Club Drugs

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California Society of Addiction Medicine

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CONFLICT OF INTEREST DISCLOSURE

I, Isabella Morton, have nothing to disclose, and I will not be discussing “off label” use of drugs or devices in this presentation.

EDUCATIONAL OBJECTIVES

After attending this presentation, participants will be able to:

1. Explain the mechanism of action for common synthetic drugs, hallucinogens, dissociative anesthetics, and other club drugs.
2. Describe the clinical presentation of the above drugs.
3. Identify common toxicities of the above drugs.

1. Which of the following is FALSE about PCP, Dextromethorphan (DXM) and Ketamine?

A. At one point, they were all available as FDA approved medications.

B. Hallucinations and vital changes are extremely rare with use at moderate-high doses.

C. They are all considered dissociative anesthetics and NDMA antagonists.

D. They have similar pharmacodynamics to Nitrous Oxide (NO).

B. HALLUCINATIONS AND VITAL CHANGES ARE EXTREMELY RARE WITH USE AT MODERATE-HIGH DOSES.

- PCP, DXM, Ketamine are all dissociative anesthetics and NMDA antagonists.
- DXM, when taken as directed, has low toxicity and a high therapeutic index, and is used for cough, cold, or flu relief; however, it is one of the most abused OTC medications.
- PCP was developed as an IV anesthetic but due to a high incidence of postop emergency reactions, it is now only available through illicit sources. PCP intoxication typically includes confusion, delirium, psychosis, and can include severe agitation and nystagmus as well.

Domino EF & Miller SC (2019). The pharmacology of dissociatives. In *ASAM Essentials of Addiction Medicine (6th edition)* pp. 252-262

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PCP, DXM, KETAMINE

- Ketamine is available as a sterile solution for general anesthesia and conscious sedation. Clinical effects of Ketamine are similar to PCP though it is less potent (less agitation and sympathomimetic effects).
- Nitrous Oxide is also an NMDA antagonist and has dissociative-like clinical effects. It can lead to hypoxia, which contributes to feelings of intoxication, and euphoria, which occur rapidly and last for a short time. Inhalants like NO are most commonly used among 12-17 year olds.

Domino EF & Miller SC (2019). The pharmacology of dissociatives. In *ASAM Essentials of Addiction Medicine (6th edition)* pp. 252-262

2. A 20 yo patient presents to clinic c/o low mood for 5 days after taking a "love drug" at a rave. He says that while intoxicated, it caused increased energy and empathy, euphoria, and emotional closeness. Which of the following is FALSE about the drug he most likely used?

A. It causes release of serotonin, dopamine and norepinephrine and can also cause reuptake inhibition.

B. Agitation or anxiety from intoxication should not be treated with a benzodiazepine such as diazepam.

C. Common clinical symptoms includes dry mouth, sweating, mydriasis, bruxism, tachycardia.

D. Severe toxicities can include hyperpyrexia leading to multi-organ failure and rhabdomyolysis; serotonin syndrome; hyponatremia and cerebral edema.

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B. AGITATION OR ANXIETY FROM INTOXICATION SHOULD NOT BE TREATED WITH A BENZODIAZEPINE SUCH AS DIAZEPAM.

- MDMA is also commonly known as ‘”ecstasy” or “molly”
- MDMA causes reuptake inhibition and release of serotonin, DA and NE.
- MDMA is an entactogen, not a classic hallucinogen; it produces minimal sensory effects but consistently increased feelings of elation which likely originate from its disproportionate effect on 5HT. It also has some stimulant like effects.
- Common clinical symptoms includes elevated mood, dry mouth, sweating, mydriasis, bruxism, tachycardia.

Hall, A. P., and J. A. Henry. "Acute toxic effects of ‘Ecstasy’(MDMA) and related compounds: overview of pathophysiology and clinical management." *BJA: British Journal of Anaesthesia* 96.6 (2006): 678-685.

MDMA

- Agitation or anxiety should first be treated by placing the patient in a quiet environment with minimal sensory stimulation, though more severe anxiety/agitation can be treated with a benzodiazepine such as diazepam.
- MDMA toxicities include hyperpyrexia leading to multi-organ failure and rhabdomyolysis; serotonin syndrome; hyponatremia and cerebral edema. Hyperpyrexia is more common in circumstances such as dancing all night in a warm environment.

Wilkins JN, Danovitch I, Gorelick D (2019). Management of stimulant, hallucinogen, PCP and club drug intoxication and withdrawal
In *ASAM principles of Addiction Medicine*, 6th edition, p 770.

3. Which of the following is part of the mint family and long recognized for its hallucinogenic properties, used in healing ceremonies?

A. Salvia

B. K2

C. Methoxetamine

D. Ibogaine

A. SALVIA

- Salvia divinorum belongs to the mint family and is endemic to the Mexican Oaxaca state.
- S. Divinorum contains salvinorin A, a kappa-opioid receptor agonist, which results in hallucinations, diuresis, analgesia, and altered state of consciousness often called “trance-like”.
- Onset of effect is rapid, between 30 seconds to 10 minutes; hallucinations are typically brief and resolve within 30 minutes. Its effects are more potent when smoked rather than ingested orally. Chewing (and absorbing through oral mucosa) is another common method of use that allows better absorption than oral ingestion.
- Salvia’s popularity increased since the 1990s, due to its status as a “legal high”, its wide availability in head shops/the internet, lack of detection on UDS and perceived safety.
- There are no reports of a withdrawal syndrome.

