PHARMACOLOGY-I

UNIT 4 NOTES

DRUGS ACTING ON CNS

- NEUROHUMORAL TRANSMISSION IN CNS
- GABA, GLYCINE, SEROTONIN, DOPAMINE
- GENERAL ANAESTHETICS
- PRE ANAESTHETICS
- SEDATIVE & HYPNOTICS
- CENTRALLY ACTING MUSCLE RELAXANTS
- ANTIEPILEPTICS
- ALCOHOL & DISULFIRAM

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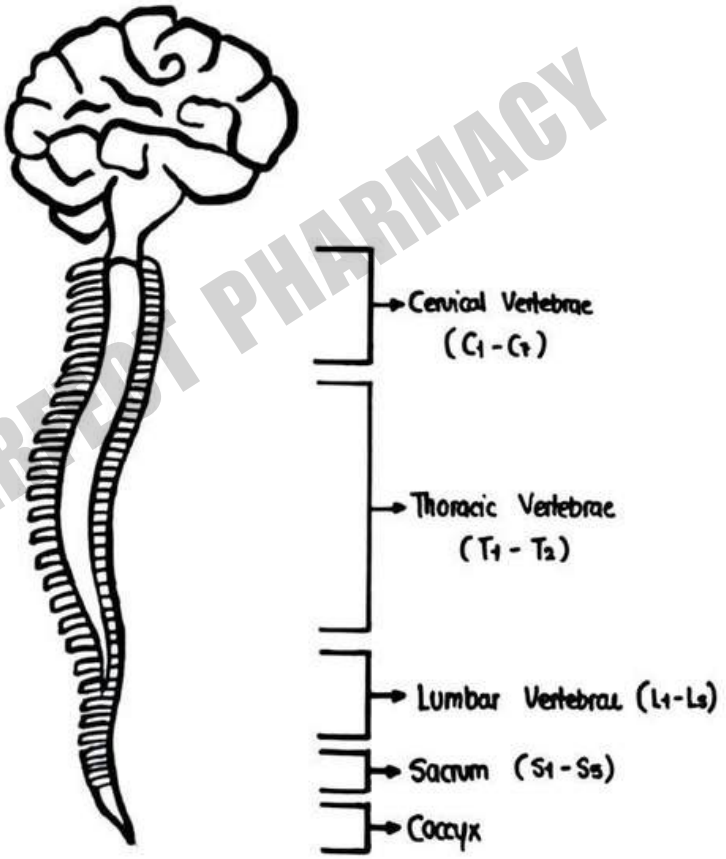
CNS

- The central nervous system is the part of the nervous system that consist of the brain & spinal cord.
- It acts as the central center of body, responsible for processing and co-ordinating sensory data, & motor the commands.



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MAIN FUNCTIONS

- Recieves sensory input from body (via peripheral nervous system)
- Process & interprets this information.
- Sends out motor responses to muscle & glands.
- Controls higher functions such as thought, memory, emotion & conciousness.

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NEUROHUMORAL TRANSMISSION

Neurohumoral transmission refers to the process by which neurons communicate with other (nervous) neurons or effector cells in the CNS, using chemical messengers (neurotransmitters) released at synapses.

STEPS OF NEUROHUMORAL TRANSMISSION

① Synthesis of Neurotransmitters

- Neurotransmitters (NTs) are synthesized in the neuron's cell body or axon terminal.
- Enzymes & Precursors are used for synthesis (eg tyrosine → Dopamine).

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② Storage

- NTs are stored in synaptic vesicles in the axon terminal until a signal arrives.

③ Arrival of Action Potential

- An electrical signal (action potential) travels along the axon to the axon terminal.

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④ Opening of Ca^{2+} channels

- Depolarization of the terminal opens voltage-gated Ca^{2+} channels.
- Ca^{2+} enters the terminal → triggers vesicle fusion with the membrane.

⑤ Release of Neurotransmitters

- NTs are released via exocytosis into the synaptic cleft.

⑥ Binding to receptors

- NTs binds to specific receptors on the post-synaptic membrane.
- Receptor types:
  - Ionotropic receptors → Fast response
  - Metabotropic receptors (G-protein coupled) → slower, modulatory.

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⑦ Post-Synaptic Response

Now this binding leads to extracellular response which can be either:

- Excitatory Post-synaptic Potential (EPSP)
- Inhibitory Post-synaptic Potential (IPSP)

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Classification Of Neurotransmitters

- Neurotransmitters are chemical messengers that transmit signals across a synapse from one neuron to another.
- They can be broadly classified as :
  - Inhibitory – Suppress the generation of an action potential.
  - Excitatory – Promotes the generation of an action potential.

- Some neurotransmitters may have dual roles depending on the type of receptors they bind to.

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① Inhibitory Neurotransmitters

- These neurotransmitters reduce the likelihood of the firing of an action potential.
- They usually cause hyperpolarization of the post-synaptic membrane.

ⓐ GABA (Gama – Aminobutyric Acid) :

Type : Major inhibitory neurotransmitter in the CNS.
Action : Opens Cl^- channels, causing hyperpolarization.
Function : Promotes relaxation, reduces neuronal exitability, involved in sleep and muscle tone.

ⓑ Glycine :

Type : Inhibitory neurotransmitter mainly in the spinal cord and brainsteam.
Action : Open Cl^- channels.
Function : Inhibits motor neurons; involved in reflexes and motor control.

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② Excitatory Inhibitors

- These neurotransmitters increase the likelihood of the firing of an action potential.
- They usually cause depolarization of the post-synaptic membrane.

ⓐ Glutamate:

Type: Major excitatory neurotransmitter in the CNS.
Action: Open Na^+ and Ca^{2+} channel.
Function: Involved in learning, memory, and cognition.

ⓑ Dopamine (Mainly excitatory, but can also be inhibitory depending on receptor type):

Type: Monoamine neurotransmitter.
Action: Acts on D_1 (excitatory) & D_2 (inhibitory) receptors.
Function: Mood regulation, reward, motivation, motor control
(Parkinson's disease is related to its deficiency.)

ⓒ Serotonin (5-HT):

Type: Mostly excitatory; some inhibitory effects depending on receptor subtype.
Action: Acts on various 5-HT receptors.
Function: Regulates mood, appetite, sleep and pain perception.

