

Pee with a purpose

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Disclosures Statement

I, **Michael Larson PhD**, do **NOT** have any relevant financial interest or other relationship(s) with a commercial entity producing health-care related product and/or services.



Objectives

- Discuss concept of “Peeing with a Purpose” and how we discuss UDT results with patients to be therapeutic
- Overview of Urine Drug Testing (UDT)
- Identify factors that can influence UDT results
- Discuss interpretation of UDT results and common errors



How do we think about UDTs historically?

- Is the historical – punishment based “we caught you” approach really the best way to handle UDTs?
- Is this really what we think a therapeutic alliance is?
- Perhaps consider a therapeutic approach!
- See the UDT results as a “**dashboard warning light**”, similar to missed appts, reported use, not engaged in visits, falling asleep.
- It is an opportunity to show **concern for the patient.**



Start with concern – it deflates the resistance.

- Start every discussion of UDTs with - I am concerned about you (insert actual concern because I hope you have it)
- Patient – Why?
- Your last UDT showed _____ and why I see this is makes me concerned about how you are doing in your recovery.
- Can you tell me more about what happened that led to the use / misuse, etc.



Pee with a purpose – review of UDTs

Example: When we have a patient that reports use of marijuana, another substance, or reports overuse / underuse of Suboxone, we need to consider the **menu of options** (not always a dose reduction – the punishment – the hammer)

What is the best option for the patient to move into recovery.

Consider the following options:

- **Remember:** the use of a substance (or some other problem) is a sign that something is not going well for the person in their recovery. **Concern for the patient and their status is always the first step in the right direction.**
- Determine what occurred around the situation (in this case stress).
- How did they handle the situation, is this is a teachable moment regarding a recovery skill?



Pee with a purpose – review of UDTs - continued

- Are they already in a place (now 2 weeks later perhaps) where they understand what they could have done differently?
 - If yes, a dose reduction may not be indicated – they have learned.
 - **We want to reinforce their understanding of what they could have done differently (not necessarily punish it).**
- **Did they reach out for assistance** from their counselor?
 - Again this may be a reason to reinforce that behavior, noticing they were struggling and reaching out for help.
 - Again, may not be indicated to reduce the dose.



Peel with a purpose – review of UDTs - continued

- There may even be a time when a patient reports overusing their Suboxone (or another substances) **where an increase in their dose may be indicated.**
- Example
 - Pt with trauma and current stress.
 - Pt working with team but has many issues.
 - Making it to all appointments but clearly struggling.
 - Pt asking for assistance, other substances showing up in UDT.



Peel with a purpose – review of UDTs - continued

- This may be a temporary increase (or longer term) because they don't have the ability to deal with the physical side of their opioid use disorder OR their trauma OR their life without further skill development OR that combination right now.
- Per Sheila Weix:
 - “Suboxone has an impact on the stress regulatory response”
 - Sometimes can be beneficial when the pt is working thru their life issues or trauma
- Another option is to get a quick focused counseling visit to address the situation. Again, dose reduction may not be required.



| Pee with a purpose – review of UDTs - continued

Summary:

- Consider the nature of the misstep / slip / relapse to determine how to move forward with the dose reduction, no dose change or a dose increase.
- It really may depend on where the pt is at and the situation surrounding the misuse. Look at the other factors (engagement in counseling, group attendance, etc.).
- The question is what is going to help the patient move forward in their recovery? This is always the question by the way!



Are UDTs consistent with Trauma-Informed Care?

- UDTs - Observed – triggers trauma?
- UDTs - “forced” upon patients, required at the moment under threat, this is not trauma-informed care.
 - Safety tip – Pt always has a choice to not do the UDT



Are UDTs consistent with Trauma-Informed Care?

- UDTs are often done to “catch” the patient doing something wrong, again not a part of a therapeutic relationship.
- Can they be done in a manner consistent with TIC, yes.
- Clearly define how urine screens are performed within your program. Discuss your trauma-informed care approach.



What would a TIC UDT protocol look like?

