PCSS MAT TRAINING
PROVIDERS' CLINICAL SUPPORT SYSTEM
For Medication Assisted Treatment

Patient–Centered Urine Drug Testing: Facts you Should Know!

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Howard A. Heit, MD, FACP, FASAM Disclosures

Commercial Disclosers	What Was Received	Role
Millennium Laboratories	Honoraria and/or consultant fees	Consultant
Millennium Research Institute	Honoraria and/or consultant Fees	Consultant

Educational Objectives

- At the conclusion of this activity participants should be able to:
  - Discuss testing methodology in urine drug testing (UDT)
  - Differentiate between qualitative vs. quantitative UDT
  - Review drug metabolism
  - Explain sample integrity check (SIC)
  - Recommend “best clinical practices” with the use of UDT

Target Audience

- The overarching goal of PCSS-MAT is to make available the most effective medication-assisted treatments to serve patients in a variety of settings, including primary care, psychiatric care, and pain management settings.

Accreditation Statement

- The American Society of Addiction Medicine (ASAM) is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

Designation Statement

- The American Society of Addiction Medicine (ASAM) designates this enduring material for a maximum of 1 (one) *AMA PRA Category 1 Credit*™. Physicians should only claim credit commensurate with the extent of their participation in the activity.
  - Date of Release: June 27, 2014
  - Date of Expiration: June 27, 2017

Participation in this CME Activity

- In order to complete this online module you will need Adobe Reader. To install for free click the link below:
  - http://get.adobe.com/reader/
- You will need to complete a Post Test. You will then be directed to a module evaluation, upon completion of which you will receive your CME Credit Certificate or Certificate of Completion via email.

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- After successfully completing the Post Test, you will receive an email detailing correct answers, explanations and references for each question of the Post Test.

Case Study: Mr. G. – A 36-year-old male

- Mr. G. presents with *documented* failed back syndrome and myofascial pain syndrome 2^0 auto accident (8/10 pain level)
  - Reviewing past medical records documented all non-opioid treatments have failed to improve Mr. G's quality of life
  - Positive family history of addiction
- He presents with chronic pain
  - Alcohol abuse started after the accident
  - Hydrocodone and heroin (IV use) was bought off the street to self-medicate his pain
  - Cocaine (snorting) is now being used to deal with stress and depression secondary to family and economic problems
- Mr. G. states "I have not used alcohol for two weeks but used hydrocodone this morning and cocaine and heroin last night."

Case Study: Mr. G. – A 36-year-old male

- Mr. G. is asked as part of this initial evaluation to do a urine drug test (UDT).
  - Question:
    1. If a point of care (POC) UDT by immunoassay is done in the office which parent molecule(s), primary metabolite(s) or "pharmaceutical contaminant"(s) abused by Mr. G.'s would most likely be positive on the POC testing if there are **no** false positives or false negatives with the test?
    2. If Mr. G's UDT is then sent to the lab for "definitive" testing by Liquid Chromatography /Mass Spectrometry (LC/MS-MS) the specimen would be positive for which parent molecule, primary metabolite or "pharmaceutical contaminant"?

Complete the module Post-Test for answers

UDT in Pain Management: An Exploding Field

- Diagnostic labs exhibits at major pain and/or addiction meetings in the U.S. have markedly increased
  - There is a trend to use UDT results beyond their scientific limits such as:
    - Quantified analyte reports to asses “compliance”
    - “Normative” data from supposedly “compliant patients”
    - In fact, even in “high risk” patients, you can test “too frequently”
- Discharging patients from practice because their “numbers” were not right!

Purpose of Urine Drug Test

- Urine drug testing in clinical practice
  - Consensual diagnostic test
  - Provide objective documentation of adherence to the mutually agreed upon treatment plan
  - Aid in the diagnosis and treatment of the disease of addiction or drug misuse, if present
  - Advocate for the patient in family and 3rd party issues
    - Not for forensics purposes!

Urine drug testing is another tool in the tool box for appropriate care of patients with SUD and/or chronic pain.

Testing Methodology in UDT

- Screening (e.g. Immunoassay) vs. “confirmation” by Liquid Chromatography/Mass Spectrometry LC/MS-MS (definitive analyte identification)
  - In the forensic world, to r/o false +ve, the concept of “confirmation by a second scientific method” was advanced
  - In the pain world, we *must* know the specific drug (LC/MS-MS) not just the class of drug (IA)
    - i.e. +ve screen for opiates (is this the ‘correct’ opioid?)

