ASAM REVIEW COURSE 2023

## Other Classes of Drugs: Pharmacology and Epidemiology

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## Financial Disclosure

Annie Lévesque, MD, MSc

- No relevant disclosures

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## LEARNING OBJECTIVE

**Identify** other classes of drugs, their physiological impacts, and treatment considerations.

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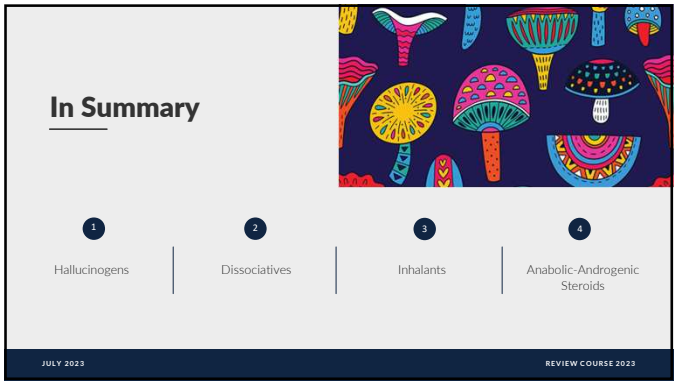
In Summary
1
Hallucinogens
2
Dissociatives
3
Inhalants
4
Anabolic-Androgenic Steroids
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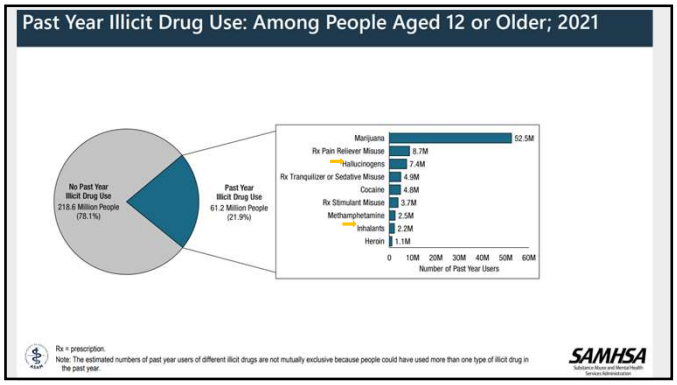
Past Year Illicit Drug Use: Among People Aged 12 or Older; 2021
No Past Year Illicit Drug Use
218.6 Million People
(78.1%)
Past Year Illicit Drug Use
61.2 Million People
(21.9%)
Marijuana 52.5M
Rx Pain Reliever Misuse 8.7M
Hallucinogens 7.4M
Rx Tranquilizer or Sedative Misuse 4.9M
Cocaine 4.8M
Rx Stimulant Misuse 3.7M
Methamphetamine 2.5M
Inhalants 2.2M
Heroin 1.1M
0 10M 20M 30M 40M 50M 60M
Number of Past Year Users
Rx = prescription.
Note: The estimated numbers of past year users of different illicit drugs are not mutually exclusive because people could have used more than one type of illicit drug in the past year.
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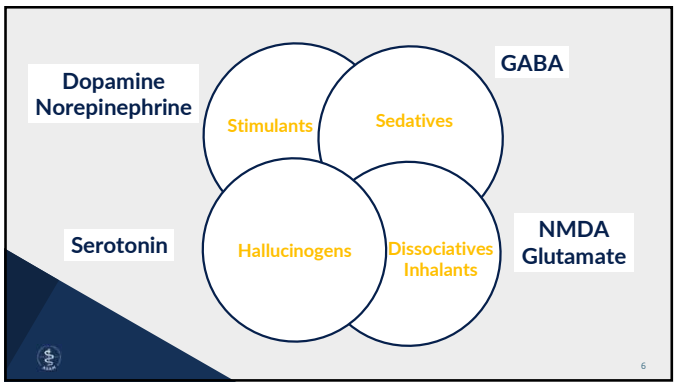
Dopamine
Norepinephrine
Stimulants
Sedatives
GABA
Serotonin
Hallucinogens
Dissociatives
Inhalants
NMDA
Glutamate
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## Hallucinogens

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## LSD and Psilocybin are:

A. Serotonin 5HT-2A receptor agonists
B. Dopamine transporter reuptake inhibitors
C. NMDA receptor antagonists
D. Opioid mu-receptor agonists

