Breath and Urine Alcohol Testing: Relationship to BAC and Use Patterns

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Disclosures

- No financial relationships to disclose
- I perform medical-legal consulting regarding drug and alcohol impairment
- My practice of Occupational Medicine uses BAT devices and I am a BAT trainer

Alcohol Biomarkers

- **Objective** measures that are helpful as:
  1. **Outcome measures** in studies
  2. **Screens** for possible alcohol problems in individuals with unreliable drinking histories
  3. **Evidence of abstinence** in individuals prohibited from drinking alcohol

These tests are complimentary to self-report assessments
Categories of Alcohol Biomarkers

- Indirect Biomarkers
- Direct Biomarkers

Indirect Biomarkers

- Assesses alcohol effects on body systems
- Non-specific, insensitive
- AST, ALT, GGT, MCV
  - Things other than EtOH abuse cause elevations
  - Some abusers do not have elevations

Indirect Biomarkers

- Newest: CDT- Carbohydrate-deficient transferrin
  - Elevated after > 2 weeks of heavy EtOH abuse (>5 drinks/day)
  - Few other things cause elevations
  - Insensitive to bingeing
Direct Alcohol Biomarkers

- Analytes of alcohol or its metabolites
  - Measures alcohol directly in body matrices
  - Or alcohol adducts in body matrices
- Most common is BAC, BrAC

Direct Alcohol Biomarkers

- Alcohol Metabolites:
  - Most alcohol is oxidized by ADH and AlDH
  - A very small amount is broken down non-oxidatively, creating analytes that can be measured for a longer period than alcohol itself
  - Analytes are measured in the blood or urine.

Alcohol Metabolism

Unchanged in breath, urine, sweat

< 5%

Ethyl Glucuronide (EtG)

< 1%

Ethanol in Blood

< 1%

Ethyl Sulfate (EtS)

< 1%

UDP-glucuronosyltransferase

< 1%

Sulfotransferase

> 95%

ACDH & ADH

Acetaldehyde and acetic acid
**Breath Alcohol Concentration (BrAC)**

- BrAC of terminal portion of a prolonged exhalation reflects the arterial BAC
- Expressed as g ethanol per 210 L breath
- Machines designed to ignore initial (2/3) of breath and measure terminal portion only
- Salivary alcohol gone in 15 minutes
  - Mandatory retest in 15 minutes
  - 2nd test must agree with first by ≤ 0.02g/210L
- Eructation, vomiting can contaminate

**BrAC testing Devices**

- BrAC testing devices must be calibrated
- Air blanks and gas cylinders with known [EtOH]
- QA procedures and device user training logs
- Device manufacturers must submit their equipment to NHTSA to get on CPL
- BrAC frequently subject to challenges by DWI defense counsel

**BrAC Testing Devices**

- Three types in common use on NHTSA CPL:
  - Infrared
  - Fuel cell
  - Chemical oxidation
- Challenges to accuracy are rampant in DWI defense
- Most attack the human element, not the technology
- Many jurisdictions use BrAC screening, get BAC confirmatory
BrAC Testing Devices:
1) Infrared Spectroscopy
- All chemicals absorb infrared light at specific wavelengths
- Ethanol absorbs strongly at 3.3-3.5 µ (acetone too), but more specific band at 9.5 µ
- Amount of infrared energy lost from Br from chamber entry to exit reflects infrared absorption by EtOH, is proportional to [EtOH]
- Acetone potential interferent if 9.5 µ not used

2) Fuel Cell, aka Electrochemical Oxidation
- Converts fuel and an oxidant into DC
- EtOH converted to acetic acid
  - Gives off two electrons
  - Current produced is proportional to [EtOH]
- Very specific for alcohols (MeOH, IsOH too)
- Can be very small, low power usage: ideal for hand-held devices
- Acetate can build up on fuel cell with many consecutive + tests, prolongs time to return to baseline

Alkosensor IV
3) Chemical Oxidation/Photometry

- First type of BrAC device developed and brought into widespread LE use
- Breath enters chamber of oxidizing mixture
- Reaction of EtOH with the oxidizers causes a decrease in UV light absorbed, measured by photometer, proportional to [EtOH]
- Still in use in a few jurisdictions
- No longer manufactured, Breathalyzer 900A was the only one left

