

DRUGS USED FOR ANXIETY AND PANIC DISORDERS

ILOs

Define some types of anxiety disorders

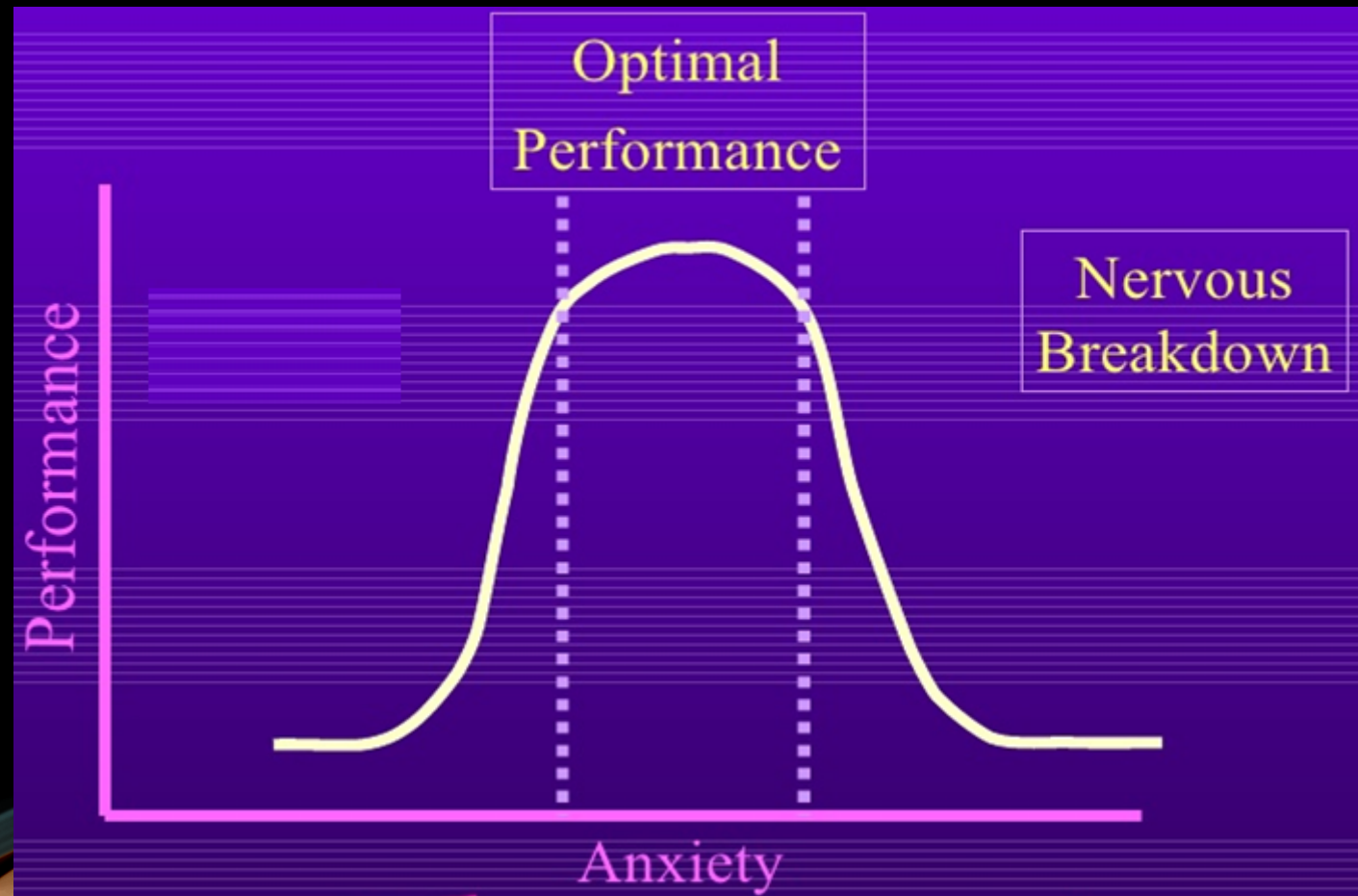
Classify types of drugs used for treatment of anxiety

