How to correctly interpret a urine drug screen result

A Project RAMP Resource

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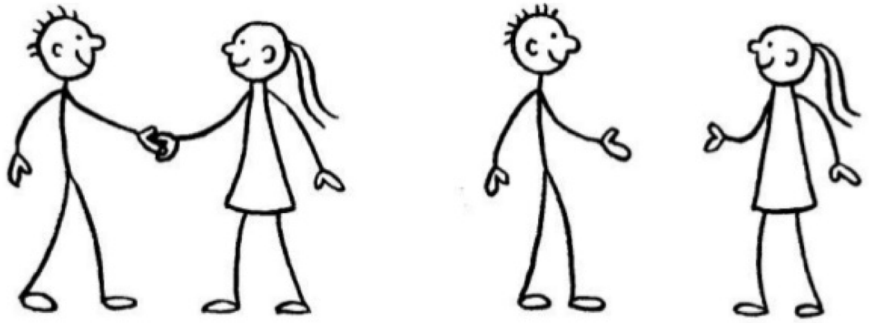
INTRODUCTIONS



CONFLICT OF INTEREST AND DISCLOSURE

- Dr. Gordon has no fiduciary conflicts of interest
- Some of the material presented herein has been previously published from work at the University of Pittsburgh, University of Utah, and the Veterans Health Administration
- The views expressed in this presentation are Dr. Gordon's and do not necessarily reflect the position or policy any institution, agency, or government

TODAY's GOALs

- Understand the role of urine drug screens in the monitoring of patients on opioids
- Understand the role of urine drug screens for patient on opioid agonist treatment
- Correctly interpret a variety of urine drug screen results

CASE 1: Adam's Chief Complaint

- Adam is a 49 year old male who presents to your primary care clinic
- He has been your patient for 10 years
- He recently was diagnosed with stage 4 colon cancer
- He has been placed on opioids for pain s/p a colon resection
- Otherwise, he is healthy except he has had a "cold" recently
- He admits to having a lot of stress and has been hanging out with his college "hippy buddies" recently. "My wife doesn't like them"
- You have called him in to discuss his urine toxicology report

CASE 1: Adam's history

- **Past Medical History:**
  - Nicotine use disorder – he smokes ½ pack per day
- **Social history:**
  - Divorced and remarried
  - Works in healthcare
- **Family history:**
  - Mother and Father are alive and well
  - Three children – no diseases

CASE 1: Adam's Medications/Studies

- **Allergies:**
  - None
- **Medications:**
  - Oxycodone 5mg po q6 hours prn
- **Labs/Studies:**
  - Urine drug screen:
    - Morphine **negative**
    - Cocaine **negative**
    - Amphetamine's **positive**
    - 6-AM **negative**
    - Marijuana **negative**

CASE 1 : Adam’s conundrums

- Interpret the lab result.

- What would you say to Adam?
- What actions would you take?

TODAY's GOALs

- **Understand the role of urine drug screens in the monitoring of patients on opioids**
- Understand the role of urine drug screens for patient on opioid agonist treatment
- Correctly interpret a variety of urine drug screen results

General Goals of Drug Testing

- Important and routine component of treatment for all patients on on opioids.
- Testing is not meant to "catch" the patient
- A positive (or negative result) should be interpreted cautiously
- A positive test result should not simply lead to discharge from treatment, but an opportunity for reviewing the current plan

- Basically, drug testing procedures and follow up should be similar to other tests we routinely do
  - Are we punitive when someone’s glucose is high?
  - Are we punitive when someone’s cholesterol is high?

General Goals of Drug Testing

- Think of Urine Drug Screen results as a test on the PROVIDER's treatment quality
  - Do you need to change care?
  - Do you need to intensify care?

- Think of Urine Drug Screens as akin to HBa1c results
  - Monitoring TREATMENT over time….