BrAC Testing Devices: Dual Detectors: FC and IR

- Employs both Fuel Cell and Infrared
- Usually one method is used to validate the other
- Any discrepancy invalidates the test
- Can be used stationary or mobile
- Very accurate and hard to challenge due to redundancy
BrAC to BAC ratio

- Assumption is that blood: breath alcohol ratio is 2100:1, and that is basis for all testing in NA
- Actual ratio is closer to 2300:1
- This actually favors the arrestee
  - Proven in side by side roadside tests
  - BrAC always underestimates true BAC

Converting Serum EtOH to BAC

- Serum: WB ratio:
  - Averages 1.15:1 to 1.10:1
  - So a serum EtOH value is divided by 1.1 to 1.15 to convert to “legal” BAC language
- Some DWI arrestees with positive BrAC present to EDs demanding a retest- will usually not be helpful to them

Other Biomarkers

- Ethyl glucuronide (EtG), ethyl sulfate (EtS), and phosphatidyl ethanol (PEth).
- Usually measured in urine; detectable for days.
  - EtG and EtS tests become positive shortly after even low-level exposure to alcohol
  - PEth requires higher levels of ethanol use, detectable in blood for weeks
Ethyl Glucuronide- EtG
Ethylsulfate- EtS

- EtG: Ethyl β-D-6-glucosiduronic acid

- Approx 0.02% of ethanol is metabolized by phase II conjugation with uridine 5'-diphospho-glucuronic acid (UDPGA) via UDP-glucurolyosyltransferase to form EtG

- EtS produced by sulfotransferase

Ethyl Glucuronide- EtG

- The most studied and the most utilized long-term biomarker

- Can be measured in very [low]

- Detected for ~ 4 days in urine after 1 drink- i.e., the “80-hour test”

Ethyl Glucuronide- EtG

- However, cannot prove beverage alcohol was the source
  - Hand sanitizers
  - Mouthwashes
  - Non-alcoholic beer
  - Old fruit juices
Ethyl Glucuronide- EtG

- Present in very low levels (<100ng/mL) even in abstainers and children
  - Endogenous ethanol by intestinal bacteria
  - Non-apparent dietary ethanol: old fruit juices, sauerkraut, old bananas

Ethyl Glucuronide- EtG

- Perfect for documenting abstinence
  - Underage patients
  - Military in combat zones
- Those requiring abstinence as condition of rehab or probation
  - Probation for EtOH-related crimes
  - Persons in court-ordered rehab as condition of release
  - Impaired professionals as condition of continued licensure

EtG, EtS Measurement Concerns

- Must confirm with LC/MS/MS
  - EIA unreliable, false positives
  - All EIA screen positives must be confirmed
- \([\text{EtG}]\) Varies with hydration, often corrected for creatinine
- Should urine be refrigerated or preserved?
  - EtOH produced from glucose fermentation in urine
  - Refrigeration or preservative in specimen prevents
  - However, UDPGA & ST-ase do not exist in urine
  - Our practice does not refrigerate urine, no preservative in our bottles
- Not FDA-approved medical test, not covered by health insurance
EtG and EtS Kinetics

Winkler Int J Legal Med.

Suggested EtG Cut-offs

- EtG >1,000 ng/mL indicates:
  - Heavy drinking in past 1-2 days
  - Light drinking the same day (or the night before)
Suggested EtG Cut-offs

- EtG between 500–1,000 ng/mL indicates:
  - Heavy drinking previous 1–3 days
  - Light drinking past 24 hours
  - Intense “extraneous exposure” within 24 hr or less

- EtG positive, above LOQ but <500 ng/mL indicate:
  - Previous heavy drinking (1–3 days+).
  - Previous light drinking (12–36 hours).
  - Recent “extraneous” exposure.

