ABC’s of Drug Testing

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Base Knowledge

• Q: If a drug test is positive, can you determine how long ago the drug was taken and over what period of time?
• Q: Is it possible for a heroin addict to test positive for morphine?
• Q: My teenager tests positive for THC but claims exposure to "second hand smoke". Is this possible?
Effects of meth (Before)

Source – Nebraska State Patrol
Effects of meth (After)

Source – Nebraska State Patrol
Urban Legends (Rumors)

and that Some Kentucky Fried Chicken is actually People’s Fingers

and that one of the ingredients of Coca Cola is cocaine.
But the one about the Kentucky Fried Finger actually happened, but it was at Wendy’s and it was a customer’s finger.

And it’s also true that one of the ingredients of Coca Cola used to be cocaine.
Why test for drugs?

• Identify inappropriate drug use

• Guide patient care: identify *in utero* exposures, manage decontamination and withdrawal symptoms, acute social management, long-term rehabilitation efforts, etc.

• Demonstrate abstinence and long-term sobriety
The perfect drug test

Detect all drugs and toxins in any sample and tell you:

- What drug was used
- How much was used
- How long the drug was used
- When it was last taken
- Why it was taken
- Whether the drug or toxin will be found

All for low cost, without a doubt!

"One Size Fits All"
Outline

• Definitions
• Specimen pros and cons
• Common strategies for “beating” the drug test
• Technologies
• Interpretation of results
Definitions

• **Screen**: a qualitative (positive/negative) test; usually designed to detect many drug classes; confidence in results may be poor, but depends on the assay

• **Confirmation**: a test designed for very high confidence in identification of individual drugs/compounds; may be qualitative or quantitative (reports the amount of drug present)

• **Cutoff**: the concentration used to distinguish between a positive and a negative result; defined by the “kit” manufacturer, or by the limit of quantification (LOQ)
Definitions (cont.)

- **Sensitivity**: the minimum concentration that is reliably detected ~ LOD ~ LOQ ~ reporting limit
- **Specificity**: assurance that the results reflect detection of the compound of interest; susceptibility of the test to interferences that could lead to false positive or false negative results
General performance characteristics of testing methods

- **Screen**
  - Easy to perform
  - Cost-effective
  - Specificity and cutoff concentrations vary

- **Confirmations**
  - Technically complex
  - May be expensive; performed by a reference lab
  - Sensitivity and specificity better than screens
  - Cutoffs are generally lower than screens
Specimens

- Breath
- Blood
- Oral Fluid
- Urine
- Sweat
- Hair
- Meconium
- Tissue
- Vitreous
Specimens (cont.)

- Breath
- Blood
- Oral Fluid: Minutes to hours or days
- Urine
- Sweat: Days to weeks
- Hair
- Meconium: Weeks to months
- Tissue
- Vitreous – Postmortem only
Specimens (cont.)

- Blood: Minutes to hours or days
- Urine: Days to weeks
- Hair
- Meconium: Weeks to months
Urine (pros)

- Easy to collect, and plenty of it!
- Many inexpensive testing options available
- Window of detection reasonable to identify regular users
- Inexpensive testing available to analyze
- Federal standardization of cutoffs and drugs detected
Conventional approach

1. Collect, mix and divide between two containers, sealed in the presence of the donor
2. Chain of Custody
3. SCREEN
   - Immunoassay
   - Adulteration, dilution detection
   - Limited panel of drugs
   - Standardized cutoffs to minimize false positives
4. CONFIRMATION
   - Second method, preferably based on mass spectrometry
Drugs covered by the “NIDA-5,” “HHS-5”, “SAMHSA” drug test

• Amphetamines (d-amphetamine)
• Cannabinoids (9-carboxy THC)
• Cocaine (benzoylecgonine)
• Opiates (morphine)
• Phencyclidine (PCP)
Why measure drug metabolites?