Discuss the different characteristics of antianxiety drugs



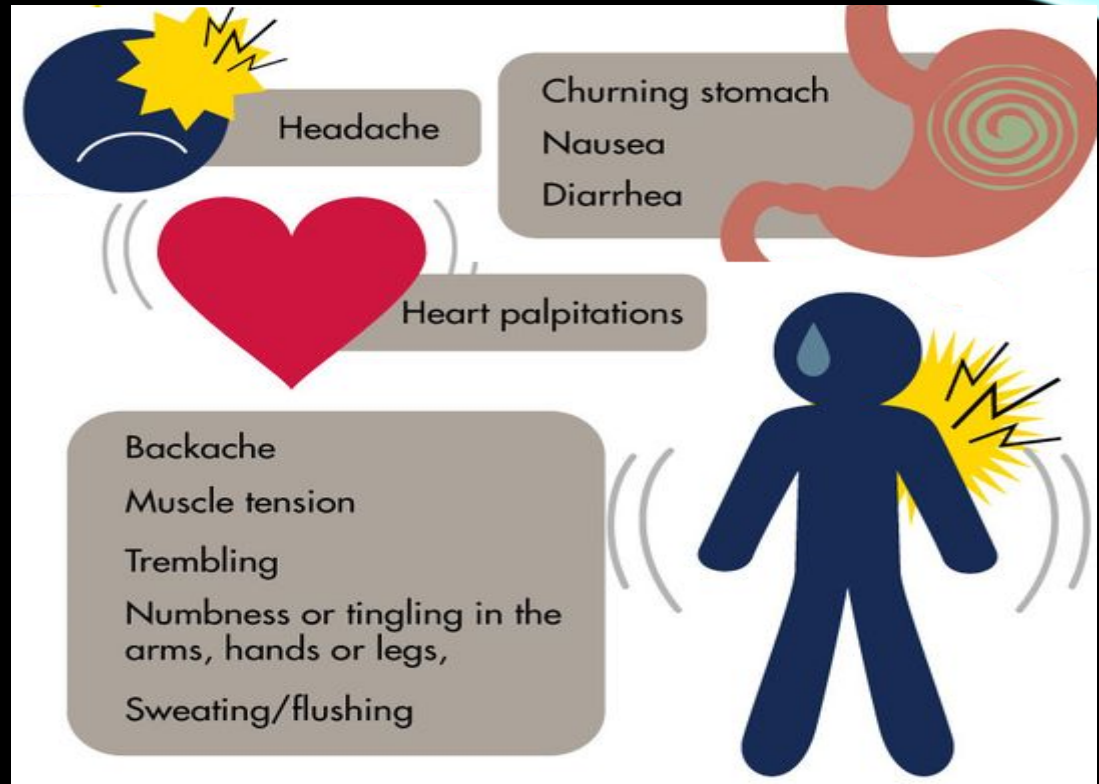
WHAT IS ANXIETY ?

Physical and emotional distress which interferes with normal life.



SYMPTOMS OF ANXIETY

1-Somatic



2- Emotional

Emotional Symptoms

- Feelings of dread
- Difficulty concentrating
- Irritability
- Restlessness
- Pessimism
- Recurring memories



TYPES OF ANXIETY DISORDERS

1- Generalized anxiety disorder

2- Panic disorder

4- Post traumatic stress disorder

3- Phobia

5- Obsessive compulsive disorder



TREATMENT OF ANXIETY

Psychotherapy



Anxiolytics



CLASSIFICATION OF ANXIOLYTIC DRUGS:

1-Benzodiazepines (BDZ).

2-5HT_{1A} agonists.

3-Beta-adrenergic blockers

4-5HT reuptake inhibitors

5-Tricyclic Antidepressants

6-MAO inhibitors

7-Pregabalin



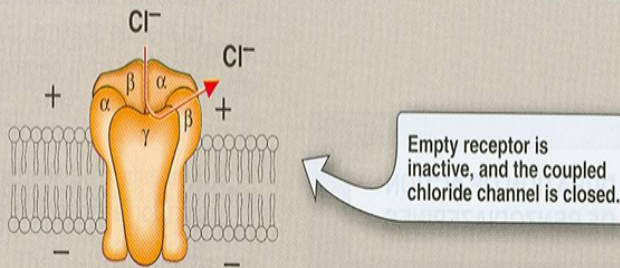
1-Benzodiazepines (BDZ).

MECHANISM OF ACTION

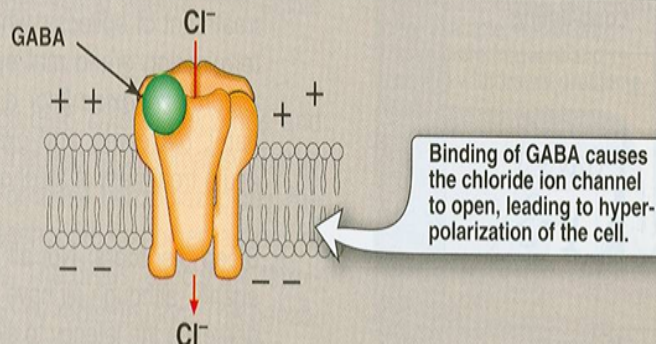
Benzodiazepines act by binding to BZ receptors in the brain → enhance GABA action in the brain



