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Toxicology Testing in Addiction Treatment: 2020 Update

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Provides support to prescribers and their practices in addressing the needs of their patients with substance use disorders and chronic pain management.

All Services are FREE

- Phone consultation for clinical questions
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- Assistance with addiction and behavioral health resources and referrals
- Technical assistance to practices implementing or expanding office-based addiction treatment services
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My Professional Profile

- Board Certified in Family Medicine and Addiction Medicine
- Medical Director, UMMC Addiction Treatment Programs at 1001 West Pratt
  - OTP
  - OBOT
  - IOP
  - DASAM
  - Health Home
  - HCV treatment, nascent integrated primary care practice
  - Research projects (biomedical and psychosocial)
- Preceptor, UM Family Medicine Residency Program

Outline

- Toxicology rationale/philosophy
- Key Vocabulary
- Common clinical test matrices & characteristics
  - Urine
    - Screening/Presumptive & Confirmatory/Definitive
  - Saliva
  - Blood
  - Hair/Nails
  - Sweat/Breath
- Cases
- Questions

Why Test?

- Therapeutic tool
  - For supporting recovery, not exacting punishment
  - Chance to explore denial, motivation, and current use.
  - Congratulate abstinence
- Assessment and treatment planning
- Monitoring of current treatment plan effectiveness
  - Ensure adherence

Key Vocab

- Analyte—what is being identified/measured
- Expected vs unexpected
- Matrix/matrices
- Positive vs negative
- Window of detection
- Presumptive vs Definitive
- Clean vs dirty

Presumptive	Definitive
Qualitative	Quantitative
Preliminary	Confirmatory
Immunoassay	Chromatography/mass-spectrometry
Point of care/in-office/lab-based	In-office/lab-based
Screen	Confirmation
Semi-quantitative/quasi-quantitative	Absolute level/creatinine-corrected
Simple (cup/strip/dipstick/cassette)	Complex
Class or category test	Specific drug identification

Hurford et al 2017

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Hurford et al 2017

The Most Cost-Effective Definitive Test

- Ask the Patient!
- Concordance between self-report and biochemical verification >80% (in treatment-seeking individuals)

Clark et al 2016

Responding to Test Results (1)

- Maintain the spirit of Motivational Interviewing:
  - Collaboration: step away from the “expert” role
  - Express empathy: don’t be a jerk
  - Evoking or drawing-out the client’s ideas about change: “change talk”
  - Support self-efficacy: highlight patient autonomy
  - Roll with resistance: “the customer is always right”

Responding to Test Results (2)

- Attach a meaningful response to all results, and deliver ASAP
  - Why POC testing is optimal
- Use a nonjudgmental, nonconfrontational, and nonstigmatizing approach
  - Acknowledge uncertainty
  - Contexualize
  - Collaborate

cf Hurford et al 2017

Choosing a Test Matrix

- Which can best answer the question at hand?
  - Urine best established
  - Other matrices provide different levels of sensitivity and specificity over different windows of detection
    - For example, after heroin use, 6-MAM remains present in saliva longer than in urine, but morphine sticks around longer in urine
  - Susceptibility to tampering?
  - Particular patient characteristics (dialysis, paruresis, baldness)

Hurford et al 2017

Choosing a Test Matrix

TABLE 4. Comparing Testing Characteristics Across Matrices

	Blood	Breath	Oral Fluid	Urine	Sweat	Hair
General detection period	<24 hours [2] 1–8 hours [25] 1–48 hours [26]	~1 hr per standard drink	<24 hours [2] 12–24 hours [27] 1–36 hours [28] 5–48 hours [29] 12–48 hours [25]	1.5–4 days [29] 1–3 days [25,26,30]	Continuous, usually 1–4 weeks [2,26]	7–90 days [2] 7–100 days [26]
POCT/On-site immunoassay available	Yes, primarily used for alcohol	For alcohol	Yes	Yes	No	No
Primarily detects	Parent drug compound; blood alcohol concentration	Parent drug compound; blood alcohol concentration	Parent drug compound	Drug metabolite	Parent drug compound	Parent drug compound
Best use in treatment setting	Determination of acute impairment or intoxication for alcohol	Determination of acute impairment or intoxication for alcohol	Short-term detection in ongoing treatment	Intermediate-term detection in ongoing treatment	Medium-term prospective monitoring	Long-term monitoring; 3-month drug use history
Ease of collection	Requires staff trained in phlebotomy	Easily collected	Easily collected	Requires specialized collection facility (restroom)	Easily collected	Easily collected
Intrusiveness of collection	High for intravenous access	Low	Low	High	Low	Low
Resistance to tampering	High	High	High, but some uncertainty	Low	High, but some uncertainty	High when chemically untreated
Retesting same sample	Difficult	Generally not possible	Difficult	Possible	Possible depending on patch used	Easy

