
Alcohol Markers and Devices

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Disclosures

• Director, Professionals Health Services, Promises Treatment Centers – employee
• Affinity Online Solutions – consultant
• Greg Skipper, MD – consultant to regulatory boards, courts, and other agencies
Background

- Innovator of EtG as an alcohol biomarker with Friedrich Wurst MD from Switzerland in 2001
- Convinced the initial lab in the USA, NMS near Philadelphia, to start performing EtG testing
- Participated in both SAMHSA committees that developed the Advisories re use of new alcohol markers in 2006 and 2012
- Accepted as an expert and have testified in 46 administrative hearings, 22 criminal, 14 custody, and 1 federal class action suit
- Maintain website: www.ethylglucuronide.com

Peer Review Articles

- Expertise in Alcohol Biomarkers
- Publications
  - Skipper GE, Liepman M, Wurst FM, Weinmann W. Breathing Vapor of Ethanol-Based Hand Sanitizing Gel Vapor Causes Positive Alcohol Marker, Ethylglucuronide (EtG), and Positive Breathalyzer. (Accepted for publication by Journal of Addiction Medicine 11/25/2008)
  - Skipper GE, Weinmann W, Wurst FM. Ethylglucuronide (EtG): A New Marker to Detect Alcohol Use in Recovering Physicians. Journal of Medical Licensure and Discipline, 2004,90(2), 14-17
Peer Review Articles

- **Publications Cont’d**
  - Wurst FM, Skipper GE, Weinmann W, Ethyl Glucuronide – the direct ethanol metabolite on the threshold from science to routine use, 2003 Society for the Study of Addiction to Alcohol and Other Drugs, pg 1-11, Oct 2003

Overview

- **New alcohol biomarkers**
  - Standard of care for use
  - To detect drinking and document abstinence
  - Used individually or together to enhance reliability
- **New devices for monitoring alcohol use**
  - Comparison to biomarkers
  - Used with biomarkers
Standard Use of Alcohol Markers
Survey of all PHPs (March 2013)

1. All programs use EtG
   – 47% have EtG on a standard panel
   – 53% have EtG on a separate panel

2. 85% use EtS
   – 82% use it because it automatically comes with EtG

3. 76% use blood PEth
   Of those 24% who don’t use it:
   – 50% don’t know why they don’t use it
   – 50% don’t use it because there is not yet adequate science to support its use – 3 programs

4. EtG cutoffs:
   a. 100ng/ml – 7%
   b. 250ng/ml – 34%
   c. **500ng/ml – 57%**

5. Reporting of EtG to regulatory board:
   a. Always – 18% - N=8 programs
   b. Depends on circumstances – 58% 25 programs
Standard of Use of Alcohol Markers

7. About ½ of programs have used hair or nail EtG.

8. Most common reasons for use of PEth test
   - 60% After positive EtG/EtS if drinking is denied
   - 63% If drinking is highly suspected
   - 23% of programs use it randomly
**Please indicate why your program does not use PEth testing. (Choose all that apply):**

<table>
<thead>
<tr>
<th>Reason</th>
<th>Response Percent</th>
<th>Response Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not sure</td>
<td>50.0%</td>
<td>2</td>
</tr>
<tr>
<td>Not allowed by our licensing board</td>
<td>0.0%</td>
<td>0</td>
</tr>
<tr>
<td>Not allowed by our PHP board or committee</td>
<td>0.0%</td>
<td>0</td>
</tr>
<tr>
<td>Not enough scientific evidence to support it</td>
<td>50.0%</td>
<td>3</td>
</tr>
<tr>
<td>Legal or liability concerns</td>
<td>0.0%</td>
<td>0</td>
</tr>
<tr>
<td>Don’t have appropriate participants</td>
<td>0.0%</td>
<td>0</td>
</tr>
<tr>
<td>Other (please specify)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>answered question</strong></td>
<td></td>
<td><strong>6</strong></td>
</tr>
</tbody>
</table>