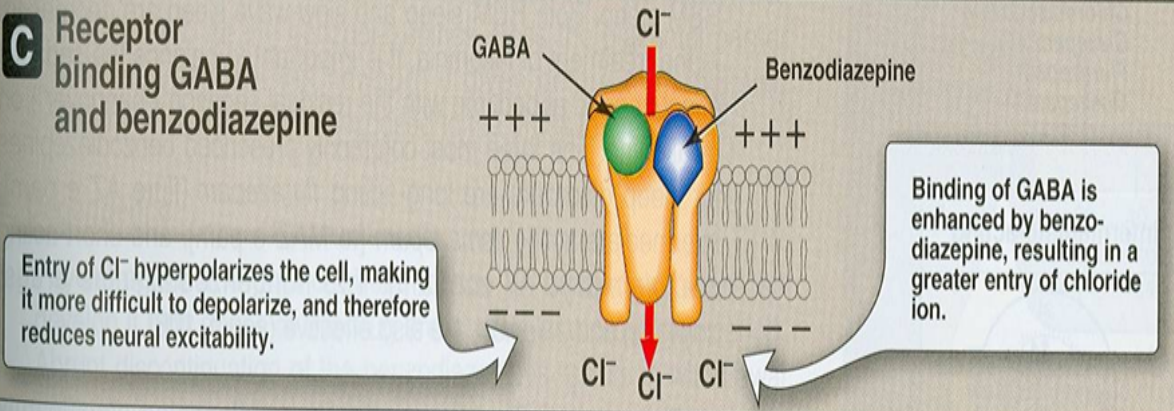
A Receptor empty (no agonists)



B Receptor binding GABA



C Receptor binding GABA and benzodiazepine



PHARMACOKINETICS

Lipid soluble

Well absorbed orally,

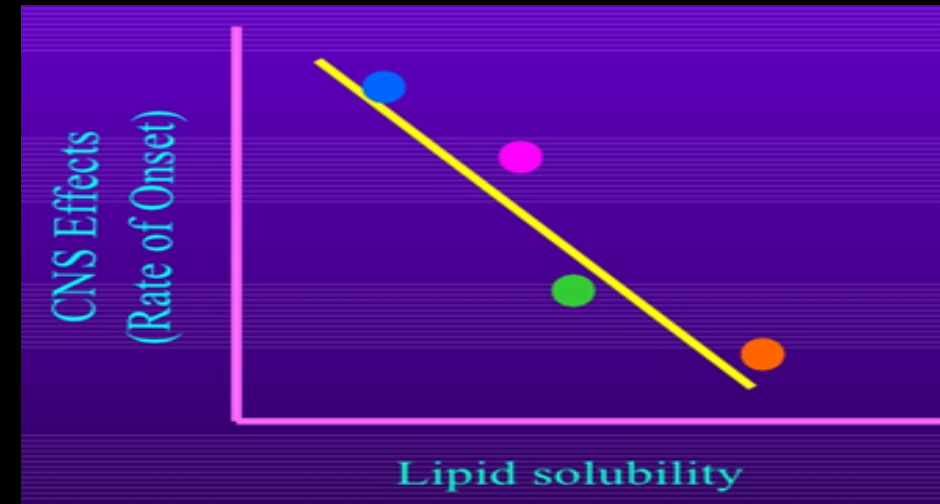
Can be given parenterally

Chlordiazepoxide- Diazepam (IV only NOT IM)

Widely distributed

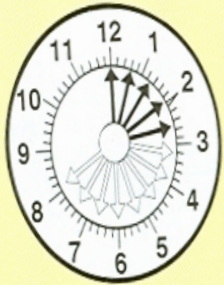
Excreted in milk (neonatal depression).

Cross placental barrier (Fetal depression)



Can be classified according to the duration of action into short, medium & long- acting

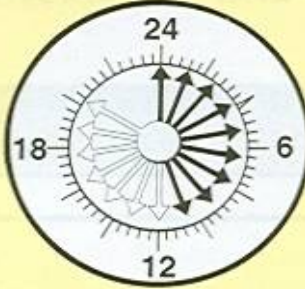
Short-acting



3-8 Hours

Oxazepam
Triazolam

Intermediate-acting



10-20 Hours

Alprazolam
Estazolam
Lorazepam
Temazepam

Long-acting



Clorazepate
Chlordiazepoxide
Diazepam
Flurazepam
Quazepam

PHARMACOLOGICAL ACTIONS

Anxiolytic action.

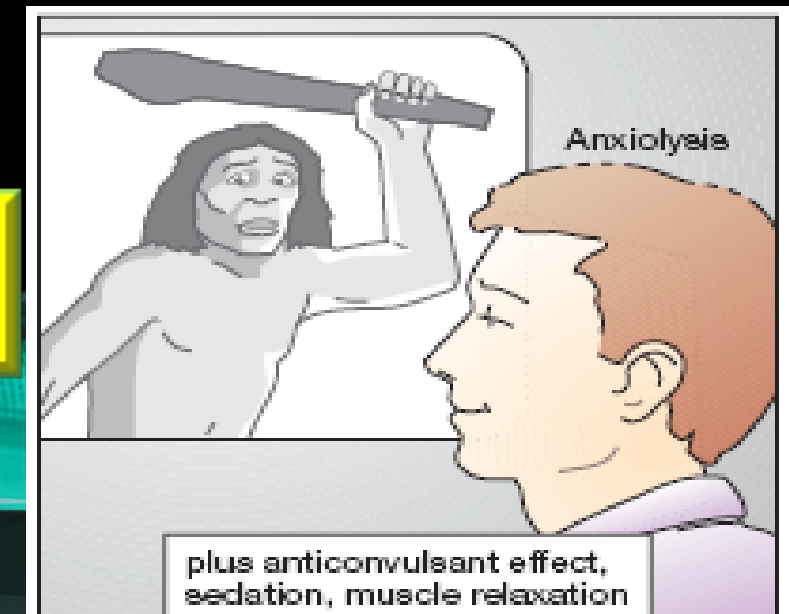
Depression of cognitive and psychomotor function

