“Urine – Luck”
All About Drug Testing

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Overview
• Basic concepts – drug testing
  – Matrices
  – TPAs
  – Laboratories
  – Panels
  – Cutoffs
  – Subrogation and Adulteration
• Alcohol markers
• Common MRO conundrums
• Relapse
• Boards and other legal entities

Drug Testing
• Any tissue can be tested - Matrices
  – Urine, blood – most available
  – Hair – excellent – longer term use
  – Saliva – less invasive
  – Sweat – valid and easy substitute for hair
  – Fingernails – similar to hair
  – Brain

Federally Regulated Testing
• US Navy incident - 1984
• 1986 – Ronald Reagan
• Drug Free Federal Workplace
• Federal Agencies Most Involved
  – DOT, NRC, FAA, FHWA, FRA, FTA, RSPA, USCG
  – “Sensitive Positions”
• Regulated Federal Industries
  – DOT, Airlines, etc
• Non-Regulated Testing - us

Benefits of Drug Testing
• Diagnosis – substance abuse and dependence
• Accountability - improves outcomes
• Documentation of recovery - advocacy
• Malpractice liability protection – defense
• Detection of relapse – early intervention
• Prevention - deterrence
• To gain support to return to work – boards, partners, etc – employment

Benefit of Urine Drug Testing
• Binary – positive or negative
• Objective – on paper
• Science based - authoritative
• Exposes the truth
  – Addiction thrives in secret
    • Dishonesty = hallmark of addiction
    • Honesty = hallmark of recovery
Drug Testing – Emerging Technologies

**2000**
- 12 million drug tests
- 5 million mandated drug tests
- Fragmented and non-centralized IT

**2010**
- 30 million drug tests
- 7 million mandated drug tests
- Consolidated and centralized IT

- Quick Test Kits
- New confirmation tests: LC/MS/MS
- More extensive testing panels
- Increased use of Flex Testing
- Improved testing for ethanol (EtG, EtS, etc)
- Monitoring devices – SCRAM, Wrist TAS
- Queuing devices - Sleepetime

Saliiva Testing
- DHHS - 5 DRUGS, ALCOHOL
- Similar to Plasma
- Increasingly used (ie dilute urines)

Hair Testing

- DHHS - 5 DRUGS
- Ongoing sequential record

Sweat Testing

- DHHS - 5 DRUGS
- Ongoing sequential record

Monitoring Devices
- Transcutaneous Alcohol Sensors
  - Continuous
  - Transcutaneous diffusion
  - Expensive - $20/d
- Wrist TAS - NIAAA
Terms

- MRO – Medical Review Officer
- NIDA Five – Opiates, MJ, Amphetamines, Cocaine, PCP
- TPA – Third Party Administrator
- DOT Certified Lab -> SAMHSA Certified
- LC/MS/MS – Liquid chromatography tandem mass spectroscopy
- ELISA – Enzyme Linked Immunosorbent Assay
- EMIT – Enzyme Multiplied Immunoassay Test

Drug Testing Problem Areas

- Collection sites – competence, subversion
- TPAs – no shows, money, service
- Panel selection
- Invalid, dilute, out of range, cancelled
- MRO review – competence
- Relapse reporting – making the complex simple

20 Steps to Foolproof Drug Testing

1. Signing of a detailed monitoring agreement with the participant (including all substances to avoid, a clause that the participant agrees to be responsible for to observed urine collection, etc)
2. Development of competent collection sites (Agreement with the collection sites regarding collection methods, including stipulation that all collections be directly observed)
3. Quality control and regular periodic follow-up of collection site to assure that proper collection methods are being maintained
4. Provision of proper urine collection kits to collection sites
5. Provision of financial arrangements
6. Periodic questioning of the participant to insure that specimen collection is being performed properly
7. Notification method to inform participant to obtain urine drug testing
8. Monitoring no-call and no-show reports w/ appropriate action
9. Monitoring of compliance of submission of specimen within appropriate time frame following notification
10. Competent testing of chain of custody urine samples at a qualified lab

