Drugs of Abuse Continued: Sedatives, Hallucinogens, PCP and Other Drugs

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AOD 101 Part 3 of 3
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Learning Objectives

1. List the common drugs of abuse and their mechanisms of action.
2. Review how drugs affect the brain and the body.
Classes of Drugs of Abuse

- Stimulants
- Caffeine
- Nicotine
- Cannabis
- Opioids
- Sedative-hypnotics
- Hallucinogens
- Dissociative Drugs
- “Club drugs”
- Anabolic Steroids
- Inhalants
Sedative-Hypnotic Drugs

Examples

- Benzodiazepines
  - Diazepam
  - Chlordiazepoxide
  - Clorazepate
  - Oxazepam
  - Lorazepam
  - Alprazolam
  - Clonazepam
  - Temazepam
  - Triazolam
  - Flurazepam

- Barbiturates
  - Phenobarbital
  - Pentobarbital
  - Secobarbital

- Others
  - Meprobamate
  - Chlormezaline
  - Methaqualone
  - Zolpidem
  - Zapelen
- Alcohol

Sedative-Hypnotics

- Most have clinical utility as hypnotics, anxiolytics, sedatives or anticonvulsants
- 12-20% of American adults use in any give year
- 90% of med-surg patients are prescribed these drugs
- 2 billion (yes, billion) tablets of diazepam are prescribed annually in the U.S.
Sedative-Hypnotics

- All exert significant activity on GABA
- Prototype: Barbiturates
- Most common: Benzodiazepine (other than alcohol)
- Major avenue of supply: Physicians
- Route of administration: Oral, IM, IV
- Tolerance and cross-tolerance occur
- Withdrawal can be life-threatening
- Benzodiazepine antagonist: Flumazenil

Sedative Intoxication and Withdrawal

- **Intoxication**
  - Euphoria (Rising BAL)
  - Dysphoria (Falling BAL)
  - Sedation
  - Slurred speech
  - Incoordination
  - Nystagmus
  - Cognitive impairment

- ** Withdrawal**
  - Dysphoria
  - Anxiety, agitation
  - Insomnia
  - Tremor
  - Diaphoresis
  - GI distress
  - Transient hallucinations
  - Seizures
Treatment of Sedative Withdrawal

- Approaches
  - Gradually wean the sedative drug itself
  - OR
  - Substitute a similar drug (usually a long half-life drug like clonazepam or phenobarbital) and wean it
  - OR
  - Substitute and anticonvulsant (Data not as strong)

Phenobarbital Equivalents for Withdrawal Management

<table>
<thead>
<tr>
<th>Phenobarbital</th>
<th>30 mg</th>
<th>Lorazepam</th>
<th>2 mg</th>
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<tbody>
<tr>
<td>Butalbital</td>
<td>100 mg</td>
<td>Oxazepam</td>
<td>30 mg</td>
</tr>
<tr>
<td>Pentobarbital</td>
<td>100 mg</td>
<td>Temazepam</td>
<td>15 mg</td>
</tr>
<tr>
<td>Secobarbital</td>
<td>100 mg</td>
<td>Triazolam</td>
<td>0.125 mg</td>
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<tr>
<td>Alprazolam</td>
<td>1 mg</td>
<td>Chloral Hydrate</td>
<td>500 mg</td>
</tr>
<tr>
<td>Clordiazepoxide</td>
<td>25 mg</td>
<td>Meprobamate</td>
<td>1200 mg</td>
</tr>
<tr>
<td>Clonazepam</td>
<td>1 mg</td>
<td>Zolpidem</td>
<td>5 mg</td>
</tr>
<tr>
<td>Diazepam</td>
<td>10 mg</td>
<td>Methaqualone</td>
<td>300 mg</td>
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</table>
Hallucinogens

“My surroundings...transformed themselves in more terrifying ways. Everything in the room spun around, and the familiar objects and pieces of furniture assumed grotesque, threatening forms. They were in continuous motion, animated, as if driven by an inner restlessness...Even worse than these demonic transformations of the outer world were the alterations that I perceived in myself, in my inner being. Every exertion of my will, every attempt to put an end to the disintegration of my outer world and the dissolution of my ego, seemed to be a wasted effort. A demon had invaded me, had taken possession of my body, mind and soul.”

