

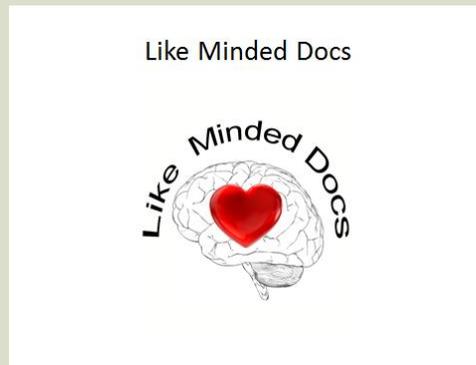
Urine Drug Testing in Addiction Medicine

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Conflict of Interest

- I do not have any financial or commercial relationship to disclose pertaining to this educational activity.

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Purpose

- To monitor adherence to the agreed upon plan of treatment
 - Not to “catch” people
- Medical Monitoring for Adherence (MMA)
 - Proposed to replace Urine Drug Test (or hair or blood)

Addiction Treatment Testing

- Similar, but not the same for chronic pain management
- Not the same as workplace drug testing
- Not the same as diagnostic or screening in primary care
- Not the same as forensic

ASAM Documents

- Drug Testing: A White Paper of the American Society of Addiction Medicine 10/26/2013
- ASAM Drug Testing Appropriateness Document 04/04/2017

Definitions

- Positive test = Unexpected (New suggested term)
- Negative test = Expected (New suggested term)
- Presumptive
- Definitive
- Qualitative
- Sensitivity
- Specificity
- Creatinine corrected

Matrix Tested

- Urine
- Saliva
- Hair
- Nails
- Breath
- Blood
- Sweat

The Interpreter Must Consider

- The purpose of the test
- The limitations of the test used
 - Potential for false positives and false negatives
- The limitations of the selected matrix (SAMHSA – TAP 32)
- The drugs being tested, and not tested
- Method of collection
- Concentration and cutoff
- Window of detection
 - Pharmacogenetic variation

Collection

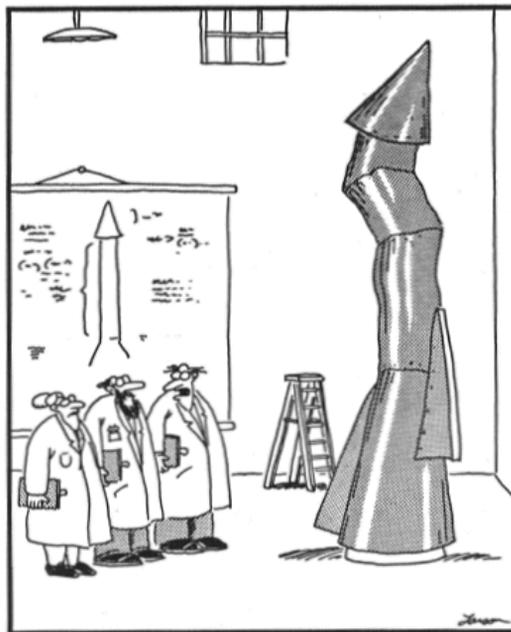
- Chain of custody collection
 - Results have the potential for significant life impact

Frequency of Collection

- ASAM Level 1
- ASAM Level 2
- ASAM Level 3
- ASAM Level 4
- Random
 - Average number of times per period (week, month)

Technologies

- POC Cups, Strips, Automated strips
- Immunoassay instruments
- GC/MS
- LC/MS
- LC/MS/MS

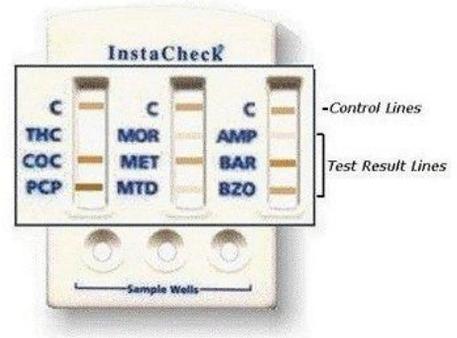


"It's time we face reality, my friends. ...We're not exactly rocket scientists."