TPA – Third Party Administrator

- Notification
- Mass purchase lab testing
- Collection site setup, maintenance, QA
- Collect reports from lab
- Report storage, display, etc
- Billing
- MRO services
- Database software
- Other

Notification (for testing)

- 800 number call in daily – Allows no call report
- Color or PIN
- Control of panels, selection dates, etc
- Vacations, etc.
- Shorter notice the better – Less time to prepare to dilute or substitute
- Call-in time can be helpful to know in some situations – ie dilutes

20 Steps to Foolproof Drug Testing, cont’d

11. Appropriate testing of specimen (ie proper test, proper analytes, etc) to include drugs of abuse used by health professionals (a more extensive and diverse panel than NIDA 5 screens)
12. Method for varying drug test panel as appropriate based on clinical situations, drug of choice, trials, etc
13. System for routine confirmation (usually by GC/MS or LC/MS) of all screened positives results
14. *Review of drug testing reports by Medical Review Officer or other qualified personnel, with appropriate investigation, interview with participant to exclude appropriate use under physician care and reporting of positives
15. Entry of report notification and submission times into a database for analysis, storage, comparison, and review
16. Review of all non-negative reports (including: dilute, positive, adulterated, invalid, or delayed reports) by staff
17. Determination of level of relapse (ie. levels I, II, III)
18. Reporting of refuse to appropriate authorities as needed or agreed
19. Intervention with participant and referral for appropriate reevaluation
20. Work with evaluation personnel to assure transfer of information and thorough reevaluation and receipt of reports

* Frequent problem areas

Notification (for testing)
Collection

- The weakest link
- Facilities – labs, hospital, clinics, etc
- Personnel
  - Direct Observation – difficult to obtain
  - Temp – Substitution (90-100 degrees or within 1.8 degrees of body temp)
  - Obvious Adulteration – Manipulation (Color, odor, objects, etc.)
  - Shy Bladder - <30cc Urine
    • 45oz of water over 3 hours

The Ideal Collection Site

- Convenient location
- Quick
- Competent personnel
- Low cost

Laboratories

- Chain of custody
  - Signatures
  - Seals
  - Delivery
- Screen – RIA – Radioimmunoassay, ELISA
- Confirmation – GC/MS – Gas Chromatography/Mass Spectroscopy
- Cut offs
- Certifications
- Availability for consultation
- Innovative

Reports

- Negative
- Positive – Confirmed by GC/MS
- Other
  - Invalid - Unable to test – ?Medication (which interfere w/ testing) - ?Adulterant
  - Substitution (Creat <2 and SpGr <1.001 or >1.020)
  - Adulteration – Nitrite >500, pH <3 or >11 or others identified adulterant (gluteraldehyde, clorox, oxidase peroxidase, pyridinium hypochlorate, drano, etc.)

MROs

- Verify the legitimacy of a positive urine and/or eliminate legitimate use
- Oversee legitimacy of the process
- Limited role – not addiction doctors
- Rare Prescriptions – Marinol, Heroin, PCP
- Food – Hemp Oil, Coca Tea, Poppy Seeds

Panels

- Most common substances abused by health professionals
  - Alcohol – 49%
  - Opiates – 35% (hydrocodone, oxycodone, fentanyl…)
  - Stimulants – 8% (adderall, ritalin, etc)
  - Sedatives – 5% (benzodiazepines)
- Fentanyl can only reasonably be detected by hair or nail testing
- Relatively rare: darvon, ketamine, LSD, ecstasy, GHB, Propofol, all gases, others
Panels
- Primary panel to include (picks up 95%)
  - EtG/EtS, common opiates, amphetamines, ritalin, and common benzos
- Periodic hair (or nail) test for fentanyl (particularly for those with access)
- Occasionally
  - Propoxyphene, ketamine, LSD, ecstasy, GHB, etc, etc
- Only when suspected
  - propofol, all gases, others
- Saliva test – for backup for suspicious dilutes