Drug Testing in the Office

- Ideally laboratory testing could be:
  - Random
  - Observed
  - Convenient for the patient
  - High quality
  - Able to offer timely result

Screening and Confirmatory Tests

SCREENING TESTS

- Relatively rapid
- Inexpensive
- Usually immunoassay
- Performed in lab or point-of-care testing (POCT)
- Results are PRESUMPTIVE until confirmed by a more definitive test
- Good for initial check (negative)

CONFIRMATORY TESTS

- Usually time consuming
- Expensive
- Usually chromatography and spectrometry
- Likely performed in certified lab
- More PRECISE and more SPECIFIC
- Results considered definitive
- Not needed all the time…

What IS in a typical *screening* test

- Opiates (detects morphine, codeine, and metabolites)
- Benzodiazepine
- Cannabinoids
- Amphetamines
- Cocaine metabolite (benzoylecgonine)

What is NOT in a typical *screening* test

- Buprenorphine (and nor-buprenorphine)
- Fentanyl
- Oxycodone
- Methadone
- Benzodiazepines
- Alcohol metabolite (ethyl glucuronide or ethyl sulfite)

Sample Authenticity

- Urine samples can be altered
  - Adding a substance so that it appears to have been ingested (adulterant)
  - Diluting with water to decrease chances of detecting that are substances present
  - Providing a sample produced earlier or by another person

Sample Authenticity

- Some of these can be detected by examining physical characteristics of the urine
  - Temperature
  - Specific Gravity
  - Creatinine

Characteristic	Normal Range
Temperature*	90-100 F
pH	4.5 to 8
Creatinine	> 20 mg/dL
Specific gravity	> 1.002 to 1.030

* within 4 minutes of collection

Duration often results in urine drug tests

Substance	Duration
Alcohol Ethyl glucuronide	7-12 hours 2-5 days
Amphetamine	2 days
Benzodiazepines (short-acting, e.g. lorazepam) Benzodiazepines (long-acting, e.g. diazepam)	3 days 30 days
Buprenorphine	4-10 days
Cocaine	2-4 days
Ethyl glucuronide	2-6 days
Heroin or morphine	1-3 days
Marijuana (single use) Marijuana (chronic use)	3 days 30+ days
Opioids	2-4 days

Moeller et al., Mayo Clinic Proc. 2017

Poppy Seeds and Opioids

- Poppy seeds can contain ***codeine*** and ***morphine*** in amounts detectable on UDT after ingestion, including after eating poppy-seeded baked goods such as bagels or pastries
- Because morphine and codeine are actually present in the seeds:
  - positive results due to poppy seeds are chemically indistinguishable from those due to use of opiates, even with confirmatory testing
- Patients being tested for opioids should be advised to avoid poppy seeds and foods containing them
  - abstinence from poppy seed-containing foods may be included as part of a treatment agreement in order to allow informative testing for opioid use
- Concentrations of codeine and morphine > 2000 ng/ml are generally considered to suggest opioid use rather than poppy seed ingestion
  - Therefore consider confirmatory/quantification testing

