Alleviating Chronic Pain While Maintaining Patient Safety: *Urine Toxicology & Interpretation in Pain Management*

American College of Osteopathic Internists
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The I Love Me Slide:

- 15 years private practice, board certified in pain medicine and addiction medicine, Certified Medical Review Officer
- Current Chair, American Osteopathic Pain Medicine Conjoint Exam Committee
- Extensive experience in that time treating not just chronic pain but also the unintended consequence of addiction; board certified Addiction Medicine
- Leadership Council, Long Island Council on Alcoholism and Drug Dependence (LICADD)
- Medical Director, LICADD Opioid Overdose Prevention Program
- Member, Nassau County, NY, County Executive's task force on Heroin and Prescription drug abuse

Disclosures:

- Speaker Bureau, Alkermes, Inc., Vivitrol
- Treatment Advocate, Reckitt Benckiser, Suboxone
- Speaker Bureau, Orexo, Zubsolv
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Objectives

- Understand the need for strategies to ensure compliance and avoid diversion with chronic opioid therapy.

- Toxicology, our only reasonable objective method to monitor compliance.

- A little history on toxicology.

- What types of testing are available?

- What does and doesn’t it tell us about a patient?

- Some special considerations in toxicology.
"The rise in abuse of and deaths from prescription opioid narcotics has reached epidemic proportions...."

"There were more than 27,000 deaths from prescription drug overdoses in 2007, a number that has risen five-fold since 1990...."

"...overdose deaths from prescription opioids are exceeding deaths from heroin and cocaine overdoses combined...."

"Also, the overall number of drug-induced deaths -- which includes all drugs, not just prescription painkillers, although it is attributable in large part to those -- is approaching the number of deaths from motor vehicle crashes."

"Drug abuse deaths have also surpassed the number of deaths from suicide, homicide, and fire arms...."
Enough prescription painkillers were prescribed in 2010 to medicate every American adult around-the-clock for a month. Although most of these pills were prescribed for a medical purpose, many ended up in the hands of people who misused or abused them.
Universal Precautions in Pain Medicine

- Described by Dr’s Heit & Gourlay in *Pain Medicine*. 2005;6:107–112
- Based on the universal precautions for infectious diseases
- Allows reasonable limits in the Physician/patient relationship
Universal Precautions in Pain Medicine

- Diagnosis with appropriate differential
- Psychological assessment with risk of addictive disorder
- Valid Urine toxicology screening
- Informed consent
- Treatment agreement (not a “contract”)
- Regular reassessment of pain level and functional level
- I recommend making chart copies of all prescriptions
- Regularly reassess the “Four A’s”:
  - Analgesia
  - Activity
  - Adverse reactions
  - Aberrant behaviors
The Treatment Agreement:

- **Random toxicology** screens to ensure compliance
- The use of **one pharmacy**
- **One physician** prescribing C.S.’es (no doctor shopping)
- Use of a **lock box** and the patient responsible for lost or stolen medications
- Clearly defines the already **implied consent** to speak with the pharmacist and other treating physicians but also to contact the authorities if illegality is suspected
- Bring in left-over medications for pill counts
- Prescribing practices (not outside of office hours, etc.)
- States the obvious, such as **no sharing**, selling or trading of medications
- Several are available, such as from the AAPM
Toxicology Screening

The single most effective and objective assessment of patient compliance is the toxicology screen, of which urine is the most common, but it is imperative that we use the information wisely…
When did we start testing???

- Before the 1960’s testing was primarily used by ME’s and ED’s
- By the 1970’s in drug treatment and the criminal system
- By the 1980’s Workplace testing and military
- In the 2000’s Schools and transportation industry but more importantly use in Pain Management to check for compliance and diversion
What’s different for testing in Pain Management?

- In most medical and non-medical applications we are looking to ensure the absence of substances.

- In Pain Management we are looking for the presence of some substances and the absence of others.

- With the growth of Pain Management in the 1990’s into the 21st century we have seen an explosion of abuse and addiction for prescription medication as well as their diversion for profit. This now makes it necessary to ensure compliance not just for the patient's benefit but the safety of society as well.
What does it detect???

- Recent use (blood, urine, breath and saliva)
- Use history (hair and nail can detect for weeks to months)

What doesn’t it detect???

- Impairment
- Abuse
- Addiction
- Physical dependence
What can we sample???

