



FSSolutions

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Monitoring FAQ's:

Presented by

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Questions:

- **Will the Test Tell Me What I Want to Know?**
- **What Won't the Test Tell Me?**
- **What laboratories do you use?**
- **What is Validity Testing? Dilution?**
 - What is an invalid specimen?
 - How do you handle a dilute?
 - How do you follow up after a Dilute Specimen?
 - What about High Creatinine?
- **What are the Detection Periods of Different Specimens?**
- **Why are some Alcohol Biomarkers Negative when some aren't?**
- **Is PEth Testing Junk Science?**
- **What Type of MRO are you?**

Will the Test Tell Me What I Want to Know?

- **Yes, if it is:**
 - The right test
 - Collected the right way
 - At the right time
 - Tested at the right lab
 - On the right specimen
 - Looking for the right drug or alcohol biomarker

Is it the Right Test?

- **Are you looking for the most sensitive current information?**
 - Urine or Oral Fluid
- **Are you looking for a pattern of use over a longer period of time?**
 - Hair, Nail, PEth
- **Are you looking to confirm intentional use vs accidental use or environmental exposure?**
 - Not always possible
 - EtG/EtS
 - Parent drugs (Cocaine, Methamphetamine, others) in hair
 - More likely with Hair/Nail, PEth

Is It Collected the Right Way?

- The “Myth” of observed collections
 - A “monitored” collection is not an “observed” collection
 - Some sites either do not do observed collections or do not do enough of them
- Questionable Collections:
 - Bottle ‘A’ and ‘B’ different colors
 - Creatinine/specific gravity mismatches
- Follow-up ASAP with either:
 - Another observed collection at a different site or with a different collector
 - An alternative specimen test

Is It a Right Laboratory?

- **Limited National Certification Standards and QC for Clinical/Recovery Monitoring Testing:**

- SAMHSA/NLCP only certifies laboratories for federal workplace testing panels and drugs
 - This certification is the strictest and is indicative of general high standards at other areas of NLCP certified labs
 - If possible we favor laboratories that have NLCP certified areas
- CAP, CLIA, various state agencies certify processes, not specific tests
- FDA
 - Clears some screening kits
 - Has no authority over certification processes (GC/MS/MS or LC/MS/MS)
 - Has no authority over LDTs
- Most testing uses Laboratory Developed Tests (LDTs)

What laboratories do you use?

- We use a number of different appropriately certified laboratories according to type, service, need and location. The labs we choose are selected for their experience in recovery monitoring panels, cost and proven turnaround time efficiencies.
- Our goal is to understand your program needs and match those needs with the best choice or mix of testing laboratories

LDT's

- **Laboratory Developed Test (LDT)**
 - Most Recovery Monitoring testing involves LDT's
 - “Test developed and characteristics determined by...”
 - LDT's should be adequately supported by peer reviewed data
 - No current national certification or clearance for LDT's
 - Laboratory selection crucial (SAMHSA/NLCP, CAP, CLIA, State)

Does enough data exist to support an interpretation of a result that will benefit both the program and the participant?

Remember:

- **The drug testing we do is not like workplace drug testing**
 - More drugs and drug metabolites
 - Lower cutoffs
 - More specimen types
 - Greater effects from specimen concentration
 - Less peer reviewed data regarding quantitative levels and their meaning
 - More room for error, usually human

Not Workplace Testing but Still Forensic:

- **Screening: The first step (Either in the lab or at Point of Collection-POCT)**
 - Sensitive but not specific
 - Most specimens are negative
 - Sensitivity: The proportion of truly positive results, as measured by the gold standard, that are identified as positive by the test under study
- **Confirmation: The second step (In the lab)**
 - Specific and sensitive
 - Most specimens that go from screening to confirmation are positive, and results must be quantitative
 - Specificity: The proportion of truly negative results, as measured by the gold standard, that are identified as negative by the test under study
- **Both Screening and Confirmation must be positive for the test to be reported positive**

Cutoffs

Cutoffs are quantitative levels. If alcohol or drug is present above cutoff, the specimen is positive, if not the specimen is negative.

- Three Types:
 - Limit of Detection (LOD): The lowest concentration at which a measurand can be identified, but (for quantitative assays) the concentration cannot be accurately calculated.
 - Limit of Quantitation (LOQ): For quantitative assays, the lowest concentration at which the identity and concentration of the measurand can be accurately established.
 - Administrative: Above both LOQ, and LOD. Balances detection and forensic defensibility requirements
- Cutoffs may vary

What Won't the Test Tell Me?

