENCE OF pH

Weakly acidic drugs – most influence when pKa is less than 8.5 and close to pH of saliva

Butabarbital – pKa 7.9
Butalbital – pKa 7.6
Phenobarbital – pKa 7.2
THC – pKa 9.5
INFLUENCE OF pH

Weakly basic drugs – most influence when pKa is more than 5.5 and close to pH of saliva

Heroin – pKa 7.6
Morphine – pKa 8.1
Oxycodone – pKa 8.5
Cocaine – pKa 8.6
PCP – pKa 8.5
Amphetamines – pKa 9.9
Benzodiazepines – pKa 2-4
Relative concentrations of Drug and Metabolites in Various Matrices
COCAINE Metabolic Profile

- Blood
- Saliva
- Urine
- Sweat
- Hair

COC = Cocaine
BE = Benzoylecgonine
EME = Emetic
CE = Coboic

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HEROIN Metabolic Profile

- Blood
- Saliva
- Urine
- Sweat
- Hair

- Heroin
- 6-MAM
- Morphine
- M-3-G, M-6-G
METHAMPHETAMINE
Metabolic Profile

Blood | Saliva | Urine | Sweat | Hair

- Methamphetamine
- Amphetamine

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CANNABINOIDS
Metabolic Profile

Blood | Saliva | Urine | Sweat | Hair

THC | 11-OH THC | THCA
WINDOW OF DETECTION

- Dose
- Time between doses
- Route of administration
- Matrix
Goal of Study: Determine Effect of Repeated Cocaine Dosing on Detection Times

- Compare detection times for cocaine and benzoylcegonine (BZE) in oral fluid and urine in two groups of subjects
  - **Group 1:** Single dose study (crossover design)
    - Six subjects received single dose of cocaine
      - 25 mg IV
      - 32 mg IN
      - 42 mg SM
  - **Group 2:** Repeated dosing study
    - Six subjects received daily escalating doses of oral cocaine to maximum tolerable doses
    - Reached daily maximum doses of 375 mg to 2000 mg cocaine
    - Specimens collected following last dose

[Analysis by GC-MS (LOD = 1 ng/mL)]
Repeated Cocaine Dosing

A.) Cocaine

B.) BZE

Accumulation and bi-exponential elimination of cocaine contribute to greater increase in oral fluid detection times compared to urine.
Single and Repeated Doses of Cocaine: Detection Times

Error bars = SEM
N=6

X4
X7
X2

Hours

SD OF COC 8: 5.03
RD OF COC 8: 21.33
SD OF BZE 8: 6.78
RD OF BZE 8: 50.00
SD UR BZE 150: 41.36
RD UR BZE 150: 93.73
Conclusions

• Repeated dosing increased oral fluid detection times by factor X4-7 compared to X2 for urine
• Single dose studies underestimate detection times
• Oral fluid detection times will be significantly longer for detection of cocaine abuse in realistic settings where multiple dosing occurs
DETECTION OF MARIJUANA: HOW LONG CAN THC LAST?

- After single use up to 12 to 24 hours
- Data available showing that urine may not be much better
- No data yet on heavy users - Not expected to be as long as urine!
THC ELIMINATION
(Baseline and 4 Hours)

Baseline

Elimination Profiles
(t=4 hours)

THC Concentration Ranges by GC/MS
(ng/mL)

Percentage of Specimens

Oral Fluid

Urine

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THC ELIMINATION
(10 Hours and 24 Hours)

Elimination Profiles
(t=10 hours)

Percentage of Specimens
Oral Fluid
Urine

THC Concentration Ranges by GC/MS
(ng/mL)

Elimination Profiles
(t=24 hours)

Percentage of Specimens
Oral Fluid
Urine

THC Concentration Ranges by GC/MS
(ng/mL)
SERUM VS ORAL FLUID
Saliva/Serum (S/P) Correlation Issues

- Saliva pH due to method of collection
- Remains of orally ingested, smoked or internasally administered drugs
  - Ethanol – 30 minutes
  - Smoked or Internasal – 4-8 hours
S/P Ratios

