



BENZODIAZEPINES

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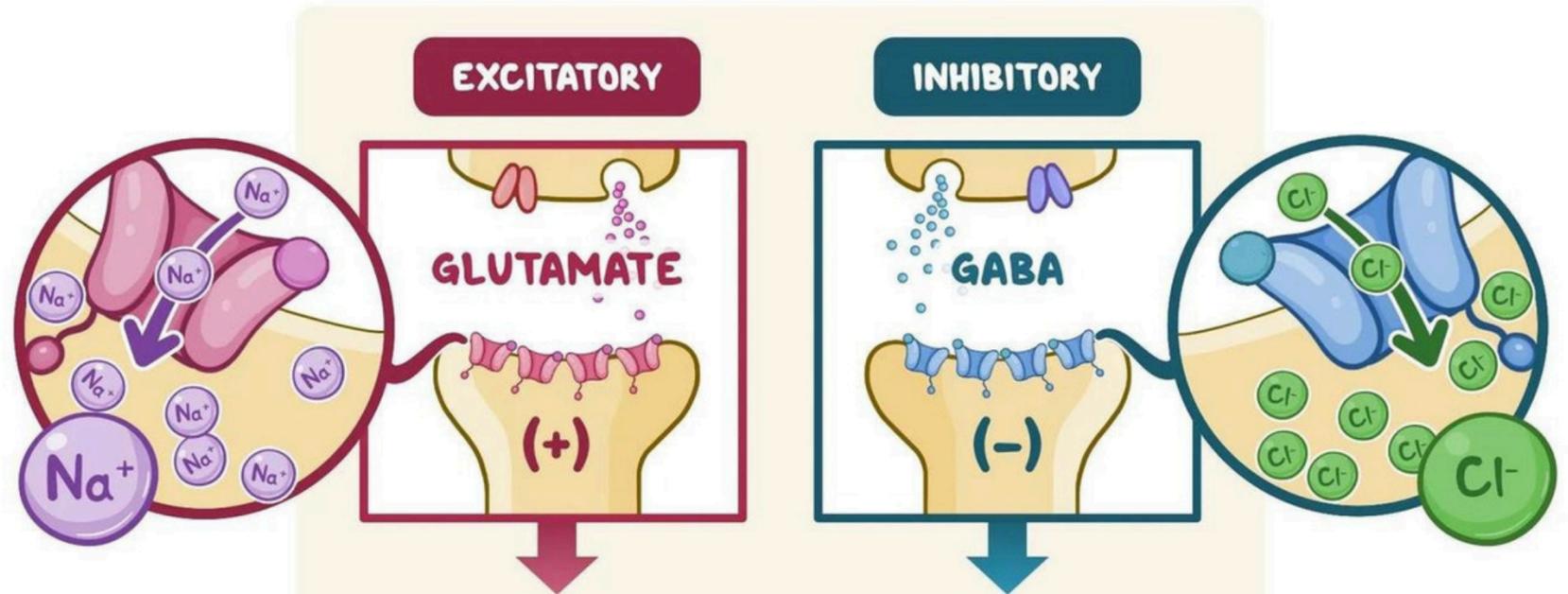
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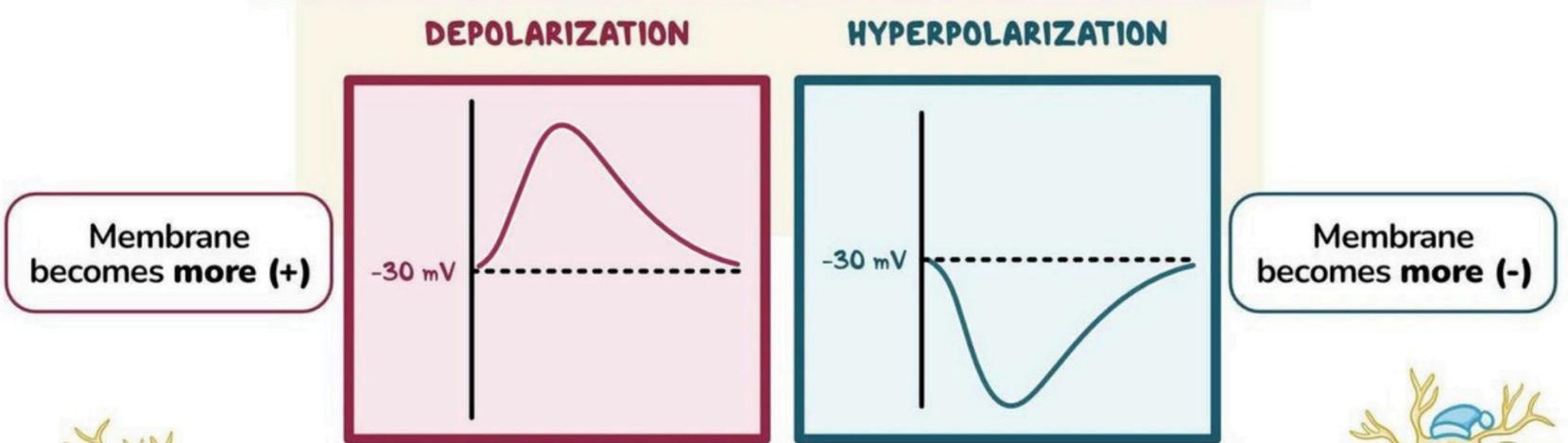
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NEUROTRANSMITTERS