• Most drugs are eliminated as metabolites
• Widens opportunity for drug detection
• Provides stronger evidence for drug use than identification of parent alone
• May suggest (alone or via ratios)
  – Use of more than one drug
  – Chronic vs recent use
  – Metabolic variation (inherited or acquired)
### ARUP vs. SAMHSA cutoffs (urine, ng/mL)

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>SAMHSA Screen</th>
<th>ARUP Screen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphets</td>
<td>500</td>
<td>300</td>
</tr>
<tr>
<td>MDMA</td>
<td>500</td>
<td>300</td>
</tr>
<tr>
<td>THC</td>
<td>50</td>
<td>20</td>
</tr>
<tr>
<td>Cocaine</td>
<td>300</td>
<td>150</td>
</tr>
<tr>
<td>Opiates</td>
<td>2000</td>
<td>300</td>
</tr>
<tr>
<td>PCP</td>
<td>25</td>
<td>25</td>
</tr>
</tbody>
</table>
Urine (cons)

- Actual concentrations are of limited value
  - Do not correlate with impairments
  - May or may not identify “new” use
  - Will not identify amount of drug taken

- Easy to adulterate or substitute when collections are not observed, and accidentally
Example of urine concentration on THC concentrations and interpretation

Sample 1:
- THC: 728 ng/mL
- creatinine: 200 mg/dL

\[
\text{THC} \times \frac{100}{\text{creatinine}} = \text{364 ng THC per gram of creatinine}
\]

Sample 2:
- THC: 374 ng/mL
- creatinine: 50 mg/dL

\[
\text{THC} \times \frac{100}{\text{creatinine}} = \text{748 ng THC per gram of creatinine}
\]
Strategies for “beating” the test

• Over-hydration
  ▫ Creatinine
  ▫ Specific gravity

• Substitution
  ▫ Synthetic urine
  ▫ Catheterization

• Additives
  ▫ Sodium chloride, Bleach, Soap, Drano, Lemon juice, Nitrites (Urine Luck), Vitamin C, Visine eyedrops, Glutaraldehyde, Peroxidase (Stealth)
Blood for drug testing (pro)

- Best specimen for correlation of clinical signs and symptoms (impairment) with drug use
- Can be useful to qualify an acute intoxication, and to monitor decontamination, particularly in an overdose situation
- Useful for people that cannot provide urine
- Collections are observed
- Adulteration difficult
Blood for drug testing (cons)

- Requires phlebotomist
- Represents only recent use (short window of detection)
- Specimen errors
  - Use of separator gels
  - Requires prompt removal of plasma or serum from the clot
- Testing not readily available
- No standardized “cutoffs”
Meconium: the first stool

water, epithelial cells, lanugo, mucus, amniotic fluid, bile acids and salts, fatty material from the vernix caseosa, cholesterol and sterol precursors, blood group substances, enzymes mucopolysaccharides, sugars, lipids, proteins, trace metals, various pancreatic and intestinal secretions, drugs and other materials ingested by the mother
Meconium

- Begins to form at \(~12\) wks gestation
- Detect exposure during \(~\)last trimester
- Relatively easy to collect
- Limited collection period; may require 5-6 days after birth, or be lost \textit{in utero}
- Testing not generally available on-site and may require several days
- Interpretation of results may be vague
Challenges with meconium analysis

- No commercial assays designed for meconium
  - Testing content (drugs detected) and cutoffs vary
  - Analytes may be different in meconium than in urine
- Interferences possible
  - False positives
  - False negative
- High-risk babies generally test positive for multiple drugs
- Limited quantity limits confirmatory testing
Hair

- Allows for detection of historical drug use
- May represent chronology of use, if segmented
- Time represented varies
  - Will not represent recent (~past week) use
  - Neonate hair represents ~last trimester
  - Head hair: 1 cm represents ~ 1 month
  - Body hair (natural) represents ~ 1 year
Concerns with hair testing

- Not all drugs are found in hair
- Color and consistency of hair affects drug deposition; processing???
- Sampling errors
  - Insufficient amount common. Need ~100 hairs or enough to approximate the diameter of ½ pencil
  - Must label root to detect chronology
  - The longer the hair, the longer the history detected (1.5 in ~ 3 months)
- Laboratory concerns: sample handling, methods used, cutoffs
Interpretation of hair testing

- Over-interpretation common
  - Cutoffs proposed but not standard
  - False negatives likely
  - Extent of use guidelines not well substantiated (use vs pg/mg)
- External contamination possible, but irrelevant if metabolites present
- Isomers may not be resolved based on technology of laboratory
- “De-tox” shampoos on market but of unknown efficacy
Comparing drug tests

