

Drug Testing for Stimulants

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What is classified as a stimulant?

- Substances that effect the central nervous system (CNS) by stimulating the brain to speed up both physical and mental processes
- Prescription, illicit and natural stimulants
 - Amphetamine
 - Methylphenidate
 - Cocaine, Methamphetamine
 - Caffeine, Nicotine
- Today we are focusing on the major sympathomimetic CNS stimulants
 - Amphetamine
 - Methamphetamine
 - MDMA

Some interesting facts

- These sympathomimetic amines are structurally similar to the natural neurotransmitter phenylethylamine
- Amphetamine first synthesized in 1887, Methamphetamine in 1893, however Meth was first used in 1930 for treatment of obesity, narcolepsy, ADD, and hypotension with Amp following in 1935
- Methamphetamine used by German military forces in WWII:
 - Stuka-Tablets or “Hermann Göring pills”
 - Soon discovered they had a drug issue on their hands
- MDMA, a derivative of methamphetamine, was first used in psychotherapy in the 1970s
 - Used in couples therapy; Love drug
 - Risky sexual behavior associated with MDMA use

Stereochemistry of Amp and Methamp

- Amp and methamp are present as racimates; d and l
- d form is more pharmacologically active
- So both prescription and illicit forms have expanded effects *in the key of D*
 - Adderall versus Vynanse
 - d-meth versus l-meth

Analysis of Amp, Methamp, and MDMA

● Immunoassay

- Lots of cross-reactivity for Amp and Methamp
 - OTC cold and allergy preps
 - Other natural products?
- MDMA not as much, but still an issue

● Point of Care (POC) devices

- Similar to immunoassay
- Consider cutoffs and cross-reactivity
- Need for definitive testing even if prescribed Amp

Analysis of Amp, Methamp, and MDMA

- Definitive

- Due to cross-reactivity of IA/POC need definitive MS testing
- Old GC/MS methods would convert ephedrine/pseudoephedrine to Methamp; YIKES!
- Also an issue with isobaric compounds, ie those with the same spectral mass
 - Methamphetamine versus phenteramine
- d,l- methamphetamine analysis
 - Use chiral separations; specialized methods that require longer analysis times

Interpretation Challenges

- Presumptive-only results
 - Despite even having a prescribed amphetamine, must ensure OTC compounds are not responsible for the positive IA/POC result
- Could a confirmed methamphetamine be due to a nasal inhaler?
 - Possible; need d,l methamphetamine analysis to differentiate
- If prescribed Adderall or Vyvanse, is methamphetamine a metabolite?
 - No
- Wide elimination half-life for amphetamines
 - Low-dose amphetamine could be “Negative” if urine is acidic due to decreased half-life (7 hours versus 22 hours)
- Methylphenidate (Ritalin) is not detected by the IA, POC or Definitive assays

What about Synthetic Stimulants?

- Khat; plant-based stimulant used in the Horn of Africa and Arabian Peninsula since 10th century
 - Involves chewing/sucking on leaves of young plant
 - Leaves chewed for its euphoric effects; 20 million daily users in the region
 - Also used by farmers and others for its ability to fight fatigue and hunger; think afternoon coffee!
 - Cathinone is the active ingredient; related to neurotransmitters such as epinephrine
 - Stages of Cathinone use:
 - Euphoria (last about two hours)
 - Deep discussion and increased irritability
 - Increased imagination
 - Depressive stage
 - Irritability

What about Synthetic Stimulants?

- Cathinone is the parent molecule for development of a series of drugs collectively known as “Bath Salts” or Novel Psychoactive Stimulants
- Referred to as Bath Salts due to the initial packaging used to sell these products in retail environment
- These derivatives possess more hallucinogenic properties that account for their abuse
- Like cathinone, most are now regulated; however, nonregulated compounds become available and are used until they are identified and undergo the regulatory process

What about Synthetic Stimulants?

- Most cultural exposed Bath Salt?
 - Alpha-pyrrolidinopentiophenone or alpha-PVP
 - More commonly known as “Flakka”
 - Became notorious as the “Face-Eater” drug during an attack in Florida
 - Adverse effects include:
 - Delusions
 - Paranoid psychosis
 - Agitation
 - Altered mental state
 - Agitated delirium and its associated symptoms

What about Synthetic Stimulants?

- Analytical challenges
- New derivatives easily made and then distributed
- Difficult for labs to stay current due to lack of analytical standards to aid identification
- Current offering:
 - **MDPV** <25 ng/mL
 - **Mephedrone** <25 ng/mL
 - **Methylone** <25 ng/mL
 - **Butylone** <25 ng/mL
 - **Pentylone** <25 ng/mL
 - **Alpha PVP** <25 ng/mL
- Ethylone and eutylone are present in some samples, despite not being a part of the offering

Quest Diagnostics

● Thank You