- Urine
- Hair, finger and toe nails
- Saliva
- Sweat
- Breath (only EtOH for now)
- Pretty much any tissue sample if willing to spend the money to create the test
Hair

**Benefits:**
- Cheating is virtually impossible
- Long DDW – 90 day history of use for a 1½” sample
- Can distinguish between light to heavy use over 90 day’s
- No (false) positive for poppy seeds
- No body fluid issues, except for the guy to the left

**Drawbacks:**
- Expensive, $30-40 per test
- Fewer vendors of these tests
- No on-site option
- To test positive for marijuana one must use BIW for the 90-day period covered by the sample
- Limited number of drugs tested for compared to other sources such as urine
Saliva

Benefits:
- Easy collection, no lavatory needed
- Cheating difficult
- More availability of laboratories performing the test
- On-site option is available
- Cost comparable to urine

Drawbacks:
- On-site not sensitive to THC yet
- Relatively short DDW, ~12 hours
- As with all bodily fluids, universal precautions
Originally called the NIDA–5 and tests for:
• Marijuana
• Cocaine
• Amphetamine/Methamphetamine
• Morphine/Codeine
• PCP (“Angel Dust”)

In 2006, officially changed to SAMSHA–5 due to restructuring in the Department of HHS

In 2008 become the SAMSHA–6 to include MDMA (“Ecstasy”)

The standard for workplace monitoring

- November 25, 2008, entry in the Federal Register on the Mandatory Guidelines
Urine testing is usually the best choice for pain management applications, not blood as commonly thought. Urine collection is just that, a collection over time and represents cumulative collection since last micturition.
3–Step Process

- Initial screen with enzyme Immunoassay
- Confirmation through Gas or Liquid Chromatography/MS
- Review by a health care professional
- If this involves employment, then a certified Medical Review Officer is necessary to be compliant with Department of Transportation guidelines
**EIA**

*Enzyme Immunoassay*

- Monoclonal antibodies are created that are VERY specific to particular compounds and/or their metabolites. The amount of antibodies bound can then be measured to assess the amount of a substance present in the sample.

- Highly sensitive but the specificity is called into question because of the reactivity to the metabolites as well as the compound in question.

- Very inexpensive.

- Can be sent to laboratories or onsite. Processing machines are available, individual dipsticks or sample cups with the EIA build into the cup itself.
Liquid and gas chromatography refers to two different ways of separating the various components in a sample.

The mass spectrometer is responsible for breaking each molecule into ionized fragments and not only detecting these fragments using their mass to charge ratio but also quantifying.

The Mass Spectrometer is HIGHLY sensitive and HIGHLY specific.

Cut-offs are much lower for LC and GC/MS. An example for this would be THC detection:
- LC and GC detect one specific metabolite while EIA detects several.
- Therefore, LC and GC/MS are usually at least 40% lower.
ATTENTION ALL MEDICAL STAFF: Due to a mix-up in urology this morning, no apple juice will be served at lunch.
Urine

**Benefits:**
- Most common form of testing
- Many vendors and inexpensive
- Onsite and off site testing
- Large number of drugs to be tested available
- Can retest down the road with saved sample
  - (not true for 6-MAM)

**Drawbacks:**
- Cheating possible (The Whizzinator) but remember the advantage of testing in our field
- Short DDW
- False + (for EIA)
- Need for a lavatory
Who to test???

- Everyone
Who to test???
Who to test???

In patient on COT who are at high risk or have engaged in aberrant drug–related behaviors, clinicians should periodically obtain urine drug screens or other information to confirm adherence to the COT plan of care.

In patients not at high risk and not known to have engaged in aberrant drug–related behavior, clinicians should consider periodically obtaining urine drug screens or other information to confirm adherence to the COT plan of care.

Who to test???

“Reliance on aberrant behavior to trigger a UDT will miss more than 50% of those individuals using un-prescribed or illicit drugs.”

So I'm probably not going to pass this urine test am I?
The beauty of dealing with Pain Management is that we are not only looking for the absence of a substance but also the presence of other substances in their proper concentrations.

The MRO or the criminal justice system are looking for clean urine making it beneficial for the individual being tested to use someone else’s “clean” urine.
The Cheater

A sure discharge from the practice is to “show clean” when we should be seeing a controlled substance.