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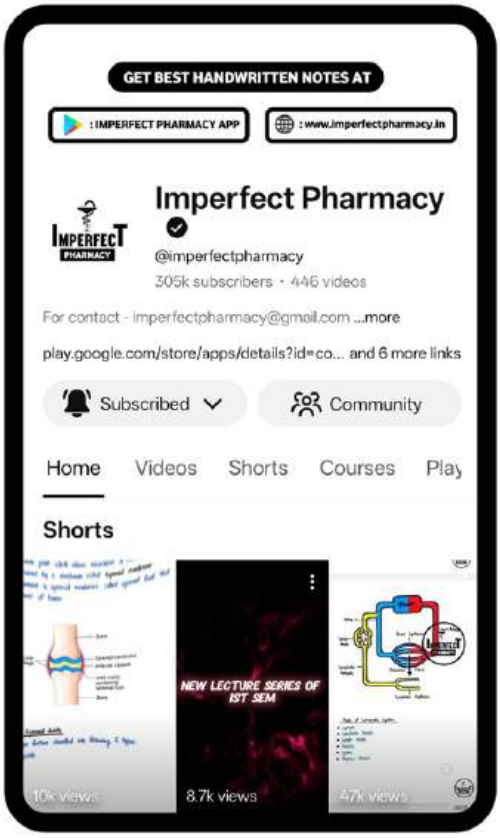

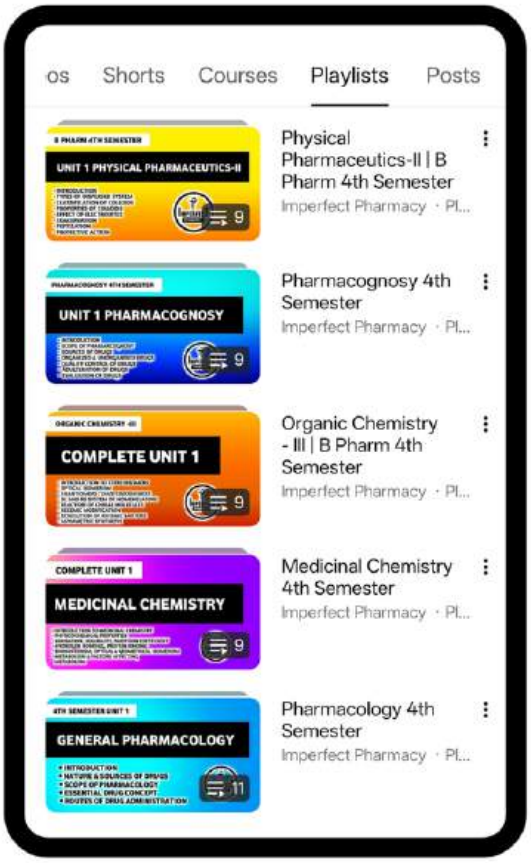

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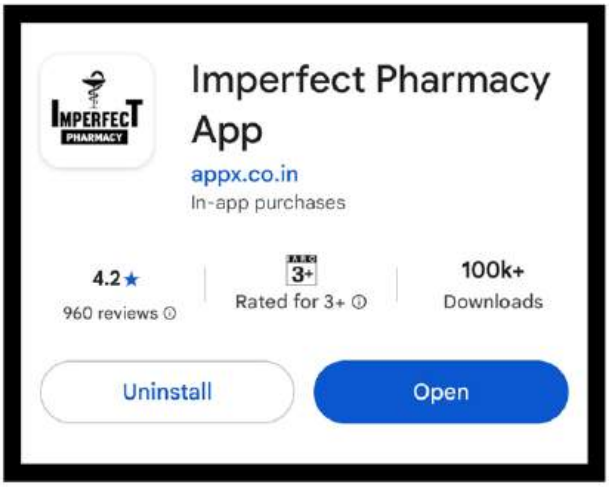

General Anesthetics

- General Anesthetics are Central nervous system (CNS) depressant drugs that produce a reversible loss of conciousness, analgesia, amenesia (loss of memory), muscle relaxation and suppression of reflexes.
- These agents are used to perform surgical and other medical procedures painlessly and without psychological trauma.

General Mechanism Of Action

- The mechanism of general anesthesia involves multiple effects on the central nervous system that result in loss of conciousness, amnesia, analgesia and immobility.
- The exact mechanism are complex and not completely understood but the general principles includes:

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① Enhancement of inhibitory pathways

- Most of General Anesthetics enhance the action of inhibitory neurotransmitters, especially GABA at the GABA-A receptor.
- This leads to :
  - Hyperpolarization of neurons
  - Reduced neuronal excitability
  - Sedation, Amnesia and unconciousness.

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② Inhibition of Excitatory Pathways

- Some anesthetics inhibit excitatory neurotransmitters such as Glutamate particularly at the NMDA (N- methy D- Aspartate) receptors.

- Example- Ketamine blocks NMDA receptors, contributing to its dissociative anesthetic effect.

③ Modulation of Ion Channels

- General Anesthetics also acts on potassium (K^+) and sodium (Na^+) channels:
- Promotes (K^+) potassium reflux — Hyperpolarization
- Inhibit (Na^+) sodium reflux — Reduced action potential generation.

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Stages Of General Anesthesia

- When a general anesthesia is given, the body goes through 4 stages.
- These stages help doctors know how deep the anesthesia is and when it is safe to do surgery.

① Stage - I Analgesia (Pain relief stage)

- Starts right after the anesthesia is given.
- The person is still awake but starts feeling less pain.
- They may feel lazy, sleepy or relaxed.
- Reflexes (like blinking or coughing) are still present.
- Used for small procedures or before giving full anaesthesia.

② Stage - II Excitement or Delirium (confusing stage)

- The person becomes unconcious (not awake).
- May show strange movements, crying, talking or laughing.
- Breathing may become fast or uneven.
- Reflexes are still present, sometimes very active.
- May have vomitting or choking.
- This is a risky stage, Doctors try to pass through it quickly.

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③ STAGE III - Surgical Anaesthesia (Safe for Surgery)

- Person is fully unconcious and doesn't move or feel pain.
- Muscles are relaxed.
- Breathing becomes regular.
- Reflexes are gone.
- This stage has four levels (planes):
  - Plane I : Light sleep - eyelid reflex gone.
  - Plane II : Medium depth - Corneal (eye) reflex gone.
  - Plane III : Deep sleep - Chest muscle ~~reflex~~ relax.
  - Plane IV: Too sleep - breathing becomes weak.
- Doctors do surgery in Plane II or III.

④ STAGE IV - Medullary Paralysis (Danger Stage).

- Too much anaesthetic has been given.
- Brain areas that control breathing and heart stop working.
- The person can stop breathing, blood pressure drops.
- Can lead to death, if not treated quickly.
- This is an emergency, Doctors try to avoid this stage.