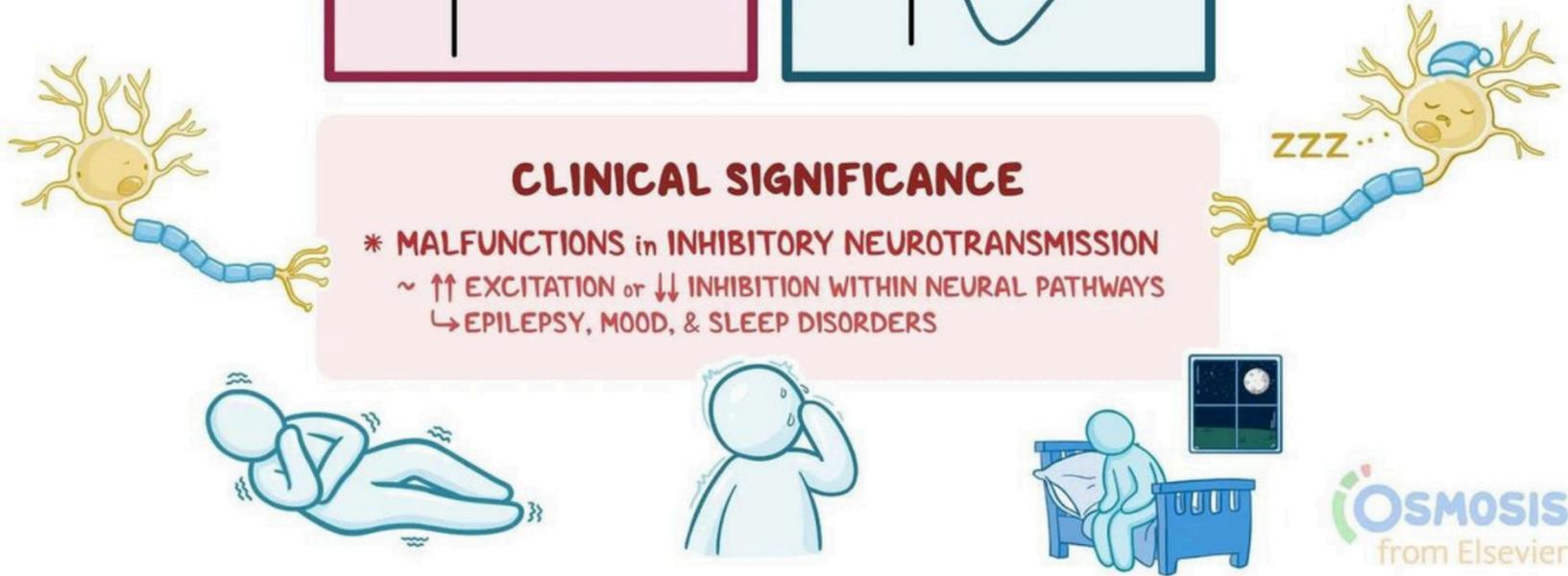


ACTION POTENTIALS



CLINICAL SIGNIFICANCE

* **MALFUNCTIONS** in **INHIBITORY NEUROTRANSMISSION**
~ ↑↑ **EXCITATION** or ↓↓ **INHIBITION** WITHIN NEURAL PATHWAYS
↳ **EPILEPSY, MOOD, & SLEEP DISORDERS**