- Discuss different levels of observation:
 - outside door - most common and appropriate
 - behind screen - only used when prior problems present
 - direct observation - very rare and only used after clear evidence of UDT adulteration



Overview of Urine Drug Testing (UDT)



Additional Disclosures and Information

All urine screens are interpreted per model developed that utilizes statistical analyses and comparison of individual urine screen data to normative data per Larson-Richards analyses guidelines

- **U.S. Patent No. 7,585,680: Method and device for monitoring medication usage M. Larson and T. Richards**
- These analyses are conducted thru the IRB approved Clinical Research Database (LAR30104)



Additional Disclosures and Information

Relevant Publications:

- **Larson, M.E.**, Berg, R.L. & Flanagan, J. (2016). Quantification of oxycodone and morphine analytes in urine: Assessment of adherence. *J Opioid Manag*, 2016;11(6):489-500.
- **Larson, M.E.** & Richards, T.M. (2009). Quantification of a Methadone Metabolite (EDDP) in urine: assessment of compliance. *Clin Med Res*, 7(4), 134-141.



UDT: Safety Tip

- Urine screens are one piece of data and should not be used in a vacuum!!!!
 - They are NOT perfect and we do not have a screen that can perfectly identify with complete certainty that the person is taking the medication as prescribed.
- They are a TOOL to ADD TO clinical judgment, refill data, outside report, etc. to help make decisions.
 - They should RARELY be the sole reason to change a person's treatment plan.



Urine Drug Testing 101

- Why use urine screens?
 - They provide objective data of recent use
 - They are accurate depending on the type of UDT being done.
 - Depending on type of testing performed, learn:
 - Use of the prescribed medication.
 - Use of non-prescribed medications.
 - Use of illicit substances.
- Why people don't use them
 - Sometimes they are difficult to interpret
 - Invasive and can come across as accusatory “you need to submit a urine to show me what you are doing because I do not TRUST your report”



- Step 2: confirmation and quantification:
 - This occurs by Gas (or Liquid) Chromatography and Mass Spectrometry (GC/MS or LC/MS) which is very reliable.
 - My simplistic explanation of GC/MS:
 - Gas/Liquid chromatography maps the various compounds.
 - Mass Spectrometry evaluates the mass (chemical weight) of the compounds.
 - Very specific and reliable.
 - Provides you with confirmation that the specific metabolite was present AND
 - Provides how much of the metabolites were present in the urine (quantification).

Review of factors that influence UDT results



Influence on UDTs: Type of Test Performed

Screening Assay – Just shows positive or negative. This is referred to as “**presumptively positive**” for the identified substance.

- Benefits: Cost, Timeliness of Results.
- Negatives: Confidence if it is true result, no levels.

Quantification or Confirmation – Provides a specific number associated with a metabolite or analyte category.

- Benefits: Levels are meaningful, Confirmation.
- Negatives: Cost, Timeliness of Results.



Influence on UDTs: Drug / Medication Type

Each substance has different excretion patterns, duration of detection, stability of level, etc.
Examples:

- **Marijuana (THCA)** is very stable over time (when corrected for hydration with urine creatinine). THCA has a LONG window of detection (4-6 weeks depending on use patterns).
- **Methadone** is very stable, when using EDDP as metabolite of interest. EDDP also has a long window of detection, 1-2 weeks after last use depending on dose.
- **Stimulants** are less stable, excretion pattern is quicker with a shorter window of detection (only 1-3 days depending on dose).
- **Benzodiazepines** vary in terms of detections times and metabolites.
- **Heroin** shows as morphine (unless testing specifically for it) and the morphine has a very short detection time with lower levels.
- **Buprenorphine** has a fairly stable level for **norbuprenorphine** (metabolite) but **buprenorphine** (parent drug) is more unstable and relates more to time since last dose.



Influence on UDTs: Hydration / Urine Creatinine

Use Urine Creatinine to adjust for sample hydration (part of Larson & Richards patent).

- **Urine creatinine (UC)** is a by-product of muscle metabolism and excretes into the urine at a relatively constant rate.
- Allows us to understand how hydrated (watery vs dense) the urine sample provided is.
- **If UC is LOW**, then the amount of metabolites in the urine from the ingested drug will also be LOW.
- **If UC is HIGH**, then the amount of metabolites in the urine from the ingested drug will also be HIGH.



Influence on UDTs: What about the levels?