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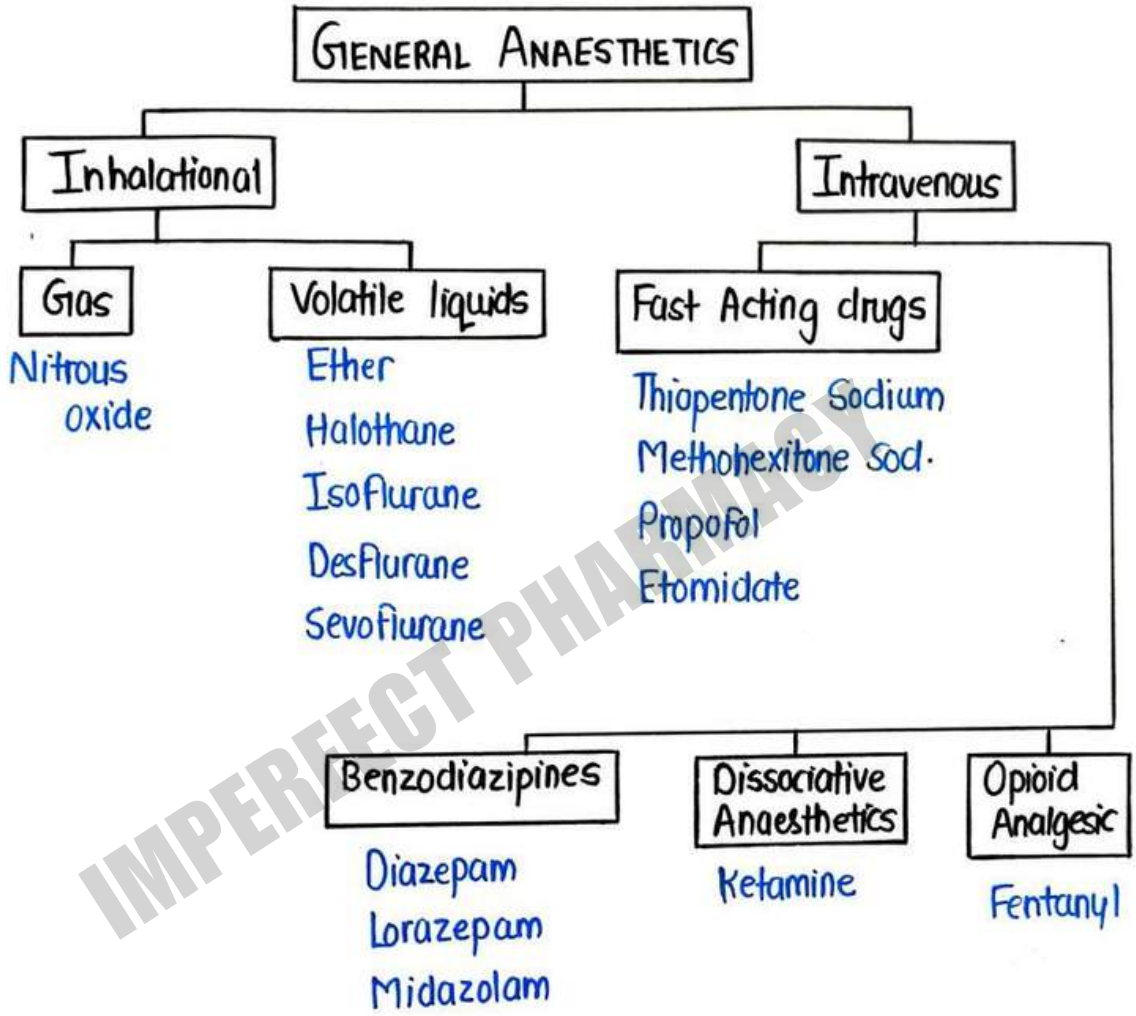
Classification Of General Anaesthesia



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INHALATION ANAESTHETICS

Inhalation anaesthetics are volatile or gaseous chemical agents that are administered through the respiratory tract (via inhalation) to include and maintain general anaesthesia, producing reversible loss of conciousness, analgesia and muscle relaxation.

Key features:

- Delivered via lungs, absorbed into bloodstream.
- Act primarily on the CNS.
- Commonly used for induction or maintenance of anaesthesia.
- Include gases (e.g., Nitrous oxide) and volatile liquids (e.g., Halothane, Isoflurane).

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Mechanism of Action (General):

- Enhance inhibitory neurotransmission mostly (GABA-A).
- Some agents (like N_2O, ketamine) inhibit excitatory NMDA receptors.

Example:

- Nitrous oxide, Halothane, Isoflurane, Sevoflurane, Desflurane, Ether etc.

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① Gaseous Agent

It mainly includes Nitrous Oxide (N_2O).

MOA

- NMDA receptor antagonists ⟶ inhibits excitatory neurotransmission.
- Produces analgesia & sedation, no muscle relaxation.

Pharmacokinetics

Absorption – Rapidly absorbed via alveoli due to low blood : gas partition coefficient.

Onset / Recovery – Very fast (almost immediate)

Distribution – Quickly reaches CNS; high diffusible

Metabolism – Not metabolized in the body.

Elimination – Exhaled unchanged via lungs.

Therapeutic Uses

- As adjuvant with other anaesthetics.
- Dental & Obstetric Analgesia.
- Minor procedures (e.g., dressing changes)

Adverse Effects

- Hypoxia
- Neuropathy
- Megaloblastic Anemia
- Nausea / Vomiting
- Mild respiratory dipression.

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② VOLATILE LIQUIDS

It mainly includes

- Ether
- Halothane
- Isoflurane
- Desflurane
- Sevoflurane

Mechanism of Action

- Potentiate GABA-A receptors ⟶ enhance inhibitory neurotransmission.
- Cause CNS depression, unconciousness, muscle relaxation (variable).
- Some also act on potassium and glycine channels.

Pharmacokinetics

~~Absorption~~

AGENT	ONSET/RECOVERY	METABOLISM	ELIMINATION
Ether	Very slow	Negligible	Exhaled
Halothane	Moderate	~20% (liver)	Exhaled
Isoflurane	Fast	<1%	Exhaled
Desflurane	Very fast	<0.02%	Exhaled
Sevoflurane	fast	3-5% (liver)	Exhaled

Uses

- Induction & maintenance of general anaesthesia.
- Sevoflurane - Preferred in children (non-irritant).
- Desflurane - Prefferred in a day-care surgery (very-fast recovery).
- Often used in combination with IV agents or N_2O.