Moeller et al., Mayo Clinic Proc. 2017

Opioid metabolism

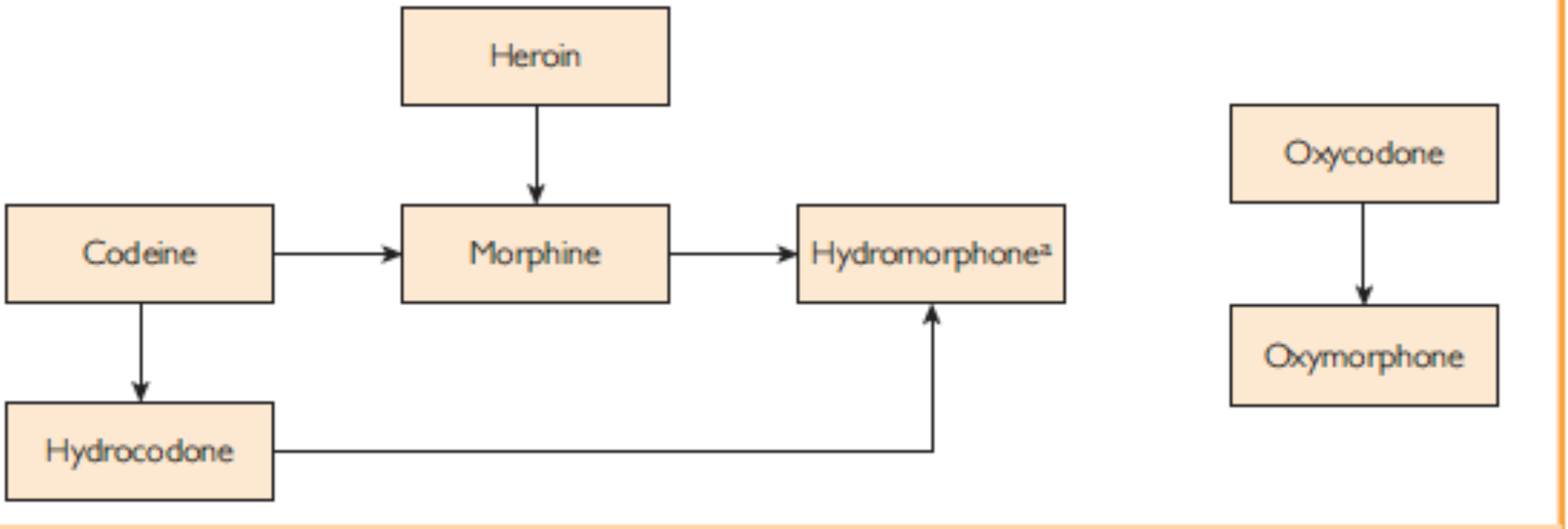


FIGURE 1. Metabolism of opioids.[136,141] [a]Morphine is metabolized to hydromorphone in very small amounts.

Moeller et al., Mayo Clinic Proc. 2017

Benzodiazepine metabolism

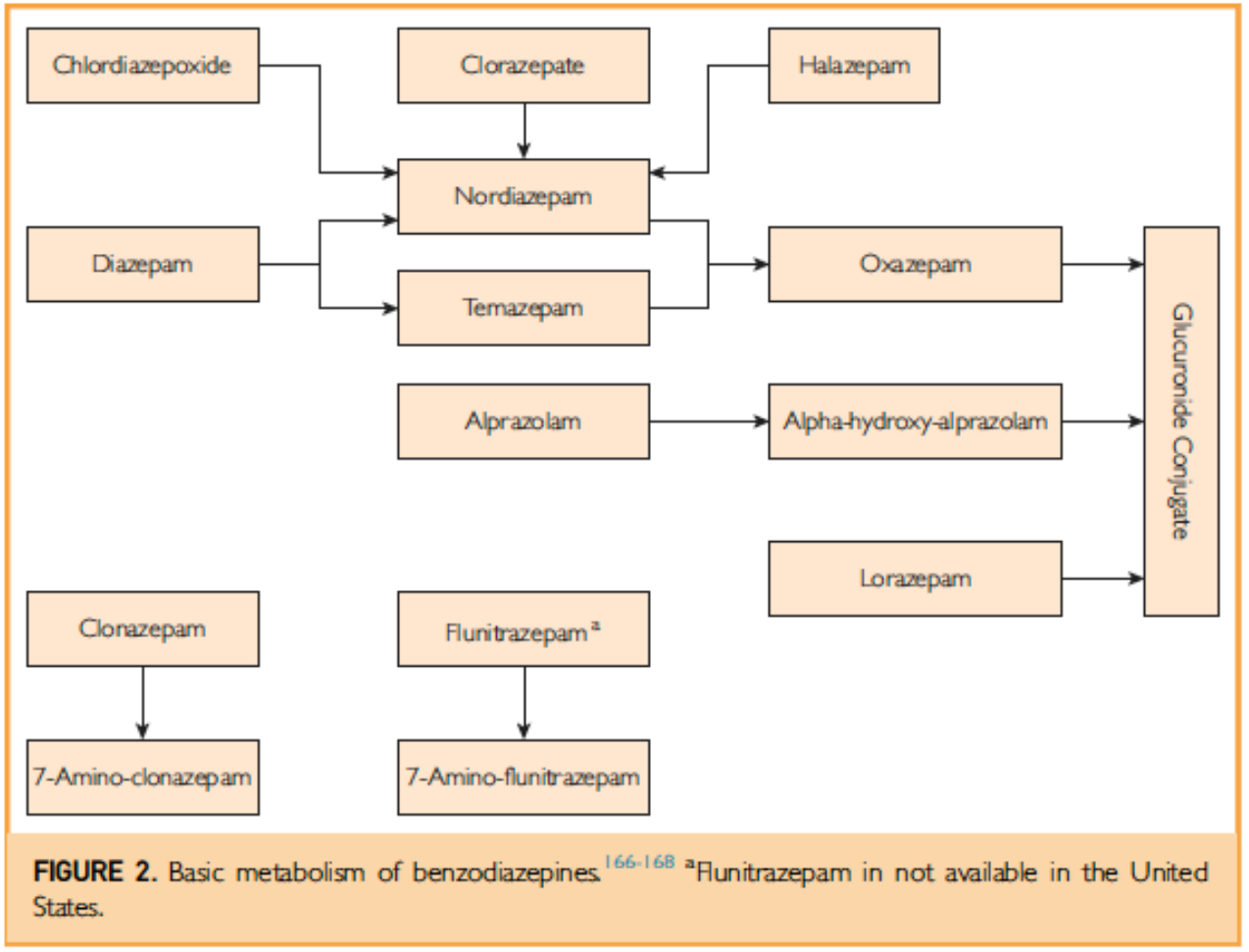


FIGURE 2. Basic metabolism of benzodiazepines.[166-168] [a]Flunitrazepam in not available in the United States.