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## Definition of Hallucinogens

- Produce alterations in thought, mood, and perception
- Produce minimal autonomic side effects or craving

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## "Illusionogen"

- Illusions = alteration or enhancement of existing sensory perception
- May be more accurate term
  - Reality testing is generally intact
  - Effect varies greatly with expectations and environment

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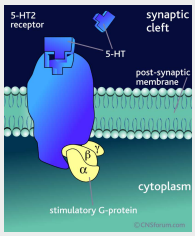
## Classical Hallucinogens (Serotonergic Hallucinogens)

- 5HT-2A agonists or partial agonists
- Fall within the group of chemical compounds called arylalkylamines:
  - Not all arylalkylamines are hallucinogenic
  - Also includes some stimulants and empathogens

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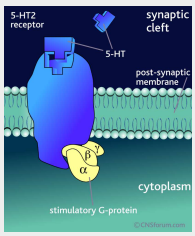
## Classical Hallucinogens (Serotonergic Hallucinogens)

- 2 subclasses of arylalkylamines
  - Indolealkylamines (serotonin analogs)
    - Bind at multiple receptors (5HT-2A, 5HT-2B, 5HT-2C, 5HT-1A)
  - Phenylalkylamines (norepinephrine analogs)
    - Fairly selective for 5HT-2A

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## Effects of Hallucinogens

- Altered shapes and colors
- Synesthesia
- Alterations in mood (can be tension and anxiety)
- Distorted sense of time
- Difficulty expressing thoughts
- Depersonalization
- Dreamlike feeling

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## Effects of Hallucinogens *Somatic*

- Dizziness
- Weakness
- Tremors
- Nausea
- Drowsiness
- Paresthesias
- Blurred Vision

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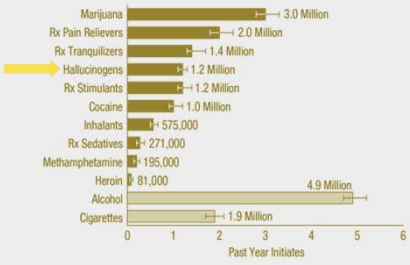
## Numbers of Past Year Initiates of Substances among People Aged 12 or Older: 2017 NSDUH

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## DMT

- DMT (N,N-Dimethyltryptamine)
  - Naturally occurring (plants, toad)
  - Rapid onset (<5 min), short duration of action (30 min)
    - Inhalation (smoking) or injection (rare)
    - Can be taken orally, but requires MAOI

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## Ayahuasca

- Brew containing DMT, MAOIs, and other hallucinogens
- Used ceremonially in parts of the Amazon and in some Native American religions
- Can cause significant vomiting

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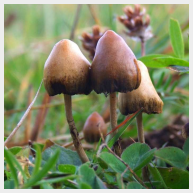
## Psilocybin

- Psilocybin → psilocin
  - Found as naturally occurring tryptamine in certain varieties of mushrooms
  - Detachment from reality: inability to discern fantasy from reality
    - Can lead to panic attacks, psychosis
  - Rapid tolerance to effects
    - Cross tolerance with LSD
  - Duration: 4-6 hours



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## Psilocybin

- Reported mystical-like experiences
  - Inner peace, patience, optimism, self-confidence
- Adverse effects
  - Nausea, vomiting, anxiety
  - May interact with MAOI
- Duration: 4-6 hours

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## Lysergic Acid Diethylamide (LSD)

- Water soluble, clear, white, odorless crystals
  - Thin blotter paper with dried solution of LSD
  - Breath mints/sugar cubes ("dropping" acid), pressed into pills or thin gelatin squares
- Onset: 30-60 min, Peak: 2-4 hours, Duration: 8-12 hours
- Effects
  - Altered shapes and colors, heightened sense of hearing
  - Depersonalization, visual hallucinations, alterations in mood

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## Lysergic Acid Diethylamide (LSD)

- Onset: 30-60 min, Peak: 2-4 hours, Duration: 8-12 hours
- Effects
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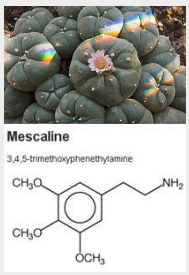
## Mescaline/Peyote