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Intravenous General Anaesthetic

- Intravenous general anaesthetics are drugs that are administered directly into the bloodstream through IV injection to produce rapid induction of unconciousness and are often used as part of balanced anaesthesia for surgical procedure.
- It can be further divided into two types:

① Fast Acting Agents
② Slow Acting Agents

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① Fast Acting Intrvenous Anaesthetics

Fast acting intravenous (IV) anaesthetics are agents given through IV routes that produce rapid loss of conciousness (within 30 seconds) and are mainly used for the induction of general anaesthesia.

Example:

- Thiopentone Sodium
- Propofol
- Etomidate
- Ketamine
- Midazolam

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Mechanism Of Action

Drug	MOA
Thiopentone, Propofol, Etomidate	Enhance GABA-A activity → CNS depression
Ketamine	NMDA receptor antagonist → dissociative anaesthesia
Midazolam	Potentiates GABA-A → sedation, anxiolysis

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Pharmacokinetics

Feature	Description
Onset	Very rapid (10-30 sec)
Duration	Short (5-10 min) due to redistribution (not metabolism)
Metabolism	Mostly hepatic
Elimination	Renal (metabolites)

Uses

- Induction of general anaesthesia.
- Short procedures (e.g., Endoscopy, Cardioversion)
- ICU sedation
- Ketamine – emergency anaesthesia, asthma patients
- Etomidate – Cardiac patients (minimal CV depression)

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② Slower Acting Intrvenous Anaesthetics

- Slower acting IV anaesthetics are drugs given intravenously that produce gradual or special types of anaesthesia such as sedation, analgesia or dissociative anaesthesia, and are commonly used premedication or in special cases during general anaesthesia.
- It includes :

① Benzodiazepines - Midazolam, Diazepam, Lorazepam
② Opioids - Morphine, Fentanyl
③ Dissociative Anaesthetics - Ketamine

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Mechanism Of Action

Drug Class	MOA
Benzodiazepines	Enhance GABA-A activity → Sedation, Amnesia
Opioids	Mu-opioid receptor antagonist → Analgesia, Sedation
Ketamine	NMDA receptor antagonist → Dissociative anaesthesia, Analgesia

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PHARMACOKINETICS

PROPERTY	BENZODIAZEPINES	OPIOIDS	KETAMINE
Onset	1-3 minutes	Fentanyl: ~ 1 min	~30 seconds (IV)
Duration	Midazolam : short	Fentanyl: short & Morphine: Long	10-15 minutes (anaesthesia, longer analgesia)
Metabolism	Hepatic (CYP enzymes)		Liver (CYP3A4. Active metabolite: norketamine)
Excretion	Renal	Renal	Renal

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USES

DRUG TYPE	USES
Benzodiazepines	Premedication, Sedation, status epilepticus
Opioids	Analgesia during surgery, adjunct to GA, post-op pain management
Ketamine	Emergency anaesthesia, asthma patients, trauma center, short procedures in children.

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PRE-ANAESTHETIC AGENTS

- Pre- Anaesthetics (also called premedications) are drugs administered before the induction of general anaesthesia to prepare the patient to surgery and improve the safety and improve effectiveness of anaesthesia.
- They are given prior to general anaesthesia to reduce anxiety, minimize side effects, ensure smooth induction and recovery, and decrease the required dose of anaesthetic agents.

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OBJECTIVES

Anxiolysis - Relieave anxiety and apprehension.
Sedation - Calm the patient before induction.
Analgesia - Provide pain relief before and during surgery.
Amnesia - Reduce unpleasant memories of the procedure.
Anti-secretory effect - Reduce salivary and bronchial secretions.
Anti-emetic effect - Reduce risk of postoperative nausea/vomiting.
Decrease anaesthetic dose - allow for lower, safer doses of general anaesthetics.

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Common classes of Pre-anaesthetics

Class	Example Drugs	Purpose
Sedative-hypnotics	Diazepam, Midazolam	Sedation, anxiolysis, Amnesia
Opioid analgesics	Morphine, Fentanyl	Preoperative analgesia
Anticholinergics	Atropine, Glycopyrrolate	Reduce secretions, prevent bradycardia
H_2 blockers / PPI	Ranitidine, Omeprazole	Reduce gastric acidity
Anti-emetics	Ondansetron, Metoclopramide	Prevent nausea and vomiting
Neuromuscular blockers	Succinylchloride, Vecuronium	Facilitate intubation

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Sedatives & Hypnotics

- Sedatives & Hypnotics are class of drugs that depress the CNS (central nervous system), producing a calming (sedative) or sleep-inducing (hypnotic) effect.

- **Sedatives** are medicines that calm you down, they help reduce stress anxiety and excitement.
- **Hypnotics** are medicines that help you fall asleep, they are used when someone has trouble sleeping (insomnia).

- Both sedatives & hypnotics slow down the brain, but they are used for different reasons depending on the dose.