Sedative & hypnotic actions

Anterograde amnesia

Minimal depressant effects on cardiovascular system & respiratory system

Some have anticonvulsant effect:
Clonazepam, diazepam.



THERAPEUTIC USES

Anxiety disorders:

Short term relief of severe anxiety

General anxiety disorder

Obsessive compulsive disorder

Panic attack with depression →

Alprazolam (antidepressant effect)



Sleep disorders (Insomnia).

Triazolam, Lorazepam, Flurazepam

Treatment of epilepsy

Diazepam – Lorazepam



THERAPEUTIC USES

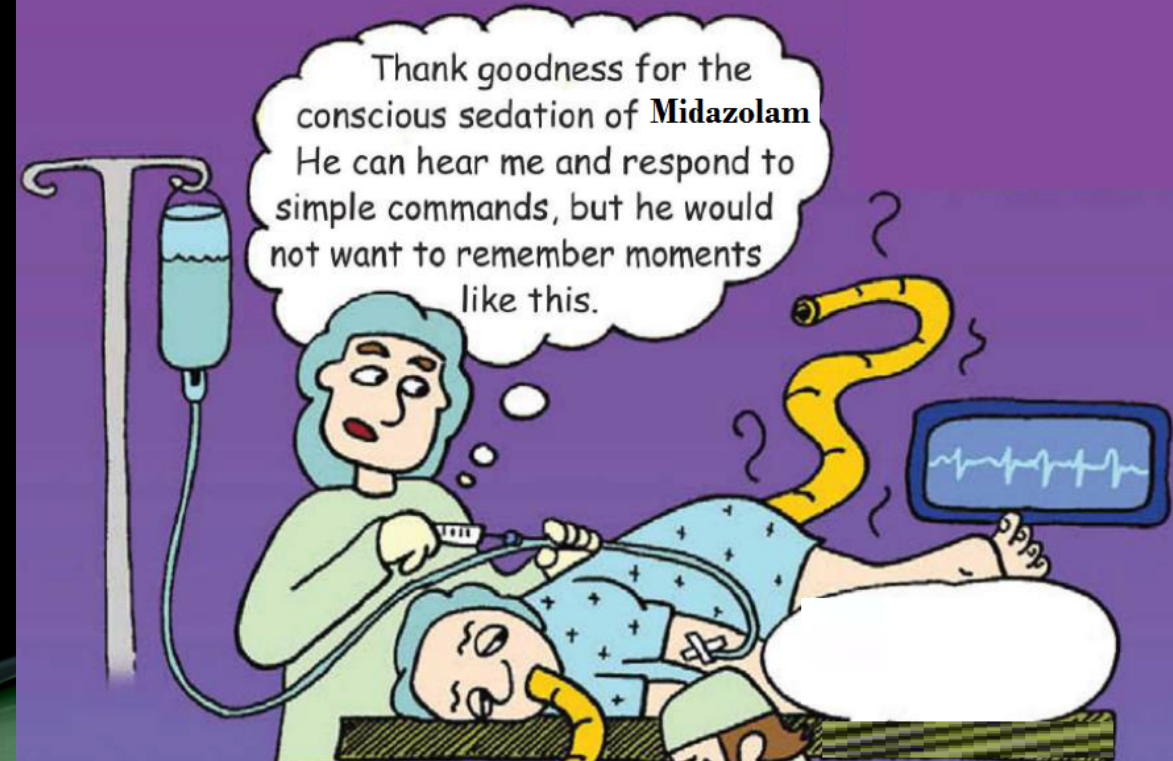
In anesthesia

- Preanesthetic medication (diazepam).

