Depressants
Sedative Hypnotics

Psychology 470
Introduction to Chemical Addictions
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Alcohol
- Oldest Sedative Hypnotic
- Used thousands of years
- Used mostly for self medication

Used for Many Things
- To relieve stress
- Induce sleep
- Reduce anxiety

General Names
- Downers
- Sedatives
- Hypnotics
- Minor Tranquilizers
- Anxiolytics
- Anti Anxiety Medications

Classes of Compounds Based Historically
- Non-Barbiturates
- Barbiturates
- Antianxiety Medications/Minor Tranquilizers

Non-Barbiturates
- Use began before 1900
- Many compounds
  - Bromides *
  - Chloral Hydrate *
  - Paraaldehyde*
  - Urethane
  - Sulfonal
- Most are not used today
Bromides

- Sodium Bromide
- One of the earliest Sedative Hypnotics
- Behaves like a chloride ion
- Shuts down the action potential
- Is eliminated slowly
- Need to gradually increase the dosage over days (titrate the patient) until the desired effect occurs

Problems

- Lots of side effects
- Takes a long time to administer and eliminate from the system
- Can be toxic
- Can still be used for epileptic seizures and sedation but other drug groups are better
- Not used much today

Chloral Hydrate (Noctec)

- Oldest sleep inducing (hypnotic) depressant
- First synthesized in 1832
- Induces sleep in approximately ½ hour
- Therapeutic Doses
  - Little effect on respiration or BP
  - Toxic Doses
    - Severe respiration depression and low BP
    - Alcohol + Chloral Hydrate = Knockout Drops
    - Mickey Finn
    - Still used today but not as much

Paraldehyde

- Is a polymer of acetaldehyde
- Occasionally used to treat DT’s
- Sleep occurs in about 15 minutes
- Drug is metabolized to acetaldehyde by the liver and eliminated through the lungs – gives an odor.
- Highly toxic to the liver, stomach and kidneys

Barbital

- Is a derivative of Barbituric acid
- Was introduced in 1903
- Became extremely popular
- 1912 Phenobarbital was introduced
- Since then >2500 analogues have been synthesized
- 50 commercially available
- About 20 are still on the market

Barbiturates

- Barbituric Acid is the parent compound of all barbiturates
- Basic structure lacks CNS depressant activities
  - Need other alkyl or methyl groups to get sedative activity
  - How you get all the different types
Based on onset and duration of action:
- Ultra short
- Short
- Intermediate
- Long

**Ultra short**
- Usually used in IV anesthesia
- Onset of action: seconds to about one minute
- Some Drugs:
  - Methohexital (Brevital)
  - Thiamylal (Surital)
  - Thiopental (Pentothal)
  - Propofol (Diprivan)
  - Gamma-Hydroxybutyric Acid (GHB)***
- Not preferred by drug abusers
- Works fast

**Gamma-Hydroxybutyric Acid (GHB)**
- Is a barbiturate
- Called "Natures Quaalude"
- Is primarily used as a general anesthetic
- Used also for:
  - Sleep disorders
  - Alcohol and Opiate Abuse
  - Classic Date Rape Drug
- Is a potent sedative/depressant
- Produces:
  - Disinhibition
  - Excitement
  - Drunken-like behavior (but without alcohol)
  - Amnesia
- Increases dopamine levels in the brain
  - Results in euphoria

**Side Effects**
- Commonly see:
  - Respiratory Depression
  - Seizures
  - Vomiting

**Short**
- Preferred by users
- Onset of action: 20-30 minutes
- Lasts 3-6 hours (usually 4)
- Primarily used for sleep or sedation
Variety of Drugs

- Pentobarbital (Nembutal) Yellows
  - Yellow Jackets
  - Is often used in Veterinary anesthesia
- Secobarbital (Seconal) Reds
  - Used primarily as a sleep medication

Intermediate

- Also preferred by abusers
- Onset of action - 40-60 minutes
- Duration of action - 4-6 hours
- Used primarily for sleep or sedation

Types of Drugs

- Amobarbital (Amytal) Blues
- Aprobarbital (Alurate)
- Butabarbital (Butisol)

Long

- Used for continuous sedation
- Used in epilepsy
- Used for mild anxiety
- Onset of Action 1-2 hours
- Duration of Action 6-12 hours

Types of Drugs

- Phenobarbital (Luminal)
- Mephobarbital (Mebaral)

Mechanism of Action

- Binds on the Picrotoxin binding site of the GABAA receptor
- Result:
  - Decrease excitability of all tissue
  - CNS is more sensitive to Barbiturates
  - RIA system is most sensitive
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Behavioral Effects

- Disinhibition
- Slurred Speech
- Disorientation
- Appears drunk but has no alcohol odor
- Decreased respiration
- Weak, rapid pulse
- Dilated Pupils

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Side Effects of Barbiturates

- Decrease REM sleep
  - Result – Person is not as rested in the morning
- High potential for abuse
- 25% of all suicides (mostly among women)
- Induces other enzymes and thus breaks down other drugs faster.

