

AACC Online Conference  
The Laboratory's Role in Drug Monitoring for Pain  
Management

Analytical Methods I  
Overview of Test Menu and Testing Strategies from  
“Beside to the Reference Laboratory”

Tai C Kwong, PhD  
University of Rochester Medical Center  
Rochester, New York

# Analytical Methods

➤ Overview of Test Menu and Testing Strategies from “Beside to the Reference Laboratory”

II. Immunoassay

III. Mass spectrometry

# Learning Objectives

After this presentation, you should be able to:

1. Describe the role of the laboratory in pain management
2. List the laboratory issues of urine drug testing for pain management
3. Describe the different approaches to urine drug testing, and pros and cons of each approach
4. Develop a plan to optimize the clinical effectiveness and laboratory efficiency of urine drug testing

# Chronic Pain Patients on Opioids: Aberrant Drug Behaviors

- ❑ Not using prescribed medications
- ❑ Not using prescribed medication as prescribed
- ❑ Using non-prescribed medications
- ❑ Diverting prescribed medication
- ❑ Using illicit drugs

# Urine Drug Test in Chronic Opioid Therapy

- ❑ Supplement self-reporting and behavioral monitoring
- ❑ Identify problems otherwise undetected:
  - ❑ Use of undisclosed medications
  - ❑ Not using prescribed medications
  - ❑ Undisclosed use of alcohol and illicit drugs

Objective means to document aberrant drug behaviors

- ❑ Check for ‘Compliance’ to prescribed medication(s)

# Drug Testing for Pain Management

Laboratory Issues to consider:

- ❑ Specimen types (**urine**, oral fluids, others)
- Test menu/drug list
- ❑ Analytical methodologies
  - ❑ Immunoassay (Analytical Method II)
  - ❑ LC-MS/MS (Analytical Method III)
- ❑ Testing strategy

# Confirmed Results for 10,922 Pain Clinic Specimens

<b>Drug Class</b>	<b>% Specimen Positive</b>
Amphetamines	1.5
Barbiturates	2.8
Benzodiazepines	21.9
Cannabinoids	8.9
Carisoprodol	5.6
Cocaine	2.8
Fentanyl	4.2
Meperidine	0.5
Methadone	11.1
Opiates	82.4
Propoxyphene	3.5

# What Medications/Drugs To Test For?

- ❑ Typical illicit drugs
  - ❑ Amphetamines, cannabinoids, cocaine
- ❑ Opioids
- ❑ Benzodiazepines

# What Medications/Drugs To Test For?

- ❑ Typical illicit drugs
- ❑ Opioids
  - ❑ Opiates: morphine, hydromorphone, codeine, hydrocodone, dihydrocodeine, oxycodone, oxymorphone,
  - ❑ Non-opiate opioids: methadone, fentanyl, buprenorphine, tramadol, tapentadol
- ❑ Benzodiazepines

# Opioids

## **Buprenorphine**

Buprenex<sup>®</sup>

Subutex<sup>®</sup>

Suboxone<sup>®</sup>

Butran<sup>®</sup>

## **Hydrocodone**

Hycodan<sup>®</sup>

Vicodin<sup>®</sup>

## **Methadone**

Dolophine<sup>®</sup>

## **Fentanyl**

Duragesic<sup>®</sup>

## **Morphine**

MSContin<sup>®</sup>

## **Oxycodone**

OxyContin<sup>®</sup>

Percodan<sup>®</sup>

Oxceta<sup>®</sup>

## **Hydromorphone**

Dilaudid<sup>®</sup>

## **Tramadol**

Ultram<sup>®</sup>

## **Tapentadol**

Nucynta<sup>®</sup>

# What Medications/Drugs To Test For?

- ❑ Typical illicit drugs
- ❑ Opioids
- ❑ Benzodiazepines
  - ❑ Clonazepam/7-aminoclonazepam (Klonopin<sup>®</sup>)
  - ❑ Alprazolam/ $\alpha$ -OH-alprazolam (Ambien<sup>®</sup>)
  - ❑ Lorazepam/lorazepam glucuronide (Ativan<sup>®</sup>)
  - ❑ Nordiazepam, oxazepam (Serax<sup>®</sup>), tempazepam (Restoril<sup>®</sup>)

## Immunoassay Test Menu

- ❑ Limited by availability of FDA-cleared test kits
- ❑ Menus depending on local prevalence practice groups

Amphetamines

Benzodiazepines

Buprenorphine

Cannabinoids

Cocaine metabolites

Methadone/metabolite

Opiates

Oxycodone

## Confirmation Test Menu

Amphetamines	amphetamine, methamphetamine, MDMA, MDA
Benzodiazepines	$\alpha$ -OH-alprazolam, 7-aminoclonazepam, lorazepam, nordiazepam, oxazepam, temazepam
Buprenorphine	buprenorphine, norbuprenorphine
Cannabinoids	$\Delta^9$ -THC-carboxylic acid

## Confirmation Test Menu, cont'd

Cocaine	benzoylecgonine
Fentanyl	fentanyl, norfentanyl
Methadone	methadone, methadone metabolite (EDDP)
Opiates	6-acetylmorphine, codeine, dihydrocodeine, hydrocodone, hydromorphone, morphine, oxycodone, oxymorphone

# Drug Testing for Pain Management

## Laboratory Issues to consider:

- ❑ Specimen types (**urine**, oral fluids, others)
- ❑ Test menu/drug list
- Analytical methodologies
  - ❑ Immunoassay (Analytical Method II)
  - ❑ LC-MS/MS (Analytical Method III)
- ❑ Testing strategy