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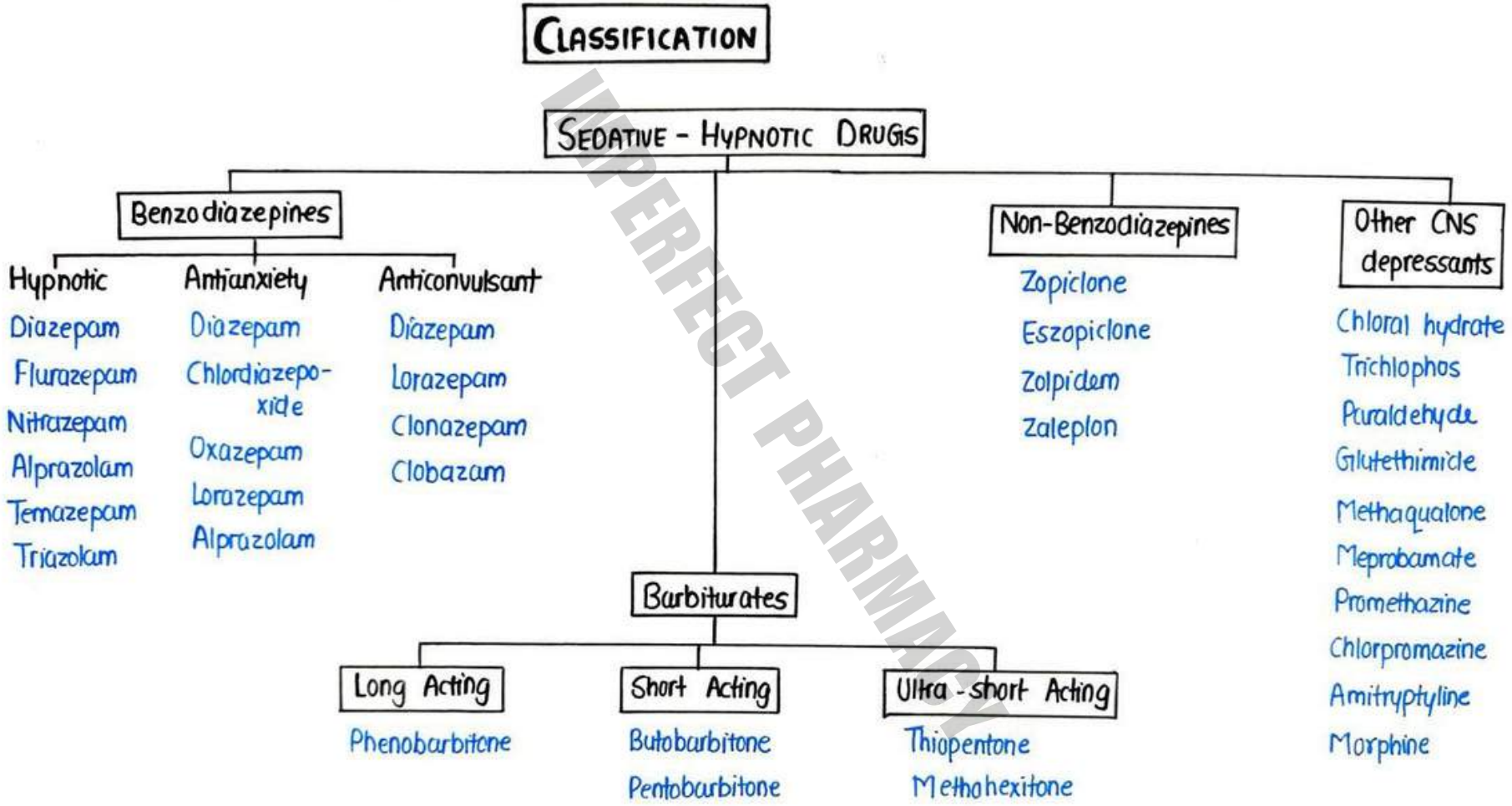
Classification



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BENZODIAZEPINES

- BZDs are class of drugs used as:
  - Sedatives (to calm)
  - Hypnotics (to induces sleep)
  - Anxiolytics (to reduce anxiety)
  - Anticonvulsants (to control siezures)
  - Muscle relaxants
- Safer than older drugs like barbiturates

MECHANISM OF ACTION

- BZDs act on the GABA-A receptor (GAMa-aminobutyric Acid type A)
- GABA is main inhibitory neurotransmitter in the CNS.
- BZDs bind to a specific site on the GABA-A receptor complex.
- They enhance the effect of the GABA by increasing the frequency of chloride channel opening.
- This leads to hyperpolarization of neurons.
- CNS depression.

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PHARMACOKINETICS

- Absorption - Well absorbed orally.
- Distribution - High lipid soluble → quickly crosses blood-brain barrier.
- Metabolism - Mainly metabolized in the liver (CYP450 Enzymes).
- Excretion - Excreted via kidneys (urine) as inactive or conjugated forms.

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Therapeutic Uses

- Anxiety disorders
- Insomnia (short-term)
- Siezures
- Pre-operative sedation

Adverse Effects

- Drowsiness
- Sedation
- Dizziness
- Confusion
- Muscle weakness

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BARBITURATES

- Barbiturates are older CNS depressants used for:
  - Sedation
  - Hypnosis
  - Anaesthesia
  - Siezure control
- Nowdays, its used less because of high risk of overdose tolerance, and dependence.
- It includes:
  - Phenobarbitone
  - Butobarbitone
  - Thiopentone etc.

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MECHANISM OF ACTION

- Barbiturates also act on the GABA-A receptor and increases the duration of chloride channel opening.
- But at high doses, they can directly open GABA-A channels without GABA.
- It leads hyperpolarization of neurons ⟶ CNS depression.

PHARMACOKINETICS

- **Absorption** - Rapid oral absorption & some given IV (eg., thiopentone)
- **Distribution** - Very lipid soluble ⟶ fast brain entry.
- **Metabolism** - Metabolized in liver (CYP450 enzymes).
- **Excretion** - Mainly through kidney's, as metabolites.

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Classification Based On Duration Of Action

Type	Drugs	Uses
Ultra-short Acting	Thiopentone, Methohexitone	IV anaesthesia (fast induction)
Short Acting	Pentobarbitone, Butobarbitone	Hynotic (now rarely used)
Long Acting	Phenobarbitone	Siezures control (epilepsy), sedation in children.

Therapeutic Uses

- Anaesthesia (induction) → Thiopentone, Methohexitone
- Siezures (epilepsy, status epilepticus) → Phenobarbitone
- Sedation / Hypnosis (now obsolete) → Butobarbitone, Pentobarbitone

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Adverse Effects

- Drowsiness
- Dizziness
- Severe Respiratory depression (dose-dependent)
- Coma / death in overdose.
- Tolerance & Dependence.

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NON BENZODIAZEPINES

- Non - benzodiazepines, often called Z- drugs, are class of sedative-hypnotic agents that are structurally unrelated to benzodiazepines, but act via the same GABA receptor complex.
- They are mainly prescribed for short - term management of insomnia due to their favorable side - effect profile and low risk of dependence compared to traditional benzodiazepines.
- It includes :
  - Zolpidem
  - Zoleplon
  - Zopiclone
  - Eszopiclone

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MECHANISM OF ACTION

- Z- drugs selectively bind to the benzodiazepines site on the GABA receptor.
- This enhances the inhibitory effect of GABA, the primary
- CNS inhibitory neurotransmitter.
- The result is :
  - Sedation
  - Hypnosis

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Pharmacokinetics (ADME)

Parameter	Zolpidem	Zaleplon	Zopiclone / Eszopiclone
Absorption	Rapid oral absorption	Rapid	Rapid
Onset	10-15 minutes	~15 min	30-60 minutes
Duration	~ 6-8 hours	3-4 hours	6-8 hours
Half-life	2-3 hours	~1 hours	5-7 hours
Metabolism	Liver (CYP3A4)	Liver (aldehyde oxidase + CYP3A4)	Liver (CYP3A4, 2E1)
Excretion	Urine	Urine	Urine and feces

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Therapeutic Uses

- Insomnia
- Cardiac rhythm disturbance etc.

Adverse Effects

- Drowsiness
- Dizziness
- Headache etc.

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OTHER CNS DEPRESSANTS

- These are older or alternatives drugs that depress the CNS and are used for sedation, hypnosis or calming effects.
- Many are now used less frequently due to side effects or availability of safer drugs.