	Minutes	Hours	Days	Weeks	Months
Blood					
Breath					
Oral Fluid					
Urine					
Sweat					
Hair					

Hurford et al 2017

Urine

- Both parent drug and metabolites present, usually in higher concentrations than in blood/serum.
- About 2 hours from use to detection
- Point of care testing available, reliable
  - Need CLIA waiver, FDA approval
  - Possibility of misinterpretation
- Presumptive tests are immunoassays
  - Risk of cross-reactivity, false positives
- Definitive tests are GCMS/LCMS
- Remember cut-offs & detection windows

Moeller et al 2017

Detection Windows (maybe)

TABLE 2. Approximate Drug Detection Time in the Urine[9-17]

Drug	Length of time detected in urine
Alcohol	7-12 h
Amphetamine	48 h
Methamphetamine	48 h
Barbiturate	
Short-acting (eg, pentobarbital)	24 h
Long-acting (eg, phenobarbital)	3 wk
Benzodiazepine	
Short-acting (eg, lorazepam)	3 d
Long-acting (eg, diazepam)	30 d
Cocaine metabolites	2-4 d
Marijuana	
Single use	3 d
Moderate use (4 times/wk)	5-7 d
Chronic use (daily)	10-15 d
Chronic heavy smoker	>30 d
Opioids	
Codeine	48 h
Heroin (morphine)	48 h
Hydromorphone	2-4 d
Methadone	3 d
Morphine	48-72 h
Oxycodone	2-4 d
Phencyclidine	8 d
Synthetic cannabinoids	
Single use	72 h
Chronic use	>72 h
Synthetic cathinone	Variable

Moeller et al 2017

Urine problems

- Looking for adulteration, substitution, and dilution
- Expected characteristics:
  - T between 90 and 100 deg F
  - pH between 4.5 and 8
  - Spec Grav 1.002 to 1.030
  - Cr > 20mg/dL
- If out of the expected range, get another sample

Moeller et al 2017

Saliva/Oral Fluid

- Saliva levels corollate with plasma levels
- Typically has a shorter window of detection
- Easier to collect
- Levels are affected by oral route of administration
- Problems: dry mouth (particularly problematic with cannabis and stimulants), leftovers

cf Hurford et al 2017

Blood

- Requires specialized staff
- Handing samples is hazardous
- Invasive
- Ability to obtain sample in emergency situations

cf Hurford et al 2017

Hair/Nails

- Can be thought of as a “continuous collection device”
- Head hair window of detection: 3 months
- Body hair window of detection: 12 months
- Potentially discriminatory, subject to external contamination, expensive
- Usually used in forensic settings; ASAM says “not appropriate” in addiction treatment

cf Hurford et al 2017

Breath

- Most commonly used as POC EtOH testing
- Biggest problems: sample contamination, breath volume
  - Auto-brewery syndrome a bit less common!
- Use for other substances is compelling but still exploratory

cf Hurford et al 2017

Sweat

- Collected with an adhesive patch
- Not ready for prime time at this point

cf Hurford et al 2017

Most Useful Presumptive Analytes

- Amphetamine/Methamphetamine
- Barbiturates
- Benzodiazepines
- Buprenorphine
- Cannabis (THC)
- Cocaine metabolite
- Fentanyl
- Heroin metabolite (6-acetylmorphine)
- Methadone metabolite (EDDP)
- Opiates
- Oxycodone
- PCP

Important Metabolites

- Norbuprenorphine
- 2-ethylidene-1, 5-dimethyl-3, 3-diphenylpyrrolidine (EDDP)
- Benzoylecgonine
- 6-MAM
- Norfentanyl (or lack thereof)
- Oxymorphone & hydromorphone (see below)

Opiates

- Urine screening specific to morphine
- Possible cross-reactivity: quinolones, poppy seeds
- Need separate screening assays for semisynthetic and synthetic opioids