Excitatory Neurotransmitters:
Glutamate, norepinephrine, dopamine

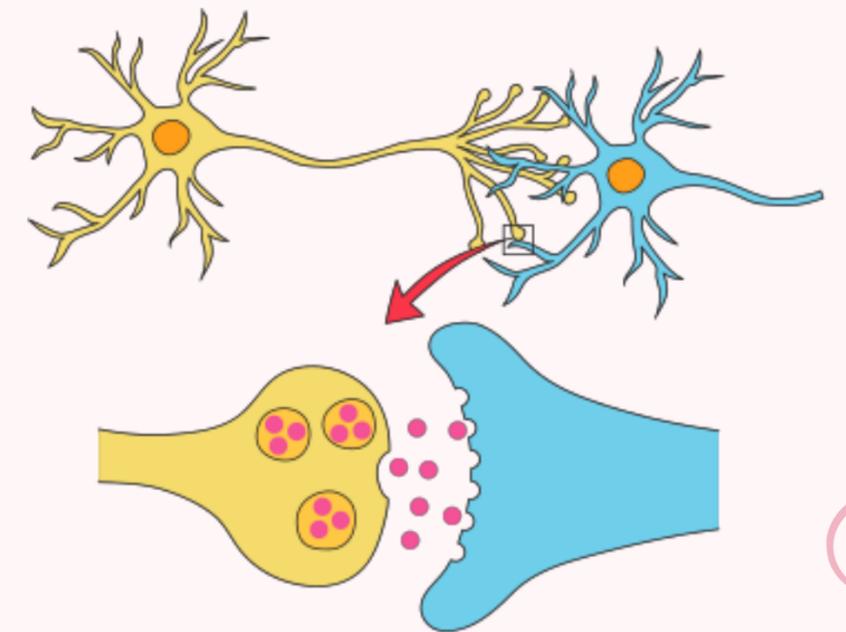
Inhibitory Neurotransmitters:
GABA, serotonin, dopamine

Introduction

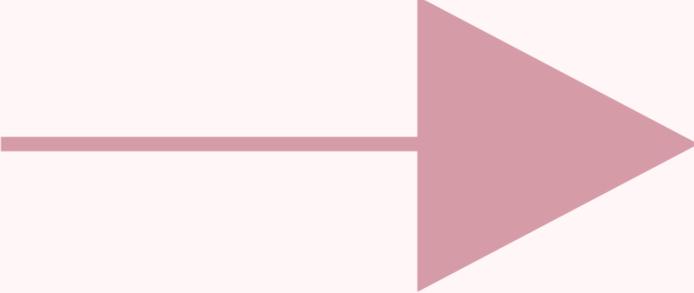
Benzodiazepines are a class of medications that act as a central nervous system depressant.

They have a wide variety of uses including anxiolytic effects, or to relieve anxiety; as anticonvulsants, or to manage seizure disorders; as a hypnotic for insomnia; as an anesthetic; and to treat withdrawal syndromes.

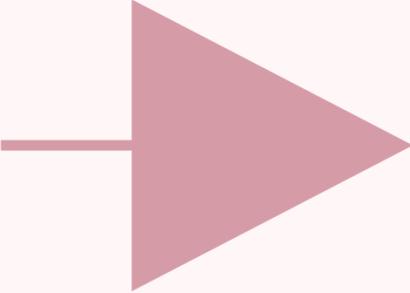
They act by enhancing the main inhibitory neurotransmitter gammaaminobutyric acid, or GABA, by binding to its receptor.



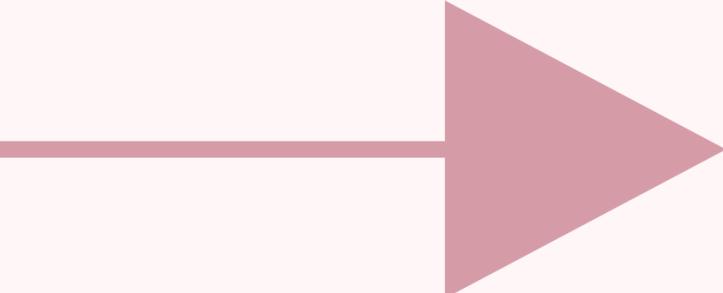
Neurotransmissions



Neurons communicate with each other through neurotransmitters.