Induction of anesthesia (Midazolam, IV)

MIDAZOLAM

Moments Not Remembered



ADVERSE EFFECTS

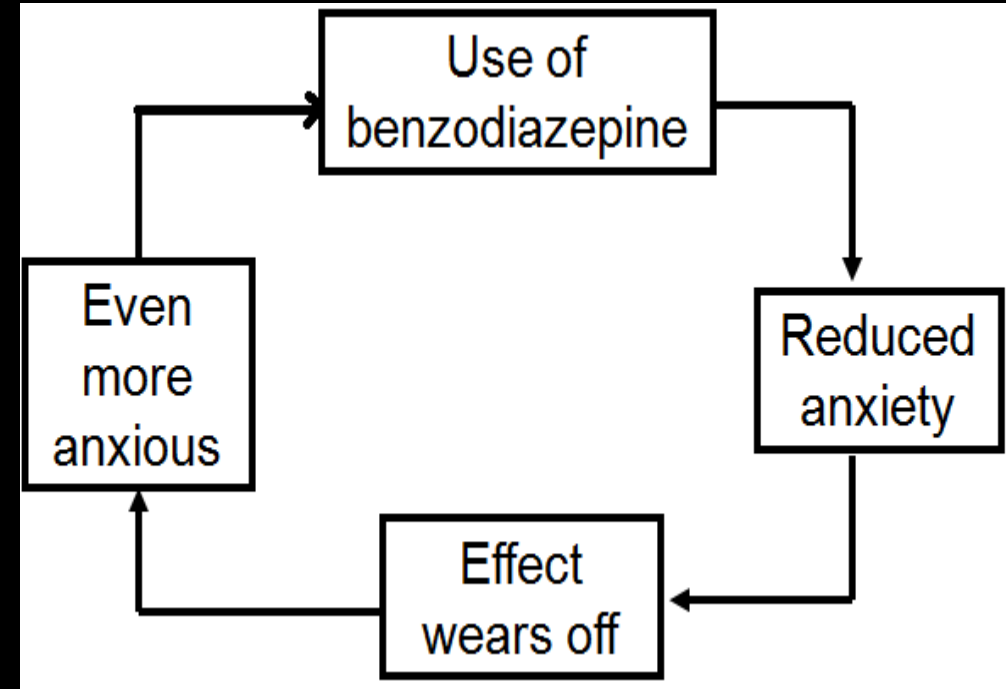
- Ataxia (motor incoordination)

Cognitive impairment

- Hangover: (drowsiness, confusion)

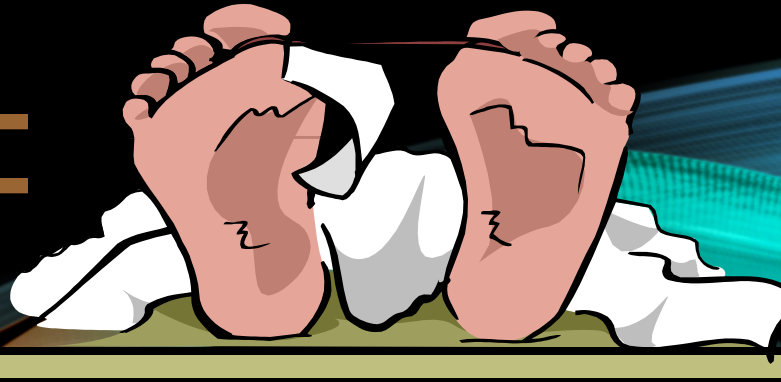
Tolerance & dependence

- Risk of withdrawal symptoms (Rebound insomnia, anorexia, anxiety, agitation, tremors and convulsion)



ADVERSE EFFECTS

Toxic effects: respiratory
cardiovascular depression in large doses.



DRUG -DRUG INTERACTIONS

	Examples
CNS depressants	Alcohol & Antihistaminics ↑ effect of benzodiazepines
Cytochrome P450 inhibitors	Cimetidine & Erythromycin ↑ $t_{1/2}$ of benzodiazepines
CYT P450 inducers	Phenytoin & Rifampicin ↓ $t_{1/2}$ of benzodiazepines



BENZODIAZEPINE ANTAGONIST

FLUMAZENIL

Binds competitively to GABA receptors displacing benzodiazepine

Has a short plasma half life → repeated dosing

Used in benzodiazepine overdose

Precipitates withdrawal symptoms in benzodiazepine addicts

Henry ignored his benzodiazepine's warning to avoid operating dangerous machinery while using it and loses his right foot.



5HT_{1A} AGONISTS

Buspirone

Acts as a partial agonist at brain 5HT_{1A} receptors, presynaptically inhibiting 5HT release

Adaptive changes after chronic treatment, reduction in 5HT₂ receptors in cortex

Weak dopamine D₂ action, but not antipsychotic



5HT_{1A} AGONISTS

Buspirone

Rapidly absorbed orally.

$t_{1/2}$: (2 – 4 h).

Undergoes extensive hepatic metabolism, some of the metabolites are active

Liver dysfunction → ↓ its clearance



PHARMACODYNAMIC EFFECTS

Only anxiolytic

No hypnotic effect.

Not muscle relaxant.