Based on my research, the most relevant factors that influence LEVELS that are present in the Urine (in order of importance):

- Drug Dose and Urine Creatinine (Hydration of sample) are consistently primary factors
- Consistency of use / time since last use
- Liver (high and low), Kidney function (low) and Hepatitis C
- Diet and individual metabolism
- Gender and BMI



Interpretation of UDTs and common interpretation errors



UDT Errors in Interpretation

- **Presumptive Positive Results:**
 - This is not a confirmation that they used that substance, there can be cross-reactivity.
 - Example: Cocaine positive may be due to certain antibiotics.
Methamphetamine may be due to amphetamine / psychostimulant use.
 - Confirm if it is important to know for sure.
- **NOT CORRECTING WITH URINE CREATININE:**
 - Levels are **ONLY** relevant when you correct for hydration of the urine sample.
 - Actual Data: THCA = 115 vs THCA = 331 vs THCA = 601



THCA and URINE CREATININE Example:

- **Actual Data:** 601 with Urine Creatinine = 139.5; THCA to Urine Creatinine Ratio of 4.31 (Divide THCA level by Urine Creatinine to get ratio) **This is the LOWEST level of use.**
- **Actual Data:** 115 with Urine Creatinine = 26.6; THCA to Urine Creatinine Ratio of 4.32 (This person is using slightly more marijuana but they are essentially the same). **Slightly higher level of use**
- **Actual Data:** 331 (THCA) with Urine Creatinine = 39.5; THCA to Urine Creatinine Ratio of 8.4, nearly double the adjusted level. **This is clearly the HIGHEST LEVEL OF USE.**

Marijuana Interpretation: Use of Urine Creatinine Ratio

1. Rules for Marijuana (THCA) interpretation:
2. Divide the THCA level by Urine Creatinine (example $100 / 50.0 = 2$).
3. Identify that ratio and locate in table below.
4. If THCA / Urine Creatinine ratio is LESS THAN 0.5, this may be due to PASSIVE INHALATION (e.g., being in a closed space with other smoking marijuana and you are passively inhaling that smoke). This could also suggest a very infrequent user or a person who has not used for a several weeks and the THCA is excreting out of the system.
5. If THCA / Urine Creatinine ratio is 0.5 OR HIGHER, then we can accurately identify that the person has had ACTIVE INHALATION at some point in the recent past (e.g., 1-30 days or so).
6. CAUTION: Individuals with kidney dysfunction may show higher levels due to kidney problems, so if person has those known problems (e.g., recent low eGFR) the some caution may be indicated.

Low	High	Comment
0.0 to	0.49	Possible PASSIVE INHALATION or remote use or very low level use. Possible CBD Oil (Wisconsin Version) use.
0.5 to	3.0	ACTIVE INHALATION CONFIRMED but likely fairly low level use (e.g., 1 x per week or less).
3.0 to	7.0	Active inhalation but likely more frequent. This may be in the several times a week user.
7.0 to	10.0	DAILY USERS will fall in this category. Likely chronic users.
10.0 or	Above	MULTIPLE TIMES PER DAY USERS. Likely CHRONIC AND CONSISTENT USERS.



UDT Errors in Interpretation

Not understanding the metabolites:

- BZE = **BENZOYLECGONINE** and is **NOT** a benzodiazepine. It is the cocaine metabolite.
- Several medications have more than one metabolite:
 - Methadone – can have methadone and EDDP
 - Oxycodone – oxycodone, noroxycodone, oxymorphone
 - Hydrocodone – hydrocodone and hydromorphone
 - Morphine – morphine and hydromorphone
 - Methamphetamine – methamphetamine and amphetamine
 - Codeine – morphine and codeine (pathway for even hydrocodone or hydromorphone but it is rare)



Cocaine Example

3/11/10 13:10 Pain Clinic Survey w/ Confirm

Beuscher, Tara L NP (77061)

Performing Facility: Jt Venture Lab

Collecting Facility: Minocqua Center

<u>Result</u>	<u>Value</u>		<u>Units</u>
Cannabinoids	POS		
THCA	9	A	ng/mL
Cocaine	POS		
BZE	44	A	ng/mL
Benzodiazepines	POS		
Nordiaz/Oxaz	159	A	ng/mL
Diaz/Temaz	1268	A	ng/mL
Barbiturate	NEG		
Amphetamines	NEG		
Phencyclidine	NEG		
Propoxyphene	NEG		
Methadone	NEG		
Opiate	NEG		
OxycodoneGrp	POS		
Oxycodone	79	A	ng/mL
Oxymorphone	346	A	ng/mL
Ethanol	NEG		
Creat-Ur	46.1		mg/dL

A quantitative confirmatory test for Cannabinoids was done & billed for.

A quantitative confirmatory test for Cocaine metabolite was done & billed for.

A quantitative confirmatory test for Benzodiazepines was done & billed for.