① CHLORAL HYDRATE

- One of the oldest hypnotics.
- It is metabolized to trichloroethanol (active form).
- Produces sleeps quickly but may cause:
  - Gastric irritation
  - Hangover effect
- Rarely used today.

② TRICLOFOS

- A prodrug of Trichloroethanol.
- Less irritating to the stomach.
- Mainly used as a sedative in children, especially for procedures like ECG or MRI.

③ PARALDEHYDE

- CNS depressant with anticonvulsant properties.
- Used in the past for alcohol withdrawl siezures.
- Has a strong, uppleasant smell and causes airway secretions.
- Very rarely used now.

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④ GLUTHEMIDE

- A sedative - hypnotic once used for insomnia.
- Similiar action to barbiturates.
- High risk of dependence and abuse.

⑤ METHAQUALONE

- Popular in the past as a sleeping pill.
- Withdrawn from the market due to widespread abuse.

⑥ MEPROBAMATE

- Used as anxiolytic and sedative.
- Acts on GABA-A receptors.
- Risk of dependence, rarely used today.

⑦ PROMETHAZINE

- Antihistamine with sedative properties.
- Used for nausea, allergy, and preoperative sedation.
- Causes drowsiness.

⑧ CHLORPROMAZINE

- A typical antipsychotic, but also has sedative effects.
- Used for psychosis, agitation and preoperative sedation.

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⑨ AMITRIPTYLINE

- A tricyclic antidepressant (TCA).
- Causes sedation due to antihistamine and anticholinergic action.

⑩ MORPHINE

- A strong opioid analgesic.
- Can cause CNS depression, sedation and respiratory depression.
- Not used as a hypnotic, but included due to CNS depressant action.

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Centrally Acting Muscle Relaxants

- Centrally acting muscle relaxants are drugs that reduce skeletal muscle tone and spasms by acting primarily on the central nervous systems (CNS) rather than directly on muscle.
- They are mainly used for muscle spasticity, painful muscle conditions, and neurological disorders involving increased muscle tone.
- It includes:
  - Baclofen
  - Tizanidine
  - Methocarbamol
  - Chlorzoxazone
  - Cyclobenzaprine
  - Carisoprodol
  - Diazepam

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Mechanism Of Action

- They works by relaxing / depressing the CNS, especially at the level of the brainstem and spinal cord.
- They inhibit polysynaptic reflexes, reduce motor neuron excitability, and sometime enhance GABAergic activity, leading to reduced muscle tone and spasms.
- Some also act via α_2 adrenergic receptors (eg. Tizanidine).

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PHARMACOKINETICS

PARAMETER	GENERAL INFO
Absorption	Well absorbed orally
Distribution	Crosses BBB ; CNS Acting
Metabolism	Mostly hepatic (liver) metabolism
Excretion	Primarily renal (urine)

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THERAPEUTIC USES

- Relief of acute muscle spasms (e.g., lower back pain, neck pain).
- Treatment of spasticity.
- Muscle relaxation during orthopedic procedures.
- Musculoskeletal pain due to strain or injury.
- Supportive care in neurological disease with increased muscle tone.

ADVERSE EFFECTS

- Sedation
- Dizziness
- Drowsiness
- Weakness
- Hypotension
- Hepatotoxicity etc.

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ANTIEPILEPTIC DRUGS

Antiepileptic drugs (AEDs) — also known as antiepileptic agents or anticonvulsants — are a class of medications used to prevent and control siezures in indivisuals with epilepsy or other siezure disorders.

MECHANISM OF ACTION (GENERAL)

- AED works by one or more of the following mechanisms:
- Inhibition of voltage-gated sodium channels (e.g. Phenytoin, carbamazepine)
- Enhancement of GABAergic (inhibitory) neurotransmitters (e.g., benzodiazepines, phenobarbital)
- Inhibition of voltage-gated calcium channels (e.g., ethosuximide, for absence siezures).
- Inhibition of glutamate-mediated excitatory neurotransmitter (e.g. topiramate)

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EPILEPSY

- Epilepsy is one of the most common chronic neurological disorder characterised by recurrent & unpredictable seizures due to disorder of brain cells.
- Seizures occurs due to sudden, uncontrolled electrical disturbances in brain that can cause changes in behaviour, movement, sensation & loss of consciousness.
- It is an Paroxysmal Disorder.
- It often occurs due to too much excitation or too low inhibation.

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TYPES OF EPILEPSY

It is of mainly two types :

① Generalised Epilepsy
② Focal Epilepsy

GENERALISED EPILEPSY

- A Generalised Epilepsy is a type of seizure that involves abnormal electrical activity throughout the entire brain.
- It affects both Hemispheres.
- It is further subdivided as follows :

① Tonic Clonic Seizure
② Absence Seizure
③ Tonic Seizure
④ Clonic Seizure
⑤ Atonic Seizure
⑥ Myoclonic Seizure

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① **Tonic - Clonic** :
- It is also known as Grand-Mal Seizure.
- It is characterised by loss of consciousness, stiffening of muscles (Tonic Phase) & Jerking movements (Clonic Phase)
- It leads to Post Seizure Depression.

② **Absence** :
- It is also known as Petit-Mal Seizures.
- It is characterised by sudden loss of consciousness (For 30-60 seconds) in middle of an activity.
- In this patient shows absent minded behaviour & typically occurs in children

③ **Tonic** :
- Tonic seizure involves sustained muscle stiffness/rigidity.
- It usually affects muscles in back, arms & legs.

④ **Clonic** :
- It is characterised by repeated jerking movement of muscles.
- It usually affects neck, face & arms.

⑤ **Atonic** :
- It involves sudden loss of muscle control, leading to collapse or fall.

⑥ **Myoclonic** :
- These seizure involves sudden brief muscle contraction.
- It can occur in specific muscle group or involve in entire body

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FOCAL EPILEPSY

- It is also known as Partial Epilepsy.
- In this only a single / specific part of brain is affected
- It is further subclassified into two types

① Simple Partial Seizure
② Complex Partial Seizure

① **Simple Partial** :
- These seizures do not cause loss of consciousness.
- They may cause localised symptoms such as tingling, changes in emotion, sensation & perception.

② **Complex Partial** :
- These seizures involves loss of consciousness accompanied by unusual behaviour or automatism.
- The person may not remember seizure afterwards.

