Clinical Chemistry Trainee Council
Pearls of Laboratory Medicine
www.traineecouncil.org

TITLE: Drugs of Abuse Testing

PRESENTER: Shannon Haymond, Ph.D.

Slide 1:
Title Slide

Slide 2: Drugs of Abuse Testing Models
There are 2 main models of drugs of abuse testing: Forensic and Therapeutic. The forensic model is focused on detection of illicit drugs or non-prescribed medications and the normal result is a negative. This model is most commonly referred to as urine drug screening and is used in criminal situations, for workplace testing, to screen athletes and military personnel, in addition to use in domestic situations. It is also the model employed in hospital settings by various units, including emergency, intensive care, psych, labor & delivery.

The therapeutic model is focused on monitoring the presence of prescribed medication to aid in treatment, primarily in pain management settings. The expected result is a positive for the drug/metabolite of interest and negative for non-prescribed substances and alcohol.

Slide 3: Basics of Drugs of Abuse Screening
There is often much confusion about the interpretation of drug screen results, despite their seemingly straight-forward results of positive or negative. In order to appropriately assess results from a drug screen, one must remember some basic principles. It is important to know what drugs are included in a panel and that drug screens do not test for any or all drugs. The methodology used for the drug screen may have a significant impact on the result; therefore, it is necessary to understand the advantages and limitations associated with immunoassay and chromatographic methods such as GC/MS or LC/MS. It is also important to know the cutoff that was used to generate the result. The detection timeframe differs among different specimen types so the same drug may be positive in one specimen but negative in another type. Drug screens cannot distinguish between acute and chronic exposure.

Slide 4: Drug Screening Tests

Most drug screening tests are qualitative and are designed to detect classes of drugs and/or metabolites. The drug classes included in a panel vary from lab-to-lab and a single lab may offer more than one type of drug screening panel. The Substance Abuse and Mental Health Service Administration (known as SAMHSA) defined a panel of 5 drug classes for use in workplace drug screening. This panel is also known as the NIDA 5. This is a commonly utilized panel in the clinical setting as well. It includes Amphetamines, Cocaine, Opiates, PCP, and Marijuana. Quantitative immunoassays are available that are specific for a drug or metabolite of interest.

Slide 5: Drug Screen Results

Qualitative results are typically reported as positive or negative. Positive results indicate that the measured value was greater than or equal to an assigned cutoff. Negative results indicate that the value was less than the cutoff. Negative results do not mean that the drug was not detected. Cutoffs should be included with results on the drug screen report. Many labs utilize cutoffs that are specified by the assay manufacturer and are based on SAMHSA limits that were defined for workplace testing. These cutoffs may not be sensitive enough for pediatric or clinical practice.

Slide 6: Positive Drug Screens

A positive drug screen is a presumptive positive and may require confirmation using a different methodology with improved specificity and sensitivity. For example, a positive immunoassay screen for opiates should not be confirmed by the same immunoassay using a lower cutoff, by an immunoassay from a different vendor or by an immunoassay that is specific for an opiate. It should be confirmed by a chromatographic method that provides quantification of each opiate and associated metabolite.

Slide 7: Drug Testing by Immunoassay

Immunoassay is the most common format used for drugs of abuse screening in urine. The advantages include availability of automated platforms able to simultaneously screen for multiple drugs on a small sample volume. These tests are relatively inexpensive and fast to perform so they are offered STAT 24 hours a day, 7 days a week. Point-of-care devices are also available to screen for drugs of abuse and are used in physician office and home settings.

Slide 8: Drug Testing by GC/MS or LC/MS

GC/MS and LC/MS are chromatographic methods used to quantify specific drugs/metabolites and confirm results of immunoassay screens. For example, such methods are capable of confirming that morphine is the opiate causing a positive drug screen. Chromatographic methods may identify drugs not included in immunoassay panels or are not available in an immunoassay format, and are useful when results may be contested or have legal consequences. They can be used to test specimens other than urine or oral fluid. Although these methods tend to be more specific than immunoassays, false positives and negatives are possible.

Slide 9: Detection in Various Specimen Types

This figure shows the relative detection window for various specimen types. Blood and oral fluid have the shortest detection windows and show the best correlation between concentration and signs of intoxication. The window of detection varies with different drugs and drug classes but, in general, urine drug screens detect substances for 1-3 days after exposure. Hair is an alternative matrix that is useful for detection of long-term exposure. Meconium is indicative of in utero drug exposure over the last 20 weeks of gestation.