- Buttons from top (crown) of peyote cactus
  - 6-10 buttons for intoxication
- Slow onset (30-60 min)
  - First hour: minor perceptual changes, increased resp rate, nausea
  - Next several hours (5-10):
    - Visual illusions/hallucinations
    - Synesthesia

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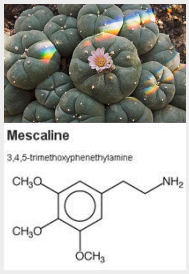
## Mescaline/Peyote




- Slow onset (30-60 min)
  - First hour: minor perceptual changes, increased resp rate, nausea
  - Next several hours (5-10):
    - Visual illusions/hallucinations
    - Synesthesia

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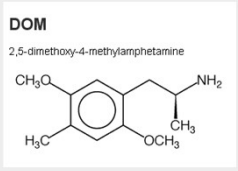
## DOM

- Results from structural modification of mescaline-like substances
- Extremely potent
- Used as model hallucinogen in drug discrimination studies

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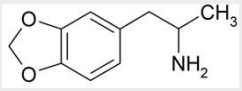
## MDA

- Produces stimulant and hallucinogenic effects
  - Similar to combined effects of cocaine and LSD
- Can be modified to MDMA (ecstasy)
  - Stimulant effects
  - Empathogenic
- Has been represented and sold as MDMA

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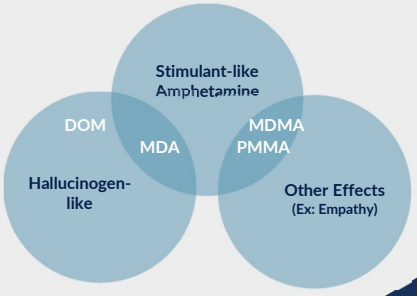
## Classification by Effect

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## Salvia

- Naturally grows in the US
- Traditionally ingested by chewing / drinking juice for healing rituals
- Sometimes smoked when used as drug
- Active ingredient in Salvia is salvinorin A, a kappa opioid agonist

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## Salvia Effects


- Intense and short-lived
  - Onset < 1 minute
  - Duration < 30 minutes
- Changes in visual perception
- Decreased ability to interact with surroundings
- Increased sense of well-being (or not)

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## Salvia Effects


- Feelings of detachment
- Modified perception of external reality and the self
- Decreased ability to interact with surroundings

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## Summary: Hallucinogen Intoxication

- Clear Sensorium
- Intact Memory
- Hyperalert
- Intact reality testing
  - Can sometimes be reasoned with or calmed by talking
- Visual Hallucinations >> Auditory

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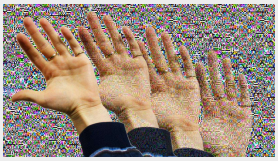
## Hallucinogen Persisting Perception Disorder (HPPD)

- Re-experiencing of perceptual symptoms experienced while intoxicated following cessation of use = flashbacks



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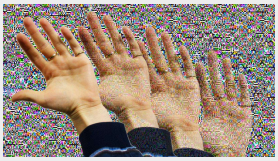
## Hallucinogen Persisting Perception Disorder (HPPD)

- Unrelated to dose or number of exposures
- Usually resolves within 1-2 years of last use
- Can be triggered by other substance use



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## Dissociatives

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## PCP and Ketamine are:

A. Serotonin 5HT-2A receptor agonists
B. Dopamine transporter reuptake inhibitors
C. NMDA receptor antagonists
D. Opioid mu-receptor agonists

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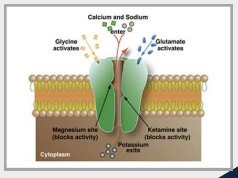
## Definition

- NMDA receptor antagonists
  - Glutamate activates NMDA receptors to filter sensory stimuli
  - Dissociatives noncompetitively block NMDA receptors → sensory overflow
  - Visual hallucination relatively rare

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## Members of the Class

- Arylcyclohexylamines
  - PCP
  - Ketamine
- Dextromethorphan (DXM
- Nitrous Oxide


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## Effects

- Dissociation
- Sensory Isolation
- Mental Distortions
- Increased HR, BP, Temp

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## Epidemiology

- Men > Women
- More common in large urban areas
- Often used in combination with alcohol or other illicit substances