# Drug Testing for Pain Management

## Laboratory Issues to consider:

- ❑ Specimen types (**urine**, oral fluids, others)
- ❑ Test menu/drug list
- ❑ Analytical methodologies
  - ❑ Immunoassay (Analytical Method II)
  - ❑ LC-MS/MS (Analytical Method III)
- Testing strategy

# Testing Strategy

Strategy depends on:

- ❑ Meeting clinical needs
- ❑ Drug positivity and negativity rates
- ❑ Turnaround time
- ❑ Laboratory capacity and technical capability

# Testing Strategies

Strategies:

1. Screen by immunoassays
  - 1a. Report positive result without confirmation
  - 1b. Report positive result with confirmation
2. Direct testing by Mass Spectrometry (MS) assays

# 1. Screen by Immunoassays

- ❑ Widely used technology. Can be performed as:
  - ❑ Point of care testing (POCT)
    - ❑ In doctor office or clinic
    - ❑ Rapid turnaround time
    - ❑ 'Waived' tests available
  - ❑ Laboratory testing; instrument based testing
    - ❑ High volume testing possible by automation
    - ❑ Testing performed by professional personnel
    - ❑ Longer turnaround time

# 1. Screen by Immunoassays

- ❑ Widely used technology. Can be performed as
  - ❑ Point of care testing (POCT)
  - ❑ Laboratory testing
    - ❑ Instrument-based testing
    - ❑ High volume testing is possible by automation
    - ❑ Performed by professional personnel
    - ❑ Longer turnaround time

# 1. Screen by Immunoassays

Strategies:

1. Screen by immunoassays
  - ➔ 1a. Report positive result without confirmation
  - 1b. Report positive result with confirmation
2. Direct testing by Mass Spectrometric (MS) assays

## 1a. Report Positive Result Without Confirmation

- ❑ Confirmation of immunoassay positives is neither mandatory nor always necessary
- ❑ Providers may forgo confirmation testing if results are 'clinically expected'
  - ❑ Proper interpretation requires understanding of the limitations of immunoassays (details in next session: Analytical Methods II)

## 1b. Report Positive Result With Confirmation

- ❑ Initial tests by immunoassays, positive results reflexed to confirmation by mass spectrometry - most widely used strategy
- ❑ Confirmation test often ordered when:
  - ❑ Specimens screen negative for prescribed drugs
  - ❑ Specimens screen positive for non-prescribed drugs (including suspected false positive)
  - ❑ Specimens screen positive for illicit drugs
  - ❑ Aberrant drug behavior is suspected

## 2. Direct Testing By Mass Spectrometric (MS) Assays

### Advantages

- ❑ Immunoassays are class-specific; MS assays are analyte-specific (benzodiazepines vs. clonazepam)
- ❑ Specific identification of drug(s) present
- ❑ MS assays have lower cutoffs, e.g., opiates assay:
  - ❑ Immunoassay: 300 ng/ml
  - ❑ LC-MS/MS: 50 ng/ml or lower
- ❑ Immunoassays are qualitative assays; MS assays can be quantitative

## 2. Direct Testing By Mass Spectrometric Assays

### Disadvantages

- ❑ Slow throughput
  - ❑ Sample preparation is labor intensive
  - ❑ Multiple-drug assay may be time consuming
  - ❑ Multiple assays may be needed for different drug groups
- ❑ Costly instrumentation
- ❑ Advanced technical expertise

## 4. Optimization of Test Menu and Strategy

Optimize test menu and strategy based on:

- ❑ Consult with clinicians and other providers
- ❑ Review of test result database:
  - ❑ Screen positivity rates:
    - ❑ low (e.g., PCP, methaqualone): drop from menu
    - ❑ Low (e.g., cocaine, amphetamines); may keep in menu-serious clinical consequences of a positive result
    - ❑ High (e.g., opiates, benzodiazepines): bypass screening, go directly to MS testing

## 4. Optimization of Test Menu and Strategy

- ❑ Review of test result database:
  - ❑ Screen false negative rates
    - ❑ high (e.g., opiates and benzodiazepines): bypass screening, go directly to MS testing
  - ❑ Screen cutoffs
    - ❑ Too high (e.g., cocaine metabolite, amphetamines): lower cutoff; but may increase false positive rate

Thank you for attending!

**Please join me in the Networking Lounge for  
an online Q&A session.**

Visit the Resource Center to get the CE code for this presentation

## Self-Assessment Questions

1. Which of the following statements on urine drug testing in pain management is INCORRECT?
  - a. UDT can detect aberrant drug behaviors that are otherwise undetected by self-reporting
  - b. UDT can detect use of undisclosed medications
  - c. UDT detects the use of alcohol and illicit drugs
  - d. UDT can assure a patient's compliance to taking medication as prescribed (dosage and timing intervals)

## Self-Assessment Questions

2. Which of the following statements on urine drug testing is INCORRECT?
  - a. Immunoassays are commonly used as the initial tests
  - b. An immunoassay positive result can be a false positive and should be confirmed
  - c. A positive immunoassay result that is in accordance with the patient's clinical history does not need to be confirmed
  - d. There are no immunoassay false negative results

## Self-Assessment Questions

3. Which of the following statements on urine drug testing is INCORRECT?
  - a. The screen-first-if-positive-confirm approach to urine drug testing is inefficient if the positivity rate is low
  - b. The screen-only approach with no confirmation can result in false positive reports
  - c. Confirmation tests should be able to provide specific identification of the drug or drugs present
  - d. Confirmation tests should be more specific and equal to or more sensitive than the screening test