Slide 10: Urine Drug Screens

There is no direct correlation between blood and urine drug concentration or between urine concentration and signs of intoxication. Urine is the preferred specimen type for most screening purposes because it is non-invasive and generally has adequate collection volume. The practices of adulterating or substituting urine samples to 'beat' drug tests are constantly evolving. Most of these practices can be discovered by comparing the sample to the expected characteristics of human urine. If the specimen integrity is suspected, the sample should be rejected and recollected as this may impact results.

Slide 11: Meconium Drug Screens

Meconium is the preferred sample type for detection of in utero drug exposure. It is the dark green, viscous first stool of newborns that is typically passed in the first 24-72 h of life. Meconium is formed at 12-16 weeks gestation, accumulates throughout the pregnancy and is not excreted until after birth; therefore, it is indicative of in utero drug exposure during the last 20 weeks of gestation. Methods to detect drugs in meconium are lab-developed and involve extensive sample extraction. The cutoffs applied for meconium screens are typically lower than those that are used for urine drug screens.

Slide 12: Oral Fluid Drug Screens

Oral fluid drug testing is gaining popularity in workplace, legal (driving under the influence of drugs) and pain management applications. Oral fluid is collected via expectoration, passive drool technique or by using specialized collection devices. Testing may be performed in a laboratory or point-of-care and there are SAMHSA guidelines for workplace testing cutoffs for oral fluid testing.

Slide 13: Oral Fluid Drug Screens

The advantages of oral fluid drug screens include simple, non-invasive collection that does not require specialized facility or a same-sex observer/collector. The parent drug is frequently present in oral fluid, meaning there is correlation between concentration and signs of intoxication. The disadvantages include possibility for contamination from orally ingested or inhaled substances, unknown adulterants, and low concentrations of drug. The collections often yield inadequate or small volumes and there is significant variation within and across sampling devices. Most immunoassays designed for oral fluid testing are non-homogeneous so they are not readily amenable to automated, high-throughput systems.

Slide 14: Drug Screen Interpretation

A negative result does not mean no drug is present. A common mistake in interpreting negative drug screens is to be unaware of the panel components or cutoffs of the assay used. For example, it is often assumed that methadone, an opioid, is detected by opiate screens. In reality, methadone, has no cross-reactivity and will not be detected by a drug screen for opiates. It is important to understand the limitations and interferences associated with the assay and methodology. Lastly, information about the detection window or effects of specimen integrity on results will aid in interpretation.

Slide 15: Drug Screen Interpretation

Knowing common interferents and assays prone to false positives will assist in interpretation of positive drug screens. Immunoassays for amphetamines have the highest reported false positive rate and cocaine assays have few false positives. It is often difficult to differentiate heroin from morphine or codeine. Detection of 6-monoacetyl morphine and the ratio of codeine to morphine are useful for this purpose but may be misleading depending on the timing of exposure and specimen type. Awareness of the intended and unintended (cross-reactivity) targets for different drug and drug classes is important to interpret positive results of a drug screen. For example, hydrocodone is an opioid that is highly cross-reactive with opiate screens, whereas, a different opioid, oxycodone, will only be detected by the same assay at high concentrations. Information describing the analytes and degree of cross-reactivity and effects of interferents for a specific assay may be available in method validation reports, the manufacturer's package insert, and as reports published in the scientific literature. Positive results indicate exposure but cannot distinguish acute from chronic exposure. Delineating prescribed versus illicit use may be difficult with a qualitative drug screen due to polydrug use and contamination of 'street' drugs.

Slide 16: Pain Management Testing

There have been significant changes in the medical treatment of pain, including availability of new drugs. This has led to increased utilization of drug testing to support pain-management therapies. Drug screening is used to establish compliance with prescribed medications and identify use of illicit or non-prescribed medications and alcohol. Testing for this purpose must distinguish codeine, morphine, hydrocodone, norhydrocodone and hydromorphone and also differentiate oxycodone, noroxycodone and oxymorphone. Urine is the primary specimen but oral fluid is gaining popularity for such applications. Testing typically involves a POCT or laboratory immunoassay screen with follow up confirmation by a chromatographic method.

Slide 17: Points to Remember

In forensic testing, commonly referred to as urine drug screens, the normal result is negative. In therapeutic testing, primarily used for pain management, the expected result is positive. To accurately interpret drug screen results and provide consultation on discrepant or confounding results, one must consider the components of the panel, the method and cutoffs used, the detection window for different drugs in different specimen types and be aware of any reported or potential cross-reactivity and interfering or adulterating substances and their effects. Positive drugs screens are presumptive results and often require confirmation. There is no direct correlation between urine and blood drug concentrations. Oral fluid testing has seen significant improvements in the past five years and is gaining popularity for a variety of applications.