Moeller et al., Mayo Clinic Proc. 2017

CASE 1: Adam's conundrums???

- **Interpret the lab result**
- **What would you say to Adam?**
- **What actions would you take?**

RECALL:

On oxycodone

UDS results:

Morphine	**negative**
Cocaine	**negative**
Amphetamine's	**positive**
6-AM	**negative**
Marijuana	**negative**

What about Amphetamine result?

- False “positive”!

Screening test	Reported causes of false positives (*not* comprehensive)
Amphetamines	amantadine aripiprazole bupropion *l*-methamphetamine (present in some nasal sprays) phenylephrine pseudoephedrine
Benzodiazepines	sertraline
Cannabinoids	NSAIDs proton pump inhibitors
Fentanyl	trazodone
Methadone	diphenhydramine doxylamine
Opiates	dextromethorphan

Moeller et al., Mayo Clinic Proc. 2017

CASE 2: Angry Adam's Chief Complaint

- Adam is a 49 year old male who presents to your primary care clinic
- He has been your patient for 10 years
- He is on buprenorphine/naloxone for opioid use disorder
- You have called him in to discuss his urine toxicology report

CASE 2: Angry Adam's history

- **Past Medical History:**
  - Opioid Use Disorder (OUD)
  - Nicotine use disorder – he smokes ½ pack per day
- **Social history:**
  - Divorced and remarried
  - Works in telecommunication
- **Family history:**
  - He is adopted
  - Three children – no diseases

CASE 2: Angry Adam's Medications/ Studies

- **Allergies:**
  - None
- **Medications:**
  - Buprenorphine/naloxone 8/2mg qd
- **Labs/Studies:**
  - Urine drug screen:
    - Morphine — negative
    - Cocaine — negative
    - Amphetamine — negative
    - 6-AM — **positive**
    - Marijuana — negative
    - Buprenorphine — **positive**
    - Nor-buprenorphine — **negative**

CASE 1 : Angry Adam's conundrums

- Interpret the lab result.

- What would you say to Adam?
- What actions would you take?

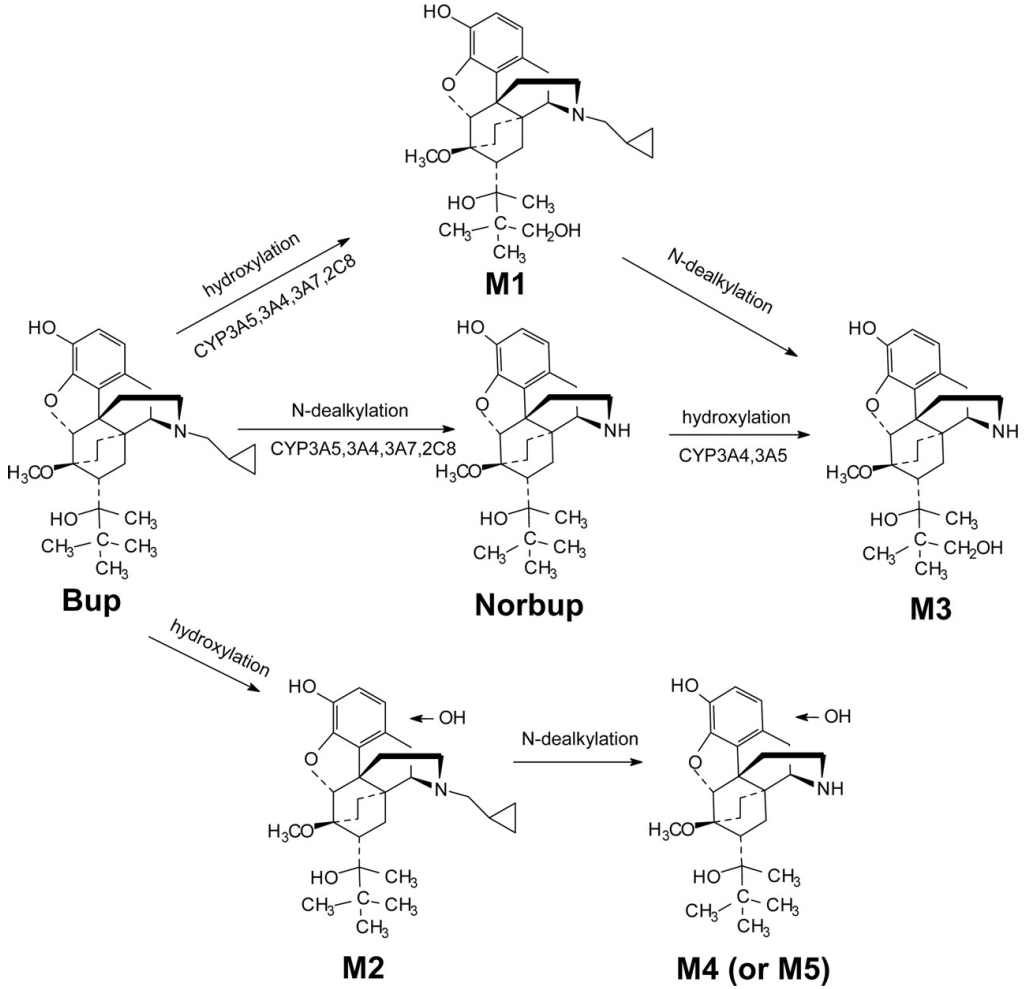
Drug Testing in the Office for Medication Treatment