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CAUSES / ETIOLOGY

- Genetic Factors
- Head Injury
- Brain Tumour
- Meningitis
- Alzheimer's Disease
- Stroke
- Hypoglycemia
- Idiopathic Reasons
- Certain Medications

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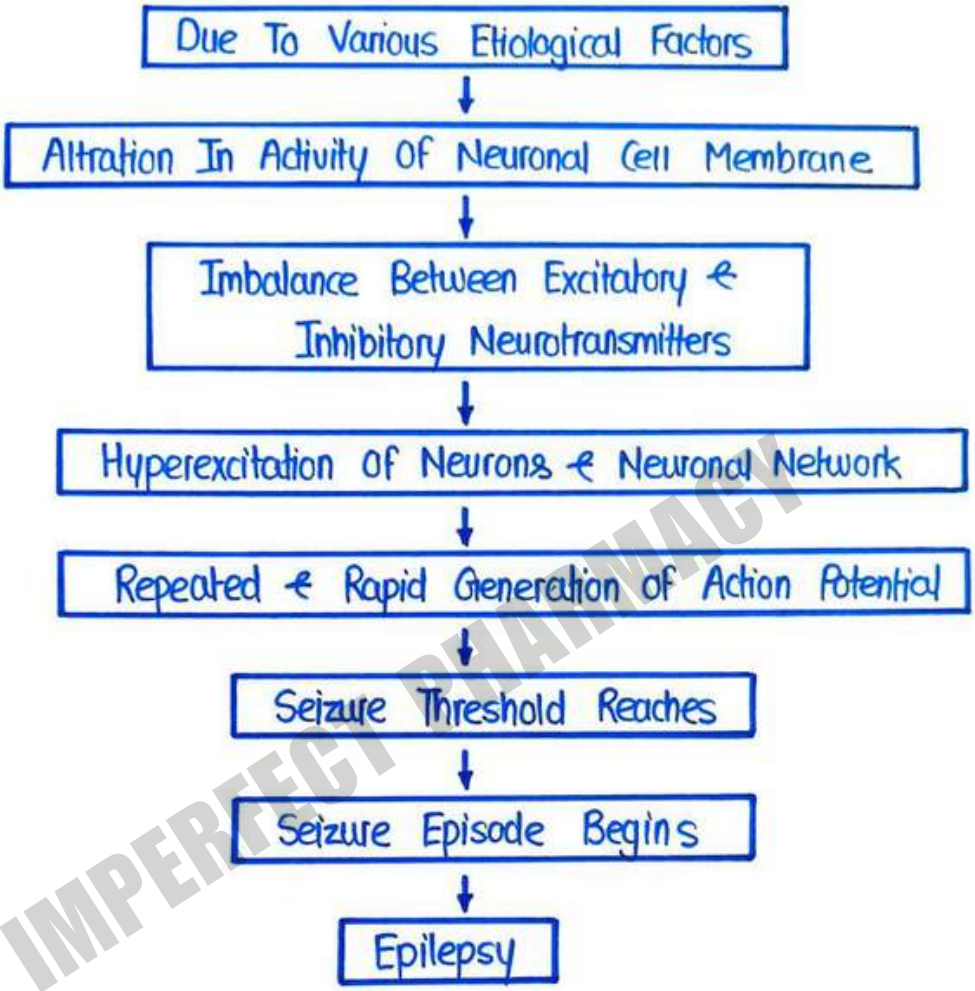
PATHOGENESIS

The pathogenesis of Epilepsy can be explained as follows :



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SYMPTOMS

- Temporary Confusion
- Muscle Contraction
- Muscle Stiffening
- Loss Of Consciousness
- Uncontrolled Jerking
- Sudden rapid eye movement
- Sudden Mood Changes

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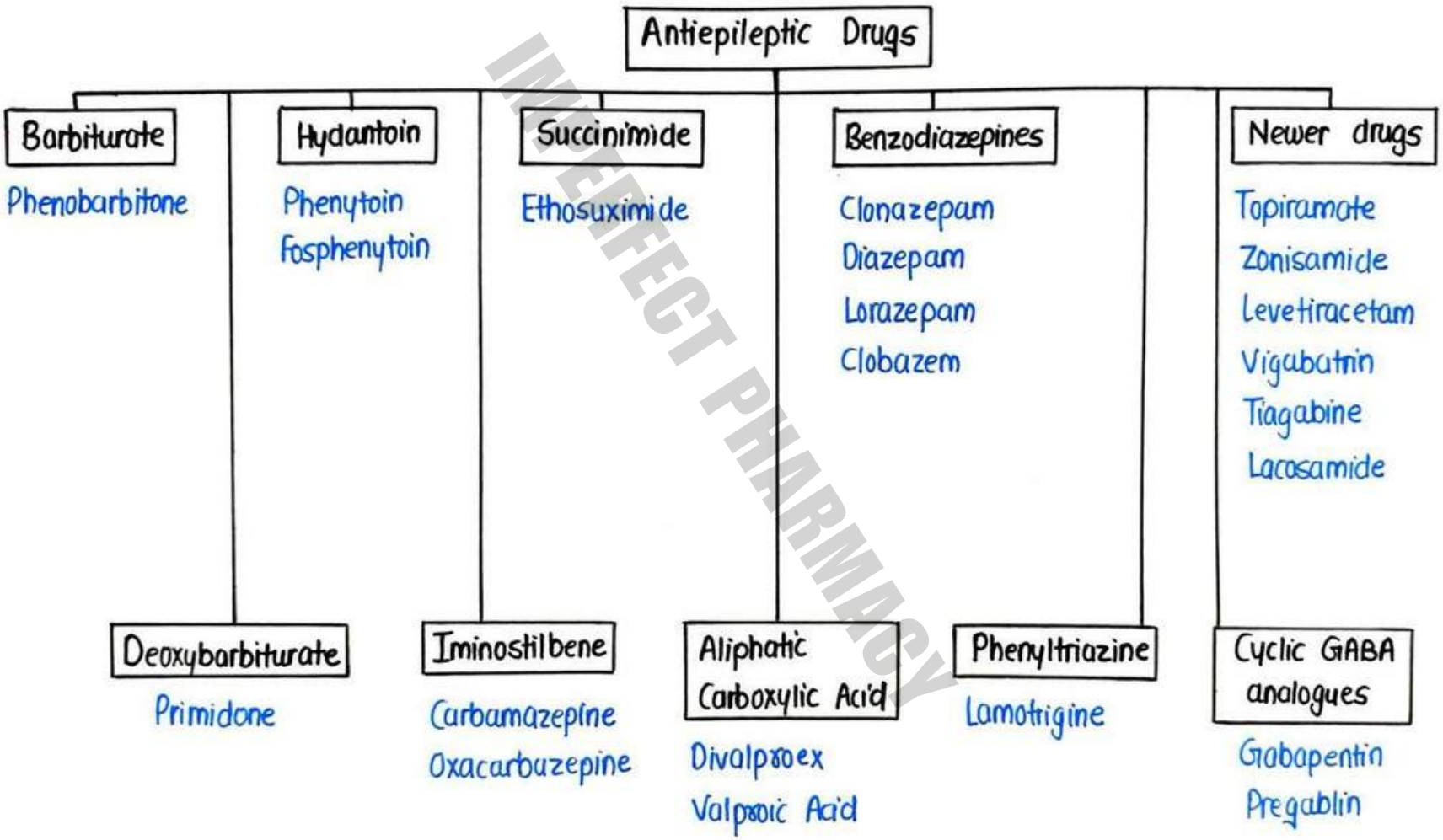
CLASSIFICATION