POC = Immunochromatography

- Antibodies are made in such a way that they bind with a specific drug, such as morphine. In one approach, manufacturers of point of care (POC) devices embed test strips with antibodies and install them in devices designed to interact with urine specimens (Amedica Drug Screen Test Cup). A urine specimen with the drug in it (in this example, morphine) will displace the drug-indicator molecule on the test strip causing the morphine drug indicator line to disappear or change color. These test strips are then visually inspected by the person administering the test. The absence or presence of a line or the change in color, such as on a home pregnancy test, indicates whether the result is positive or negative.

Immunochromatography



Negative Screen Result: Colored lines adjacent to each target drug name and in the control (C) regions will appear. The color intensity of the line for the target drug may be weaker or stronger than that of the control line however any line, no matter how faint should be interpreted as a negative result. Do not attempt to correlate the intensity or color of the test lines between the targeted drug panels.

Positive Screen Result: Colored lines appear in the control regions (C) but do not develop in the test region. The absence of any line in any target drug test region indicates a positive result for that drug or drug metabolite. In this example the screen is positive for THC and negative for all other targeted drugs. Note that test lines are not of equal intensity or color. Because of the various sensitivity cut-off levels for each specific drug this result is expected.

Note: In general, practically all drug tests using the lateral flow based immunoassay method and technology have the same result for positive and negative sample screens; the presence of a test line indicates a negative test while the absence of a test line indicates a positive test.

POC Testing

- Quick
- Cheap
- Presumptive
- Qualitative
- High false positive rate
- High false negative rate
- Subject to reading errors

Instrumented IA

- Technology is Immunoassay
 - Enzyme multiplied immunoassay technique (EMIT)
- Does not involve chromatography (or spectroscopy)
- Presence of analyte in question causes color change in reagent
 - This is measured by a colorimeter
- Office based
 - CLIA Low Complexity
 - CLIA High Complexity
- Commercial laboratory based

Instrumented IA (Office/Program)



Instrumented IA (Lab)



Instrumented IA

- More accurate
- More reliable and more reproducible
- Longer turn around time (TAT)

- Remains presumptive
 - Confirmation by MS strategies should be performed for
 - Unexpected results
 - Contested results

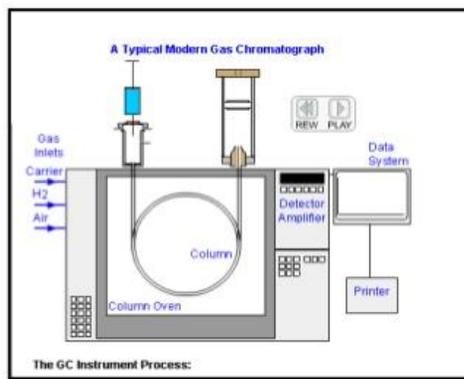
GC/MS

- Definitive
- Quantitative
- Lower cutoff level possible

GC/MS

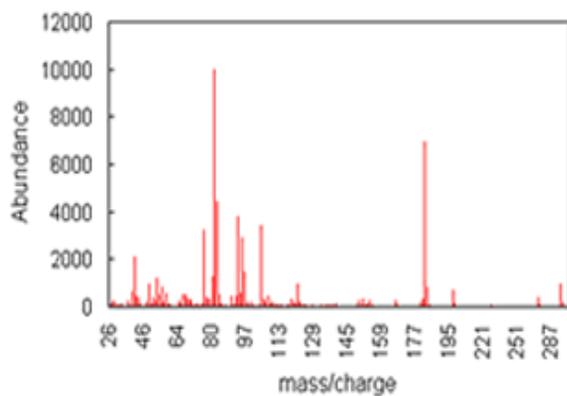
3 GAS CHROMATOGRAPHY

- Gas chromatography leads to Separation of volatile organic compounds
- Separation occurs as a result of unique equilibrium established between the solutes and the stationary phase (the GC column)
- An inert carrier gas carries the solutes through the column

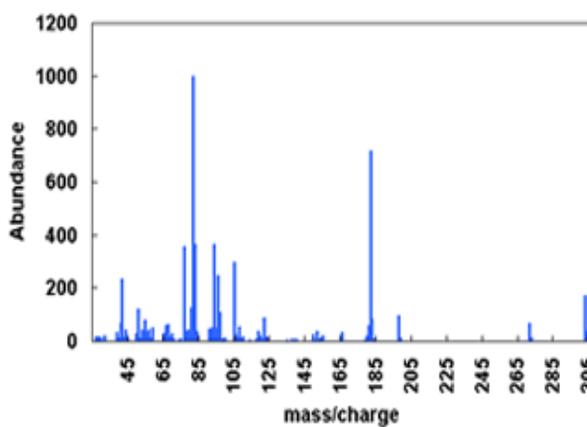


Mass Spectroscopy

Mass Spectrum of Peak at 6.39 min.