- A negative result does not guarantee the absence of alcohol or drug
- Positive alcohol or drug levels do not differentiate acceptable use from abuse even if elevated
- Positive alcohol or drug levels do not indicate impairment
- There is no dose/result relationship because there is no way to tell if level is rising or falling
- Monitoring programs push the edges of the testing envelope with the number of analytes tested for and the low cutoffs used
- We collect two bottles so that reconfirmations are possible, and they should be done at a different lab
- We cannot distinguish THC from CBD

Cannabidiol (CBD) vs Tetrahydrocannabinol (THC)

- CBD is extracted from cannabis plants
 - THC content is considered contamination, but it's almost always there!
 - THC levels vary greatly
- Epidiolex is a prescription form of CBD
 - Schedule V
 - FDA cleared for treatment of two rare and severe forms of epilepsy, Lennox-Gastaut syndrome and Dravet syndrome, in patients two years of age and older.
- Except for Epidiolex, CBD is a Schedule I substance (no medical use)
 - Participants should be advised not to use CBD
 - They should also be advised that THC positive drug test results will not be excused because of CBD use.

Please Discuss Invalid Specimens

Definition:

- Laboratory report of a drug test for a specimen that contains:
 - An unidentified adulterant, or
 - Unknown interfering substance, or
 - Has abnormal physical characteristics, or
 - Has an endogenous substance at an abnormal concentration that prevents the lab from obtaining a valid drug test result.

Urine Validity Testing Includes

- Measures of urine concentration/dilution
 - Creatinine on all specimens
 - Specific gravity only if creatinine <20 mg/dL
- pH
- General screen for oxidants
- Specimen appearance
- Abnormal Physical Characteristic (Specified)
- Bottle A and Bottle B – Different Appearance

Causes of Testing Interference

- **Interference with screening:**
 - Immunoassay interference:
 - Certain prescriptions cause screening interferences: some NSAIDs, Cipro and other fluoroquinolones, metronidazole
- **Interference with confirmation:**
 - Specific GC/MS or LC/MS interference or
 - the inability to obtain a forensically defensible data peak
 - Frequently caused by oxidants
- **Specimen ageing**
 - causes pH and nitrite (oxidant) elevations
 - UTI also may cause nitrite (oxidant) elevations
- **No reconfirmations for invalid specimens**

Two Measures of Urine Specimen Concentration

Values selected for analysis should be expected to parallel each other as specimen concentration increases or decreases

- Creatinine and Specific Gravity
- Dilute
 - Both measures out of acceptable range
 - Low creatinine by itself is a warning flag
- Substituted
 - Both measures so far out of range that specimen is not consistent with normal human urine

Why Two Measures?

- Forensic testing always involves two different tests
- If Creatinine and Specific Gravity do not parallel each other, the specimen is invalid:
 - Observed recollection is strongly recommended if no legitimate medical explanation
 - If collection was observed the observation was not done properly
 - If significant time has elapsed since the problem collection, consider alternative specimen collection

Remember the “Myth” of observed collections

How Do You Handle Dilute Specimens?

- We will implement your required protocols
- We suggest using the Dilute Specimen Protocol

Dilute or Low 'C' Protocol

- One way to address the dilution problem is with your authorization:
 - FSSolutions inquires of the Certifying Scientist whether or not there appeared to be any data for a particular analyte at 50% of the screening cutoff
 - If the laboratory reports that there is no screening data below cutoff, then there is nothing more to do with this specimen. The program *may* elect to test by using an alternative specimen, usually hair, nail, or PEth.
 - If the laboratory reports that there is suspected analyte present at 50% of cutoff, then authorize the laboratory to do an immediate confirmation of that analyte at the laboratory's lower limit of quantitation (LOQ).
 - If this LOQ confirmation is positive, this will produce a confirmed and actionable result.
- Probably not worth doing unless creatinine is less than 20 mg/dL

Dilute Specimens, Why Do We Care?

- Average creatinine concentration range is 100 mg/dL -150 mg/dL
- Creatinine not considered low if above 20 mg/dL
- The solution to pollution is dilution
- 4460 workplace specimens studied, creatinine corrected to 100:
 - Opiates positives increased 18%
 - Amphetamines positives increased 58%
 - THCA positives increased 105%