When one neuron is stimulated, it'll release excitatory neurotransmitters like glutamate which bind to receptors on the next neuron.



This causes the next neuron to depolarize and release its own excitatory neurotransmitters, propagating the signal throughout the brain.

Now, we also have inhibitory neurons that will shut down this chain of events.

Neurotransmissions

there are cases where neurons in the brain start sending out more excitatory signals than normal.

This can occur due to either too much excitation by the excitatory neurotransmitters, or too little inhibition by the inhibitory neurotransmitters like GABA.

Excessive excitatory signals can cause psychiatric disorders like anxiety, and neurological disorders like seizures and epilepsy.

so one way we can decrease the excitatory signals is by enhancing the effect of inhibitory neurons through medication like **benzodiazepines**.

benzodiazepines

* DECREASE EXCITATORY SIGNALS → ENHANCING THE EFFECT OF INHIBITORY NEURONS

SHORT-ACTING

A ALPRAZolam
T TRIAZOLAM
O OXAZEPAM
M MIDAZOLAM



INTERMEDIATE-ACTING

T TEMAZEPAM
L LORazepam
C Clonazepam



LONG-ACTING

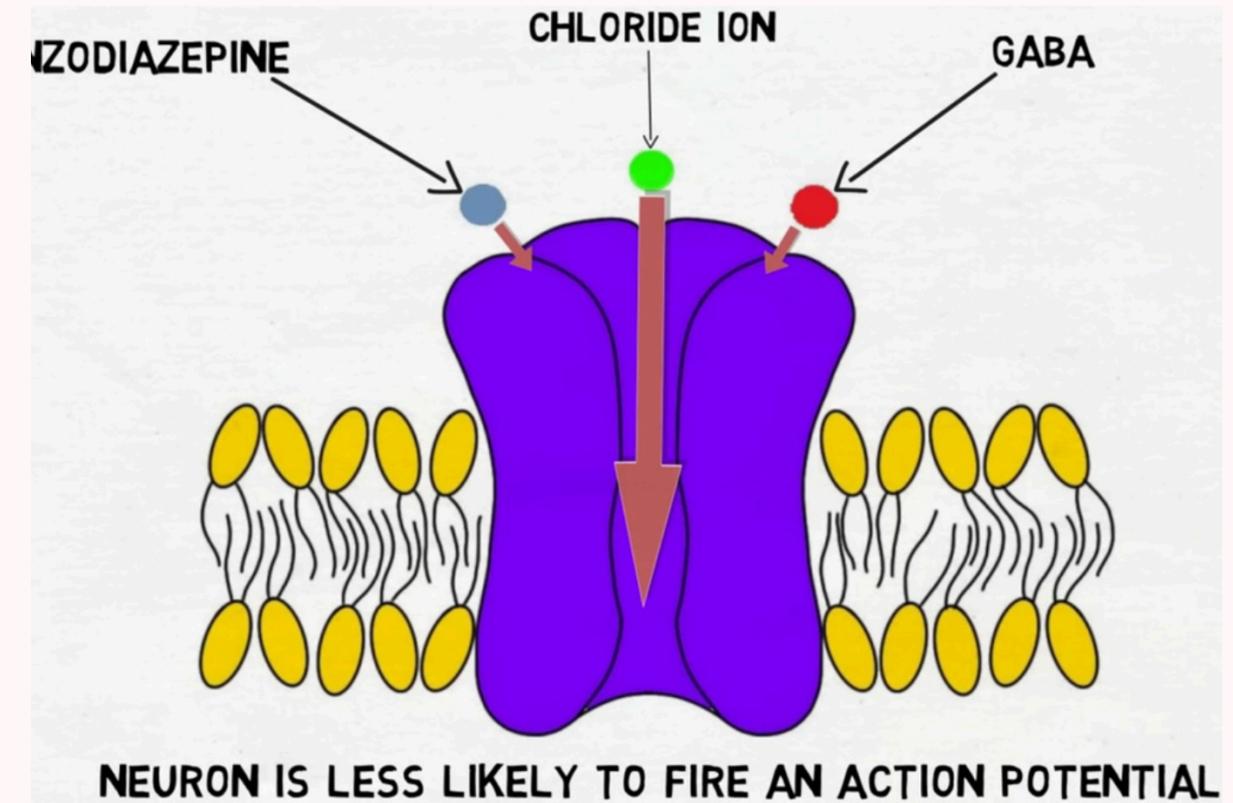
C Chlordiazepoxide
D Diazepam
(e) FLURAZEPAM
F