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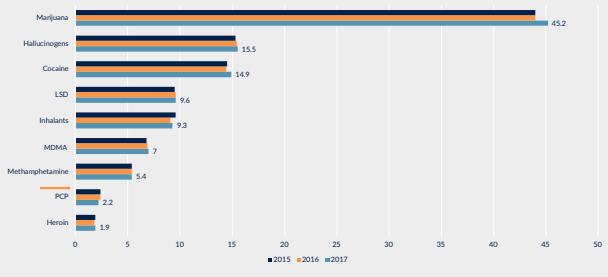
## Lifetime Prevalence of Specific Drug Use: Percentages, NSDUH

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## Phencyclidine (PCP, Angel dust)

- Developed as IV anesthetic
  - No longer FDA-approved; now Schedule I
    - Associated with prolonged delirium
- Risk of seizures or death
- Available as powder, tablets, liquid, and sprayed onto plant leaves and then smoked

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## PCP Effects

- Vary widely with dose
  - Confusion, delirium, psychosis
  - ⬇
  - Semi-coma and coma (less common)
  - ⬇
  - Coma with seizures (rare)

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## PCP

- Psychotomimetic = model of psychosis
  - Positive Symptoms (Delusions, hallucinations)
  - Negative Symptoms (Blunted affect, asociality)

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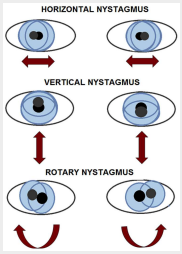
## PCP

- PCP Intoxication
  - Nystagmus (rotary, vertical, horizontal)
  - Hyperreflexia
  - HTN
  - Feelings of invulnerability
  - Management: low stimulus environment, benzos/antipsychotics as indicated

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## Ketamine (K, Special K)

- FDA-approved for general anesthesia in animals and humans
- Schedule III
- Administered as IV or IM in medical settings
- Used by inhalation, smoking, or oral administration
- Less potent, shorter-acting than PCP


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## Effects of Ketamine

- Analgesia / numbness
- Spacey feeling ("K-hole")
- Amnesia
- Delirium (higher doses)

- Nystagmus (vertical and/or horizontal)
- CV + renal complications
- Long-term
- Dysphoria, memory impairment, apathy, irritability

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## Dextromethorphan (DXM)

- OTC cough medicines
  - Capsules, tablets, lozenges, syrup
  - AKA "skittles"
- Anti-tussive dose: <120mg daily; recommended dose 10-20mg q4hours
- 300-1800mg produces PCP-like effects

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## Effects of DXM

- Euphoria and hallucinations (increasing w/ higher dose)
- Drowsiness, blurred vision, slurred speech
- N/V, hypertension, diaphoresis

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## Effects of DXM

- Significant serotonergic properties
  - ↑ serotonin synthesis and release
  - ↓ reuptake

- Deaths have been reported with large doses (200x dose)
  - CNS & respiratory depression, seizure, arrhythmias

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## Dissociative: Additional Information

- PCP included on most screening panels (high false positive rate)
  - Need special testing (GC-MS) for ketamine, DXM
- Increased serum CPK & urine myoglobin

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## Summary: Dissociative Intoxication and Overdose

- Rarely see dilated pupils
  - Different from stimulant or hallucinogen intoxication, opioid withdrawal
- Visual hallucinations relatively rare

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## Inhalants

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Many abused inhalants produce an intoxication that most closely resembles which of the following?

A. Alcohol
B. Cocaine
C. Cannabis
D. LSD

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## Inhalants


Breathable chemicals that can be self-administered, also known as:

- Whippets
- Poppers
- Huff
- Bang
- Kick
- Sniff

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## Terminology

- Sniffing = inhaling from an open container
- Huffing = holding fabric soaked in substance to the nose or mouth and inhaling
- Bagging = concentrating vapors in a bag and inhaling

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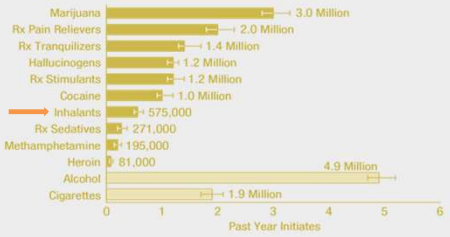
Numbers of Past Year Initiates of Substances Among People Aged 12 or Older: 2017 NSDUH