J Price, J, *J. Addict. Med.* Volume 7, Number 2, March/April 2013

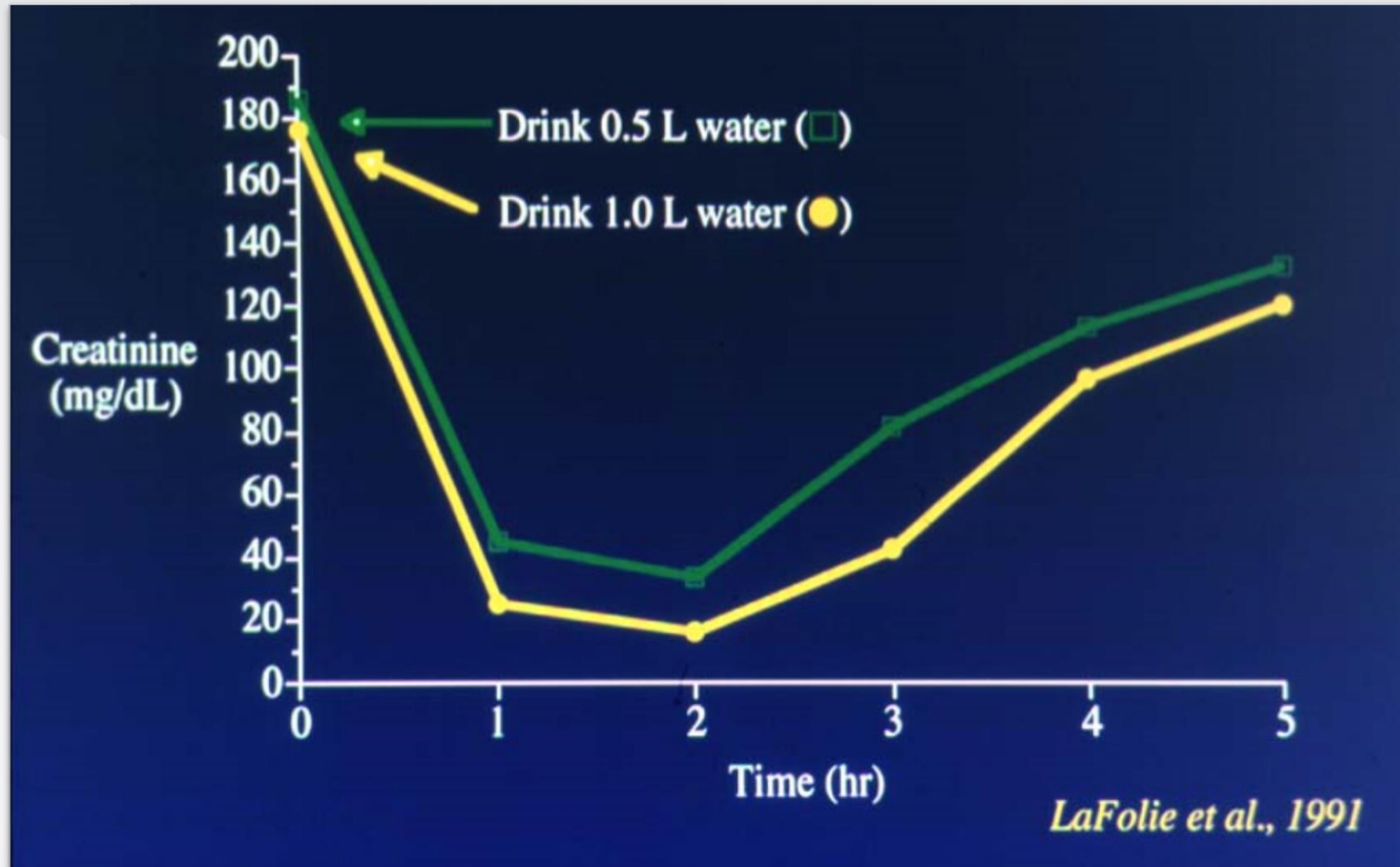
What About Really High Creatinine?

- Dilution makes it more difficult to find drugs in the specimen, high concentration makes it easier
- No good evidence to prove high creatinine is related to anything other than relative dehydration
- Still raises suspicions in my mind

“Shy Bladders”

- Occurs when a donor cannot provide an adequate specimen on demand
 - 30 mL in bottle ‘A’
 - 15 mL in bottle ‘B’
- Collector discards inadequate specimen
- Collector allows donor up to 40 ounces of fluid over a time period of up to three hours
- Donor not allowed to leave the collection site
- Refusal to drink is not a refusal to test
- Medical evaluation if no specimen produced after three hours