Not anticonvulsant

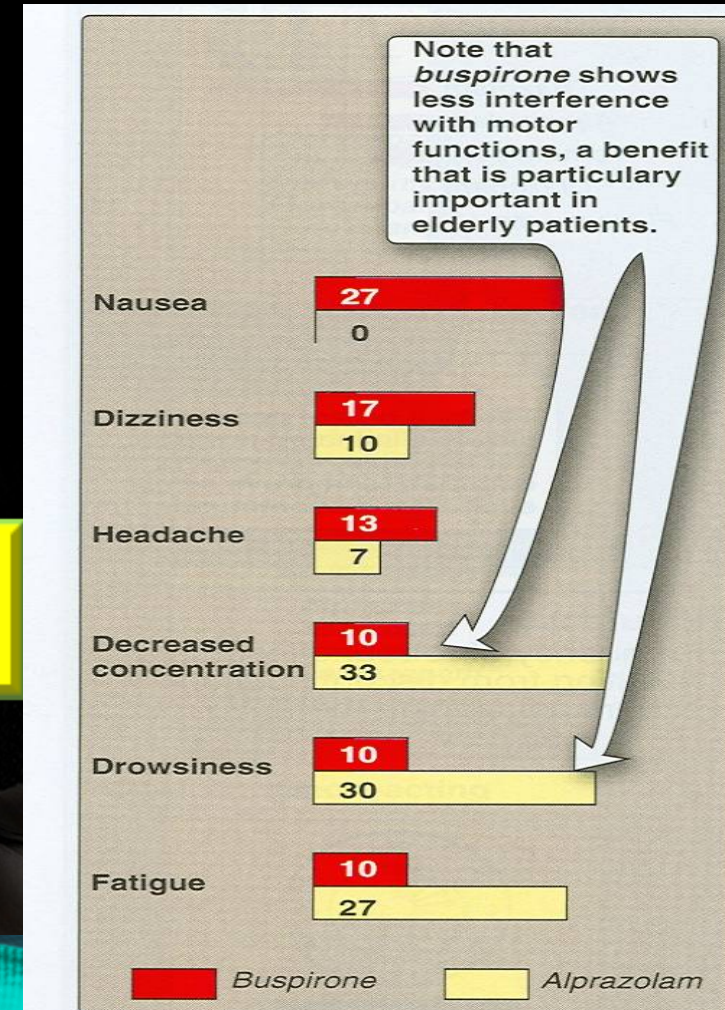
No withdrawal signs

No potentiation of
Other CNS depressants

Minimal psychomotor &
Cognitive dysfunctions.

Does not affect
driving skills

Minimal risk of dependence



CLINICAL USES

As anxiolytic in mild anxiety & generalized anxiety disorders.



DISADVANTAGES OF BUSPIRONE

Slow onset of action (delayed effect)

Not effective in severe anxiety/panic disorder

GIT upset, dizziness, drowsiness

Drug Interactions with CYT P450 inducers and inhibitors



**Inhibitors of CYP450 3A4 , verapamil,
diltiazem → ↑ buspirone level**

Rifampin cause 10 fold ↓ buspirone level

**Increase blood pressure in people
taking MAOi**

DOSE SHOULD BE REDUCED IN

- **Liver disease**
- **Old people**

Precautions

- Should be used with precaution in pregnant women or breast-feeding.
- People over 65.



BETA BLOCKERS

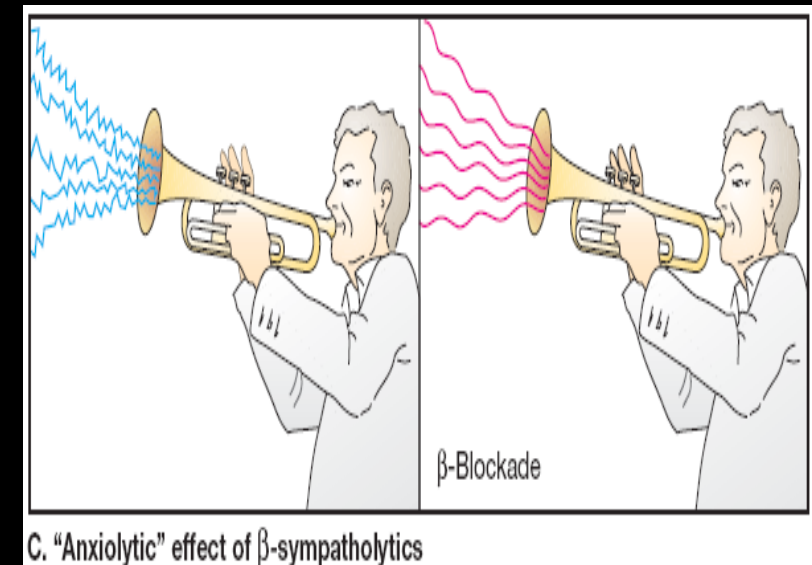
Act by blocking peripheral sympathetic system.

Reduce somatic symptoms of anxiety.

Decrease BP & slow HR.

Used in performance anxiety.