Moeller et al 2017

Opioids

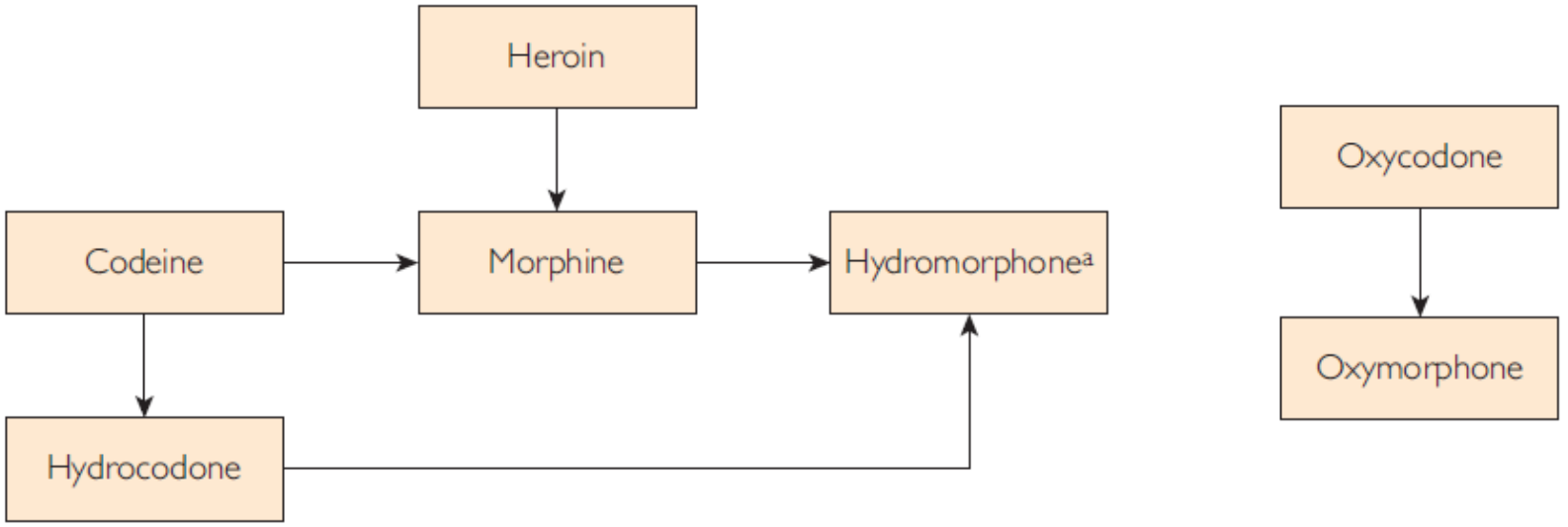

FIGURE 1. Metabolism of opioids.[136,141] [a]Morphine is metabolized to hydromorphone in very small amounts.

Moeller et al 2017

Fentanyl

- Seems to stick around a lot longer than the textbooks say!
- Occasionally see people that test positive for fentanyl and negative for norfentanyl
- Norfentanyl only: consistent with relatively distant use
- Dipsticks are cheaper than reputation would suggest...

Buprenorphine

- Not detected by opiate or oxycodone screen
- POC urine testing may be vulnerable to tampering
- Definitive testing gives you bup and norbup
- Some fancy test panels also give naloxone levels