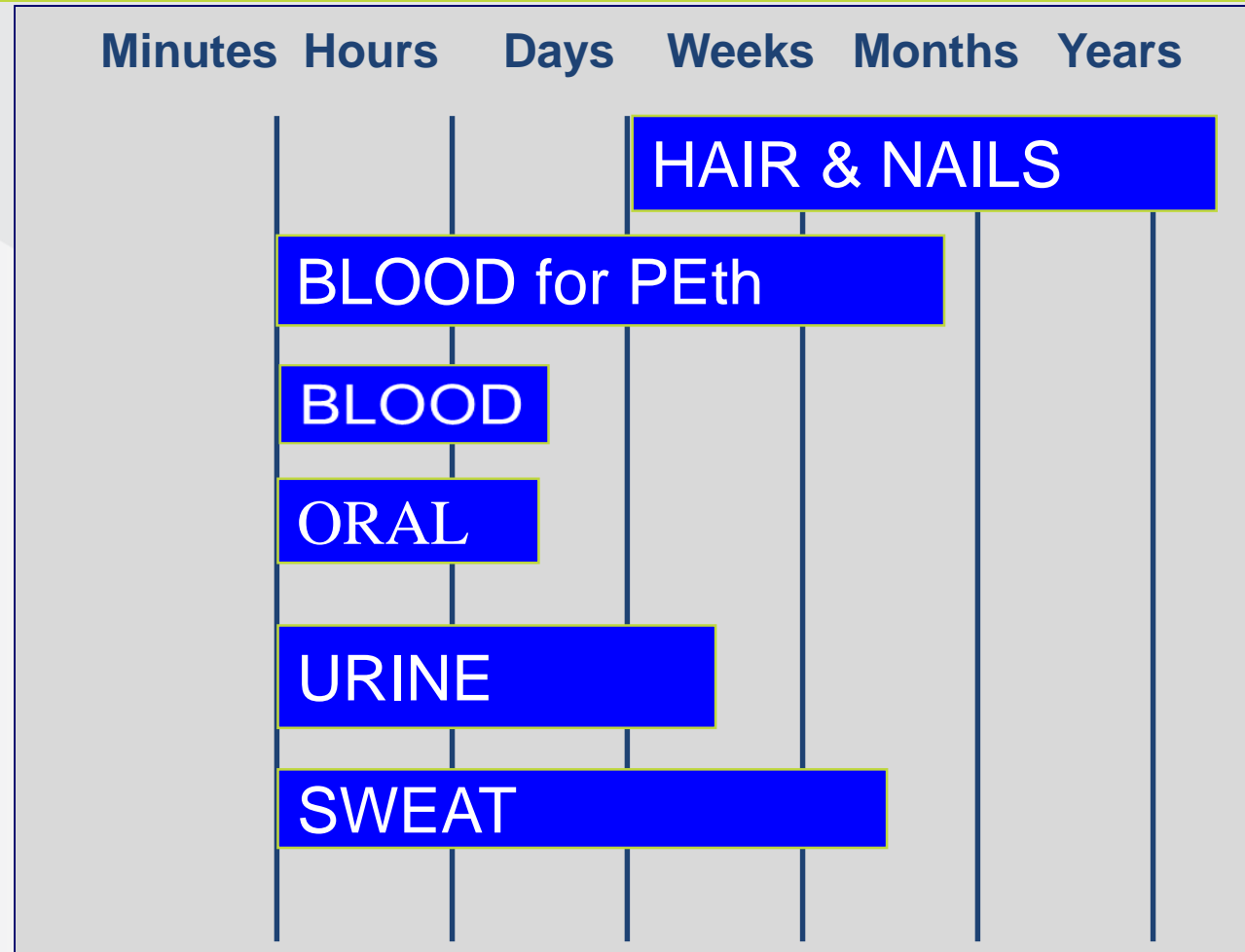
The Effect of Water Consumption on Urinary Creatinine



What is The Best Way to Follow Up After a Dilute Specimen?

- The best way to pass a drug test is not to take one
- Short detection period
 - If dilution or tampering was intended to hide a drug, the drug may be gone by the time re-collection is performed
- Recommendation: Test an alternative specimen with a longer detection period
 - Hair/nails for drug/s
 - PEth for alcohol
- Sensitivity
 - Urine is a more sensitive matrix
 - Alternative specimens less sensitive: More ingestion needed before hair, nails, PEth become positive.
- Using all available matrices gives better perspective on what is actually happening, but
- A negative hair test does not invalidate a positive urine test and vice versa

What are the Detection Periods of Different Specimens?