Are less effective for other forms of anxiety



TRICYCLIC ANTIDEPRESSANTS

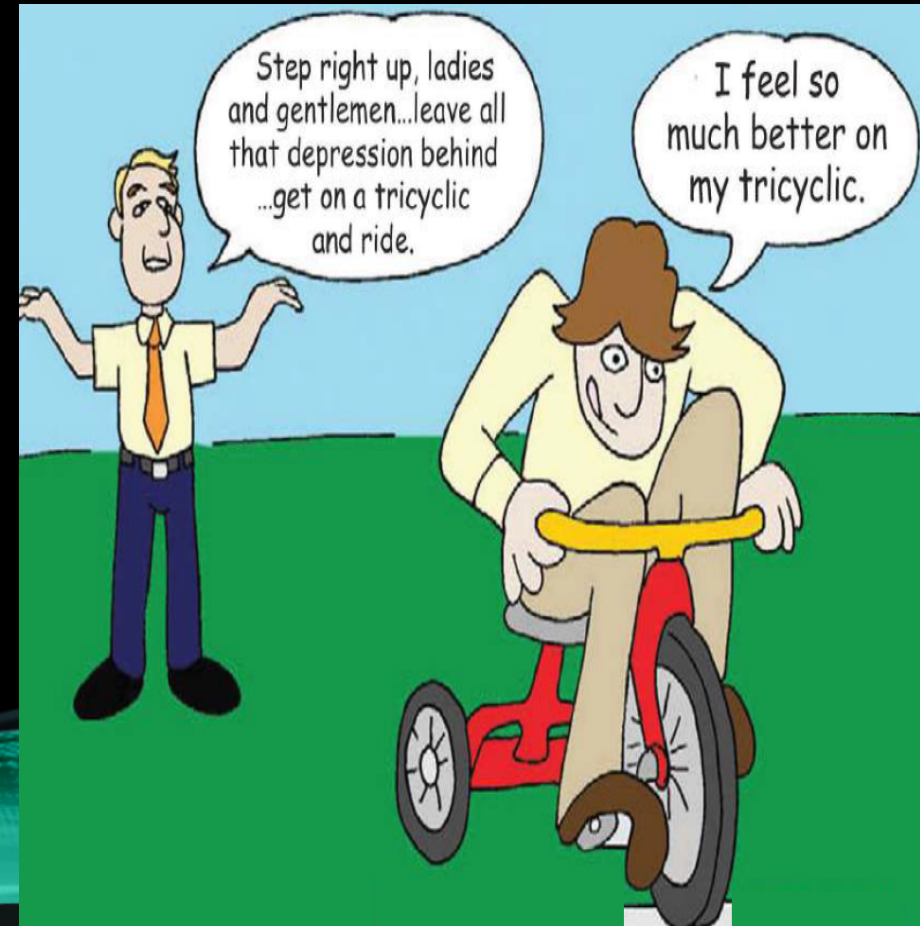
Doxepin- imipramine – desipramine

Act by reducing uptake of 5HT & NA.

Used for anxiety especially associated with depression.

Effective for panic attacks.

Delayed onset of action (weeks).



ADRS

Atropine like actions (dry mouth-blurred vision).

α -blocking activity (Postural hypotension).

Sexual dysfunction

Weight gain

Because of the high frequency of ADRS compared to SSRIs, SSRIs should be tried first



MONOAMINE OXIDASE INHIBITORS (MAOIS)

Phenelzine

Acts by blocking the action of MAO enzymes.

Used for panic attacks and phobia.

Require dietary restriction

Avoid wine, beer, fermented foods and old cheese that contain tyramine.

ADRs:- Dry mouth, constipation, diarrhea, restlessness, dizziness.

Reserved for patients who have not responded to, or proved intolerant of, other treatments

- Sweating
- Tremors
- Elevated temperature
- Bounding heart
- ↑ BP

No...

- Barbiturates
- Tricyclic antidepressants
- Antihistamines
- Central nervous system depressants
- Antihypertensives
- Over-the-counter cold medications

No...

- Cheese
- Wine
- Preserved meats



SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIS)

