Chapter 7

Depressants and Inhalants

Depressants & Inhalants

Depressants = drugs that slow activity in the central nervous system

- Include prescription drugs that treat anxiety (sedatives) and insomnia (hypnotics)
- As a group, **also called sedative-hypnotics**
- **Alcohol** is the most widely used depressant
- **Benzodiazepines** are the most widely prescribed depressants

Inhalants: Volatile solvents and other compounds used for intoxicating purposes

- Have depressant effects similar to sedative-hypnotics

History: **Before Barbiturates**

- **Chloral hydrate** ("knockout drops," "Mickey Finn")
  - Synthesized in 1832; used clinically in 1870
  - Induces sleep in less than an hour
  - Abuse leads to gastric irritation
- **Paraldehyde**
  - Synthesized in 1829; used clinically in 1882
  - Effective with a wide safety margin
  - Noxious taste and odor
- **Bromides**
  - Widely used as a sleep agent in patent medicines; appeared in OTC drugs through the 1960s
  - Can accumulate in the body and cause toxic effects

Barbiturates

- **Discovery/Introduction**
  - 1903: Barbital (Veronal) became the first barbiturate to be used clinically
  - Other popular barbiturates include phenobarbital, amobarbital and secobarbital
- **Grouped on the basis of the time of onset** and duration of activity
  - Low-dose, long-acting forms used for daytime relief of anxiety
  - Higher-dose, shorter-acting forms used to induce sleep

Barbiturates

- **Short-acting** (pentobarbital, secobarbital)
  - Time of onset: 15 minutes
  - Duration of action: 2 to 3 hours
- **Intermediate-acting** (amobarbital, butabarbital)
  - Time of onset: 30 minutes
  - Duration of action: 5 to 6 hours
- **Long-acting** (mephobarbital, phenobarbital)
  - Time of onset: 1 hour
  - Duration of action: 8 hours or longer

Sodium Pentathol

- **Ultra-short acting barbiturate**
- Administered intravenously
- Used as **an anesthetic for brief surgical** procedures
- Moves very rapidly into the brain
- Also used to make people relaxed and talkative (***truth serum***)
- Thiopental is currently the first of the three drugs administered for the **death penalty**

Methaqualone ("ludes" or "sopors")

- 1965: Despite problems in other countries, methaqualone (Quaalude, Sopor) was introduced in the United States
  - No initial monitoring- Package insert read "Addiction potential not established"
  - Overprescribed; quickly became widely misused and abused
  - 1973: Put on Schedule II
  - 1985: Put on Schedule I

Benzodiazepines

- **1960: Introduction of Librium** (chlordiazepoxide), the first commercially marketed benzodiazepine
  - Reduces anxiety without inducing sleep
  - Much larger safety margin than barbiturates
  - Physical dependence rare
  - Overdose rare and usually only when combined with other depressants like alcohol
- **1970s: Valium** (Diazepam), a lower-dose benzodiazepine, became for a time the best seller among all prescription drugs

Benzodiazepines

- **Dependence and overdose can occur**; dosage and time course are critical factors
  - *Overdose deaths* more likely for drugs sold in *higher doses*
  - *Psychological dependence* more likely with drugs that have a *rapid onset of effects*
  - *Physical dependence* more likely with drugs that have a *short duration of action*
- Perhaps there are more differences *among* the barbiturates and *among* the benzodiazepines than there are *between* these two classes of drugs

Benzodiazepines: **Rohypnol**

- Rohypnol – "R2, rib, roofies, rope" – is a 1990s' version of a "Mickey Finn"
- Produces **profound intoxication when mixed with alcohol**
- Reports surfaced of the drug being slipped into drinks and used as a **"date-rape" drug**
  - Changes in laws and in the formulation of the pills should reduce its abuse

Mechanism of Action

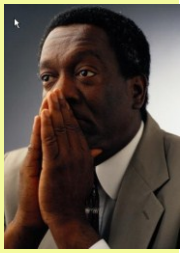
- **Benzodiazepines and barbiturates**
  - Bond with brain receptors
  - Enhance the normally inhibitory effects of GABA
- **Nonbenzodiazepine hypnotics**
  - Selectively target the GABA-A receptor
  - Seem to work better as sleeping pills than as antianxiety drugs
  - Include zolpidem (Ambien), zaleplon (Sonata), and eszopiclone (Lunesta)

Beneficial Uses: Summary

- Anxiolytics
- As sleeping agents
- As anticonvulsants

Beneficial Uses

- **Anxiolytics (anxiety-reducers)**
  - Sedatives often prescribed to reduce anxiety
  - Four benzodiazepines (Xanax, Ativan, Klonopin, Valium) are among the top 100 most commonly prescribed medications in the United States



Beneficial Uses

- Concerns about use of sedatives as anxiolytics:
  - Some anxiety disorders respond to anxiolytics while others seem to be treated more effectively by antidepressants or behavior therapy
  - Patients may take the drugs for long period
  - Anxiolytics may be overprescribed
    - *Is a person taking the drug to treat a disorder or to feel better in a general way?*