If you choose to continue to prescribe to a patient that shows negative for the substances being prescribed, you need to be ready to explain your decision to a diversion investigator or law enforcement if they review that case.
Michael Belfiore, Merrick doctor, arrested in illegal painkiller case
Updated October 8, 2014 10:46 PM
By ROBERT E. KESSLER robert.kessler@newsday.com

- A doctor who practiced in Merrick was charged Wednesday with illegally distributing the narcotic painkiller oxycodone, the culmination of a probe that began, in part, after authorities discovered he had written about 5,000 prescriptions for 600,000 of the pills over a three-year period, court records show.

- Michael Belfiore, 51, of Westbury, was charged after prescribing oxycodone six times from March 15 to Aug. 12, 2013, "with no legitimate medical need" to an undercover Nassau County detective, a complaint said.

- According to the complaint, the undercover detective approached after allegations came from "several pharmacists, law enforcement officers and multiple confidential sources" that the osteopathic physician was "illegally issuing prescriptions to individuals who were abusing and/or diverting oxycodone pills."
The undercover detective first met with Belfiore last March and falsely claimed that he had back and shoulder pain, the complaint said.

The detective added that a former girlfriend had given him oxycodone and he "liked the way it felt," the complaint said.

Belfiore "examined" the detective for 30 seconds and gave him a prescription for 90 pills for $425 in cash, the complaint said.

A similar pattern was repeated on five later visits, in which the undercover detective provided no "documentation of his injury," the complaint said.
Once, Belfiore is quoted in the complaint as urging the undercover detective to get an X-ray of his back so that "when the state calls and says, "'Why are you giving meds?' I can say something."

Another time, Belfiore is quoted as saying, "If the DEA comes into the office and asks about [the undercover's] prescriptions, there will be a problem."

Each visit ... was recorded on video and audio, the complaint said.
On four of the visits, technicians for Belfiore took swabs of the detective's saliva to check that he was taking the pills, but the tests were negative, a strong indicator that the detective was diverting or selling the pills, the complaint said.
Look Mommy, Now You Don't Have To Go To The Ghetto To Get Your Smack!
Metabolites

- Hydrocodone ⇒ hydromorphone ⇒ none
- Oxycodone ⇒ noroxycodone (only from oxycodone) & oxymorphone
- Oxymorphone ⇒ none
- Fentanyl ⇒ norfentanyl
- Codeine ⇒ morphine
- Methadone ⇒ EDDP
- Buprenorphine ⇒ norbuprenorphine
- Cocaine ⇒ benzoylecgonine
- Heroin ⇒ morphine, codeine & 6-MAM (6-MAM is what confirms it is from Heroin!!!)
- Carisoprodol (Soma) ⇒ meprobamate
Interpretation

- Remember EIA is not as specific as LC/GC–MS.
- EIA for opiates is actually looking for only some opioids such as hydrocodone, hydromorphone, morphine, codeine.
- Synthetics such as oxycodone, oxymorphone, fentanyl, etc. require their own EIA.
Interpretation

- Large amounts of poppy seeds can give positive for morphine (very low levels), this is NOT a false positive. A false positive is when another substance shows positive for what it is not (poor specificity).

- Studies have shown that passive exposure to marijuana and/or crack cocaine does NOT result in positive findings.
When one is on chronic opioid therapy, you should see a higher level of metabolite than parent compound except under two circumstances:

- The patient is a poor metabolizer
- Recent ingestion to show positive on the test and maintain the supply of medication
Interpretation

- Oxycodone’s metabolite is oxymorphone and with chronic daily use, the latter will be at higher levels.
- If the patient is on oxymorphone and you see noroxycodone, that person has ingested oxycodone in place of or in addition to oxymorphone.
Interpretation

BE AWARE!!