Bogenschutz MP & Nichols D (2019). The pharmacology of hallucinogens. In *ASAM Essentials of Addiction Medicine (6th edition)* pp. 244-245

4. Which of the following is FALSE regarding hallucinogens ?

A. LSD, mescaline, and psilocybin are all 5-HT2A partial agonists.

B. LSD's duration of action is 8-14h, compared to 4-8h for psilocybin and 30-60 min for DMT.

C. Tolerance develops quickly, and frequent use typically leads to physical withdrawal symptoms.

D. Common symptoms of intoxication include altered state of consciousness, enhanced capacity for introspection, illusions and pseudohallucinations, and alterations of time.

C. TOLERANCE DEVELOPS QUICKLY, AND FREQUENT USE TYPICALLY LEADS TO PHYSICAL WITHDRAWAL SYMPTOMS.

- LSD, mescaline, DMT and psilocybin are all 5-HT2A partial agonists.
- LSD's duration of action is 8-14 h, compared to 4-8 h for psilocybin and 30-60 min for DMT. DMT is typically smoked or inhaled.
- Tolerance develops quickly with use of hallucinogens though physical withdrawal symptoms typically do not occur. Use of the classical hallucinogens rarely meets criteria for DSM-5 SUD.

Bogenschutz MP & Nichols D (2019). The pharmacology of hallucinogens. In *ASAM Essentials of Addiction Medicine (6th edition)* pp. 230-244

HALLUCINOGENS

- Common symptoms of intoxication include altered state of consciousness, enhanced capacity for introspection, illusions and pseudohallucinations, and alterations of time.
- Research was interrupted in the 1960's but renewed research is exploring the potential of hallucinogens for the treatment of various SUDs, depression, and PTSD. However, racial minorities have been highly underrepresented in these studies. (Michaels, 2018)

Bogenschutz MP & Nichols D (2019). The pharmacology of hallucinogens. In *ASAM Essentials of Addiction Medicine (6th edition)* pp. 230-245

HALLUCINOGENS

“We can’t start history of psychedelics in the‘60s in the Americas; that needs to stop. We [indigenous people] used this medicine before Jesus Christ walked this Earth.”–Lisa M. Macias Red Bear, Injustice, Intersectional Trauma, and Psychedelics, 2017

Various Mushroom Stones (approx 1 ft tall - 1000 B.C. to 500 A.D.)

5. A 23 year old patient tells you that during his medical residency he began using GHB before going clubbing with friends. Which of the following is FALSE regarding GHB?

A. GHB has a short half-life of around 20-30 min with a narrow margin of safety.

B. GHB has been used as a muscle developer and fat burner, as a party drug for its euphoric effects, and is FDA approved for the treatment of narcolepsy-associated cataplexy.

C. GHB overdose is often brief with rapid recovery.

D. GHB intoxication typically causes hypertension, tachycardia and violent behavior.

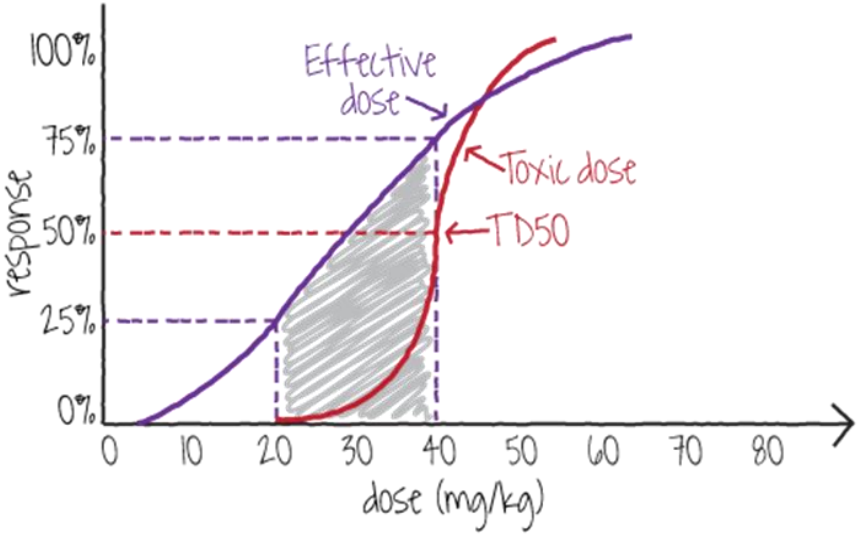
D. GHB INTOXICATION TYPICALLY CAUSES HYPERTENSION, TACHYCARDIA AND VIOLENT BEHAVIOR.