A quantitative confirmatory test for Oxycodone and/or Oxymorphone was done & billed for.

3/21/09 15:29 Urine Dipstick Reflex Micro

Urine Screen was reviewed per Larson-Richards Protocol, findings:

(*) APPROPRIATE: Ratio Z-score of -1.11 for oxycodone, on low end of expected range.

(*) APPROPRIATE: Ratio Z-score of -1.06 for temazepam.

(*) PROBLEMATIC: Positive for THCA at a very low level with ratio of 0.20, which could represent passive inhalation.

(*) PROBLEMATIC: Positive for COCAINE at very low level with ratio of 0.95.

BZE stands for BENZOYLECGONINE the cocaine metabolite (NOT benzodiazepine).

UDT Errors in Interpretation

Not understanding the specific test that is done and what it covers:

- Fentanyl is usually covered but may be assessed only when a fentanyl specific test is done
- Tramadol is much the same way as fentanyl, may require a specific test
- Methylphenidate is much the same way as fentanyl and tramadol, may require a specific test
- Each company has different menu options and that is important
- Must understand what is being tested and what is NOT



Buprenorphine UDT Interpretation Specifics #1

Buprenorphine when ingested leads to two analytes that will be present in a urine screen:

- Buprenorphine: This is the parent drug.
- Norbuprenorphine: This is due to the body's metabolism of the buprenorphine, this is an active metabolite in the body.



Buprenorphine UDT Interpretation Specifics #1

If the person is taking the medication in a STEADY STATE or consistently we will see:

- Norbuprenorphine > (greater than) buprenorphine.
- Usually the ratio will be 2 to 1 or more (e.g., norbuprenorphine will be 2 x higher than buprenorphine generally) but there is a fairly broad range.

Buprenorphine UDT Interpretation Specifics #1

This ratio allows analysis of the following:

- Steady state use.
- Loading Dose, where Buprenorphine is higher than Norbuprenorphine.
- Weaning Dose, where Norbuprenorphine is significantly higher than Buprenorphine.
- FILM DIPPING, where ONLY buprenorphine is present because the body has not shown any metabolism.



Buprenorphine UDT Interpretation #2

- Norbuprenorphine is most stable metabolite from our review, though total (buprenorphine + norbuprenorphine can be helpful at times).
- When we then CORRECT the NORBUPRENORPHINE with UC (simply divide NORBUPRENORPHINE by UC) we get a NORBUPRENORPHINE RATIO.



Buprenorphine UDT Interpretation #2

- We then statistically COMPARE this ratio to other individuals (adjusted for liver / kidney function if present and gender, possibly age) to a Normative Dataset of people on the same dose that have been ASSESSED TO BE ADHERENT.
- The results of this statistical comparison is what we call a Ratio Z-score, where roughly 66% should be between +/-1.00 and 95% should be between +/-2.0.
 - We adjust our scale due to our inclusion of the actual sample in the distribution (which intentionally broadens our variability to be assured of adjustment for individual characteristics, such as fast or slow metabolizers).
 - We use +/- 1.5 Z-scores CLINICALLY due to inclusion of the new sample in the distribution calculations.



Steady State User

10/30/15 10:48 Pain Clinic Drugs w/ Confirm			URINE
Performing Facility: Marshfield Labs, 1000 N OAK AVE, MARSHFIELD, WI 54449			
Cannabinoids NEG	Cocaine NEG	Benzodiazepine NEG	
Barbiturate NEG	Amphetamines NEG	Methadone NEG	
Opiate NEG	OxycodoneGrp NEG	Ethanol NEG	Buprenorphine Group POS
Norbuprenorphine 482 A	Buprenorphine 202 A	Creat-Ur 95.8	
A quantitative confirmatory test for Buprenorphine was done & billed for based on initial immunoassay screen positive result.			
Buprenorphine Group: This test was developed and its performance characteristics determined by Marshfield Labs. This laboratory is certified under the Clinical Laboratory Improvement Amendments (CLIA) to perform high complexity testing.			

Pt currently on buprenorphine or Suboxone therapy, urine screen was review per Larson-Richards Protocol, findings:

(***) LEVEL ANALYSIS: Buprenorphine Total Metabolites Ratio Z-score of -0.88 (female dose norms) is appropriate.

(***) STEADY STATE ANALYSIS: NorB to Bup Ratio Z-score of -0.67 suggests steady state use.