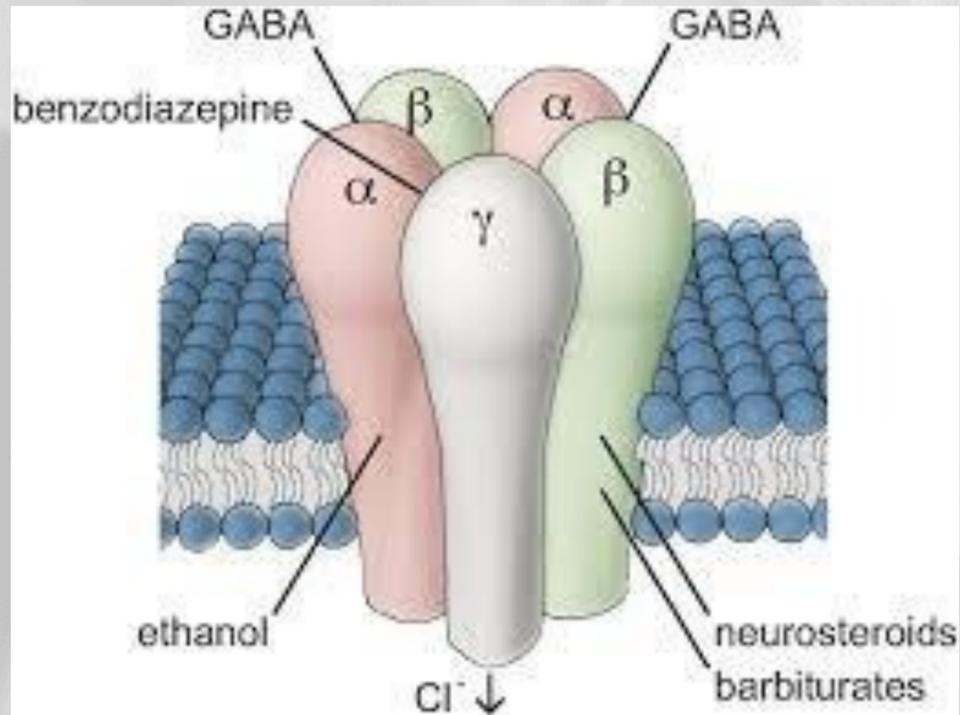
GABA in the brain

- When GABA binds to its receptor (GABA_A), it opens a chloride (Cl⁻) ion channel.
- → Cl⁻ ions flow into the neuron → the inside becomes more negative → hyperpolarization occurs.
- → This makes it harder for the neuron to fire an action potential.
- → Result: inhibition of neural activity

- GABA_A** receptors are pentameric (made of 5 subunits).
- The most common structure: 2α, 2β, and 1γ subunit.
- Benzodiazepines bind at a specific site between the α and γ subunits — different from the GABA binding site.
- → This means benzodiazepines do not directly activate the receptor; they need GABA to be present.
- When benzodiazepines attach to their site, they change the receptor's shape (allosteric modulation).
- This conformational change makes the receptor more responsive to GABA — in other words, GABA's effect is amplified.



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- **Specifically:**
- **→ When GABA binds, the Cl⁻ channel opens more frequently (not for longer).**
- **→ More chloride ions enter → stronger hyperpolarization → stronger inhibition of the neuron.**



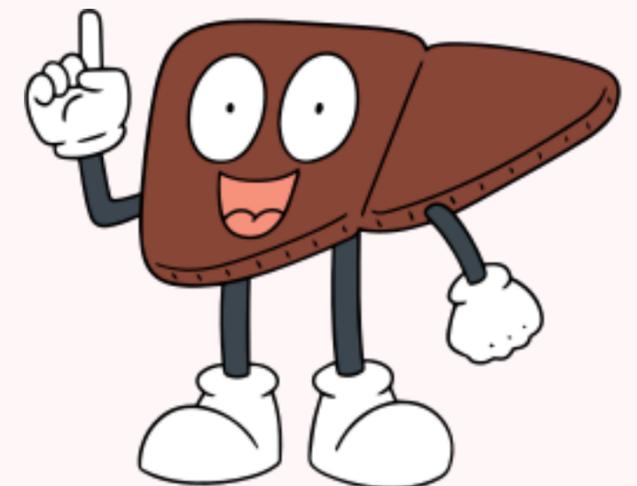
Feature	Benzodiazepines	Barbiturates
Binding site	Between α and γ subunits (benzodiazepine site)	Different site on GABA _A receptor
Effect on GABA action	↑ frequency of Cl ⁻ channel opening (needs GABA present)	↑ duration of Cl ⁻ channel opening (can work even without GABA at high doses)
Safety margin	High (less likely to cause fatal CNS depression alone)	Narrow (can cause respiratory depression and coma)