**Our program uses PEth testing in the following ways (Choose all that apply):**

<table>
<thead>
<tr>
<th>Use PEth testing</th>
<th>Response Percent</th>
<th>Response Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>after a positive EtG or EtS and drinking is denied</td>
<td>60.0%</td>
<td>21</td>
</tr>
<tr>
<td>with assessments when indicated</td>
<td>51.4%</td>
<td>18</td>
</tr>
<tr>
<td>following participant vacations</td>
<td>40.0%</td>
<td>14</td>
</tr>
<tr>
<td>following low creatinine</td>
<td>37.1%</td>
<td>13</td>
</tr>
<tr>
<td>following suspected drinking</td>
<td>62.9%</td>
<td>22</td>
</tr>
<tr>
<td>randomly (indicate approximate frequency below)</td>
<td>22.9%</td>
<td>8</td>
</tr>
<tr>
<td>for other reasons (please specify below)</td>
<td>20.0%</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>quarterly</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>We have used PEth test when results are ETG/ETS results are positive, but low and a report to the Board must be made. Because Peth is expensive, not all vacations are followed by a PEth. Some professionals are tested with urine tests randomly, but also PEth tests at times selected by the case manager.</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>We are positioned to use PEth testing but have not yet had a situation that required us to do so.</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>We do Peth testing on a quarterly basis for alcohol dependency. More frequently if recommended by the facility.</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>For some who don't practice clinical medicine and who travel a lot we use PethStat every 3-4 weeks on a schedule and on several in addition to urine because of prior relapses.</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Only one PEth test b/c of several dilute test results</td>
<td></td>
</tr>
</tbody>
</table>

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>For some physicians, we test with PEth every 2 weeks.</td>
</tr>
<tr>
<td>8</td>
<td>Reasonable suspicion or confirmation of history of drinking.</td>
</tr>
<tr>
<td>9</td>
<td>We are just starting to use this test.</td>
</tr>
<tr>
<td>10</td>
<td>PEth is less sensitive than ETG/ETG for low-level alcohol consumption and is used as such. While we have used as a confirmatory test when alcohol use is denied, a negative PEth does not mean the person was not drinking, just means they were not drinking moderately to heavily in the PEth window (2 weeks).</td>
</tr>
<tr>
<td>11</td>
<td>We had a board just approve PEth testing but have not yet started to use.</td>
</tr>
<tr>
<td>12</td>
<td>We use on suspicion or with positive ETG/ETG if they do not admit instead of a full eval. especially on nondoctoral level participants</td>
</tr>
<tr>
<td>13</td>
<td>We will test if there are compliance issues, or if someone has a dilute screen (not just for low creatinine). We are doing one random test per year for alcohol dependent participants. We will test after vacations if there is reason for suspicion. We tell our participants that we MAY PEth test after vacations, and I believe this is a beneficial deterrent.</td>
</tr>
</tbody>
</table>
Direct metabolites of alcohol

Ethylglucuronide (EtG)

Formation

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

Stephan Seidl et al.

Figure 1. Formation of ethyl glucuronide (EtG) by conjugation of UDP-glucuronic acid and ethanol.

Ethylglucuronide (EtG)

• Urine EtG (Immunoassay or LC/MS/MS)
  – Better than urine alcohol
  – False negatives – common w/ minimal alcohol use
  – False positives – from extraneous alcohol
    • Most common 3-6 hours after exposure
  – Slightly improved sensitivity and specificity w/ EtS
  – Can be used in combination with PEth (when drinking is denied)

Ethylglucuronide (EtG)

• An hour after alcohol consumption, EtG in urine will be positive
• Peaks at 3-6 hours
• Detectable up to 1-5 days after the complete elimination of alcohol from the body

(Schmitt et al., 1997, Wurst and Skipper, 1999, 2001; Seidl et al., 1998)
EtG levels daily x 4 days – alcohol detox unit

Male, 27 years, 0.12 [g/Kg] ethanol, BMI 22

Single dose of alcohol, 1 oz vodka

Male, 27 years, 0.12 [g/Kg] ethanol, BMI 22
Ethylglucuronide (EtG)

- Sensitivity of EtG (19 subjects, 1-6 drinks, all urine tests were negative after 26 hours)

<table>
<thead>
<tr>
<th>Dosing Group</th>
<th>Waiting period 24 h (%)</th>
<th>Waiting period 48 h (%)</th>
<th>Waiting period 72 h (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>100 (3 of 3)</td>
<td>0 (0 of 2)</td>
<td>0 (0 of 2)</td>
</tr>
<tr>
<td>Medium</td>
<td>67 (2 of 3)</td>
<td>0 (0 of 2)</td>
<td>0 (0 of 2)</td>
</tr>
<tr>
<td>Low</td>
<td>0 (0 of 2)</td>
<td>0 (0 of 1)</td>
<td>0 (0 of 2)</td>
</tr>
</tbody>
</table>


Urine Ethylsulfate (EtS)

- When performed with EtG improves sensitivity and specificity
- 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 window of detection
- Not confirmation of drinking!
Conclusion

