



Episode 154 (Ch. 150 9th) – Hallucinogens

Episode Overview:

1. What are four categories of hallucinogens? Give three examples of each. How do they work?
 - a. Serotonergic agents
 - b. Dissociative agents (multiple)
 - c. Marijuana and synthetic cannabinoids
 - d. Miscellaneous plants/herbs/mushrooms
2. List three important clinical management points for each of:
 - a. Serotonergic agents
 - b. Dissociative agents
 - i. Dextromethorphan
 - c. Marijuana and synthetic cannabinoids
3. Describe the management of PCP toxicity
4. How does cannabinoid toxicity present?
5. What are the isoxazole mushrooms? What is their clinical significance?
6. What is Iboga?

Key Concepts:

- Hallucinogens include many types of drugs and chemicals with different associated effects, including action at serotonin receptors, dopamine receptors, and NMDA receptors.
- Diagnosis and management are based primarily on the history and physical examination, with hallmarks of therapy including supportive care, a calm quiet environment, and sedation with benzodiazepines such as diazepam or lorazepam. Severely agitated patients may benefit from butyrophenone antipsychotic agents such as haloperidol and droperidol.
- Screening tests for drugs of abuse are of limited value in the acute management of intoxicated patients.
- Novel synthetic hallucinogens continue to emerge and may have effects from hallucinogenic, serotonergic, and dissociative toxidromes. These drugs are rarely detected by screening tests, and cases of toxicity may occur in regional outbreaks.
- Patients with PCP toxicity can have unpredictable, violent behavior, and may sustain traumatic injuries. Extreme agitation, although possible, is less common with ketamine and methoxetamine.
- Extremely agitated, violent PCP-intoxicated patients may require rapid sedation to decrease danger to the patient and providers. For hyperthermic patients, sufficient



sedation to decrease neuromuscular hyperactivity may require intubation, paralytics, and active external cooling to decrease the risk of multiorgan failure and mortality.

- The care of patients intoxicated from marijuana and synthetic cannabinoids consists of prevention of injury and reassurance for those who have panic reactions. An extremely agitated patient can be sedated with oral or parenteral administration of benzodiazepines or antipsychotics. High doses of antiemetics may be necessary to treat the nausea and vomiting associated with synthetic cannabinoids and heavy daily marijuana use—cannabinoid hyperemesis syndrome.
- The central nervous system and physiologic effects of mescaline use are similar to those of lysergic acid diethylamide (LSD) derivatives, but more vivid hallucinations can occur. Nausea and vomiting are pronounced and almost always precede the hallucinogenic effects.

Rosen's in Perspective:

Hallucinogens (aka psychedelics) cause *alterations in perception*. Remember back to the psych chapters. Hallucinations are defined ... “as perception of an object or sensation that does not exist in reality.” Very different from delusions - where there is a misperception of reality.

The main mechanism in which most hallucinogens work is via the serotonergic pathway. Thus, the typical presenting toxidrome is that of a sympathomimetic toxidrome. However, can also act via agonism of dopamine pathway and NMDA blockade

Watch out for:

- Hyperthermia
- Rhabdomyolysis
- Seizures
- Acute Kidney Injury

[1] What are four categories of hallucinogens? Give examples of each. How do they work?

a. Serotonergic agents

- “ALPs”
- Ayahuasca (tryptamine)
 - Also synthetic tryptamine aka foxy
- Lysergic acid diethylamide (LSD)
- Psilocybin (mushroom)
 - Actually a tryptamine
 - Similar to venom seen in some toads



b. Dissociative agents (multiple)

- Work via NMDA receptors
- Ketamine
- PCP
- Dextromethorphan

c. Marijuana / synthetic cannabinoids / Miscellaneous plants/herbs/mushrooms

- Marijuana (THC)
- Salvia
- Absinthe
- Amanita (isoxazole mushrooms)

d. Enactogens (Hallucinogenic stimulants - discussed in sympathomimetic chapter)

- MDMA
- PMMA
- Bath Salts
- Piperazines (aka “Molly” - like MDMA)
- Mescaline / peyote
- Nutmeg (works like mescaline)

[2] List three important clinical management points for each of:

a. Serotonergic agents:

- Panic attacks treated with non-pharmacologic and supportive care
 - Complications include harm to self/others
 - Rhabdo/seizures/coagulopathy
- Watch out for worsening depression post use
- Sedate with Benzos Benzos Benzos
- Haldol second line for psychosis

b. Dissociative agents: PCP & Ketamine

- Tx agitation / Emergence phenomena
- Benzos, Cool
- More on this later

c. Dextromethorphan

- Crazy molecule with actions similar to PCP at NMDA and Opioid receptors!!
- Consider narcan in dextromethorphan induced apnea
- Typical clinical findings include:



- Lethargy
- Agitation
- Slurred speech
- Ataxia
- Diaphoresis
- Hypertension
- Nystagmus
- Nausea
- Vomiting
- Hallucinations

TREAT SEVERE AGITATION AND EXCITED DELIRIUM AGGRESSIVELY

- Chemical sedation with Benzos or haloperidol / droperidol (if you have it)
- Cool, tx hypoglycemia
- Intubate and paralyse if needed
- Watch for rhabdo etc
- Watch for Torsades with intoxication plus tx
- Priorities:
 - SAFETY - patient and staff
 - Chemical sedation
 - IM benzo's (e.g. Midazolam 0.2 mg/kg IM = usually 10 mg)
 - Assessment
 - Glucose, FULL set of vital signs
 - Full physical examination
 - IV access and oxygenation via NRB (doubles as a spit mask)
 - Chemical sedation
 - Benzo's** - Diazepam can be administered intravenously in increments of 5 to 10 mg every 5 minutes in adults until sedation is achieved.
 - Prn Haldol IM 2.5-5 mg [see note]
 - Investigations
 - Cooling
 - AGGRESSIVELY cool if temp > 41 (rectal temp)
 - IV fluids - repletion of salt and water depletion
 - Consider need for paralysis and intubation

d. Marijuana and synthetic cannabinoids

- Δ 9-Tetrahydrocannabinol (THC) = main psychoactive agent
- Cannabidiol (CBD) = major non-psychoactive component (little abuse potential and less amounts are found in synthetic cannabis; thought to offset the psychoactive effects of THC).
- Synthetic Compounds