Metabolism:

Most of these medications are metabolized in the liver by CYP450 enzymes into active metabolites; therefore they should be avoided in individuals with liver impairment.

But, it's important to note that these individuals can use LORazepam, Oxazepam, and Temazepam because they are primarily metabolized by a process known as glucuronidation, This process is not associated with active metabolites and therefore is safe.

- Produces water-soluble inactive compounds that are excreted in urine by



Uses of benzodiazepines



-benzodiazepines are used for pre anesthetic medication



they are an effective treatment for insomnia,



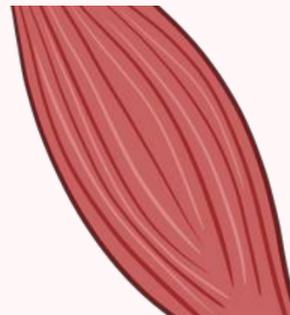
-Benzodiazepines are very effective anticonvulsants and are considered the treatment of choice for status epilepticus.



benzodiazepines are indicated when the neurons get "super excited" and we want to calm them down like in anxiety disorders, or during a panic attack.



-Diazepam can also be used as the second-line treatment for eclampsia, which is a life-threatening complication of pregnancy that is associated with seizures.



- they are sometimes used as muscle relaxants to treat spasms, like those caused by cerebral palsy.



-Since alcohol and barbiturates also work by targeting GABA receptors, benzodiazepines can be used to manage their withdrawal symptoms by decreasing their severity.

High doses uses

- **Status epilepticus (emergency seizures)**
- **Severe alcohol or drug withdrawal**
- **Pre-anesthetic / procedural sedation**
- **Severe agitation / catatonia (psychiatric emergencies)**
- **Severe muscle spasm / spasticity**

Low doses uses

- **Anxiety disorders (generalized anxiety, social anxiety)**
- **Insomnia (mild, short-term)**
- **Mild procedural anxiety or pre-medication**
- **Reduces nervousness before minor procedures**
- **Adjunct for depression or panic disorder**

Drug	Low Dose (typical for anxiety / mild insomnia)	High Dose (used for severe anxiety, seizures, or sedation)
Diazepam	2–5 mg, 1–2 times/day	10–40 mg/day (sometimes higher IV in seizures)
Lorazepam	0.5–1 mg, 1–3 times/day	4–10 mg/day (IV up to 8 mg in status epilepticus)
Clonazepam	0.25–0.5 mg/day	Up to 4 mg/day (seizure control)
Oxazepam	10–15 mg, 1–3 times/day	60–120 mg/day
Temazepam	7.5–15 mg at bedtime	30–45 mg at bedtime
Midazolam	1–2 mg (sedation before procedure)	5–15 mg IV (induction / deep sedation)
Chlordiazepoxide	10–25 mg, 2–4 times/day	50–200 mg/day (withdrawal management)

Side effects :

- Drowsiness
- dizziness
- Memory Impairment: Short-term memory issues, particularly with forming new memories (anterograde amnesia) .
- Muscle weakness: Can lead to a sense of reduced physical coordination.
- Dependence and Withdrawal tolerance:

Benzodiazepines may interact with ethanol, other benzodiazepines, and sedatives such as barbiturates, resulting in increased respiratory depression via a synergistic effect .
should be used with caution in the elderly because they can cause ataxia and precipitate falls.



Overdose

Benzodiazepine overdose is very rarely life-threatening unless associated with the co-ingestion of alcohol, opioids, barbiturates or other respiratory or CNS depressants.

A benzodiazepine overdose can lead to :

- extreme sedation or drowsiness
- confusion and difficulty thinking
- slurred speech
- Hypotonia and hyporeflexia

Ataxia

Respiratory depression (benzodiazepines have a wider margin of safety than barbiturates and, consequently, a lower risk of coma and respiratory depression)

Note :

overdose can be managed with flumazenil, which acts as a competitive antagonist for benzodiazepines, which means that it binds to the same site as benzodiazepine and blocks its action.