- Laboratory testing for evidence of substance use has several roles in treatment for opioid use disorder
  - Initial assessment
  - Treatment planning
  - Screening to identify non-prescribed substances/medications
  - Monitoring adherence to pharmacotherapy
  - Evaluating efficacy of treatment and assist in treatment planning

Testing for Buprenorphine

- Testing for buprenorphine can be useful to monitor adherence and detect possible diversion
- Buprenorphine is **not** detected by screening tests for opiates
- Confirmatory testing will distinguish buprenorphine and its metabolite norbuprenorphine
- Individuals vary in the ratio of buprenorphine to norbuprenorphine due to individual metabolism and co-administered inducers or inhibitors of CYP3A4
  - buprenorphine with little or no metabolite (i.e. a ratio of norbuprenorphine:buprenorphine: < 0.02) suggests that a sample was tampered by adding buprenorphine directly to the urine

Testing for Buprenorphine



Nor-Buprenorphine is an active metabolite

So what if the test result is wrong? Talk to your team!

- Develop policies ahead of time of specific consequences of positive tests specified by presence or absence of prescribed medications
- Incorporate policy into the signed treatment agreement
- Consider additional steps
  - Review medication dose – may need to increase dose
  - Intensity of treatment
    - More frequent visits
    - observed dosing
    - additional evidence-based counseling
    - addressing co-occurring disorders
  - Frequency of testing can be increased
- Discuss with multi-disciplinary treatment team in clinic

So what if the test result is wrong? Talk to patient!

- Discuss rationale for testing
  - Means of supporting recovery, not for punitive purpose
- Review test?
  - Results, pH, urine concentration
- Review medication list?
  - Consider possibility of false-positive
  - Consider discussing with an expert (pathologist, pharmacist, chemist)
- Confirmatory testing?
- Review Goals of Care
  - Discuss changes in treatment plan
  - Review consequences of continued use of illicit/non-prescribed substances

Frequency of Testing in MAT Controversial

- No strict, established guidelines or specific evidence to guide frequency
- Frequency of UDT depends on several factors:
  - Stage of Treatment
    - Monthly testing has been suggested as a minimum during ongoing addictions treatment
    - More frequent testing may be more appropriate early in treatment or if there is concern for diversion or recurrence of substance use
  - Stability of Patient
  - Half-life of drugs being tested
  - Treatment setting
    - Office based
    - Opioid Treatment Programs: Federal law mandates a minimum of ***eight*** drug tests per year
- Random testing, rather than at appointments or other pre-scheduled times, is recommended in order to obtain a representative sample

CASE 1 : Angry Adam's conundrums

- **Interpret the lab result.**
- **What would you say to Adam?**
- **What actions would you take?**

RECALL:

Patient on buprenorphine

Urine drug screen:

Morphine	**negative**
Cocaine	**negative**
Amphetamine	**negative**
6-AM	**positive**
Marijuana	**negative**
Buprenorphine	**positive**
Nor-buprenorphine	**negative**

DISCUSSION