- **Cocaine** - 3.8 to 0.4 (BE is a zwitterion and not affected by changes in salivary pH)
- **THC** – 0.1 (high protein binding prevents transfer from serum)
- **Opiates** – 3.8 to 0.2
- **Amphetamines** – 4 to 2.6
- **PCP** – 3 to 1.5
- **Barbiturates** – 0.2 to 0.5
- **Benzodiazepines** – 0.02 to 0.5 depending on Benzo
URINE VS ORAL FLUID
Intercept® Collection--OraSure Technologies
Intercept Sample Volume

- Collector contains 800 µL preservative buffer
- Swab collects ~ 400 µL saliva
- Results in 1:3 dilution of saliva
# Positive Rates by Drug

<table>
<thead>
<tr>
<th></th>
<th>2002-2003 Oral Fluid Intercept (n=527K)</th>
<th>January - June 2003 Drug Testing Index - Urine Gen. Workforce (n=2,800K)</th>
<th>Federal (n=600K)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total Positives</strong></td>
<td>4.62%</td>
<td>5.00%</td>
<td>2.50%</td>
</tr>
<tr>
<td><strong>Marijuana</strong></td>
<td>3.08%</td>
<td>3.02%</td>
<td>1.39%</td>
</tr>
<tr>
<td><strong>Cocaine</strong></td>
<td>1.32%</td>
<td>0.74%</td>
<td>0.58%</td>
</tr>
<tr>
<td><strong>Opiates</strong></td>
<td>0.19%</td>
<td>0.34%</td>
<td>0.19%</td>
</tr>
<tr>
<td><strong>Amphetamines</strong></td>
<td>0.47%</td>
<td>0.46%</td>
<td>0.29%</td>
</tr>
<tr>
<td><strong>PCP</strong></td>
<td>0.03%</td>
<td>0.03%</td>
<td>0.04%</td>
</tr>
</tbody>
</table>

## Comparable results for all drug targets

Drug Testing Index courtesy of Quest Diagnostics, Inc., Teterboro, NJ
Urine/Oral Fluid Correlation

- Diluted urines: Dr. Barry sample reported before the Oversight and Investigations Committee that a drug positive specimen is twice as likely to have a creatinine of less than 20 mg/dL.

- Other means of urine adulteration

- Chronic users will be detected longer periods of time
From 2/1/99 to 4/30/99:

- 315,743 Specimens Tested
- 531 Nitrites (0.17%)
- 15 Urinaids (0.01%)
- 129 Pyridine (0.02%)
- 196 Substituted (0.06%)

Total 871 Specimens (0.28%)
and 11,857 (3.8%) Dilute Specimens
THC Passive Studies
Closed Room Study Design

Subjects

- Active smokers: five healthy, male cannabis users
- Passive subjects: four healthy, drug-free males
- Staff members (specimen collections, monitored study)

Conditions: sealed room, 36 m³ (3 m X 4 m X 3 m)

Active users: smoked single cannabis cigarette

- 1.75% THC mixed with tobacco
- Purchased in The Netherlands from a commercial source
- 20 minute smoking period
- 4 hour session

Passive subjects: remained in sealed room for the 4 hour session

- Located approximately 1.5 m from smokers
Closed Room Study Design (cont.)

- **Specimen collection (timed from end of smoking)**
  - Oral fluid (baseline, 0, 15, 45, 75, 105, 135, 165, 195, and 225 min)
  - Urine (baseline, 0, and 225 min)

- **Oral fluid collection with Intercept® DOA Oral Specimen Collection Device**

- **THC oral fluid analysis (OraSure Technologies)**
  - Screened with the Cannabinoids Intercept® MICRO-PLATE Enzyme Immunoassay; cutoff = 3 ng/mL (adjusted for neat concentration)
  - Confirmation by GC-MS-MS; LOD/LOQ = 0.75 ng/mL THC

- **Urine analysis: GC-MS-MS (THCCOOH); LOD/LOQ = 1 ng/mL**
Passive Room Study
(linear scale)