Urine Drug Test

- Urine may be “the best” biologic specimen for determining the presence or absence of relevant analytes
- Increased window of detection compared to blood
  - Typically 1-3 days for most drugs and/or their metabolites
  - Less costly than serum testing
  - Less invasive

Testing Methodology in UDT

- In the clinical world, one has different needs
  - Need results you can count on, but NOT take to court (forensic testing)
  - Need to know
    - The presence or absence of classes of drugs
    - Most importantly what is the specific drug(s) or metabolites that are/are not present?
      - Is the UDT +ve or -ve for the prescribed drug?
  - Is the UDT appropriately +ve for the current prescribed medication list of the patient
    - And –ve for all others

Purpose of UDT

- UDT is a test we do ***for*** the patient, not ***to*** the patient
  - However, it is just a clinical tool
  - Should increase communication with the patient, not decrease it
  - An “objective” tool to document the results in the medical-legal record for the “subjective” complaint of pain
    - May be helpful to document treatment adherence, legal matters (divorce, child custody, disability claims etc.)

What UDT Does Not Do!

- UDT does ***not*** diagnose
  - Disease of addiction
  - Physical dependence
  - Impairment
  - Diversion
- An unexpected result should lead to a differential rather than a definitive diagnosis

Frequency of Testing

- Best clinical judgment vs. “mandated/guideline directed”
  - Disease of addiction i.e. “established high risk”
    - Test as frequently as is necessary to document that the patient is adhering to the mutually agreed upon treatment plan
  - Pain management i.e. “apparently low risk”
    - Random testing two to three times per year may be adequate
    - If the patient is displaying aberrant behavior, tighten boundaries including more UDT

Who and When to Test

- Patients
  - New patients to be started or already on a controlled substance
  - When or after making a major change in treatment or modification of therapy
  - Resistant to full evaluation
    - Should opioids be considered contraindicated in this situation?
  - Requesting a specific drug?
  - Display aberrant behavior
  - **Support referral for assessment/treatment**
    - **Suspected psychiatric comorbidities including drug misuse/addiction**

Qualitative vs. Quantitative UDT

Qualitative Testing in UDT

- Done by point of care cups, desk top analyzers or laboratory
- Qualitative testing is often based on an arbitrary threshold
  - Reported as
    - +ve or –ve
    - Detected/Not detected

Qualitative Testing in UDT

- Immediate results
  - POC testing excels in “results at the bedside”
    - But often, at the expense of accuracy
- High incidence of false negatives and positives
  - Would not make a major clinical decision with the qualitative results, alone without more advanced testing, especially in contested cases

Quantitative Testing

- There is no reliable relationship between amount of drug taken and quantity of drug/metabolite found in the test sample
  - Urine, serum, sweat or saliva
- Quantitative results do not provide enough information to determine
  - Exposure time
  - Dose
  - Frequency (pattern) of use

Quantitative Testing

- Software and laboratory products have not been fully validated scientifically to give this information
  - Nor is it likely to ever be the case – simply too many variables to consider
- Interpreting drug tests beyond our current scientific knowledge will put clinicians and patients at medical and/or legal risk

Quantitative Testing

- May be helpful in trend monitoring
  - Parent vs. primary metabolite vs. pharmaceutical "contaminant"
  - Steadily falling THC levels in an abstinent former heavy user
  - The "poppy seed" defense
    - Other food stuffs
  - Over the counter medications
    - Vicks Nasal Inhaler (l-desoxyephedrine)