-Albert Hoffman, 1943
(Sandoz Pharmaceuticals)
Hallucinogens

- Examples
  - LSD [Lysergic acid diethylamide]
  - Psilocybin [mushrooms; 4-hydroxydimethyltryptamine]
  - Mescaline [peyote cactus; 3,4,5-trimethoxyphenethylamine]
  - STP [2,5-Dimethoxy-4-methylamphetamine or DOM]
Hallucinogens

- Examples (cont.)
  - Nutmeg [Myristicin]
  - Morning glory seeds [LSA, d-lysergic acid amide]
  - Bufotenine [toad-licking; 5-hydroxy-tryptamnine]
Hallucinogens

- Hallucinogens: include all drugs that cause hallucinations. Also cause sympathetic arousal.
- Primary mechanism seems to be upon serotonergic systems, most prominent in cerebral cortex and locus coeruleus.
- Contaminants are common, esp. anticholinergic.
- LSD is the most commonly used hallucinogen.
  - Sold as “microdots,” “window panes,” or “blotter.”
  - Effects begin 30-90 minutes after ingestion (usually oral) and last up to 12 hours.
  - Rapid tolerance can develop.
  - No withdrawal syndrome reported.

Hallucinogens-Lasting Effects

- Hallucinogen Persisting Perception Disorder:
  - Episodic, spontaneous recurrences of hallucinogen sensory experiences, visual disturbances, light trails, flashing lights, etc.
  - Commonly referred to as “flashbacks.”
- Psychosis:
  - Persistent symptoms including mood swings, vivid visual disturbances and hallucinations.
  - Can last for years.
Hallucinogen Intoxication and Withdrawal

- Intoxication
  - Euphoria, anxiety, panic reactions
  - Perceptual abnormalities
  - Incoordination/tremor
  - Tachycardia
  - Blurred vision
  - Dilated pupils
  - Diaphoresis

- Withdrawal
  - None described

Dissociative Drugs

- Distort visual and auditory perceptions without genuine hallucinations
- Produce feelings of detachment from environment
- Exert effects via glutaminergic and dopaminergic mechanisms
- Examples:
  - Phencyclidine (PCP)-prototype
  - Ketamine
  - Dextromethorphan
Phencyclidine Intoxication

- Unpredictable behavior
- Decreased pain perception
- Vertical, horizontal and rotatory nystagmus
- Dysarthria
- Ataxia
- Rigidity and bizarre posturing
- Hyperacusis
- Increased reflexes
- Tachycardia, hypertension, hyperpyrexia
- Delirium and persistent psychosis

Phencyclidine (PCP)

- Initially developed as a general anesthetic
- Never approved for use in humans due to delirium and profound agitation occurring as patients emerged from anesthesia
- Often used to “lace” other drugs
- Route of administration: Oral, smoked, injected
- Effects occur within minutes and are unpredictable
- Effects last for several hours to several days
- No tolerance or withdrawal is described
Ketamine
- Slang names: Special K, “K,” Vitamin K, Cat valiums
- Anesthetic agent used most commonly in veterinary medicine
- Effects are similar to PCP (NDMA antagonist)
- Can cause neurotoxicity
- Route of administration: Oral, snorted, smoked, injected
- Less potent than PCP
- “Date Rape” drug

Dextromethorphan
- NMDA antagonist
- Available in OTC cough preparations
- 2-4 oz: mild stimulation, visual disturbances
- > 4 oz: begin to see dissociative effects
- Antihistamines and decongestants often also in DM containing preparations
Inhalants

- Include various volatile substances
  - Aerosols
  - Gasoline
  - Airplane glue
  - Paint thinners
  - Gases
  - Nitrites
- Inexpensive, readily available, not regulated, easy to conceal
- Use is most common in teens and pre-teens who move on to other drugs
Trends in Inhalant Use

Inhalant Intoxication and Withdrawal

- Intoxication
  - Euphoria
  - Ataxia
  - Nystagmus
  - Diplopia
  - Slurred speech
  - Depressed reflexes
  - Hallucinations

- Withdrawal
  - None described
Inhalants

- Ways administered:
  - “Huffing”
  - “Bagging”
  - Sniffing or snorting
  - Inhaling from balloons filled with Nitrous Oxide
  - Rapid onset of intoxication with relatively short duration

Inhalants

- Signs of abuse:
  - Detectable odor on breath
  - Paint or chemical stains on face, hands, clothing
  - Hidden bottles of paint, solvents, soaked rags
  - Evidence of intoxication
Lifetime Prevalence of Use of Various Drugs

<table>
<thead>
<tr>
<th>Grade</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>8th</td>
<td>20%</td>
</tr>
<tr>
<td>10th</td>
<td>30%</td>
</tr>
<tr>
<td>12th</td>
<td>40%</td>
</tr>
</tbody>
</table>

Source: Monitoring the Future Survey, 2003

Inhalants

Medical Consequences

- Asphyxiation
- Suffocation
- Choking/Aspiration
- Accidental injury
- Neurotoxicity
- Nephrotoxicity
- Hepatotoxicity
- Cardiotoxicity
- Bone marrow suppression
Anabolic Steroids

- Medical indications:
  - Hypogonadism
  - Delayed puberty
  - Breast cancer
  - Wasting syndrome
  - Certain anemias