- GHB has been used as a muscle developer and fat burner, as a party drug for its euphoric effects, and is FDA approved for the treatment of narcolepsy with cataplexy.
- GHB intoxication may cause **hypotension**, **hypoventilation, bradycardia, sedation/LOC, amnesia.**

Busardò, F. P., & Jones, A. W. (2015). GHB pharmacology and toxicology: acute intoxication, concentrations in blood and urine in forensic cases and treatment of the withdrawal syndrome. *Current neuropharmacology*, *13*(1), 47–70.

GHB

- GHB has a short half-life of around 20-30 min with a narrow margin of safety.
- GHB overdose is often brief with rapid recovery.



Busardò, F. P., & Jones, A. W. (2015). GHB pharmacology and toxicology: acute intoxication, concentrations in blood and urine in forensic cases and treatment of the withdrawal syndrome. *Current neuropharmacology*, *13*(1), 47–70.

6. An 18 year-old patient presents to the ED with paranoia, dilated pupils, BP 158/108, HR of 119, His UDS is negative, but his friend tells you that he had been using bath salts from a headshop near his apartment. Which of the following is FALSE regarding bath salts?

A. Bath salts are synthetic cathinones, which stimulate release and inhibit reuptake of dopamine, serotonin, and norepinephrine.

B. Cathinone is a monoamine alkaloid found in the khat plant which is native to East Africa.

C. Medical complications of synthetic cathinone intoxication can include disseminated intravascular coagulation, acute kidney injury, serotonin syndrome and seizures.

D. Bath salt intoxication can be reversed with flumazenil.

D. BATH SALT INTOXICATION CAN BE REVERSED WITH FLUMAZENIL.

- Bath salts are synthetic cathinones, which stimulate release and inhibit reuptake of dopamine, serotonin, and norepinephrine.
- Cathinone is a monoamine alkaloid found in the khat plant which is native to East Africa.
- Intoxication effects include euphoria, increased alertness and energy, agitation, psychosis. Complications can include disseminated intravascular coagulation, AKI, serotonin syndrome and seizures. Bath salt intoxication cannot be reversed with flumazenil (an antagonist at the benzodiazepine binding site of the GABA-A receptor).

Banks, M. L., Worst, T. J., Rusyniak, D. E., & Sprague, J. E. (2014). Synthetic cathinones ("bath salts"). *The Journal of emergency medicine*, *46*(5), 632–642.

7. Your patient tells you “I love smoking weed, but I had to stop because I was getting tested at my job. Now I go to my local head shop and get this stuff that does the same thing but doesn’t get me in trouble.” What is the most likely substance he’s using?

A. Psilocybin

B. MDMA

C. K2

D. Dextromethorphan

C. K2 (AKA SPICE/SYNTHETIC CANNABINOIDS)

- K2, or spice, refers to synthetic cannabinoids which are full CB1 receptor agonists (vs THC which is a partial agonist)
- Up to 100 times more potent than THC
- Synthetic cannabinoids typically do not show up on routine UDS
- Peak effects are around 2-5 hrs, though effects can last for days
- Can cause diaphoresis, conjunctival injection, tachycardia & psychosis
- Treatment of intoxication generally centers around supportive care, though benzodiazepines can be used to treat agitation.
- Higher use among LGB vs heterosexual adolescents (Goldbach, 2017)

Castaneto, M. S., Gorelick, D. A., Desrosiers, N. A., Hartman, R. L., Pirard, S., & Huestis, M. A. (2014). Synthetic cannabinoids: epidemiology, pharmacodynamics, and clinical implications. *Drug and alcohol dependence*, *144*, 12–41.

8. Which of the following is FALSE regarding Methoxetamine (MXE)?

A. Methoxetamine is a synthetic analog of ketamine with longer duration of action.

B. Methoxetamine is a CB1 receptor agonist and kappa opioid receptor agonist.

C. Methoxetamine is an NMDA receptor antagonist which inhibits reuptake of serotonin and dopamine

D. Effects of Methoxetamine include hallucinations, euphoria, dissociation, rotatory nystagmus, and confusion.

B. METHOXETAMINE IS A CB1 RECEPTOR AGONIST AND KAPPA OPIOID RECEPTOR AGONIST.

- Methoxetamine is a synthetic analog of ketamine with longer duration of action.
- It is an NMDA receptor antagonist which inhibits reuptake of serotonin and dopamine.
- Effects of Methoxetamine include hallucinations, euphoria, a disconnected feeling; rotatory nystagmus, tachycardia, and confusion; N/V/D, paranoia and anxiety.

Coppola, M., & Mondola, R. (2012). Methoxetamine: from drug of abuse to rapid-acting antidepressant. *Medical hypotheses*, *79*(4), 504–507.

SUMMARY/TAKEAWAYS

- Classical Hallucinogens (LSD, psilocybin, Mescaline) are 5-HT2A partial agonists, which have low risk of progression to a substance use disorder.
- MDMA is an entactogen, which causes reuptake inhibition and release of serotonin, DA and NE, leading to euphoria and emotional closeness.
- Synthetic drugs like K2 and bath salts escape detection on routine UDS, and are more potent and can lead to various medical & psychiatric complications.
- Dissociative anesthetics (DXM, PCP, Ketamine) are NMDA antagonists, with differing duration of action but which cause feelings of disconnection and distorted sensory perceptions.

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