Cutoffs
- Primary cutoffs
  - Determined by lab – associated with limits of machines to provide reliable data
- Secondary cutoffs
  - Used to differentiate actual use vs secondhand, incidental, accidental exposure
  - Raising cutoffs always lowers sensitivity!
  - Better, if you have the manpower and bureaucratic leeway, to avoid raising cutoffs
  - Must then learn to deal with “gray zone”

Substitution
- Detection
  - Temp
    - Immediately provide 2nd urine under direct observation
  - Creatinine & Specific Gravity
    - (Dilute vs inconsistent with human urine)
- Methods
  - Water or other liquid
  - Someone else’s urine
  - Substitution devices, self cath, etc

Adulteration
- Detection
  - Nitrate concentration ≥ 500 μg/mL
  - pH ≤ 3 OR ≥ 11
  - Glutaraldehyde, Stealth or other oxidizing agents
- Methods
  - Nitrites – Klear (KNO3), PH – Urine Luck – (was HCl now Pyridinium Chlorochromate), Drano,
  - Other oxidizing agents - Stealth (Oxidase Peroxidase), Urin Aid – glutaraldehyde, hydrogen peroxide
  - Other
    - Soap
    - Clorox
    - Ginseng Tea
    - Water

Hey, man. . . when you get caught . . . Urine Luck™!
Tommy Chong, formerly of ‘Cheech & Chong’
Complete Line of Detoxifying Products
Click on Products for More Information
$20.00
- Flushes all unwanted toxins in under 3 hours.
- Extended effectiveness for up to 5 hours.
- Contains vitamin B-complex and creatine.
- Made with safe, all-natural, herbal ingredients.
- More convenient than teas - no preparation needed.
Never worry about a drug test again.

Can't urinate on command?
Can't urinate on the spot?
Need to find a job?
Need to keep a job?

Mystique's Urine Transport System "UTS"
DON'T GET PEE'D OFF!!

UTS Unit $79.95 Complete Unit with 3 Heating Pads

New Alcohol Biomarkers
(EtG, EtS, PEth)

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Exotic Dessert?
• 19 y/o autistic man
• Convicted of auto-theft, intoxicated at the time of theft
• Near end of sentence - released for weekend to custody of attorney father
• Positive EtG on return to jail
• Father claimed they had “banana’s foster” dessert and didn’t know about EtG testing

I drank a few beers!
• 35 y/o anesthesiologist in monitoring b/o alcohol abuse
• Positive EtG 110 ng/ml
• Contacted and told his test showed he’d been drinking again
• He immediately admitted drinking “a few beers”

Overview
• Terminology and measurement
• When to use these markers
• When not to use these markers
• Understanding incidental exposure
• Cutoffs - is there one that is right?
• Informed consent for participant
• How to confront re a positive test
• What to do when drinking is denied

Alcohol - number one drug of abuse!

Alcohol legal - but not for everyone!
• Alcoholics in recovery
• Others in recovery from drug addictions
• Custody cases involving alcohol abuse
• Underage (under 21 in most jurisdictions)
• Parole or probation when abstinence is ordered by judge
• Liver transplant clinics
• US military
• Race horses

Who uses EtG/EtS testing?
• Addiction treatment programs
• Addiction aftercare and monitoring pgms
• Probation and parole
• Schools (elementary and high schools)
• Parents – home testing
• Medical clinics (transplant, IM, FP, etc)
• Military
• Life insurance companies
• Race tracks
Previous Markers

- Alcohol (urine, breath, saliva, blood) – not hair
- MCV and GGT – (Mean corpuscular volume, gamma glutamyl transferase) – measures effects of chronic heavy alcohol use on bone marrow and liver – only detects chronic heavy use and sometimes positive for other reasons (B12 deficiency, liver disease, etc)
- % CDT (carbohydrate deficient transferrin) – measures the effect of alcohol on a blood protein – only detects chronic moderate - heavy use (ie not for abstinence testing)

Problems w/ Previous Markers

- Blood alcohol – short duration
- Urine alcohol – short duration, fermentation
- All
  - Lacked acceptable time spectrum for detection
  - Lacked sensitivity and specificity
  - Influenced by
    - age,
    - gender
    - a variety of substances
    - non-alcohol-associated diseases and
    - other factors (i.e. in vitro fermentation)