Brain images show marked atrophy (shrinkage) of brain tissue in a toluene abuser (B) compared to a normalizing individual (A). Note the smaller size and the larger empty (dark) space within the toluene abuser’s brain. (The white outer circle in each image is the skull.)
Anabolic Steroids

“Firsts:”
- Isolated in 1935
- Used as performance enhancers by German soldiers in WW II
- Used as performance enhancers in sports in late 1940s
- Testing began in 1976 Olympic Games
- Ben Johnson of Canada stripped of gold medal in 100 m dash due to positive steroid testing

Anabolic Steroids

- Street names: “‘roids,” “juice”
- Have anabolic and androgenic effects
- Schedule III controlled drug
- Characteristic users:
  - Body builders
  - Athletes
  - Law enforcement
  - Up to 3% of high school males, 1% of females
Anabolic Steroids

• Reasons for use:
  • Performance enhancement
  • Increase muscle size/reduce body fat (body image distortion)
  • Self-protection

Anabolic Steroids

• Can meet DSM-IV criteria for dependence
• High rate of Cluster 2 personality disorders
• Tend to be used in elaborate way with cycled use:
  • “Stacking”
  • “Pyramiding”
• Use of dietary supplements is common
• Other drugs frequently used in combination:
  HGH, GHB, Ephedrine, Diuretics, HCG
Steroid Use and Perceived Risks

Anabolic Steroids

- **Adverse effects:**
  - Cardiovascular: MI, Increased lipids, HTN, CVA
  - Hepatic: Increased LFTs, Hepatocellular CA, Hepatitis B and C
  - Musculoskeletal: Tendon avulsion, Premature closure of epiphysis
  - Dermatological: Acne, alopecia
  - Reproductive: Testicular atrophy, azoospermia, Prostatic hypertrophy, change in sex drive (increased or decreased)
  - Psychiatric: “‘Roid rage,” Mania, Psychosis, Depression
  - Withdrawal effects: Depression, Fatigue, urge to readminister
Club Drugs

- Refers to a variety of drugs first widely used by young adults at all-night dance parties called “raves”
- Raves:
  - Large, organized social events
  - Held in warehouses, dance halls, clubs
  - Attendees dance all night to pre-recorded music, often accompanied by light shows and computer generated images
  - Reports of over 10,000 at one event
- Use of these drugs has extended well beyond “Raves” in the past several years
Club Drugs

- Use appears to be escalating
- Have developed an undeserved reputation for safety
- Can lead to serious health problems and death, especially if combined with alcohol
- Most are tasteless, odorless and colorless and can be easily slipped into drinks
- Multiple contaminants, potency varies widely

Club Drugs

- Examples:
  - Ecstasy
  - Gamma-hydroxybutyrate (GHB)
  - Ketamine
  - Rohypnol
Ecstasy

- 3,4-Methylenedioxymethamphetamine (MDMA)
- Was a legal drug until 1986
- Slang names: Ecstasy, XTC, Adam, Lover’s speed
- Structurally similar to amphetamine and hallucinogens and has both stimulant and psychedelic effects
- Contaminants and adulterants are common
  - Methamphetamine, caffeine, ephedrine, cocaine
- Frequently used with other drugs

Ecstasy

- Onset of action: about an hour
- Duration of action: 3-6 hours
- Mechanism: release of serotonin, norepinephrine and dopamine from pre-synaptic neurons
- Effects:
  - Stimulation
  - Sympathetic arousal
  - Sense of well-being and emotional warmth
  - Increased alertness
  - Enhanced enjoyment of tactile experiences
  - Undesirable effects: paranoia, hallucinations, panic reactions, recklessness
Ecstasy

Adverse Effects

- Medical effects: malignant hyperthermia, renal failure, cardiovascular collapse, hyponatremia
- Use in conjunction with Viagra increases risk of medical sequelae
- Causes long-term, perhaps irreversible damage to serotonergic neurons
- Behavioral (withdrawal) effects: depression, confusion, impairment of working memory and attention
Gamma-Hydroxybutyrate (GHB)

- Slang names: GHB, Grievous Bodily Harm, G, Georgia Home Boy, Liquid Ecstasy
- Easily manufactured
- FDA approved for treatment of cataplexy
- Often mixed with alcohol
- “Date rape” drug

Gamma-Hydroxybutyrate (GHB)

- Route of administration: Oral
- Onset of action: 10-20 minutes
- Duration of action: up to 4 hours
- Effects: Sedation/drowsiness, dizziness, amnesia, nausea and vomiting, loss of consciousness, respiratory suppression
- Death reported in Columbus in 2000 due to GHB overdose
Rohypnol (flunitrazepam)

- Slang names; Roofies, Rophies, Roche, Forget-me pill
- Usually imported from Mexico
- Route of administration: usually oral
- “Date rape” drug
- Can impair a victim 8-12 hours
- Causes profound anterograde amnesia
- Effects and side effect profile are the same as any other benzodiazepine

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