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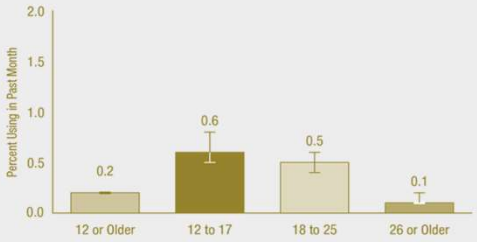
Past Month Inhalant Use Among People Aged 12 or Older, by Age Group: Percentages, 2017 NSDUH

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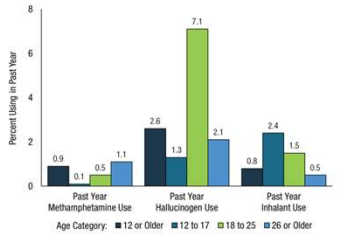
Past Year Methamphetamine Use, Past Year Hallucinogen Use, and Past Year Inhalant Use: Among People Aged 12 or Older; 2021

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## Source of Inhalants: Products

| | | | |
|---|---|---|---|
| Air freshener | Lighter fluid | Household cleaners | Gasoline |
| Hair spray | Mothballs | Nail polish remover | Paint thinner |
| Markers | Refrigerant | Rubber cement | Spray paint |
| | Video head cleaner | Whipped cream canisters | |

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## Sources of Inhalants:

Possible Contents

- Amyl, butyl, cyclohexyl nitrite; butane
- Butane
- n-Hexane, tetrachloroethylene, xylene
- Benzene, toluene, xylene, (lead)
- Butane, propane
- Naphthalene, paradichlorobenzene
- Acetone, toluene
- Toluene, trichloroethylene, xylene
- Xylene
- Freon
- Acetone, benzene, n-Hexane, toluene
- Butane, propane, toluene
- Amyl, butyl, cyclohexyl nitrite
- Nitrous oxide

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## Abuse Liability

- Number of factors increase abuse potential
  - Free or low cost
  - Readily available
  - Difficult to test for
  - Perceived as low risk
- Inquire about inhalant use, especially when working with adolescent population
- Provide education regarding consequences of use

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## Inhalant Pharmacology

- Highly lipophilic
- Rapidly absorbed through the lungs
- Crosses blood-brain barrier
- Accumulates in brain, liver and fatty tissue
- Rapid onset, short duration
- Synergistic effect: alcohol, benzos

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## Effects of Inhalants

| Acute Effects | Toxic Effects and Overdose |
|---|---|
| • Euphoria<br>• Disinhibition<br>• Dizziness / lightheadedness<br>• Slurred speech<br>• Ataxia | • Respiratory depression<br>• Arrhythmias<br>• Asphyxia, cardiac arrest and death can occur |

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## Chronic Effects of Inhalants

| | |
|---|---|
| CARDIAC<br>arrhythmia<br>cardiomyopathy | DERMATOLOGICAL<br>perioral infection<br>rash |
| GASTROINTESTINAL<br>hepatorenal failure | MUSCULOSKELETAL<br>Rhabdomyolysis |

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## Chronic Effects of Inhalants

**PULMONARY**
emphysema
hypoxia
aspiration pneumonia

**GENITOURINARY**
glomerulonephritis
hypokalemia

**HEMATOPOIETIC**
aplastic anemia
leukemia
bone marrow suppression

**NEUROLOGICAL**
peripheral neuropathy
delirium/dementia
cerebellar atrophy
irreversible white matter changes

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## Treatment Considerations

- User may experience prolonged residual effects because chemicals are stored in fatty tissue
- Neurological impairment is often present
  - Cognition should be continually re-assessed
  - Talk therapy / group therapy may not be appropriate

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## Anabolic-androgenic Steroids

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## Which of the following is a side effect of anabolic steroid use?