Windows of Detection

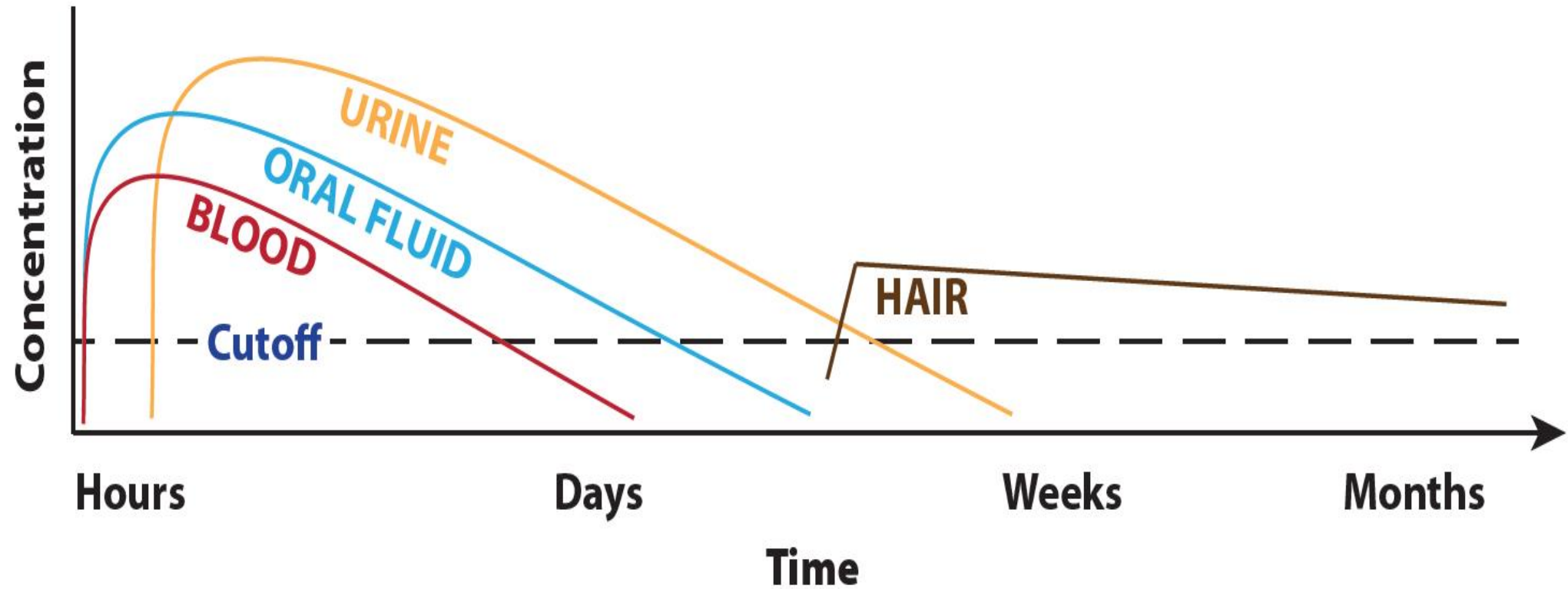


Figure 1. "Look-back" Timeframes for Urine, Oral Fluid, and Hair Compared to Blood (Cone EJ, personal communication, December 2016).

What are the Detection Periods of Different Specimens?

Urine:

- In urine all detection periods depend on several factors:
 - the dosage strength,
 - the time the dose was taken,
 - and the concentration of the specimen being tested.

Urine Detection Periods

- All things being equal the approximate detection periods are:
 - EtG/EtS 80 hours (Urine alcohol should not be used by itself)
 - Opioid detections are 3-5 days
 - Benzodiazepine detection periods vary widely:
 - Diazepam, chlordiazepoxide and metabolites temazepam and oxazepam 4-8 weeks
 - Alprazolam 4-6 days
 - Clonazepam 10-14 days
 - Lorazepam 9-12 days

What are the Advantages of Urine Drug Testing?

Advantages

- Extensive Scientific Base
- Accurate & Reliable
- Mature Technology

Disadvantages

- 2-3 Day Window of Detection for most
- Easy to Adulterate/Dilute
- No Dose/Concentration Relationship

What are the Detection Periods of Different Specimens?

Hair and Nail:

- Hair testing using scalp hair: 90 days
- Hair testing using hair from other parts of the body: 90 days to one year
- Nail testing using fingernails: 120 days
- Nail testing using toenails: 150 days
- These are all approximations

What are the Advantages of Alternative Specimens?

- Collection may have less “Yuck Factor”
- Multiple Sampling may be possible
- Greater Specimen Stability (e.g., hair)
- Lower Disease Risk in Specimen Handling (e.g., hair, sweat)
- Easier Shipment and Storage
- Differences in Window of Detection
 - Example: Pre-employment (Hair) vs. Post-Accident (Oral Fluid)
- May be more difficult to Substitute/Adulterate

How about the Disadvantages of Alternative Specimens?

- Dealing with Lower Analyte Concentrations
 - Urine/blood: ng/mL= parts per billion; Hair/nails: pg/mg = parts per trillion
- Requires More Sensitive Analytical Methods
 - Examples: Elisa, GC/MS/MS, LC/MS/MS
- May Confirm Parent Drug, Metabolite, or Both Parent and Metabolite
 - Metabolite/s are necessary to confirm ingestion
- Hair/nails require “chronic use” of substance for detection at achievable cutoff concentrations
- Limited amount of specimen: qns or insufficient specimen quantity concerns
- Lower levels of confirmed drug

Urine vs Hair/Nail

Urine testing is the forensic backbone of any testing program

- Very sound and well-studied scientific background
- Long established case history in legal situations
- Urine is easily tampered with at collection even if collection is observed
- Urine is a more sensitive testing medium and will show positive where there is less usage of drug
- Urine confirmed positives are easily forensically reconfirmed at other certified laboratories

