Differences Between Benzodiazepines (BZD) and Barbiturates

1. Mechanism of Action

- **BZD**:

Bind to benzodiazepine receptors on the GABA_A chloride channel → increase the **frequency of chloride** channel opening → require the presence of GABA.

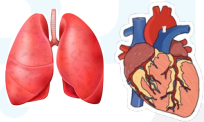
- **Barbiturates**:

Bind to a barbiturate receptor on the GABA_A complex → **increase the duration** of chloride channel opening; at high doses can act as **GABA-mimetics.**

They also **block Na^+ channels and inhibit NMDA receptors.**

2. CNS Depression

- **BZD**: Produce dose-dependent CNS depression but have a **wider therapeutic index and safer profile.**
- **Barbiturates**: Cause steeper **dose-response CNS depression,** ranging from sedation → anesthesia → coma → **fatal respiratory depression.**

3. Effect on Respiration & Cardiovascular System 

- **BZD**: Minimal respiratory depression at therapeutic doses; effects increase with IV use or with other depressants.
- **Barbiturates**: Strong **respiratory depression** and **cardiovascular collapse** at high or toxic doses.

4. Effect on Sleep

- **BZD**:

Decrease sleep latency; **least reduction of REM sleep** among hypnotics; decrease slow-wave sleep (stages 3 & 4).

- **Barbiturates**:

Strong suppression of REM sleep and can cause significant sleep architecture disruption.

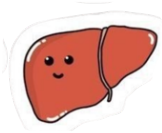
5. Tolerance & Dependence ⚠️

- **BZD**:

Tolerance mainly due to down-regulation of receptors; dependence occurs but **less than barbiturates.**

- **Barbiturates**:

High risk of **tolerance**, **dependence**, and **addiction**; tolerance partially due to increased drug metabolism.

6. Enzyme Induction 

- **BZD**:

Do not induce liver microsomal enzymes.

- **Barbiturates**:

Strong inducers of P450 enzymes → many drug interactions; also increase porphyrin synthesis (contraindicated in porphyria).

7. Safety & Overdose Management 

- **BZD**:

Overdose causes CNS depression but is usually less fatal; **flumazenil** works as a specific antagonist.

- **Barbiturates**:

Overdose is **life-threatening;** no specific antagonist; management includes airway support, urinary alkalinization, and possibly hemodialysis.

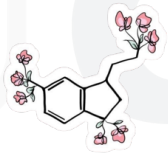
8. Therapeutic Uses

- **BZD**:

First-line for anxiety, insomnia, status epilepticus, muscle spasm, pre-anesthetic medication, alcohol withdrawal.

- **Barbiturates**:

Used today mainly for anesthesia induction (thiopental), anticonvulsant therapy (phenobarbital), procedural sedation, neonatal jaundice, and headaches.

9. Pharmacokinetics 

- **BZD**:

Weak bases; highly lipid soluble; many have **active metabolites;** do not significantly alter drug metabolism.

- **Barbiturates**:

Weak acids; redistributive; metabolized by liver; induce enzymes; cross placenta → fetal respiratory depression.

10. Contraindications 

- **BZD**:

Avoid in COPD, asthma, sleep apnea, myasthenia gravis, pregnancy (category D/X), alcohol or opioid abusers.

- **Barbiturates**:

Contraindicated in **porphyria**, severe respiratory disease, and pregnancy due to fetal depression. 

Table: Differences Between Benzodiazepines (BZD) and Barbiturates

Barbiturates	Benzodiazepines (BZD)	Feature
Increase **duration** of Cl^- channel opening; at high doses act as **GABA-mimetics**	Increase **frequency** of Cl^- channel opening; require GABA	**Mechanism of action**
Block **Na^+ channels** & inhibit **NMDA receptors**	—	**Additional actions**
Steep dose-response; can progress to coma & death	Dose-dependent but **safer**; wide therapeutic index	**CNS depression**
Marked respiratory depression; major cause of death in overdose	Mild respiratory depression (↑ with IV or other depressants)	**Respiratory effect**
Hypotension & **cardiovascular collapse** in toxicity	Possible depression at high/toxic doses	**Cardiovascular effect**
Strong REM suppression; disrupts sleep cycle	Least reduction in **REM sleep**; ↓ slow-wave sleep	**Effect on sleep**
High; partly due to ↑ metabolism (enzyme induction)	Due to **down-regulation** of receptors	**Tolerance**
High risk of dependence & addiction	Present but **less** than barbiturates	**Dependence & abuse**
Strong P450 inducers → drug interactions	**Do not** induce liver enzymes	**Enzyme induction**
No specific antidote; supportive treatment	**Flumazenil** (specific antagonist)	**Antidote for overdose**
Anesthesia induction, anticonvulsants (phenobarbital), procedural sedation, neonatal jaundice, headache disorders	Anxiety, insomnia, seizures, muscle relaxation, pre-anesthesia, alcohol withdrawal	**Main uses**
Major ↓ REM	Slight ↓ REM	**Effect on REM**
Porphyria, severe respiratory disease, pregnancy	COPD, asthma, sleep apnea, myasthenia gravis, pregnancy (D/X), alcohol/opioid abusers	**Contraindications**
Weak acids; redistributive; enzyme induction; cross placenta → fetal depression	Weak bases; many with active metabolites; **no enzyme induction**	**Pharmacokinetics**