Buprenorphine

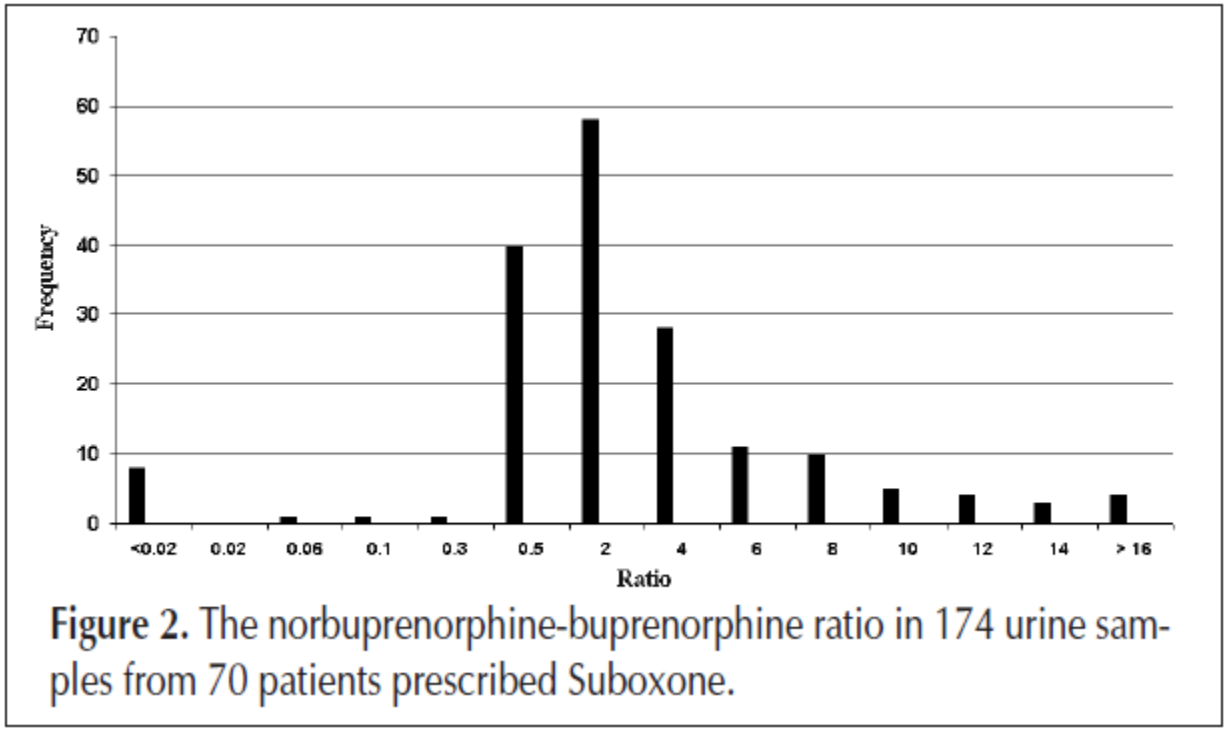

Figure 2. The norbuprenorphine-buprenorphine ratio in 174 urine samples from 70 patients prescribed Suboxone.

Hull et al 2017

Benzodiazepines

- Most immunoassays detect oxazepam or nordiazepam, not glucuronide conjugates
- Relatively high cutoff for potent BZDs prescribed in lower doses
- False positives relatively rare (despite patient reports), other than sertraline.