A. Mania
B. ↓LDL,↑HDL
C. Hypersomnia
D. Weight loss

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## Anabolic - Androgenic Steroids (AAS)

- Anabolic = skeletal muscle-building
- Androgenic = masculinizing
- Includes testosterone and >100 related synthetic substances

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## Misuse

- Enhance performance and/or improve physical appearance
  - May be taken at 10-100x the intended dose

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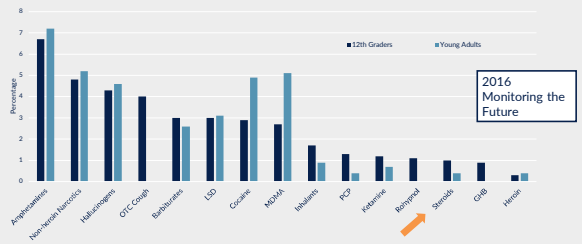
## Annual Prevalence of Various Drugs for 12th Graders and Young Adults (18-25) by % Using

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## Epidemiology

- 3 most common populations:
  - Athletes
    - Performance enhancement
  - Aesthetes
    - Improve physical appearance (often adolescents)
  - Fighting Elite
    - Increase aggression and/or job performance (security, law enforcement)

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## Steroid Side Effects

| | | | |
|---|---|---|---|
| Acne | Liver damage | ↑LDL, ↓HDL | Complications of Injections |
| Aggressive / violent behavior ("Roid Rage") | Hypomania or Mania | Paranoia | Extreme irritability |

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## Steroid Side Effects

| Women | Men |
|---|---|
| • Deepening of voice<br>• Facial hair<br>• Menstrual changes<br>• Male-pattern baldness<br>• Genital hypertrophy | • Testicular atrophy<br>• Prostatic hypertrophy<br>• Gynecomastia<br>• Baldness<br>• Infertility |

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## Psychiatric Side Effects

- Aggressive / violent behavior
  - "Roid Rage"
- Hypomania or Mania (high doses)
- Paranoia
- Extreme irritability
- Impaired judgment
- Delusions

- Treatment
- Remove AAS
- Use mood stabilizers or anti-psychotics as needed
- Generally, resolves within 1-2 weeks after cessation

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## Other Associated Syndromes & Treatment

- Steroid Withdrawal-Associated Depression
  - Can be responsive to SSRIs
- Comorbid SUD, especially opioid
- Body Dysmorphic Disorder / Muscle Dysmorphia

- Rarely seek treatment
- Not euphorigenic; no immediate high
- Goal is long-term reward associated with physical changes
- May be seen as socially acceptable or positive

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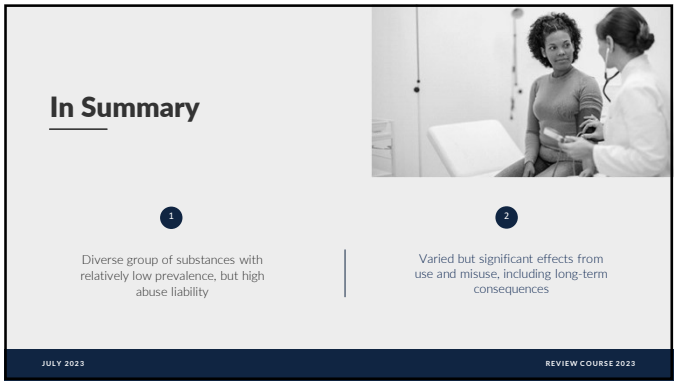
In Summary
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Diverse group of substances with relatively low prevalence, but high abuse liability
2
Varied but significant effects from use and misuse, including long-term consequences
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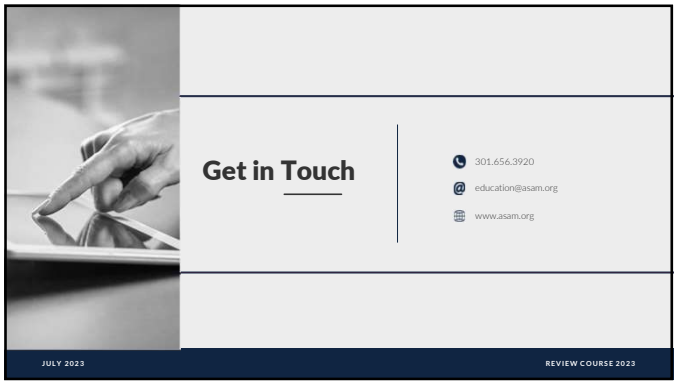
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