- Spice, K2 Summit, Banana Cream Nuke, Yucatan Fire, Genie, Black Mamba, Crazy Clown
- All cannabinoids work via CB receptors
 - CB1R, found mostly in the CNS, and CB2R, found primarily on peripheral immune cells.
- Tx: supportive care
 - Consider IV antiemetics
 - Hot water to reset hypothalamus dysfunction in dysregulatory syndrome
 - Consider capsaicin cream for Cannabinoid induced hyperemesis syndrome

[3] Describe the management of PCP toxicity

These “naked ninjas” can be super dangerous to themselves, staff and other patients.

- Take control early!!!
- Avoid oxygen and glucose testing until adequate chemical restraint
- These patients are unpredictable and unreliable, so take em down:
- Benzos Benzos Benzos Benzos Benzos
- Cooling for hyperthermia (Conduction/Convection/Radiation/Evaporation)
- Correct electrolyte disturbances
- Watch out for Torsades
- Treat rhabdo aggressively
- May need intubation and paralysis to facilitate the above

[4] How does cannabinoid toxicity present?

Remember cannabis works via CB receptors.

- Smoking marijuana= rapid and predictable signs and symptoms
- Ingestion= delayed and sometimes unpredictable effects.
- NB effects:**
 - smoking** = immediate (within 8min up to 4hrs) alteration of mood and usually relaxation and euphoria.
 - Oral ingestion** = longer duration of effect ($\geq 6-12$ hours), and patients with a massive oral marijuana ingestion may develop profound ataxia, vomiting, agitation, anxiety, and CNS depression. In addition, symptoms may not manifest until 2-4 hrs post ingestion (by that time the person has eaten the whole bag of “edibles”....)
 - Physiologic effects = mild increase HR & conjunctival injection.**
- Other acute peripheral changes include:
 - Urinary retention



- Decreased testosterone levels
- Decreased intraocular pressure
- Short-term memory is impaired
- Impaired ability to perform complex tasks
- Excessive appetite

WATCH OUT FOR PEDIATRIC INGESTIONS:

- Pediatric exposures
 - Hypothermia, ataxia, nystagmus, tremor, tachycardia, injected conjunctiva, and labile affect
- “Oral ingestion in peds: can produce rapid onset of drowsiness, hypotonia, and lethargy, which can lead to coma and **airway obstruction and respiratory compromise** requiring intubation and ventilatory assistance.”

Synthetic Cannabinoids:

- First-generation synthetic cannabinoids = tachycardia, agitation, nausea and vomiting, altered mentation, and hallucinations & seizures
- Second-generation synthetic cannabinoids = profound agitation and aggression, seizures, tachycardia followed by bradycardia
- POSSIBLE RARE COMPLICATION: ischemic stroke and cardiac toxicity**

[5] What are the isoxazole mushrooms? What is their clinical significance?

- Isoxazole-containing mushrooms include
 - Amanita muscaria
 - has a red or yellow cap, with “white warty structures”
 - Amanita pantherina
 - Amanita gemmata
 - Amanita cothurnata
- Active ingredients = isoxazole derivatives
- Ibotenic acid and its decarboxylation product, muscimol, = structural analogues of:
 - glutamic acid (excitatory)
 - Elation, giddiness, hyperactivity, muscle tremors, and distortion of space and time
 - Begin approximately 30 minutes to 2 hours after ingestion
 - Likely to be mediated by ibotenic acid
 - GABA (inhibitory)
 - Tiredness and deep sleep, difficult to rouse
 - Vivid hallucinations and manic excitement may oscillate with periods of deep sleep.
 - Duration of effect = up to 12 hours



Management =

- Excitatory phase supportive care
- Prolonged sleep = no intervention but observation
- Tonic-clonic seizures are reported

*** Clinical Pearl***

- Isoxazole poisoning **CAN RESEMBLE** anticholinergic toxicity
- BUT THEY DON'T CONTAIN** belladonna alkaloids
- Some people mistake the name = *A. muscaria* with that of muscarine, a cholinergic toxin.
- Atropine can worsen anticholinergic effect. Don't use it
- But the most important not of this podcast is here:
- "It is important to differentiate isoxazole-containing *Amanita* mushrooms from the deadly hepatotoxic cyclopeptide- containing *Amanita* mushrooms, of which *Amanita phalloides* is a member."
- People dabble in shrooming, but even seasoned academics get identification wrong. Cyclopeptide poisoning has a very high mortality, so don't miss it!!!

[6] What is Iboga?

- Ibogaine = naturally occurring indole alkaloid
- Found in the roots of the African rain-forest shrub *Tabernanthe iboga*.
- Involve opioid, dopaminergic, serotonergic, glutaminergic, γ -aminobutyric acid (GABA)-ergic, glutamatergic, adrenergic, and cellular ion channel signaling systems.
- Becoming popular as treatment for opiate withdrawal!!!
- Increasing reports of sudden cardiac death, likely from prolonged QTC and PMVT
- Tx torsades with Mg and possible overdrive pacing