Mass Spectrum of Cocaine Standard



LC/MS and LC/MS/MS

- Also definitive
- Quantitative
- Lower cutoff level possible

LC/MS and LC/MS/MS

- Liquid Chromatography/Mass Spectrometry (LC/MS) is fast becoming the preferred tool of liquid chromatographers. It is a powerful analytical technique that combines the resolving power of liquid chromatography with the detection specificity of mass spectrometry. Liquid chromatography (LC) separates the sample components and then introduces them to the mass spectrometer (MS). The MS creates and detects charged ions. The LC/MS data may be used to provide information about the molecular weight, structure, identity and quantity of specific sample components.

Validity Testing

- pH - >3 - <11
- Specific gravity - >1.002
- Creatinine - $>20\text{mg/dl}$
- Adulterants

Profile (not Panel)

- Individualized
- Usual
 - Developed for population served
- Modified
 - Based on some distinction of an individual
 - Based on community characteristics
- Special
 - Concern for unusual drug use
 - i.e. GHB

Interpretation

- No drug identified
 - Expected = Negative
 - Unexpected = Positive
 - Contested
- Drug identified
 - Expected = Negative
 - Unexpected = Positive
 - Contested

Recommendations

- Collection frequency
- Type of testing
 - POC
 - Instrumented EIA
 - Definitive
 - GC/MS, LC/MS, LC/MS/MS
- Response

Collection Frequency

- Level of care
- Turn around time
- Cost-benefit analysis
 - Including reasonableness of specimen collection in time and travel
 - Availability of staff, etc
- History
 - Abstinence
 - Recovery activity

POC

- First encounter
- Return from pass

- Consider results presumptive
- Accept if clinically congruent and not contested
 - May forward for instrumented testing

Instrumented EIA

- Cost effective for screening
- May accept as “good enough” if consistent with clinical
- Unexpected drug present specimens should be sent for definitive testing
 - i.e. finding a drug that was not prescribed or illegal
- Unexpected no drug present specimens should be sent for definitive testing
 - i.e. a negative test for a drug that is prescribed

Mass Spectroscopy Testing

- Unexpected drug present
- Unexpected no drug present
- Contested results
- Modified profile
 - Special testing

Response to Abnormal Findings

- Consider a modification of the treatment plan
 - Motivational Enhancement Therapy
 - More frequent visits
 - Higher level of care
- Avoid non-therapeutic responses
 - Discontinuation of treatment
 - Messages of failure

Cases

- The “false positive” LC/MS/MS
- The “almost positive” POC
- The uncontested positive benzo POC

The False Positive LC/MS/MS

- Several patients with addiction involving opioids presented to IOP with Medical Monitoring for Adherence (MMA’s) positive for Tramadol. Some of the patients denied using Tramadol. All of them were taking Effexor.
- N-desmethylenlafaxine has exactly the same elution time and same mass/charge ratio on a tandem LC/MS/MS
- The lab added O-desmethylenlafaxine to the Tramadol method.
- Using a different chromatography technology, Time of Flight (TOF), the retention times are different, so it isn’t a problem.

Almost Positive POC

- John is a 22yo male with addiction involving opioids, amphetamines, and alcohol. He has a significant history of selling as well as using and has been seen by the counselors as less than honest.
- John has been in treatment for 1 month and returns from his first pass with his family. Staff chose to use a POC cup for his MMA in order to get quick results.
- The counselor reading the test felt the line for THC was “almost unreadable.” So he asked John what he had used during his pass. When John said, “nothing,” the counselor told him the POC was positive for THC.

Uncontested Pos Benzo

- Jim has admitted to your IOP one week ago. You use POC cups for screens in your MMA process and you see a positive for Benzodiazepines. You have a process by which you ask your patients to confirm this before reflexively confirming. Jim tells you that he was at his mother’s house and had a headache and she gave him a pill. “You know, she takes valium. That must have been it. I’m sorry. I have to be more careful around her.”
- The next week, he’s positive again and this time it is reflexively confirmed showing alprazolam. Jim tells you he lied about the valium the first time after seeing the confirmed positive.