Pharmaceutical grade morphine is not as pure as you might think. Codeine and hydromorphone can be seen in the sample as a contaminant in the process, usually with very high dosages of morphine and hydromorphone can be a minor metabolite of morphine.
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Blood</th>
<th>Urine</th>
<th>Hair</th>
<th>Saliva</th>
<th>Sweat Patch</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immunocassay screen</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>GC/MS confirmation option (laboratory-based)</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Chain-of-custody option</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Retained positives for retest option</td>
<td>Difficult</td>
<td>Possible</td>
<td>Easy</td>
<td>Difficult</td>
<td>Possible</td>
</tr>
<tr>
<td>Medical review officer option</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Common surveillance window</td>
<td>3-12 hours</td>
<td>1-3 days</td>
<td>7-90 days+</td>
<td>3-24 hours</td>
<td>1-21 days</td>
</tr>
<tr>
<td>Intrusiveness of collection</td>
<td>Severe</td>
<td>Moderate</td>
<td>None</td>
<td>Slight</td>
<td>Slight</td>
</tr>
<tr>
<td>Retest of same sample</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Compatibility of new sample if original test disputed</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Number of drugs screened</td>
<td>Unlimited⁴</td>
<td>Unlimited⁴</td>
<td>Large⁵</td>
<td>5+alcohol</td>
<td>5³</td>
</tr>
<tr>
<td>Cost/sample (NIDA 5)</td>
<td>About $200</td>
<td>About $15-$30</td>
<td>About $40-$65</td>
<td>About $50</td>
<td>About $35</td>
</tr>
<tr>
<td>Can distinguish between light, moderate, and heavy use</td>
<td>Yes (short term)</td>
<td>No</td>
<td>Yes (long term)</td>
<td>No</td>
<td>Yes (ongoing)</td>
</tr>
<tr>
<td>Resistance to cheating</td>
<td>High</td>
<td>Low</td>
<td>High</td>
<td>High</td>
<td>High</td>
</tr>
<tr>
<td>Best application</td>
<td>Postaccident and overdose testing for alcohol and other drugs</td>
<td>Reasonable-cause testing</td>
<td>Frequent testing of high-risk groups such as those in postaccident follow-up and the criminal justice system</td>
<td>Unannounced, random tests with observed collection</td>
<td>Preemployment testing Random and periodic testing Testing to determine severity of drug use for referral to treatment Testing of subjects suspected of seeking to evade urine-test detection Opiate addicts claiming false positive</td>
</tr>
</tbody>
</table>

Note. DOT=U.S. Department of Transportation; GC/MS=gas chromatography/mass spectrometry; NIDA=National Institute on Drug Abuse.

⁴ Blood testing for alcohol is routine, costing about $25/sample, but blood testing for drugs is done by only a few laboratories in the United States. Blood testing for drugs is relatively expensive, costing about $60 for each drug tested for.
⁵ Urine tests for nonroutine drugs are available from most reference laboratories, and costs for broad screens are generally less than $200.
⁶ Hair testing using the NIDA 5 (cocaine, opiates, marijuana, amphetamines, and phencyclidine) is usually performed in several toxicology reference laboratories. The cost of nonroutine testing of hair is less than $300 in most cases.
⁷ Commonly limited to the NIDA 5. Tests can also be performed for alcohol.
DDW’S (in urine)

- In general the opioids will be detectable for up to 2–3 days and with chronic use the metabolites slightly longer
- Methadone and its metabolite EDDP at high doses as much as two weeks
- THC is 6–11 weeks with heavy use
- Benzodiazepines can be several weeks with chronic use
If discharge is necessary, do it right:
• Check with the counsel for your Medical Society or malpractice carrier for local laws and regulations.
• All states require a 30-day notice of discharge, this does not necessarily mean a 30-day supply of narcotics.
• Send a letter certified mail with return receipt (some patients may think not signing for it means they did not get it, wrong!)
• You may discharge for any reason so long as it is non-discriminatory.
• You are not required to state the reason but if you do, keep it simple and brief without elaboration or general statements. Remember you could have lawyers or regulatory people trying to pick apart what you say, or take it out of context.
Conclusions

• Urine toxicology is only one tool in ensuring compliance and avoiding diversion.
• The practitioner must understand what he or she is reading and if any questions call the toxicologist at the lab for further clarification.
• Treat the patient not the report. If illicit substances are found address it and offer the patient what they need, not necessarily what they want.
Conclusions

Remember, this is like a mammogram. An early screening tool to detect an abnormal condition or even a disease before it kills. Please do not use it as a tool to discharge.
References

- DuPont RL, Newel R, Brethen P. *Drug Testing in Drug Abuse Treatment*. Center City, MN: Hazelton, 2005
AND THEN THEY GAVE ME THIS NEW DRUG AND I THOUGHT WHAT THE HECK, WHY NOT, I'VE TAKEN EVERYTHING ELSE ...

LAB RAT REHAB