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High Tolerance

- Rapid down regulation
- During withdrawal
  - Increased stimulation
  - Seizures
  - Delirium
  - Anxiety

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Non Barbiturates

- Chloral Hydrate is technically here too
- Many types
  - Glutethimide (Doriden)
  - Methaqualone (Quaalude, Sopor)
  - Methyprylon (Noludar)
  - Ethchlorvynol (Pladidyl)
  - Valmid

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Effects

- Actions and addiction properties are similar to classic barbiturates
- Act as sedatives or hypnotics
- Side effects are the same as barbiturates
- Overdoses are harder to treat
- Have same behavioral effects
- Luding out (Quaaludes with wine)
- Very dangerous with alcohol

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Behavioral Effects

- Slurred speech
- Disorientation
- Drunken behavior without the odor of alcohol
Antianxiety Medications / Minor Tranquilizers

- Two Different Groups
  - Carbonates
  - Benzodiazepines

Carbonates

- Meprobamate
  - Miltown
  - Equanil

Action

- Works similar to intermediate-acting barbiturates but is less toxic
- Produces less sedation but can be long lasting
- Doesn’t give as great of respiratory suppression as barbiturates

Behavior

- Same as traditional barbiturates
  - Sedation
  - Muscle relaxation
  - Reduces anxiety
  - Can help prevent seizures
  - Mild euphoria

Interesting Points

- Primarily used up until the 1950’s but still occasionally used today.
- Can overdose on 20-30 pills
- When overdosing, causes a ball of pills in the stomach. Requires the stomach to be pumped to ensure all of the drug is out of the stomach.
- Benzodiazepines do a better job and are safer

Benzodiazepines

- Newest class of sedative-hypnotics
- Are one of the most widely prescribed medications
- Are frequently abused
- Like carbonates are used to:
  - Produce sedation
  - Induce sleep
  - Relieve anxiety
  - Muscle relaxation
  - Prevent seizures
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Classification

• Two groups
  • Short-acting
  • Intermediate-acting
  • Long term duration

• Differ based on
  • How fast they take effect
  • Duration of action

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Short Acting

• Rapid onset, short duration
• Used to treat insomnia

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Types

• Midazolam  (Versed)
• Oxazepam  (Serax)
• Temazepam  (Restoril)
• Triazolam  (Halcion)
• Alprazolam  (Xanax)
• Estazolam  (ProSom)
• Quazepam  (Doral)

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Intermediate

• Liozepam  (Ativan)
• Clonazepam  (Klonopin)
• Quazepam  (Dormanin)

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Types

• Alprazolam  (Xanax)
• Chlordiazepoxide  (Librium)
• Diazepam  (Valium)
• Clorazepate  (Tranzene)
• Halazepam  (Paxipam)
• Oxazepam  (Serax)
• Prazepam  (Centrax)
• Flurazepam  (Dormanin)

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Long Term

• Are primarily used to treat general anxiety.
• Can also be used for:
  • Muscle relaxation
  • Adjunct to Anesthesia
Other Uses

- Midazolam (Versed)
  - Injectable Anesthetic
  - Short acting
- Clonazepam (Klonopin)
  - Used for the treatment of seizure disorders
  - Intermediate-Acting

Site of Action for Benzodiazepines

- GABAa Receptor
- Can
  - Completely block
  - Partially Block
  - Most completely block

For Anxiety

- Shut down structures associated with fearful responses
- Amygdala
- Orbitofrontal Cortex
- Insula
- Other structures

For Muscle Relaxation

- Shut down structures in
  - Spinal Cord
  - Cerebellum
  - Brain Stem

Antiepileptic

- Shut down structures in the
  - Cerebellum
  - Hippocampus

Pleasure

- Shut down structures in the
  - Nucleus Acumbens
  - Ventral Tegmentum
Partial Agonists

- Block only particular types of receptors
- Reduces anxiety
- Doesn't give you the high
- Where new research is going

Flunitrazepam (Rohypnol)

- Is technically a Benzodiazepine
- Commercially marketed outside the US
- Is similar to Halcion
- Reduces anxiety
- Causes sedation
- Causes amnesia

Combined with Alcohol

- Acts like Chloral Hydrate
- Acts like GHB
- Also called a date-rape drug

Side Effects

- Similar to Barbiturates
  - Sedation
  - Motor impairments
  - Drowsiness
  - Mental confusion
  - Amnesia (especially when taken with alcohol)
  - Others
  - Generally is dose related

Other Issues

- Can significantly impair cognitive performance (especially memory)
- Decreases academic performance
- Reduces psychomotor functioning
- Effects can occur for long periods after the drugs are discontinued
- Impairments decrease over time (usually)

Differences from Barbiturates

- Not as dangerous
- Can increase the effects of barbiturates
  - Synergistic effects
- Do not usually give as great of sedation
  - Better for daytime use
- Work on different binding sites
- Can be used with alcohol withdrawal
- Don’t see as great of tolerance effects and takes longer too
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In General

- Both Barbiturates and Benzodiazepines tend to slow the system down
- Work on the GABAa receptor (and others as well)
- When used correctly are very effective for what they do.
- Both develop tolerance
- Both have opposite withdrawal effects