Hair/Nail vs Urine

Hair and possibly nail testing are useful adjuncts to a sound urine program

- Significant amount of scientific data but not as much as urine
- More controversial case history that is still being worked out
- Limited data on nails
- Hair is less easy to tamper with
- Hair is not as sensitive as urine to drug usage and is thought to show a pattern of use rather than a single use
- No reconfirmation possible for nail testing

Interpretation Guidelines

- **Generally speaking, the longer the detection period of the specimen, the more drug usage required to produce a positive result**
- **All specimen results are two dimensional:**
 - Is the analyte concentration going up or down?
 - Results from different collections using the same specimen matrix within the detection window can help answer that question
 - Multiple results using alternative specimens may be less clear, but may hint at total amount of usage

Rate of Hair Growth (mm/day)

Scalp Crown	0.35
Vertex	0.44
Beard	0.27
Chin	0.38
Eyebrow	0.16
Axilla	0.30
Chest	0.40
Thigh	0.20

Growth Stages of Hair

ANAGEN PHASE - persists for years
Growing stage (80-90% of hair)



CATAGEN PHASE - lasts 2-3 weeks
Transition



TELOGEN PHASE - lasts a few months
Resting stage (10-20% of hair)

Telogen (Resting) vs Anagen(Growth)

Body Area	% Telogen Hair	% Anagen Hair	Telogen Duration	Follicles Density (1/Cm ²)	Depth of Follicle
Scalp	13	85	3-4 Months	350	3 - 5 mm
Beard	30	70	10 Weeks	500	2 - 4 mm
Upper Lip	35	65	6 Weeks	500	1 - 2.5 mm
Axillae	70	30	3 Months	65	3.5 - 4.5 mm
Trunk				70	2 - 4.5 mm
Pubic Area	70	30	12 Weeks	70	3.5 - 4.5 mm
Arms	80	20	18 Weeks	80	
Legs and Thighs	80	20	24 Weeks	60	2.5 - 4 mm
Breasts	70	30		65	3 - 4.5 mm

Unresolved Issues in Hair Testing

- Relationship of dose to hair concentration
- Relationship of time of use vs. detection
- Mechanism of drug entry into hair
- Environmental drug exposure vs ingestion
- Effectiveness of wash procedures in removing external contamination, especially cocaine
- Influence of hair color and texture on test results
- Interpretation of results: metabolites required to confirm ingestion

Action on Alternative Specimen Results?

- Alternative specimens can provide a beneficial back-up approach to strong forensic urine based monitoring programs
- One drug test result by itself does not make a diagnosis, but..
- It can provide a helpful perspective of the total picture
- Alternative specimen testing may be able to do the same thing for “gray area” urine results
- Remember we need metabolite present to assume ingestion

Urine and Alternative Specimens in Monitoring

- **Urine Testing is the Forensic Backbone of the Program**
- **Follow up invalid or indeterminate results with an alternative specimen (hair, nails, PEth, with appropriate detection period)**
- **Randomness is Key**
 - Random testing frequency
 - Random choice of specimen
 - Follow-up to all unexpected results

Example: If Urine Test Frequency is:

- Diagnostic Monitoring or Substance Use Disorder, Mild:
 - Weekly urines for 12 months, then no less than twice monthly, minimum 38 tests per year
- Substance Use Disorder, Moderate-severe:
 - Year 1 - urines 48 times a year
 - Year 2 - urines 36 times a year
 - Year 3 - urines 24 times a year
 - Year 4 - urines 18 times a year
 - Year 5 - urines 24 times a year

Then Hair Frequency Can Be:

- Diagnostic Monitoring or Substance Use Disorder, Mild:
 - Twice yearly during contract
- Substance Use Disorder, Moderate-severe:
 - Year 1 - 3 times a year (starting at 4th month)
 - Year 2 - 3 times a year
 - Year 3 - 3 times a year
 - Year 4 - 3 times a year
 - Year 5 - 4 times a year

Alcohol Consumption Monitoring

Alcohol Testing - Common Matrices

- Blood: Short and longer windows of detection, invasive
 - Short: Blood ethanol
 - Longer: PEth, AST, GGT, ALT, CDT
- Breath: Short window of detection
 - EBT
 - Personal breath testers i.e. Soberlink
- Oral Fluid: Short window of detection
 - Ethanol
- Urine: Longer window of detection
 - Fermentation issue for urine alcohol
 - EtG. EtS,

Why is a Specimen Negative for Alcohol But Positive for EtG/EtS?

- The urine detection period for alcohol is significantly less than it is for EtG/EtS
- Additionally, there are so many causes for positive urine alcohol readings other than drinking that urine alcohol should never be used without EtG/EtS
 - Glucose present
 - Microorganisms present in the urine
 - Urine stored at room temperature without preservative for one or more days

Why is EtG Positive but PEth Negative?