EtG and Hand Sanitizer Use

- 9 adults, used ethanol skin sanitizers 20x/day
- EtG levels + but < 120 ng/mL in first morning specimens
- EtG accumulation with repeated dermal ethanol did not occur
EtG and Hand Sanitizer Use

- 11 adults, used Purell® (62% EtOH) q 5' for 10 hours (120 uses each)
- Urine specimens end of each day
  - Mean [EtG] @ end of Days 1, 2, and 3 were 493, 601, and 542ng/mL respectively
  - Range of 0–2001 ng/mL
- EtS may be a good discriminator
  - Very few had + EtS
  - All EtS values < 100ng/mL
  - The sweet spot is probably EtG > 500, with EtS > 250 (this is what our program uses)

EtG and Mouthwash Use

- 10 adults gargled with Listerine® (27% EtOH), 20mL, 30 sec. each, 4 X/d
- Only one subject had + urine EtG
  - 173ng/mL
  - 2 hr post-gargle
- No one had +EtG specimens at first void of each day
- Several + EtS in 7 subjects
  - Maximum EtS value 104ng/mL
- EtS cut-off of 250-500ng/mL seems reasonable

Suggested EtG Cut-offs

- EtG >1,000 ng/mL indicates:
  - Heavy drinking in past 1-2 days
  - Light drinking the same day.
- EtG between 500–1,000 ng/mL indicates:
  - Heavy drinking previous 1–3 days
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  - Intense "extraneous exposure" within 24 hr or less
- EtG positive, above LOQ but <500 ng/mL indicate:
  - Previous heavy drinking (1–3 days).
  - Previous light drinking (12–36 hours).
  - Recent "extraneous" exposure.
Phosphatidyl Ethanol- PETH

- PETH, a group of glycerophospholipid homologues
- Formed exclusively in the presence of ethanol via the action of phospholipase D
- Found primarily in the RBC membranes
- Long detection window – weeks- due to life of the RBC

Phosphatidyl Ethanol- PETH

- Phosphatidyl ethanol (PETH) is a direct blood-based biomarker
- 48 species of PETH identified
  - PETH 16:0 and PETH 18:1 seem to be the most abundant species.
- Persists in blood for as long as 3 weeks
  - After a few days of moderately heavy drinking (>about four drinks per day)
- Perfect for detecting binge drinking
- Not readily available, being studied
Phosphatidyl Ethanol- PEth

Kwak et al – Clin Tox 2012

- Monitored 2 groups of pregnant women
- Group 1- 26 women-No ethanol use
  - Negative for PEth
- Group 2- 13 women- 2.5- 20 drinks/wk
  - Positive for PEth at >5nmol/L
  - Detectable for up to 4 wks

Comparison of biomarkers with PEth in blood and urine
Winkler- Int J Legal Med. 2012 Dec 29

- Studied the correlation between PEth and other biomarkers (ethyl glucuronide, ethyl sulfate, CDF, GGT)
- 18 alcohol-dependent patients in withdrawal therapy monitored for up to 19 days.
- No correlation between the different markers.
- PEth showed an initial rapid decrease
  - Then a slow decline after the first few days
  - Could still be detected after 19 days of abstinence

Window of Assessment for Various Alcohol Biomarkers
Alcohol Biomarkers and their Usefulness

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Screen for Heavy Drinking</th>
<th>Identifying Relapse</th>
<th>Time to Return to Normal</th>
<th>Monitoring for Abstinence</th>
</tr>
</thead>
<tbody>
<tr>
<td>CDT</td>
<td>✓</td>
<td>✓</td>
<td>2-3 weeks</td>
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<tr>
<td>EtG, EtS</td>
<td>✓</td>
<td>✓</td>
<td>1-3 days</td>
<td>✓</td>
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<tr>
<td>GGt</td>
<td>✓</td>
<td></td>
<td>2-4 weeks</td>
<td></td>
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<tr>
<td>MCV</td>
<td>✓</td>
<td></td>
<td>Several months</td>
<td></td>
</tr>
<tr>
<td>PEth</td>
<td>✓</td>
<td>✓</td>
<td>2-4 weeks</td>
<td></td>
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<tr>
<td>BAT</td>
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<td>hours</td>
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</tr>
<tr>
<td>AST</td>
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<tr>
<td>ALT</td>
<td>✓</td>
<td></td>
<td>2-4 weeks</td>
<td></td>
</tr>
</tbody>
</table>

Bibliography

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