Fluoxetine

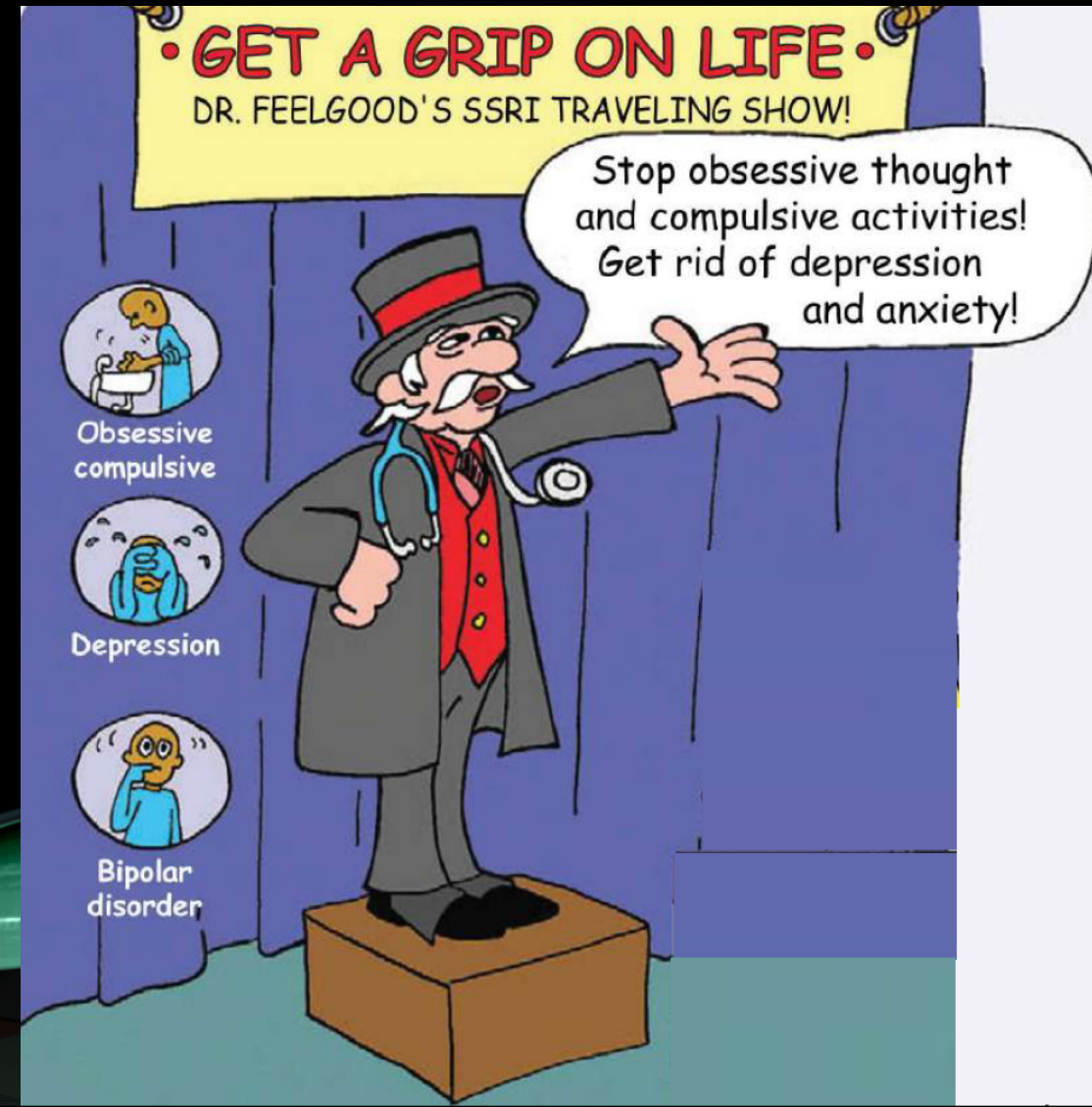
Acts by blocking uptake of 5HT

Orally

Delayed onset of action (weeks).

Long half life

Used for panic disorder – OCD -
Generalized anxiety disorders -
phobia.



ADRS

Increase in anxiety symptoms, insomnia or headache in the first days or weeks of treatment may ↓ compliance

Nausea, diarrhea

Weight gain

Sexual dysfunction

Dry mouth

Seizures

Sleep disturbance



PREGABALIN

Modulates calcium channels in CNS, \downarrow Ca⁺⁺ influx & modulates release of neurotransmitters

Onset occurs in the first days of treatment

Excreted unchanged in the urine,

Effective in treatment & prevention of relapse of GAD (1st line as SSRIS)

ADRs:-dizziness and somnolence

Withdrawal symptoms may occur but less severe than benzodiazepines

Used in epilepsy & neuropathic pain



Case

A 22-year-old woman is brought in the emergency department via ambulance because of a suicide attempt. Soon after a “night on the town,” she called her boyfriend saying that she took a handful of sleeping tablets. On examination, she appears lethargic, but groans and moves all her extremities to painful stimuli. Her blood pressure is 110/70 mm Hg, heart rate is 80 bp/m, and oxygen saturation is 99 percent. Her pupils are of normal size and reactive to light. Her deep tendon reflexes are normal bilaterally. In the field, she was given an intravenous bolus of dextrose and an ampoule of naloxone without response. Her boyfriend, with whom she had an argument, brings in the bottle of sleeping medication which reads “lorazepam.”



Case

Q1

What is the danger of an overdose with this class of medication?



Case

Q2

What is the cellular mechanism of action of this class of medication?



Case

Q3

What pharmacologic agent can be used to treat this patient, and what is its mechanism of action?



The image features a motivational quote centered on a blurred background of flowers. The quote is written in a white, serif font. The background shows a large yellow flower in the center, with pink and purple flowers to the left and right. The overall tone is soft and inspirational.

Don't stress
Do your best
Forget the rest