- **Could also ask the opposite: EtG negative but PEth positive?**
- **Or urine positive but hair negative?**
- **Different specimens have different drug uptake characteristics and different detection periods.**
 - Urine: Fast uptake, very sensitive, very specific
 - Hair/Nails: Slow uptake (7-10 days or more for nails), not sensitive, very specific
 - PEth: Slow uptake (3-4 days), not sensitive, very specific

EtG/EtS Interpretation Issues

- EtG can be both formed and degraded in a urine sample – retests often differ greatly in concentration due to bacterial contamination
- EtS is not produced *in vitro* and is stable
- EtG is one factor used to suggest alcohol ingestion but,
 - *A thorough Medical Review is recommended to identify other potential sources for the alcohol exposure*
- Results are affected by hydration: lower creatinine leads to lower EtG results
- All results require EtS to be present with EtG to confirm the presence of EtG from alcohol ingestion.
- This information has been successful in defending positive EtG results.

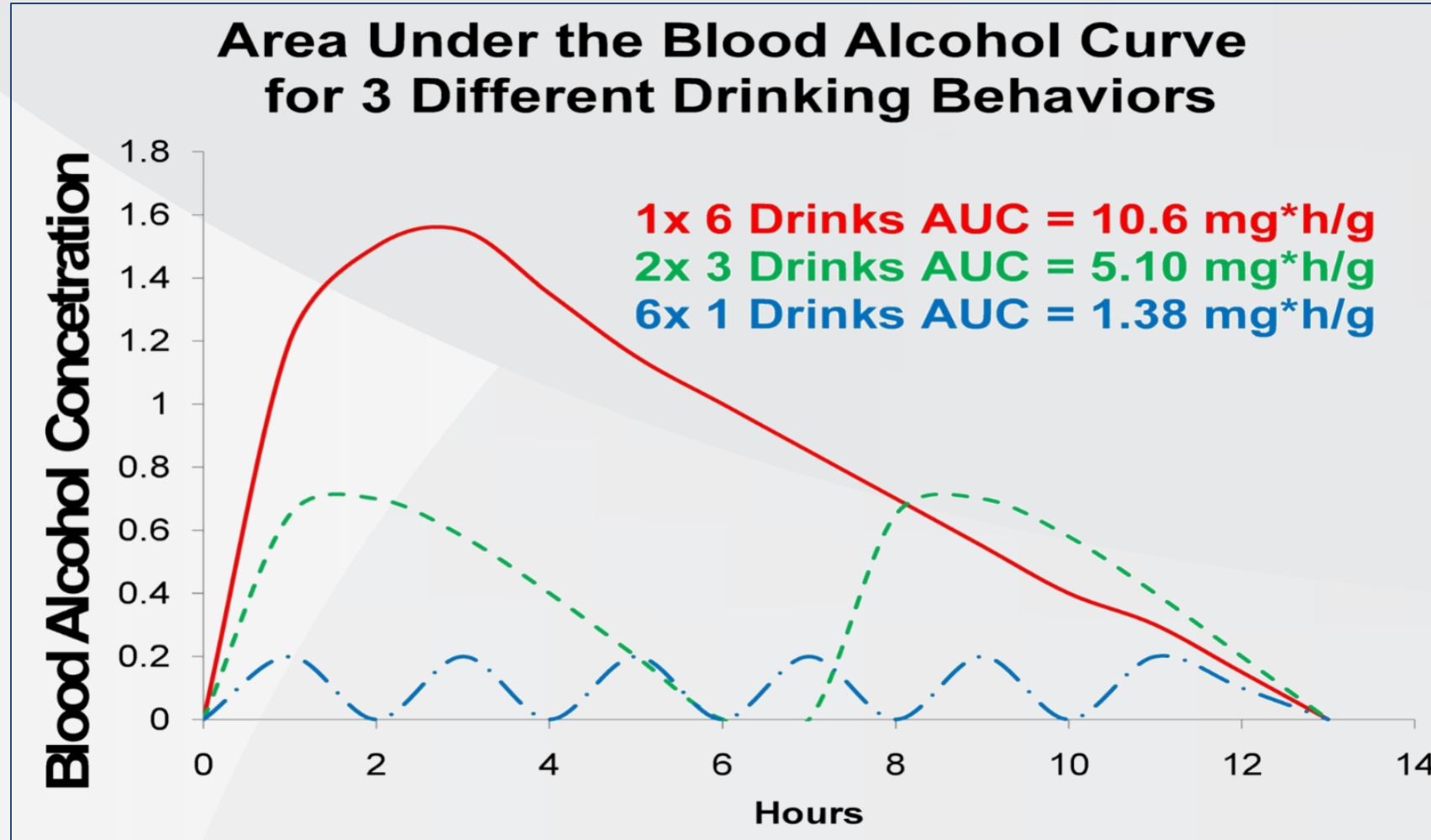
Phosphatidyl Ethanol (PEth)