New Markers with Potential

Urine

- Ethyl glucuronide (EtG) – 1-5 days*
- Ethyl sulfate (EtS) – 1-5 days*

Blood

- Phosphatidyl ethanol (PEth) – (7 drinks) - 1 week

Hair

- EtG/EtS – several months (problem – water soluble)

Ethylglucuronide (EtG)

Formation

- via conjugation of ethanol with activated glucuronic acid in the presence of membrane bound mitochondrial UDP glucuronyl transferase (UGT)

Ethylglucuronide (EtG)

- Europe 1mg/L = USA 1,000ng/ml
- A minor metabolite but exclusive to alcohol (ethanol, ethyl alcohol) – so far...
- Variable amounts produced from given amt alcohol
  - Represents about 0.05-1.0 % of total

Ethylglucuronide (EtG)

- A few hours after alcohol consumption, EtG in urine will be positive
- Detectable up to 1-5 days after the complete elimination of alcohol from the body

(Eschmann et al., 1997, Wurst and Skipper, 1999, 2001; Seidl et al., 1998).

Urine EtG not a quantitative measure of alcohol use (ie Impossible to predict how much was consumed by urine EtG value!)

- Variable production of EtG due to enzyme system variations (20 fold or more)
- Urine concentration varies (20 fold or more)
- Unknown variables
  - Time since last drink
  - Rate of consumption of alcohol
  - Chronicity of drinking

Ethyl glucuronide in urine after intake of 9 g of ethanol – single subject (27y/o 72kg male)

EtG - production

- Things that can increase ↑ or decrease ↓ EtG production due to changing enzyme systems (CYP450)
  - Genetics - ↑ ↓
  - Chronic use - ↑ until - liver failure ↓
  - Foods – grapefruit juice ↓, greens ↑
  - Medications – erythromycin ↓, St John’s Wart ↑ (many others…)
  - Diseases – pregnancy ↑, Gilbert’s Syndrome, others ↓ (5% of population), (many others…)
Urine concentration issues

- More water = less analyte per ml
- Less creatinine per ml = less EtG/EtS per ml
- Creatinine 20-400 mg/dl can be normal
- Concentration can vary EtG 20 fold by itself
- Concentrated urine – Creat 400 – EtG 10,000 whereas if same urine were diluted to Creat 20 the EtG would be 500
- U50EtG/EtS = EtG or EtS reading x 50/urine creatinine

Stability of ethyl glucuronide

Anders Helander, Helen Dahl.

_Urinary Tract Infection: A Risk Factor for False-Negative Urinary Ethyl Glucuronide but not Ethyl Sulfate in the Detection of Recent Alcohol Consumption._
Clinical Chem 2005

False-negative EtG (but not EtS) from in-vitro bacterial degradation
And then later
False-positive EtG (but not EtS) from in-vitro bacterial synthesis

Anders Helander, Ingrid Olsson, Helen Dahl.

_Post Collection Synthesis of Ethyl Glucuronide by Bacteria in Urine May Cause False Identification of Alcohol Consumption._ Clinical Chem August 23, 2007

Urine Concentrations of EtG/EtS

- Comparable cutoffs by LC/MS/MS?
  - 100 ng/mL / 25 ng/mL
  - 250 ng/mL / 50 ng/mL
  - 500 ng/mL / 100 ng/mL
  - 1000 ng/mL / 200 ng/mL

Comparable detection timeframes

Linear correlation between EtG and ETS

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**Ethyl sulfate**

- direct ethanol metabolite
- 1959 first reported: formed via conjugation of activated sulfate and ethanol by rat liver: Vestermark and Boström
- formed by sulfotransferases (polymorphism but different than EtG)
- molecular weight: 126 g/mol (smaller molecule than EtG)
- molecular formula: C₈H₅SO₄H
- enzymatic breakdown: via sulfatase
- Determination: LC/MS - MS with d₅-EtS as internal standard