Benzodiazepines

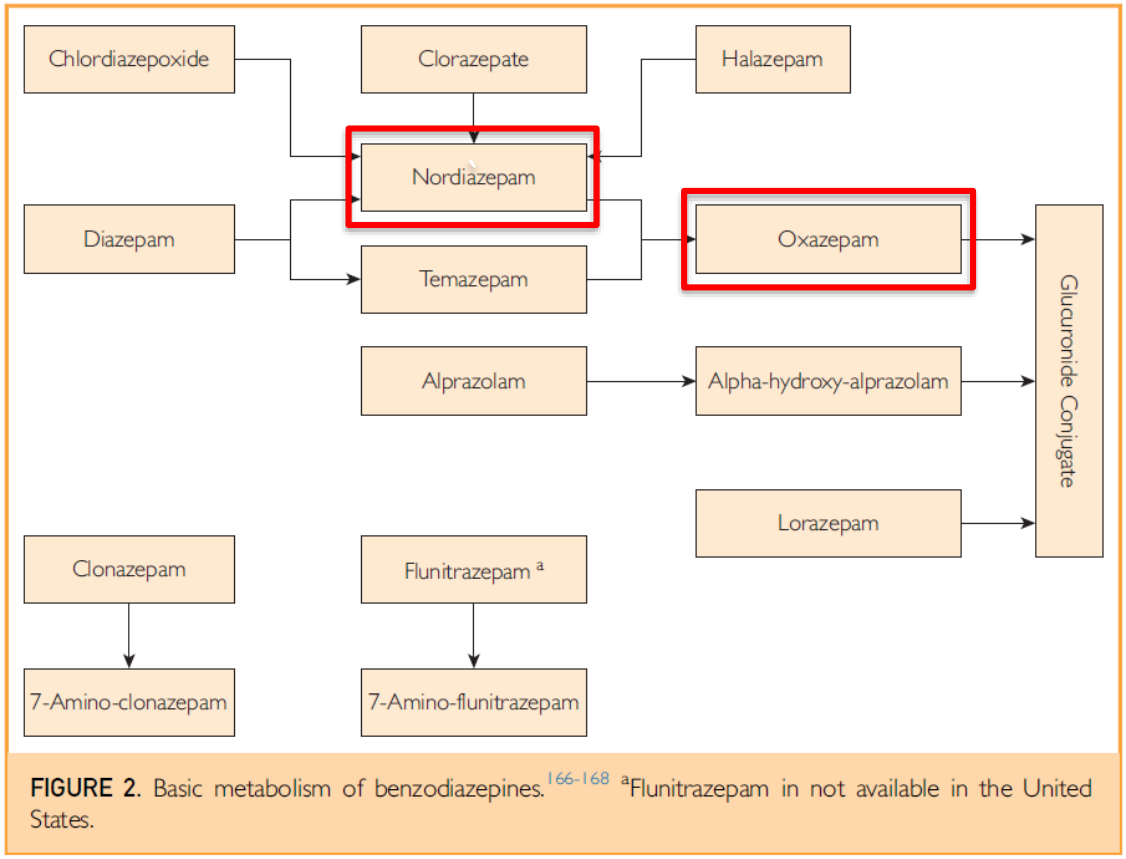

FIGURE 2. Basic metabolism of benzodiazepines.[166-168] [a]Flunitrazepam in not available in the United States.

Moeller et al 2017

Amphetamines

- Lots of false positive results: pseudoephedrine, bupropion, labetalol, ranitidine, metformin, selegiline, Vick's vapor inhalers, dietary supplements
- Will not detect methylphenidate
- *Should* detect Adderall, Vyvanse

Cocaine

- Urine assays looking for benzoylecgonine.
- Minimal cross-reactivity with other substances
- “I may have handled it though…”

Cannabis

- Urine screening sensitive to several metabolites
- GCMS specific for THC-COOH
  - (9-tetrahydrocannabinol-9 carboxylic acid)
- Possible cross-reactivity: pantoprazole (?), NSAIDs (rare—maybe ~0.2%), and efavirenz
- Prolonged exposure to secondhand smoke in unventilated—may get closer to the cutoff

Drill: Buprenorphine Test Results

Patient	Creatinine (mg/dL)	Buprenorphine (ng/mL)	Norbuprenorphine (ng/mL)	Ratio*	Naloxone (ng/mL)
A	101.8	220	< 5.0	†	< 100
B	54.6	610	6.7	0.011	113
C	13.5	1400	19	0.014	624
D	< 5.0	10,000	Present‡	†	4103
E	51.6	13,000	230	0.018	4260
E	56.0	29,000	270	0.009	11,636
F	37.4	49,000	250	0.005	15,155
G	292.4	990	1200	1.212	< 100
H	308.8	1200	1000	0.833	< 100

* Ratio = urine norbuprenorphine/buprenorphine.
† Cannot be calculated.
‡ Norbuprenorphine was detected but could not be quantitated.

Hull et al 2017

Drill: Buprenorphine Test Results

Table II. Characteristics of Seven Urine Samples Judged to be Adulterated (Patients A–F) Compared to Samples Judged to be Authentic Samples (Patients G–H)

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Hull et al 2017

Respiratory Pandemic

- A fatal viral respiratory illness sweeps the globe
- ~30% of infected individuals are asymptomatic but infectious, limiting the utility of screening interventions
- Widespread safer-at-home orders are issued
- What next?

Respiratory Pandemic: ASAM recs

- Use telehealth
- Provide ample buprenorphine, including refills
- Don’t require psychosocial interventions
- Harm reduction interventions (naloxone +)
- Minimize in-person interactions, esp for high risk

Respiratory Pandemic: ASAM recs

- Toxicology specific
  - As always, test judiciously
  - Consider pausing testing
  - Continue testing only in the most pressing cases
  - Consider other means of adherence monitoring
  - Use appropriate PPE, sanitize collection areas
  - Consider remote testing

Success (?)

- After 30 years of injecting extramedical opioids and smoking crack, your patient seeks addiction treatment.
- Immediately after initiating their buprenorphine treatment, their weekly urine toxicology screens reveal +bup, +norbup, +benzoylecgonine, +THC. Given ongoing drug use, you continue short prescriptions and weekly urine toxicology testing.
- 2 years later, their urine remains remarkably consistent.

Oxymorphone interpretation

- Your patient gets urine toxicology to monitor their oxycodone treatment
- A recent confirmatory test revealed oxymorphone
- The lab provides some helpful guidance: “oxymorphone is consistent with Opana® treatment.”
- Next steps?

Review

- Toxicology testing is a therapeutic intervention
- Avoid stigmatizing language; remember MI
- Urine and oral fluid best; limited role for breath and blood testing
- Be even more parsimonious with your testing now than ever
- Engagement and adherence are paramount

QUESTIONS?

TYPE QUESTIONS INTO THE CHAT OR RAISE HAND

Additional questions:

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