Dependence and tolerance:

Tolerance :

When used chronically, their effectiveness decreases, which means that they'll need to increase the dose to get the same effects.

These drugs are habit forming and could lead to **addiction**

Moreover, short-acting benzodiazepines are associated with a higher addiction potential since they have a shorter half life!

Dependence:

Chronic use also leads to dependence, which means, when the medication is discontinued, the person experiences withdrawal symptoms like insomnia, anxiety, and seizures.

This is less likely to happen when compared to barbiturates, making benzodiazepines the preferred choice.

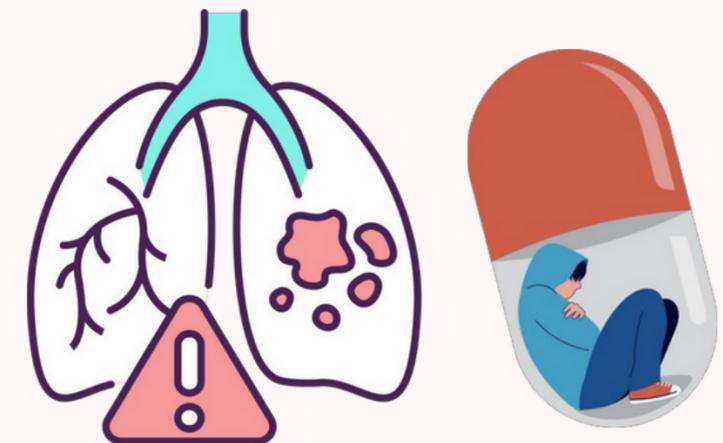
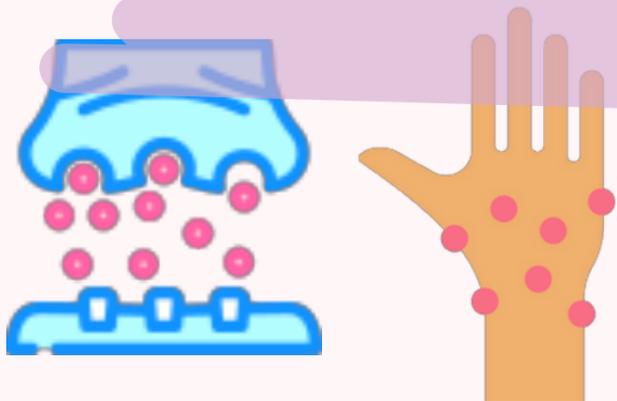
Contraindications for benzodiazepines

- Hypersensitivity to benzodiazepines.
- Neuromuscular diseases (e.g., myasthenia gravis): worsening of myasthenic symptoms.

