
Barbiturates / Sedative Hypnotic Drugs
 Psychology 472: Pharmacology of Psychoactive Drugs
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Background

- Been around a long time
 - Chloral Hydrate – Used since 1880
 - Paraldehyde – Used before barbiturates
- Barbiturates
 - Primary prescription for anxiety and insomnia from 1912-1960
 - Decreased in popularity
 - Associated with
 - Overdose
 - Dangerous drug interactions
 - Dependence and abuse

Barbiturates

Are medically used for many things

- General anesthesia
- Epilepsy (anticonvulsant)
- To maintain coma in emergency situations (e.g., head trauma)
- Bipolar disorder
- Anxiety
- Sleep

Non-Medical Use

- Decreases anxiety
- Sedation - Can be related to date rape
- Euphoria
- Used to come down from stimulants
- Favorite in Pharming parties

Slang Names

- **Amobarbital**
 - Downers, blue heavens, blue velvet, blue devils
- **Phentobargital**
 - Nembies, yellow jackets, abbots, Mexican yellows
- **Phenobarbital**
 - Purple hearts, goof balls
- **Secobarbital**
 - Reds, red birds, red devils, lilly, F-40s, pinks, pink ladies, seggy
- **Tuinal**
 - Rainbows, reds and blues, tooies, double trouble, gorilla pills, F-66s

Barbiturates

TABLE 5.2 Half-lives and uses of some barbiturates

Trade	Generic	Drug name			Distribution (min)	Elimination (hr)	Uses		
		R ₁ ^a	R ₂ ^a	R ₃ ^a			Insomnia	Anesthesia	Epilepsy
Amytal	Amobarbital	Ethyl	Isopentyl	H	10-40		X		
Alarone	Apoobarbital	Allyl	Isopentyl	H	12-34		X		
Bativel	Butobarbital	Ethyl	sec-Butyl	H	34-42		X		
Mebaryl	Mephobarbital	Ethyl	Phenyl	CH ₃	50-120				X
Brevital	Methohexital	Allyl	1-Methyl,						
			2-Pentynyl	CH ₃	1-2				X
Nembutal	Pentobarbital	Ethyl	Methyl butyl	H	15-50	X			
Luminal	Phenobarbital	Ethyl	Phenyl	H	24-120	X			X
Seconal	Secobarbital	Allyl	Methyl butyl	H	15-40	X			
Lotunate	Talbutal	Allyl	sec-Butyl	H			X		
Surital	Thiamylal	Allyl	Methyl butyl	H					X
Pentothal	Thiopental	Ethyl	Methyl butyl	H	3	3-6			X

^a Symbols R₁, R₂, and R₃ refer to chemical substitution at these positions on the barbiturate nucleus shown in Figure 5.1.



Can be categorized many ways

Duration of Action

- Ultrashort acting (e.g., thiopental)
 - Extremely lipid soluble
 - Crosses the blood-brain barrier rapidly
 - Causes sleep within seconds when used intravenously.
- Longer acting (e.g., amobarbital)
 - More water soluble, slower to penetrate CNS.

Pharmacokinetics

- Half life - 3 minutes to 120 hours
- Impacts can be within seconds to 20-30 minutes
- Metabolized by the liver

Pentobarbital

- Used for short-term insomnia treatment
- Also used as an emergency treatment for seizures
- Presurgical sleep aid

Phenobarbital

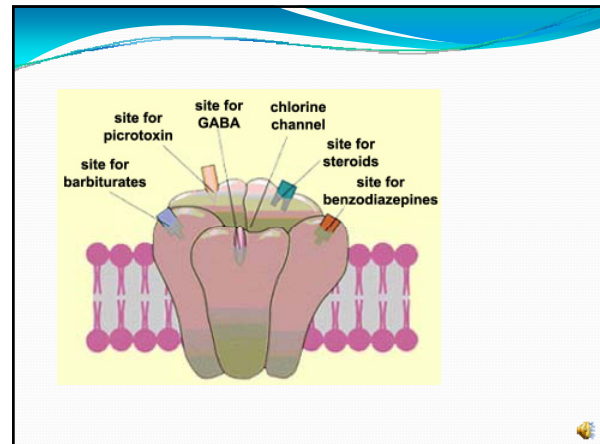
- Primarily used to treat or prevent seizures.
- Also used short-term to treat insomnia
- Sleep aid before surgery

Secobarbital

- Is used to short-term to treat insomnia
- Sleep aid sedative before surgery.

Tuinal

- Combination of secobarbital sodium and amobarbital in equal proportions.
 - Toonerville trolley, or "tooners"
- High risk of overdose
- Use has decreased



GABA_A Receptor

- Barbiturates bind on the Barbiturate binding site
- Causes Cl channels to open independently of GABA
- Causes other stimulatory PSE to shut down
- No signal in the stimulatory neuron

Pharmacologic Effects

- Are not analgesic
 - Do not reliably produce sedation or sleep in presence of pain
 - Will wake up
 - Need an opiate in surgery to help you

Sleep

- Decreases REM sleep
 - Dreaming is suppressed - restlessness
 - Become restless during continued use.
 - Sometimes not good before surgery
 - High doses –
 - Hallucinations
 - Disorientation
 - Convulsions
 - Get vivid and excessive dreaming during withdrawal.

