



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

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Used for Many Things

- To relieve stress
- Induce sleep
- Reduce anxiety

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General Names

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

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Classes of Compounds Based Historically

- Non-Barbiturates
- Barbiturates
- Antianxiety Medications/Minor Tranquilizers

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Non-Barbiturates

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

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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

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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

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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

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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

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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

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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

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Classified

- Based on onset and duration of action
 - Ultra short
 - Short
 - Intermediate
 - Long

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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 to fast

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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

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Gamma-Hydroxybutyric Acid (GHB)

- Is a potent sedative/depressant
- Produces
 - Disinhibition
 - Excitement
 - Drunken-like behavior (but without alcohol)
 - Amnesia
- Increases dopamine levels in the brain
Results in euphoria

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Side Effects

- Commonly see
 - Respiratory Depression
 - Seizures
 - Vomiting

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Short

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

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Variety of Drugs

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

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Intermediate

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

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Types of Drugs

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

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Long

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

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Types of Drugs

- Phenobarbital (Luminal)
- Mephobarbital (Mebaral)

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Mechanism of Action

- Binds on the Picrotoxin binding site of the GABA_A 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 (Placidyl)
 - 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

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Antianxiety Medications / Minor
Tranquilizers

- Two Different Groups
 - Carbanates
 - Benzodiazepines

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Carbanates

- Meprobamate
 - Miltown
 - Equanil

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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

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Behavior

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

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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

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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

- Lroazepam (Ativan)
- Clonazepam (Klonopin)
- Quazepam (Dormalin)

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Long Term

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

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Types

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

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Other Uses

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

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Site of Action for Benzodiazepines

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

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For Anxiety

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

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For Muscle Relaxation

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

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Antiepileptic

- Shut down structures in the
 - Cerebellum
 - Hippocampus

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Pleasure

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

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Partial Agonists

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

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Flunitrazepam (Rohypnol)

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

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Combined with Alcohol

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

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Side Effects

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

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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)

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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 GABA_A receptor (and others as well)
- When used correctly are very effective for what they do.
- Both develop tolerance
- Both have opposite withdrawal effects