(*) Remainder of urine screen was negative for problematic substances. This is considered a "CLEAN AND APPROPRIATE" urine screen.

Buprenorphine – The Injection Profile

- Yes – People are now reporting injecting Suboxone and Subutex. This has been confirmed.
- We have now identified the INJECTION PROFILE to assist in identifying when a patient may be injecting and trigger an Injection Site Diagram to garner supporting evidence.



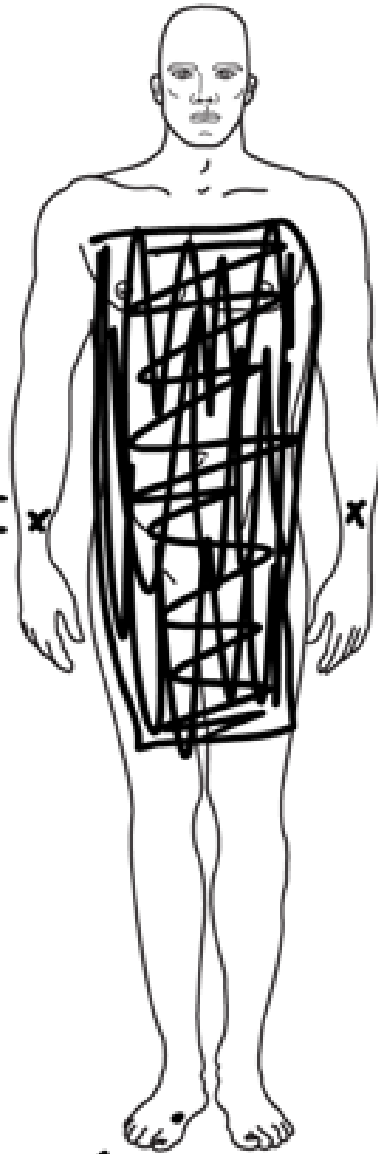
Buprenorphine – The Injection Profile

- Injection Profile Specifics:
 - BUP (parent drug buprenorphine) > NORB (Analyte norbuprenorphine)
 - BUP must be higher than expected for prescribed dose (Ratio Z-score > 2.0 in my mind)
 - NORB should be on the lower end of the expected range for prescribed dose (may not be fully low but lower end of range)
- **EXAMPLE:**
(*) CONCERN - MAT positive but levels suggest potential INJECTION PROFILE (where either BUP > NORB or BUP is elevated for norm group). BUP Ratio Z-score elevated at +3.23 and NORB Ratio Z-score is low at -1.23, this does strongly fit an injection profile.



Indicate injection site locations.

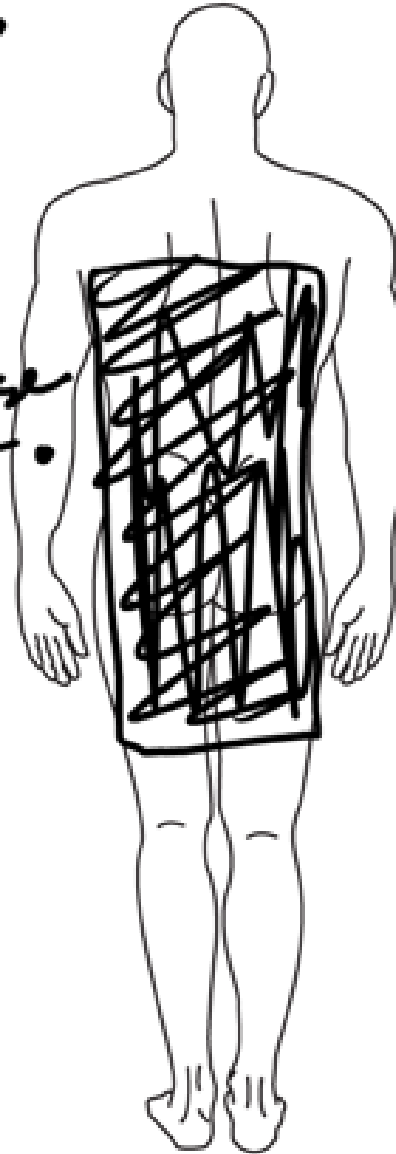
Front View



possible
injection
sites

Multiple
Scabbing on
both legs

Back View



Bruise
Left

Right

Left
possible
active
sites

Way too much information

- Contact Michael Larson PhD with questions or comments.
Larson.michael@marshfieldclinic.org
- Thank You!