Cognitive inhibition

- Result
 - Sedation
 - Memory impairment
 - Shutting down Hippocampal formation
 - Alterations in judgment and cognitive functioning.
 - Shutting down Prefrontal Cortex
 - Produce Alzheimer-like amnesia

Behavioral Effects

- Reduces inhibitions
 - Decreases motor coordination
 - Get cognitive inhibitions
- Higher doses
 - General depression
 - Sleep.
- Still higher
 - Respiratory depression
 - Death

DRINKING ALCOHOL AND TAKING BARBITURATES EQUALS DEATH



Alcohol and Barbiturates

- Combination
- Very dangerous
 - Used by users to get a better high
 - Get both accidental and intentional suicides.
 - Often used in HIV deaths

Problems

- Narrow therapeutic window TR and SF are low
 - Therapeutic Ratio = $\frac{\text{Toxic Dose } 50}{\text{Effective Dose } 50}$
 - Certain Safety Factor = $\frac{\text{Lethal Dose } 1}{\text{Effective Dose } 99}$
- Often lethal in overdose
 - Can result in coma's
 - High potential for abuse and dependence
 - Makes you feel relaxed and mellow
- Drug interactions
 - Very dangerous in combination with other drugs
 - Especially BZs and alcohol (including OTCS)

Pharmacodynamics

- Down regulation of receptors
 - Need more of the drug to get the same effect
- Liver metabolic enzymes increases
 - Faster metabolic rate
- Risk of both physical and psychological dependence.

Effects in Pregnancy

- Freely crosses placental barrier, as do all psychoactive drugs.
- Limited data, possibility of developmental abnormalities.
- Women taking drug as antiepileptic should examine the risks and take smallest effective dose.

Nonbarbiturate Sedative-Hypnotic Drugs

- Structurally resemble barbiturates
- Introduced in 1950s as anxiolytics, sedatives, and hypnotics.
- Now considered medically obsolete
- Occasionally encountered as drugs of abuse.

Meprobamate

- Miltown, Equanil, Meprospan
- Primarily used in medicine as an anxiolytic
- Was used to treat mental patients
 - Made them calmer and restored logical thinking
- Also used to treat alcoholics
- Was the best-selling minor tranquilizer for a time
 - Replaced by the benzodiazepines

Characteristics

- Is less sedating than traditional barbiturates but had similar symptoms
- Binds on GABA_A receptors
- Has impacts in the reticular formation
 - Causes sedation
 - Reduces pain
- Creates tolerance
- Not used as much today in medicine

Paraldehyde

- Polymer of Acetaldehyde;
- Has a distinct odor
- Produces sleep for up to 12 hrs.
 - Has minimal muscle, heart, or respiratory depression.
- Used to treat DTs of alcohol withdrawal
 - Usually when having delirium tremens
- Also used to calm psychiatric patients
- Also used as a preservative, preparing leather.
 - Acetaldehyde with a small amount of sulfuric acid.

Chloral hydrate (Noctec)

- Classic "Date rape" drug, "Mickey Finn"
 - Soluble in both water and alcohol
 - Makes you unconscious
 - No amnesic properties
- Past use as Bedtime sedative for elderly
- Metabolized like alcohol
- Tolerance like other Barbiturates

Methaqualone (Quaalude)

- Ludes, Lude, Panty Droppers
- Used in late 1970s and early 1980s,
- Was a top selling sedative hypnotic
- Rivalled alcohol and marijuana in popularity for abuse.
- "Date rape" drug; dose for anterograde amnesia lower than for incapacitation.

Barbiturate Anesthetics

- Ultrashort-acting barbiturates
 - Thiopental (Pentothal), methohexital (Brevital)
 - Propofol (Diprivan), etomidate (Amidate)
- Structurally resemble GABA.
- Have little analgesic or euphoriant activity.
- Onset is immediate.
 - Produce unconsciousness for surgery.
- Administered through inhalation or injection.

Ketamine

- Induces unconsciousness and amnesia.
- Also induces analgesia and psychedelic hallucinations.
 - Makes it unique for barbiturates
 - Often a drug of abuse
- Does not reduce blood pressure
 - Important for critically ill surgery patients.
 - Unlike other anesthetics

Pharmacokinetics

- Liquid form
- Absorbed quickly
- Peak in 30–75 minutes.
- Elimination half-life 30–60 minutes.

Adverse Effects

- Toxicity due to GABA_B potentiation.
- Overdose → stupor, delirium, unconsciousness, coma, death
- Nonfatal OD = coma 1–2 hours
- Acute withdrawal symptoms in dependent person.
 - Insomnia, anxiety, tremors

Conclusions

- Are a older class of drugs
 - Been replaced by other safer drugs for most things
 - Are still effectively used in surgery
- Still are abused by users
- Have major issues with effective/lethal doses
- Get lots of overdoses when combined with other drugs
 - Can kill you when consumed with alcohol