- A direct biomarker that incorporates into cellular membranes
- Long lifespan - $t^{1/2}$ 4.4 days
- Stable molecule, minimally metabolized
- Stays in red cell membrane until it decomposes or cell dies.
- 2-4 week window of detection
- 5 molecular fractions comprise 80% of total PEth in blood
 - 16:0/18:1, 16:0/18:2, 16:0/20:4, 18:1/18:1, 18:1/18:2
 - Only 16:0/18.1, 16:0/18.2, 18:1/18:1 are routinely tested
 - Only 16:0/18.1 routinely reported

PEth Indications

- Testing blood for phosphatidyl ethanol (PEth) is a reliable way to determine alcohol ingestion of at least 2-3 standard drinks or more occurring in the 2-4 weeks prior to the test
- PEth testing is ordered when there is significant concern about possible alcohol use
 - Following a low positive EtG/EtS test when participant denies alcohol consumption
 - After a third dilute UDS or any UDS with extremely low creatinine
 - As part of an initial, recovery status or appropriateness for completion evaluation
 - Following any reported suspicion of drinking

Blood Alcohol Concentration



Is PEth Testing Junk Science?

- It is an LDT, but:
- Research has been ongoing since 1983
- No false positives have been reported (Kechagias, et al, 2015)
- Single ethanol dose of 30-47gm (2-3 drinks) would be expected to produce positive 16:0/18:1 at 20 ng cutoff (Javors, et al, 2016)
- Statistically significant differences in the mean values and confidence intervals of total PEth concentrations in heavy drinkers(>60g/day) and social drinkers(<60g/day) (Wurst, et al, 2010)

More Research

- 32 males, 12 females studied for three months: 1-2 glasses of wine/day produced PEth up to 60 ng/mL (Kechagias, et al, 2015)
- 80 females aged 18-35: 2+ glasses of wine a day produced PEth 127 ng/mL (Stewart, et al 2010)
- 252 participants: PEth results in combination with previous EtG results allow differentiation between exposure and drinking (Skipper, et al, 2013)

PEth Testing and Split Specimen Reconfirmation

- **Two Testing Techniques:**
 - Whole blood is more common
 - Blood Spot done at one laboratory
- **20 ng/mL is a low but generally accepted cutoff**
- **When the donor denies ethanol ingestion, offer reconfirmation:**
 - For spot testing, the only option is the same lab tests another spot
 - For whole blood testing the specimen can have true reconfirmation at another lab
 - If drawn in a timely fashion, whole blood can be used as a follow up to blood spot even though it is not a true reconfirmation
 - Be careful about disciplinary action without reconfirmation

What Kind of MRO is Your MRO?

Healthcare Professional vs DOT?

- **DOT/HHS testing is the starting point for all MROs**
 - Purely forensic, deterrent testing
 - Medically explained positives downgraded to negatives by the MRO
 - Benefit of the doubt goes to the donor
- **Healthcare:**
 - Forensic or non forensic detection testing
 - No positives downgraded to negatives
 - All positives must be explained
 - Benefit of the doubt given or not on case by case basis

The Role of Medical Review

- Collaboration: independent and impartial
- Look for legitimate and/or acceptable explanation(s) for laboratory non-negative results.
- Consult with other experts (toxicologists, consultant physicians) when assistance is needed on problem test results, resolve the issues that can be resolved, report the findings and the result.

Healthcare Professional vs DOT?

Monitoring MRO Review is a Combination

- Forensic principles required when license action in question
- All positives reported as positives
- All positives must be explained but explanations may not be acceptable
- Prescriptions
 - DOT/HHS: Once a valid prescription, always a valid prescription
 - Monitoring: Program defines length of time RX is acceptable

Should all Positives Have an MRO Review?

I may be biased...

- Certainly, if there is any dispute about the result, MRO offers an unbiased opinion
- When legal action may be pending, an MRO review helps solidify the case and may prevent inappropriate legal action that may not stand up in a hearing
- For complicated results like EtG/EtS, PEth, benzodiazepine metabolites etc, MRO review may help clarify

What Happens During an MRO Review?

- Identify participant
- Explain verification process
- Donor Advisory Statement (Miranda)
- Ask non-result related questions (if necessary):
 - Collection inquiries?
- Inform of test result
- Seek result specific information:
 - Medical issues, RX, OTC meds, etc.
- Inform of how MRO will report
- Give split specimen testing options
- Answer questions
- Leave MRO phone number

Conclusion

Each Drug Test Result Stands on its Own:

- A second result does not invalidate the first result
- An alternative specimen result does not invalidate a urine result
- In either case the second result may support the first
- BUT: Failure of a split specimen to reconfirm the original result does invalidate the original result

Just Remember -

*No matter how hard
we work,
No matter how right
we are.....*



Questions?

Thank You!