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

PHYSIOLOGY OF ORAL FLUID PRODUCTION
- 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)

PHYSIOLOGY 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

- **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

**HEROIN**

Metabolic Profile
Goal of Study: Determine Effect of Repeated Cocaine Dosing on Detection Times

- Compare detection times for cocaine and benzoylecgonine (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)]
**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.
- Elimination Profiles (t=10 hours).
- Elimination Profiles (t=24 hours).
- 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 effected 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**
- 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>Drug Testing Index courtesy of Quest Diagnostics, Inc., Teterboro, NJ</th>
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<tbody>
<tr>
<td><strong>2002-2003</strong></td>
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<tr>
<td>Oral Fluid</td>
</tr>
<tr>
<td>Intercept</td>
</tr>
<tr>
<td>Total Positives</td>
</tr>
<tr>
<td>Marijuana</td>
</tr>
<tr>
<td>Cocaine</td>
</tr>
<tr>
<td>Opiates</td>
</tr>
<tr>
<td>Amphetamines</td>
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<tr>
<td>PCP</td>
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</tbody>
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Comparable results for all drug targets
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

LABONE'S DATA

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

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 m² (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-MSMS (THCCOOH); LOD/LOQ = 1 ng/mL

Passive Room Study

- 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

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
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

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

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

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.