Quantitative Testing

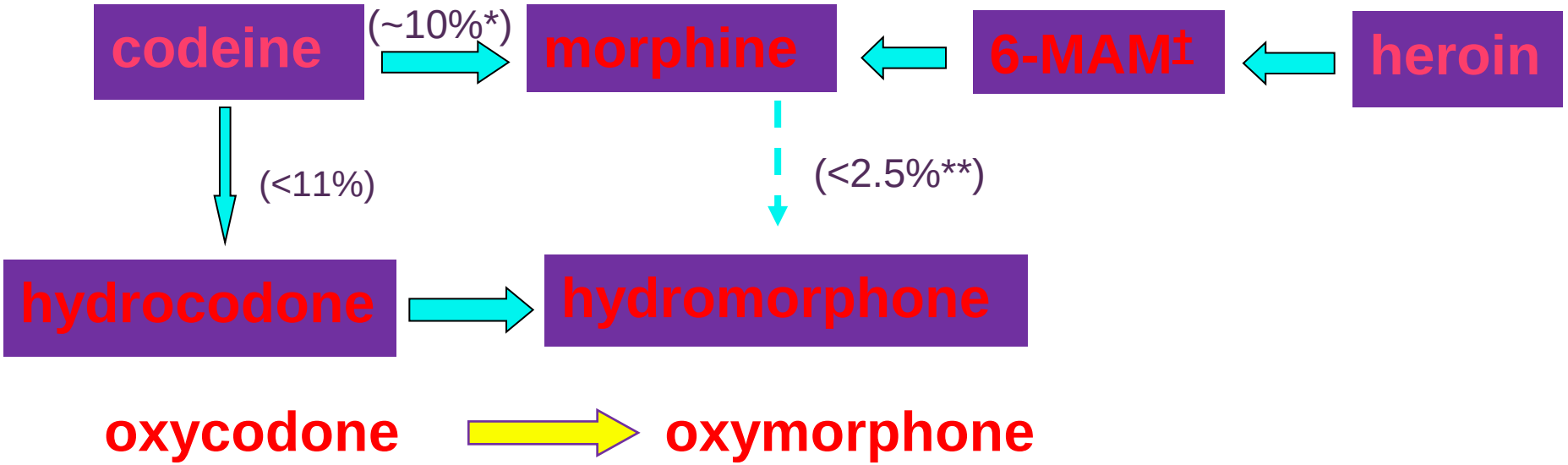
- Can help distinguish between Parent Molecule vs. Primary Metabolite vs. “Pharmaceutical Contaminant”
  - Large quantities of both oxycodone ***and*** hydromorphone
    - Two parent molecules
  - Presence of hydrocodone (<10%) in codeine users
    - Metabolite
  - Presence of trace hydrocodone in oxycodone
    - Contaminant

How to Rule Out Poppy Seed Ingestion

- Codeine concentration > 300 ng/mL without morphine being present
  - Denotes probable codeine use
- Morphine/codeine ratio <2
  - Denotes probable codeine use
- Morphine concentration > 1000 ng/mL without codeine being present
  - Denotes probable morphine use

The Medical Review Officer Handbook (1995)

Metabolism of Opioids*



*Not comprehensive pathways, but may explain the presence of apparently unprescribed drugs