Beneficial Uses

- **As sleeping pills**
  - Taking a large enough dose of a hypnotic drug helps a person get to sleep more quickly
  - Insomnia is a common complaint, although people sometimes overestimate its severity
  - Today, fewer hypnotics are prescribed than in the past, and they are usually taken for only a few nights at a time

Beneficial Uses

- Concerns about use as sleeping agents
  - Hypnotics may induce tolerance, dependence, rebound insomnia, and "hangover" effects
  - After 1976, benzodiazepines displaced barbiturates in the sleeping-pill market
    - Safety issues raised that Halcion produces adverse psychiatric reactions in some patients

Beneficial Uses

- Nonbenzodiazepine hypnotics
  - Zolpidem (Ambien) binds selectively to GABA-A receptors
    - Rapid onset and short duration of action
    - Concern about people driving while still under the influence (from not allowing 8 hours of sleep after taking drug)
  - Eszopiclone (Lunesta)
    - Approved for long-term use

Falling Asleep Without Pills

- Have a regular sleep schedule
- When you go to bed, turn out the lights and relax
- Exercise regularly but not late in the evening
- Prepare a comfortable sleep environment in terms of temperature and noise
- Eat a light snack before bed
- Avoid tobacco use
- If you don't fall asleep within 30 minutes, get up and do something relaxing before trying to fall asleep again
- Do not nap during the day
- Avoid chronic use of sleeping pills

Beneficial Uses

- **As anticonvulsants**
  - Barbiturates and benzodiazepines, in low doses or combined with other anticonvulsants, may be prescribed for seizure disorders (epilepsies)
  - Potential problems
    - Tolerance can make it difficult to find a dose that is effective but doesn't cause excessive drowsiness
    - Abrupt withdrawal is likely to cause seizures

Depressants: Causes for Concern

- **Dependence**
  - ***Psychological dependence***—especially associated with short-acting barbiturates
  - ***Physical dependence***—potentially life-threatening withdrawal syndrome linked to large doses of sedative-hypnotics
    - *Barbiturate withdrawal:* anxiety, insomnia, tremulousness, weakness, nausea and vomiting, seizures, disorientation, agitation, delusions, and visual and auditory hallucinations
    - *Benzodiazepine withdrawal* is less severe: anxiety, irritability, or insomnia
    - *Cross-dependence* occurs among the barbiturates, the benzodiazepines, and alcohol

Depressants: Causes for Concern

- **Toxicity**
  - ***Behavioral***
    - Alcohol-like intoxication with impaired judgment and coordination
    - Increased risk of injury while driving or engaging in other activities
    - Additive effects if combined with alcohol
  - ***Physiological***
    - Respiratory depression
    - Especially dangerous if combined with alcohol

Depressants: Causes for Concern

- **Patterns of abuse**
  - Most abuse associated with oral use of legally manufactured products
  - Two types of typical abusers
    - Older adults using prescription drug who develop tolerance and increase their dosage
    - Younger people who obtain drugs to get high; may take high doses and/or mix with alcohol

Inhalants: Introduction

- High-dose exposure causes intoxication, with effects similar to alcohol
- Products that can be abused by inhalation include gasoline, glue, paint, lighter fluid, spray cans, nail polish, correction fluid



Inhalants: Examples

- **Volatile solvents** (petroleum, acetone, toluene)
  - Paint, paint thinner and remover, nail polish remover, correction fluid, glues, cements
- **Aerosols, propellants, gases** (butane, propane)
  - Spray paint, hair spray, lighters, whipped cream
- **Anesthetics** (nitrous oxide, ether)
  - Current and former medical anesthetics
- **Nitrites** (isoamyl, isobutyl)
  - "Locker room," "Rush," "poppers"

Inhalants: Gaseous Anesthetics

- Nitrous oxide ("laughing gas") was first used in the early 1800s
- Still used for light anesthesia, especially by dentists
- Used as a propellant for commercial and home whipping-cream dispensers

Inhalants: Nitrites

- Relaxes blood vessels which increases blood flow, but also lowers blood pressure.
  - Used as a treatment for cyanide poisoning.
  - With high doses there maybe lightheadedness or faintness
- Consumer Product Safety Commission has taken steps to remove poppers and other nitrites from the market since 1988

Inhalants: Volatile Solvents

- Overly informative news articles and education programs actually demonstrated how to abuse volatile solvents
- Abuse tends to occur as localized fads
- Most abusers are very young—solvents are readily available and inexpensive

Inhalants: Dangers

- Kidney damage
- Brain damage
- Peripheral nerve damage
- Irritation of the respiratory tract
- Severe headache
- Death by suffocation

Gamma Hydroxybutyric Acid

- Naturally-occurring chemical found in the brain and body
- Structurally similar to the inhibitory neurotransmitter GABA
- Causes CNS depression, especially when combined with alcohol

Gamma Hydroxybutyric Acid

- Has been used as an anesthetic
- Behavioral effects similar to alcohol
  - Lack of coordination and slurred speech
- Considered a date-rape drug
- Except for a specific formulation used to treat cataplexy, GHB is listed on Schedule I