• What drugs is the test designed to detect?
• What is the cutoff concentration per drug?
• What is the specificity of the assay (i.e., likelihood of a false positive or false negative result)?
• Is adulteration testing performed?
**Drug concentrations required to generate a positive opiate IA result**

<table>
<thead>
<tr>
<th>Drug (ng/mL)</th>
<th>Abbott FPIA</th>
<th>Dade Behring (Syva) EMIT II</th>
<th>Roche CEDIA DAU</th>
<th>BIOSITE Triage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>300</td>
<td>300</td>
<td>300</td>
<td>300</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>100</td>
<td>300</td>
<td>364</td>
<td>300</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>1000</td>
<td>5,388</td>
<td>10,000</td>
<td>20,000</td>
</tr>
</tbody>
</table>

The Clinical Toxicology Laboratory, AACC Press, 2003, pp. 491-2
Detection limits reflect

• Analytical method
• Detection limit of assay (cutoff)
• Specimen
• Specimen handling (hydrolysis?)
• Patient
• Specific drug
• Pattern of drug use
Patient characteristics that affect pharmacokinetics

- Age
- Body size
- Liver function
- Kidney function
- Pregnancy
- Genetics
Drug Characteristics

- Formulation
- Route of administration
- Drug kinetics
- Dose
- Single use or chronic use?
- Used alone or in combination with other drugs?
Time
- cocaine (0.7-1.5 hrs)
- 6-acetylmorphine (6-25 min)
- morphine (1.3-6.7 hrs)
- d-methamphetamine (6-15 hrs)
- marijuana metabolite (20 hrs – 13 days)
- methadone (15-55 hrs)

Drug Concentration

Time
Time

Inducer

No other drugs

Inhibitor

Drug Concentration

Inducer

Time
Interpreting drug test results

• Are positive and negative results consistent with expectations?
  – Donor history, prescriptions
  – Pattern of metabolites

• Serial samples
  – Time interval between collections?
  – Methods consistent for serial testing?
  – Are results normalized to creatinine?

• Specimen integrity
What could cause an unexpected positive drug test?

- Inappropriate use of unprescribed drug
- Patient was previously prescribed the drug, or admitted past use, but time of specimen collection since drug discontinuation is insufficient for elimination
- Prescription obtained from another clinic
- Incorrect prescription was filled
- Clinic or lab mixup
- Drug detected is a legal form of illegal drug
- Drug detected is a metabolite of a legitimately prescribed drug
Amphetamine isomers

• $d$-isomers are CNS active and are abused
• $l$-isomers have 10% of $d$-isomer activity in CNS, but work better peripherally, so are used in nasal inhalers
• Isomers may be differentiated by immunoassays or by chiral-specific methods
• Isomeric form is preserved throughout metabolism
Prescription drugs can produce a legitimate positive result

- **Selegeline (Eldepryl)**
  - Indicated for depression, Parkinson’s
  - Metabolized to $l$-methamphetamine

- **Methamphetamine (Desoxyn)**
  - Indicated for ADHD, narcolepsy, obesity
  - $d$-methamphetamine

- **Amphetamine (Adderall)**
  - Indicated for ADHD, narcolepsy
  - $d:l$ ratio of 3:1
Simplified opiate metabolism

Notes: Those drugs appearing in boxes could be parent drug or a metabolite of another drug.
What could cause an unexpected negative drug test?

- Drug was not absorbed
- Drug was taken incorrectly (less than prescribed or less frequently than prescribed)
- Accelerated metabolism/elimination
- Urine was dilute and concentrations fell below detection limits of analytical method
- Urine was adulterated
- Specimen was not handled appropriately
- Lab or clinic mixup
Strongest drug testing results

- Results are confirmed by mass spectrometric method
- Both parent drug and drug metabolites are identified
- More than one sample is tested at two separate times (pattern of results)
- More than one specimen source/type
  - Urine, blood, meconium, hair, etc.
  - Child and parent testing
- Chain of custody
- Certified laboratory
Summary and conclusions

• All drug tests have strengths and limitations
• All specimen types have strengths and limitations, and are at risk of tampering
• Individual characteristics of a drug user will impact drug testing results
• Work with the laboratory to get the best option available that meets your needs
• Avoid over-testing, and over-interpretation