• EtG/EtS are the best markers for early detection of drinking and for documenting abstinence but:
  – Probably miss most minor drinking episodes
  – Can be positive from recent extraneous exposure

Positive test

1. Confront the participant and offer as much support as possible if they “get honest” and admit drinking
2. If they deny drinking do one or more of the following:
   a. Provide information and warning re incidental exposure – and continue testing
   b. Order blood phosphatidyl ethanol and/or hair EtG
   c. Conduct further evaluation - possibly including polygraph (to induce honesty)
   d. Consider observed antabuse
   e. Soberlink monitoring
SAMHSA Advisory (2012)

- A “high” positive (e.g., >1,000 ng/mL) may indicate:
  - Heavy drinking on the same day or previously (e.g., previous day or two).
  - Light drinking the same day.
- A “low” positive (e.g., 500–1,000 ng/mL) may indicate:
  - Previous heavy drinking (previous 1–3 days).
  - Recent light drinking (e.g., past 24 hours).
  - Recent intense “extraneous” exposure (within 24 hours or less).
- A “very low” positive (100–500 ng/mL) may indicate:
  - Previous heavy drinking (1–3 days).
  - Previous light drinking (12–36 hours).
  - Recent “extraneous” exposure.

Benefits of EtG testing

- Better to document abstinence (advocacy)
- Better than other markers for detecting recent alcohol use (early detection)
- Better to discourage drinking (deterrence)
- Better to R/O false positive urine alcohol (in-vitro fermentation) (confirmation)
- Useful in association with Soberlink or SCRAM (confirmation)
Phosphatidylethanol

- A direct biomarker that incorporates into cellular membranes.
- Takes much more alcohol to cause positive (~14 drinks within 2 weeks) – more than possible from incidental or extraneous exposure
- Longer detection window - not metabolized rather degraded (2+ week duration) – half-life 4.4 days
- Once in red cell membrane - stays there until cells die
Phosphatidyl Ethanol (PEth)

Combination Strategies

• Using PEth to confirm drinking following positive EtG/EtS when drinking denied
• Study: 18 positive EtGs

<table>
<thead>
<tr>
<th>Finding</th>
<th>#</th>
<th>%</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Admitted drinking after positive EtG/EtS</td>
<td>8</td>
<td>44</td>
<td>Drinking</td>
</tr>
<tr>
<td>Admitted drinking after PEth explained</td>
<td>3</td>
<td>17</td>
<td>Drinking</td>
</tr>
<tr>
<td>Admitted drinking after positive PEth</td>
<td>1</td>
<td>6</td>
<td>Drinking</td>
</tr>
<tr>
<td>Denied drinking after positive PEth</td>
<td>1</td>
<td>6</td>
<td>Drinking</td>
</tr>
<tr>
<td>Denied drinking - negative PEth</td>
<td>5</td>
<td>28</td>
<td>Not Drinking</td>
</tr>
</tbody>
</table>
Soberlink 2 – Digital Cellular Breathalyzer

- Pocket size, one-piece device
- Real-time alcohol results
- Instant notifications on participant violations
- Embedded Verizon cellular module for best wireless coverage
- Internal camera for user identification with infrared flash technology
- Tamper resistant features
- Evidential-grade fuel cell technology
- Long lasting rechargeable battery

SOBERLINK Monitoring Web Portal

- Case manager receives real-time results and reviews on SOBERLINK’S password protected web portal.
- Automated text reminders can be set up by case manager to remind participant when it’s time to test.
- Real-time alerts are sent to case manager for missed tests and positive BAC results.
Pilot Study Comparing 4 x Daily Soberlink v Random Weekly EtG

• 12 subjects – social drinkers
• Kept log of drinking x 5 weeks, blew in Soberlink 4 times daily, submitted random weekly urine EtG, completed questionnaire
• 84 drinking episodes
• 55 EtGs collected of possible 60
• 1609 breath tests of possible 1680

Results

• Only 1 positive EtG
• Soberlink detected all 84 drinking episodes (100%)
• Subjects all preferred using Soberlink to submitting urine tests
  – “It’s much easier to take 30 seconds 4 times per day than to drive to a collection site and wait sometimes ½ hour to submit a urine sample.”
  – “Much more convenient to blow in the Soberlink from home than to go to a collection site.”
  – “Embarrassing to submit a urine. Easy to blow in Soberlink device.”
  – “Much prefer blowing in Soberlink device.”
  – “No comparison. Prefer blowing instead of peeing.”
  – “More trouble to drive somewhere and wait to give urine sample.”