**Incidental Exposure - Concepts**

Defining terms

- Cutoffs – primary vs secondary
- "Incidental" exposure
- "Accidental" exposure
- Clinical assessment
  - Exposure studies (in or out-patient)
  - Auto-brewery syndrome testing
  - Antabuse
  - SCRAM and TAD
  - Addiction evaluation/polygraph
  - Time

**Sources of incidental exposure**

- Foods
  - Deserts
  - Cooking sherry and wine vinegar, flambé desserts
  - Vanilla extract (especially if used in large amounts, e.g. in drinks)
- Hygiene Products
  - Mouthwash (Examples)
    - Listerine Original - 26.9%
    - Listerine Fresh Burst - 21.6%
    - Scope - 14.3%
    - Cepacol - 14%
- OTC Meds (Examples)
  - Nyquil Nighttime - 25%
  - Vick’s Formula 44 - 10%
  - Etc
- Other
  - Communion Wine
  - “Alcohol-free” Beer and Wine
Communion Wine 3/4 tsp

Products Containing Ethanol

Picture of a graph showing Ethanol Concentration Levels in Human urine after consumption of Communion Wine.

Picture of a graph showing Ethanol Concentration Levels in Human urine after consumption of 2 O'Douls, labeled as “alcohol-free” beer.

Picture of a page with a chart titled “Products Containing Ethanol”, showing various products and their alcohol content.

Picture of a page with a chart titled “Products Containing Ethanol”, showing various products and their alcohol content.
**Products Containing Ethanol**

<table>
<thead>
<tr>
<th>Product Description</th>
<th>Price</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paul Mitchell Soft Sculpting Spray Gel</td>
<td>&gt;20</td>
</tr>
<tr>
<td>Cutter Uncased Outdoorsman Insect Repellant, Water-Resistant Sport Pump Spray</td>
<td>20</td>
</tr>
<tr>
<td>HOUSE SAVER Pet Stain &amp; Odor Remover</td>
<td>20</td>
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<tr>
<td>Farnam Cologne &amp; Deodorant for Pets</td>
<td>20</td>
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<tr>
<td>Avon Nail EXPERTS Strong Results</td>
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<td>29</td>
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<tr>
<td><strong>Bay Rum After Shave Balm</strong></td>
<td>30</td>
</tr>
<tr>
<td>Martin Water Solving Solution</td>
<td>31</td>
</tr>
<tr>
<td>ABN Primer &amp; Sealer</td>
<td>35</td>
</tr>
<tr>
<td>Cutter Uncased Backwoods Insect Repellant, Water-Resistant Sport Pump Spray</td>
<td>35</td>
</tr>
<tr>
<td>Cutter All Family Insect Repellent 2 Aerosol</td>
<td>35</td>
</tr>
</tbody>
</table>

**Case Reports - 2002**

- A female pharmacist in California and two pregnant RNs in Michigan tested positive for EtG at 270 and 680ng/ml respectively.
- All were suspended b/o positive EtG test.
- All vigorously denied drinking or exposure to other alcohol except for topical exposure to cologne and hand sanitizer.

**To Test Her Claim**

- She was admitted to treatment center and searched.
- Allowed to use Purrell hourly first day and then Q 1/2 hour second day.
- Morning and evening EtG tests were performed.
- 1st morning negative, 1st evening 330ng/ml, 2nd morning negative, 2nd evening 770ng/ml.

**Handsanitizing Gel**

- Contains 62 - 90% ethanol
- Hand sanitizer (often a gel hand cleaner) that rapidly kills most germs.
- Recently promoted in hospitals and everywhere as a means to reduce hospital acquired infections.
- Used without a sink or towels.
Research Questions

• Does Ethanol in Hand Sanitizer enter the body of the user?
• If so, how does the alcohol get in?

Methods

24 subjects were randomized into 4 groups

– Both Skin & Inhalation—sat in a bathroom for one hour; on cue every 4 minutes applied 4 squirts (2 cc) of Purell™ hand sanitizer (15 times)
– Inhalation only—sat in same bathroom within 2 feet of a Both subject and breathed the vapor
– Skin only—applied 4 squirts of hand sanitizer 15 times over one hour while hands were isolated in a laminar air flow chamber
– Control—no exposure to hand sanitizer.