†6-MAM: 6-monoacetylmorphine; an intermediate metabolite

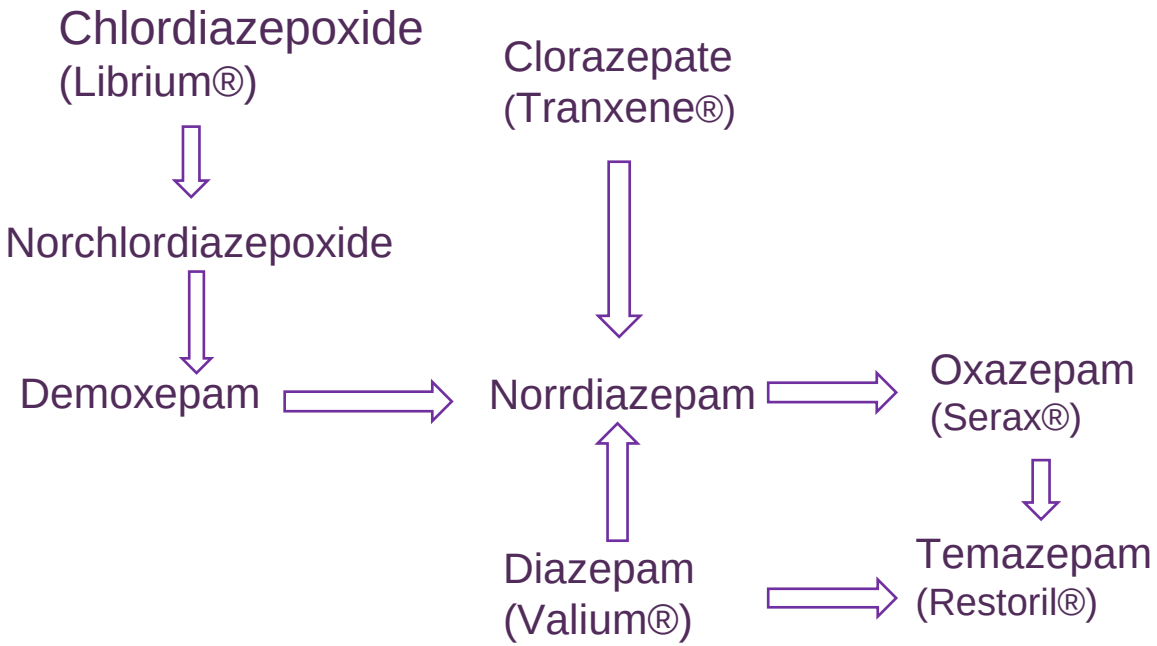
Methamphetamine Detection

- *d/l* isomer test (Chiral Chromatography)
  - *d-* form is the CNS active form
    - i.e. Didrex®, Desoxyn®
    - vs. crystal meth; Ice
  - *l-* form (prescription and OTC)
    - Selegine®
    - Vick's nasal inhaler OTC

Benzodiazepines

- Benzodiazepines are generally detected by immunoassay
  - However, due to variability of immunoassay cross-reactivity not all benzodiazepines are equally detected
    - Example:
      - Lorazepam may or may not be detected
      - Clonazepam is often missed with commonly available immunoassay reagents

Benzodiazepines Metabolism



Detection of benzodiazepines by immunoassay Is a function of the molecule on which the test is based.

Lorazepam (Ativan®) ⇒ α-hydroxyalprazolam

Alprazolam (Xanax®) ⇒ 4-hydroxyalprazolam and a-hydroxyalprazolam

Clonazepam (Klonopin®) ⇒ 7-aminoclonazepam

Communication Underpins "Best Clinical Practice" in Drug Testing

- Establish a relationship with the scientific lab director/senior technologist
- Understand the technology being used
  - A knowledgeable clinician and an informed director can help each raise the other's game
    - Ultimately leading to better clinical care

Communication Underpins "Best Clinical Practice" in Drug Testing

- In a similar fashion, the complex pain and chemical dependency patient benefits from a solid working relationship between the addiction clinician and the pain management team!
- UDT results should increase not decrease communication with the patient
  - ***"The Golden Moment"***
    - When the patient may actually see things the way they are, not the way they wished they were!

Clinical Traps in Drug Testing

- It is unwise to accept at face value, a UDT report that seems to support an impression of clinical stability if, in fact there is other clinical evidence to the contrary
  - UDT is only one clinical tool
    - Beware the “expected” UDT result in a clinically unstable patient
      - “The drug(s) most easily abused are the ones *legitimately* present in the urine”

Sample Integrity Check (SIG)

Sample Integrity Check (SIG)

- Specimen collection
- Characteristics of urine
  - Appearance
    - Color of a urine specimen is related to the concentration of its constituents
  - Temperature
    - 4 minutes of voiding should fall within the range of 90ºF to 100ºF with a volume of 30 ml. or more
  - pH
    - Range of 4.5 to 8.0

Sample Integrity Check (SIG) [cont'd]

- Urinary creatinine varies with state of daily water intake and hydration
  - Normal human urine has a creatinine concentration greater than 20 mg/dL
    - Less than 20 mg/dL is considered dilute
    - Less than 5 mg/dL is not consistent with human urine

Failed Sample Integrity Check (SIG)

- Dilute
  - If the creatinine is <20 mg/dL
- Substituted
  - The specimen does not exhibit the clinical signs of characteristics associated with normal human urine
    - If the creatinine concentration is ≤ 5 mg/dL

Failed Sample Integrity Check (SIG)

- Adulterated
  - Nitrite concentration is ≥ 500 ug/mL.
  - pH is ≤ 3 or ≥ 8.0
  - Exogenous substance
    - Substance which is not normal constituent of urine
    - Endogenous substance
      - Higher concentration than normal physiological concentration

Conclusion

- UDT is an important tool in the management of all patients on chronic opioid therapy
  - It does ***not*** replace clinical judgment
- Once a drug is legitimized through a legal prescription, the ability to monitor misuse, abuse and addiction via UDT is severely limited
- UDT should always be a test we do “for” our patients not “to” our patients

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PCSSMAT is a collaborative effort led by American Academy of Addiction Psychiatry (AAAP) in partnership with: American Osteopathic Academy of Addiction Medicine (AOAAM), American Psychiatric Association (APA) and American Society of Addiction Medicine (ASAM).

For More Information: **www.pcssmat.org**

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