

1. Depressants



b. History: 1900s (Barbiturates)

i. Discovery/Introduction

- 1903: Barbitol (Veronal) became the first barbiturate to be used clinically
- Other popular barbiturates include phenobarbital, amobarbital and secobarbital

ii. 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

1. Depressants

b. Barbiturates, cont.

iii. Classified by duration of activity

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

1. Depressants

iv. 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**

1. Depressants



c. History: 1960s – Methaqualone (“ludes” or “sopors”)

- i. **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 C.S. Schedule II**
 - **1985: Put on C.S. Schedule I**

1. Depressants

c. History: 1960s-70s – Benzodiazepines

- ii. **1960s: 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
- iii. **1970s: Valium (Diazepam)**, a lower-dose benzodiazepine, became for a time the best seller among all prescription drugs

1. Depressants

c. Benzodiazepines, cont.

iv. **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



1. Depressants

c. Benzodiazepines, cont.



- v. **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

1. Depressants

d. Mechanism of Action

i. Benzodiazepines and barbiturates

- Bond with brain receptors
- **Enhance** the normally inhibitory effects of **GABA**

ii. Nonbenzodiazepine hypnotics

- Selectively target the **GABA-A receptor**
- Seem to work better as sleeping pills than as anti-anxiety drugs
- Include zolpidem (**Ambien**), zaleplon (**Sonata**), and eszopiclone (**Lunesta**)
- **May produce paranoia** and dementia in the elderly

1. Depressants

e. Beneficial Uses

Summary:

- i. **Anxiolytics** (anti-anxiety)
- ii. **Sleeping agents**
- iii. **Anticonvulsants**



1. Depressants

e. Beneficial Uses, cont.

i. Anxiolytics (anxiety-reducers)

1. **Sedatives** often prescribed to reduce anxiety

2. **Four benzodiazepines (Xanax, Ativan, Klonopin, Valium)** are among the top 100 **most commonly prescribed medications** in the United States



1. Depressants

e. Beneficial Uses, cont.

i.3. Concerns about use of sedatives as anxiolytics:

- Some **anxiety disorders respond differently** 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?*

1. Depressants

e. Beneficial Uses, cont.

ii. Sleeping pills

1. Taking a large enough dose of a **hypnotic drug helps a person get to sleep more quickly**

2. **Insomnia** is a common complaint, although people sometimes overestimate its severity



1. Depressants

e. Beneficial Uses, cont.

ii.3. 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



1. Depressants

e. Beneficial Uses, cont.

ii.4. 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

1. Depressants

e. *Beneficial Uses, cont.*

iii. Anticonvulsants

1. **Barbiturates and benzodiazepines**, in low doses or combined with other anticonvulsants, **may be prescribed for seizure disorders (epilepsies)**

2. 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

1. Depressants

f. **Depressants: General Causes for Concern**

i. 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

1. Depressants

f. *Causes for Concern, cont.*

ii. 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



1. Depressants

f. Causes for Concern, cont.

iii. 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



2. Inhalants

a. 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**





2. Inhalants

b. Examples of inhalants

- 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
- Nitrites** (isoamyl, isobutyl)
 - "Locker room," "Rush," "poppers"
- Anesthetics** (nitrous oxide, ether)
 - Current and former medical anesthetics



2. Inhalants

i. Volatile Solvents, cont.

- 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





2. Inhalants

iii. Nitrites, cont.

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



2. Inhalants

iv. Gaseous Anesthetics, cont.

- 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 “Whip-its”



2. Inhalants

c. Dangers

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