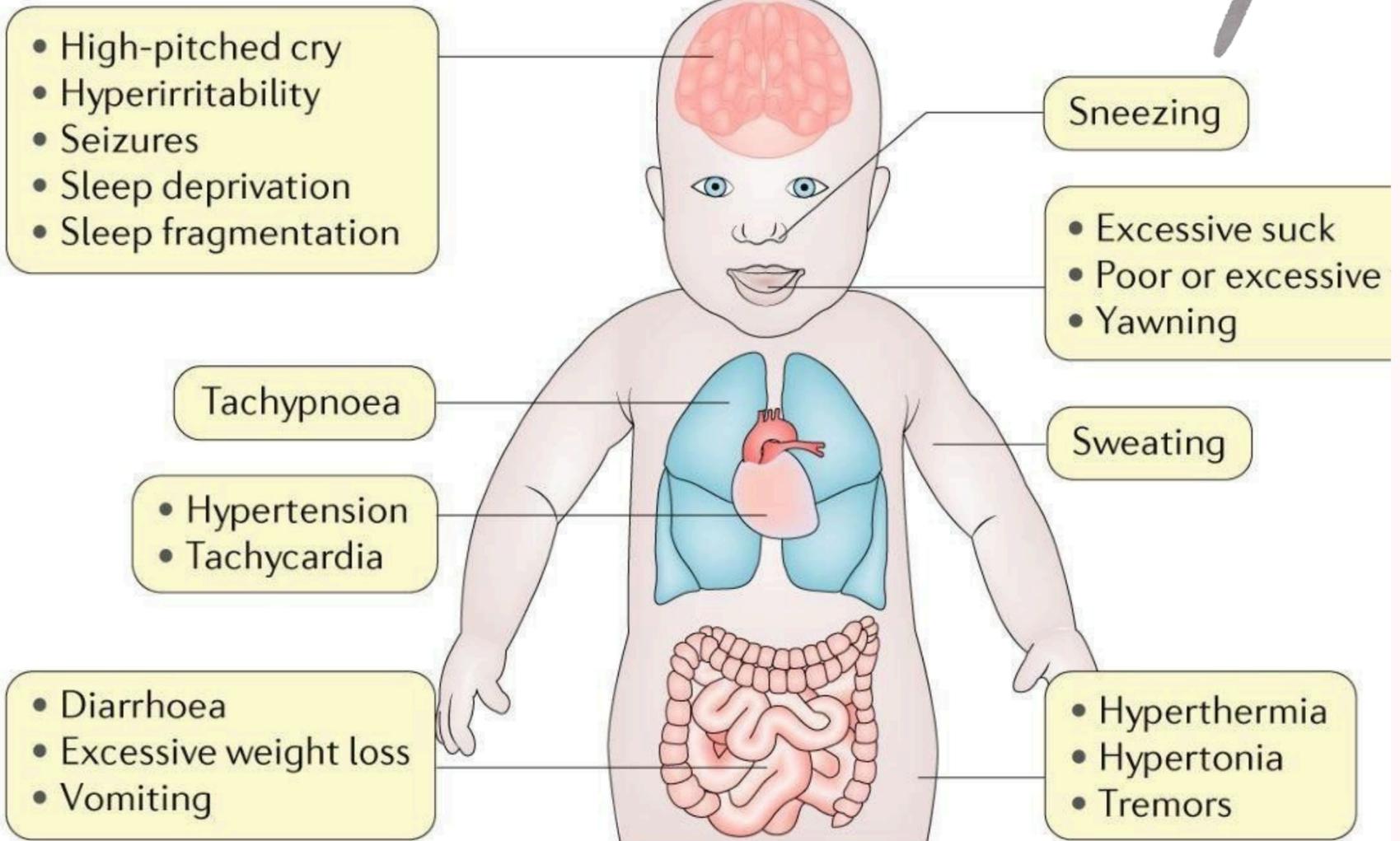
- narrow-angle glaucoma.

- Respiratory depression (COPD , respiratory failure)

- Pregnancy (except for the management of eclampsia following unsuccessful magnesium sulfate therapy): ↑ risk of floppy infant syndrome (hypotonia).



Hypotonia
(decreased
muscle tone)



Here is the information in a tidy table format:



Short acting (half-life: <6 hours)	
Medication	Characteristics
Midazolam (Versed)	<ul style="list-style-type: none"> - Very short half-life - Primarily used in medical and surgical settings

Intermediate acting (half-life: 6–20 hours)	
Medication	Characteristics
Alprazolam (Xanax)	<ul style="list-style-type: none"> - Treatment of anxiety, including panic attacks - Short onset of action leads to euphoria, high abuse potential
Lorazepam (Ativan)	<ul style="list-style-type: none"> - Treatment of panic attacks, alcohol and sedative-hypnotic-anxiolytic detoxification, agitation - Not metabolized by liver - Used with haloperidol in IM formulations to quickly sedate agitated patients
Oxazepam (Serax)	<ul style="list-style-type: none"> - Alcohol and sedative-hypnotic-anxiolytic detoxification - Not metabolized by liver
Temazepam (Restoril)	<ul style="list-style-type: none"> - Because of dependence, rarely used for treatment of insomnia - Not metabolized by liver

Long acting (half-life: >20 hours)	
Medication	Characteristics
Diazepam (Valium)	<ul style="list-style-type: none"> - Rapid onset - Used during detoxification from alcohol or sedative-hypnotic-anxiolytics, and for seizures - Effective for muscle spasm - Less commonly prescribed to treat anxiety because of euphoria
Clonazepam (Klonopin)	<ul style="list-style-type: none"> - Treatment of anxiety, including panic attacks - Avoid with renal dysfunction; longer half-life allows for once or twice daily dosing



A decorative background consisting of numerous overlapping, horizontal brushstrokes in a light purple color, creating a textured, hand-drawn effect.

Thank you