Blue = smokers
Yellow = non-smokers
Red = 2ng/mL DHHS cutoff
Passive Room Study
(log scale)

Blue = smokers
Yellow = non-smokers
Red = 2ng/mL DHHS cutoff
Room Study Summary

**Passive inhalation**
- THC oral fluid concentrations ranged < 0.75 to 26.4 ng/mL
- Present up to 30 min after exposure
- All urine specimens from passive subjects tested negative

**Active smokers**
- THC in oral fluid was X10 to X20 fold higher than passive
- Generally positive throughout 4 hour session
- Urine specimens positive at 4 hours
- Pattern of decline of THC was bi-phasic suggesting oral depot effect for THC
The Van
Motor Vehicle Study Design

Subjects
- Active smokers: four healthy, male cannabis users
- Passive subjects: four healthy, drug-free males
- Staff members (specimen collections, monitored study)

Conditions: Unventilated van, 15.3 m³ (1.7m x 1.8m x 5.0m)

Passive subjects: Each passive subject sat next to a smoker in van

Active users: each smoked single cannabis cigarette
Motor Vehicle Study Design (cont.)

Study I
- 5.4% THC mixed with tobacco (39.5 mg)
- Purchased in The Netherlands from a commercial source
- 20 minute smoking period
- 8 hour session; remained in van for first hour

Study II
- 10.4% THC, no tobacco (83.2 mg)
- Purchased in The Netherlands from a commercial source
- 20 minute smoking period
- 8 hour session; exited van immediately after smoking
Motor Vehicle Study Design (cont.)

- **Specimen collection (timed from end of smoking)**
  - Oral fluid (baseline, 0, 15, 30, 45, 60, 75, 90, 105, 120, 150, 180, 210, 240 minutes, 6 & 8 hours)
  - Urine (baseline, 60, 120, 240 minutes, 6 & 8 hours)

- **Oral fluid collection with Intercept® DOA Oral Specimen Collection Device**

- **THC oral fluid analysis (OraSure Technologies)**
  - Screened with the Cannabinoids Intercept® MICRO-PLATE Enzyme Immunoassay; cutoff = 3 ng/mL (adjusted for neat concentration)
  - Confirmation by GC-MS-MS; LOD/LOQ = 0.75 ng/mL THC

- **Urine analysis: GC-MS-MS (THCCOOH); LOD/LOQ = 1 ng/mL**
Passive Van Study
(linear scale)

Blue = smokers
Yellow = non-smokers
Red = 2ng/mL DHHS Cutoff
Orange = Exposed devices
Passive Van Study
(log scale)

Blue = smokers
Yellow = non-smokers
Red = 2ng/mL DHHS Cutoff
Orange = Exposed devices
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Intercept® Study Comparison

Blue = smokers
Yellow = non-smokers
Red = 2ng/mL DHHS Cutoff
Green = Van Study II

ng/mL THC in Intercept (corrected)

Hours
Van Study Summary

Passive inhalation
- THC oral fluid concentrations ranged < 0.75 to 82 ng/mL when collected inside Van, none exceeded 0.75 ng/mL when collected outside van
- Present up to 30 min after exposure when collected in the presence of smoke, none when subjects removed from smoke during collections
- All urine specimens from passive subjects tested negative

Active smokers
- THC in oral fluid was X10 to X20 fold higher than passive
- Generally positive throughout 8 hour session
- Urine specimens not all positive until 6 and 8 hours
- Pattern of decline of THC was bi-phasic suggesting oral depot effect for THC
Conclusions

- Passive conditions were designed to represent "extreme" exposure conditions
- Initial high levels of THC are rapidly cleared (active)
- Second phase decline of THC after active use suggests formation of "depot" of THC in oral cavity
Conclusions

- Overall, these studies indicate that collection of specimens outside an area of possible smoke contamination is necessary for accurate determination of passive exposure effects on oral fluid testing.

- Absent extreme conditions, passive exposure to marijuana smoke is not a credible explanation for a positive oral fluid test.