Methods

• BAC measured by an Intoximeters™ Breathalyzer at baseline, 20, 40, and 60 minutes into the procedure and at 90 min. (or 30 min. after completion of exposure)
• Urine samples for creatinine & EtG at baseline, 30 minutes after completion and ~6 hours later
• Urine samples sent to Northwest Toxicology for sample analysis using picric acid colorimetric technique for Creatinine and Liquid Chromatography/Tandem Mass Spectroscopy technique for EtG.

Results

• The Inhaled group was significantly higher than control p=0.0044
• The 30-minute post exposure EtG was significantly higher than baseline and 6 hours post exposure p=0.0049.
Conclusion

• Hand sanitizer is primarily absorbed via inhalation rather than through the skin
• Recovering alcoholics, especially those who are subject to urine monitoring for EtG, should avoid breathing vapor of alcohol-based hand sanitizer
• Those who are pregnant or on medications that react adversely with alcohol also should avoid using alcohol-based hand sanitizer.

Download paper @ www.ethylglucuronide.com

Cutoffs

• The higher the EtG/EtS level the more likely due to drinking
• No clear line identified so far
• Guessing at the number that might distinguish between drinking and incidental exposure for years
• Fact is, we don’t know the number!

Cutoffs

• Primary cutoff - determined by lab based on characteristics of the test, supplies, machinery, personnel - “What level is above a point where test is reliable?”
• Secondary cutoff - a level chosen to differentiate between true substance abuse and accidental or incidental exposure
  – Based on population studies
  – Individual cases

Cutoffs

• Best cutoff = lowest primary cutoff possible = 100 ng/ml EtG and 25mg/ml EtS
• If:
  – You understand it’s a screening test
  – If you have the time to deal with more positives
  – If you have the luxury of using clinical judgment
• More sensitive for picking up drinking
• But requires more sophisticated thinking

Cutoffs

• Setting a higher cutoff means choosing to officially ignore lower levels of positive because they are less likely to be due to substance abuse
• However
  – Low levels can be from drinking
  – If you set a high enough cutoff to totally eliminate “false-positives” you miss more true positives

Positive test

1. Confront the participant and offer as much support as possible if they “get honest”
2. If they deny drinking do one or more of the following:
   a. Order blood phosphatidyl ethanol and/or hair EtG
   b. Provide information and warning re incidental exposure – and continue testing
   c. Further evaluation - possibly including polygraph (to induce honesty)
   d. Consider observed antabuse
   e. Transcutaneous alcohol sensor device (ie TAD – from BI.com or other)
Benefits

- Better than other markers for detecting recent alcohol use
- Present in urine and hair
- Better to document abstinence (advocacy)
- Better to discourage drinking (deterrence)
- Better to detect relapse (detection)
- Better to R/O false positive urine alcohol (in vitro fermentation) (confirmation)
- Useful in association with transcutaneous alcohol sensors (such as the TAD – device – from BI.com) (confirmation)

Phosphatidyl ethanol (PEth)

- Blood test
- Phosphatidylcholine + EtOH and Phospholipase D
- Similar to CDT but better

Phosphatidylethanol

- A direct biomarker that incorporates into cellular membranes.
- Takes much more alcohol to cause positive (14 drinks within 2 weeks)
- Longer detection window - not metabolized (3+ week duration)
- Once in red cell membrane - stays there until cell dies.

Important to advise participants

- Have them sign an agreement that they understand they must avoid incidental exposure
- List of items to avoid
- See www.ethylglucuronide.com for example contract
Bottom Line

- Useful new tests – proven in the field - but not perfect
- EtS more sensitive and specific
- No known cutoff that clearly distinguishes between drinking and incidental exposure
- Warn ahead of time to avoid incidental exposure
- Important how you confront someone with positive EtG/EtS

Important Link:
http://ethylglucuronide.com