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Some Most Commonly Used Antiepileptic Drugs

① Phenytoin

MOA: Blocks voltage-gated Na^+ channels, stabilizes neuronal membranes, and prevents repititive firing.

ADME: Absorption - Variable; saturable kinetics.
Distribution - Highly protein-bound.
Metabolism - Hepatic (CYP450); zero-order kinetic at high doses.
Excretion - Renal (as metabolites).

Uses: Generalized tonic-clonic siezures, focal siezures, status epilepticus (IV form).

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② Carbamazepine

MOA: Blocks voltage-gated sodium channels, decreases, synaptic transmission

ADME: Absorption - Good oral bioavailability.
Distribution - High protein binding.
Metabolism - Liver; its own metabolism induction (autoinduction)
Excretion - Renal (kidneys).

Uses: Focal and generalized tonic-clonic siezures, trigeminal neuralgia, bipolar disorder.

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③ Valproic Acid

MOA: Inhibits Na^+ channels and Type-T Ca^{2+} channels.
Increases GABA by inhibiting GABA transaminase.

ADME: Absorption - Well-absorbed orally.
Distribution - Highly protein bound.
Metabolism - Hepatic (CYP and glucuronidation).
Excretion - Renal (via urine).

Uses: Broad-spectrum AED - effective in generalized, absence, and myoclonic siezures; bipolar disorder; migraine prophylaxis.

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④ Ethosuximide

MOA: Block T-type Ca^{2+} channels in thalamic neurons.

ADME: Absorption - Good oral absorption.
Distribution - Low protein binding
Metabolism - Hepatic
Excretion - Renal

Uses: Absence siezures (drug of choice).

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ALCOHOL

- Alcohol commonly refers to ethanol (C_2H_5OH), a psychoactive substance found in alcoholic beverages.
- It is a central nervous system (CNS) depressant that produces effects such as sedation, euphoria, impaired coordination, and cognitive dysfunction.

MECHANISM OF ACTION

Ethanols acts on mutiple neurotransmitter systems:

- Enhances GABA receptor activity → increased inhibitory neurotransmission (sedative/hypnotics).
- Inhibits NMDA (glutamate) receptors → reduces excitatory neurotransmission (cognitive & memory impairment).
- Increases Dopamine release in the mesolimbic pathway → produces rewarding & euphoric effects.
- Modulates serotonin, endorphin, and canabinoid systems.

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PHARMACOKINETICS

Absorption - Rapidly absorbed from the stomach (20%) and small intestine (80%); food slows absorption.

Distribution - Widely distributed in body water; crosses blood-brain barrier and placenta; Vd ≈ 0.5 - 0.7 L/kg.

Metabolism - Mainly in liver by alcohol dehydrogenase (ADH) to acetaldehyde, then by aldehyde dehydrogenase (ALDH) to acetic acid, follows zero-order kinetics.

Excretion - 90 - 98% metabolized; 2 - 10% excreted unchanged in breath, urine and sweat.

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PHARMACODYNAMIC EFFECTS

① Central Nervous System (CNS)

Acute effects: Alcohol acts as a CNS depressant, enhancing GABAergic activity and inhibiting NMDA receptors, leading to sedation, impaired coordination, and cognitive dysfunction.

Chronic effects: Prolonged used can result in tolerance, dependence and neurodegenrative conditions like Wernicke - Korsakoff syndrome, characterized by memory impairment and ataxia.

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② Cardiovascular System

Acute effect: Moderate intake may cause vasodilation, leading to a sensation of warmth and lowered blood pressure.

Chronic effects: Long-term consumption increases risk of hypertension, arrhythmias, cardiomyopathy and stroke.

③ Respiratory System

Acute effects: High doses can depress respiratory centers, leading to hypoventilation.

Chronic effects: Chronic alcohol use impairs pulmonary immune defenses, increases susceptibility to infections like pneumonia and conditions such as acute respiratory distress syndrome (ARDS).

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④ Gastrointestinal (GI) Tract

Acute effects: Alcohol irritates the gastric mucosa, increasing acid secretion and potentially causing gastritis.

Chronic effects: Long-term use can lead to esophagitis, peptic ulcers, malabsorption and increased risk of GI Cancers.

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⑤ **Liver**

Steatosis : Accumulation of fat in liver cells, often reversible with abstinence.

Alcoholic Hepatitis : Inflammation of liver, presenting with jaundice and liver dysfunction.

Cirrhosis : Long-term consumption leading to liver failure and increased risk of hepatocellular carcinoma.

⑥ **Pancreas**

Acute effects : Alcohol can trigger acute pancreatitis, characterized by abdominal pain and elevated pancreatic enzymes.

Chronic effects : Repeated episodes may lead to chronic pancreatitis, impairing both exocrine and endocrine functions, increasing the risk of diabetes and pancreatic cancer.

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⑦ **Musculoskeletal System**

Bone Health : Chronic alcohol consumption distrupts calcium balance and hormone regulation, leading to decreased bone mineral density and increased fracture risk.

Muscle Health : Alcohol-induced myopathy can cause muscle weakness and atrophy.

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⑧ Endocrine System

Harmonal imbalance : Alcohol effects the hypothalmic - pitutary - gonadal axis, leading to decreased testosterone in men and menstrual irregularities in women.

Metabolic effects : It impairs glucose metabolism, increasing the risk of hypoglycemia and type-2 diabetes.

⑨ Immune System

Immunosuppression : Alcohol impairs both innate and adaptive immunity, reducing the body's ability to fight infections and increasing susceptibility to diseases like tuberculosis and pneumonia.

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⑩ Mental Health

Mood disorders : Alcohol use is linked to depression, anxiety and increased risk of suicide.

Cognitive impairment : Chronic use can lead to memory deficits and increased risk of dementia.

⑪ Eyes

Visual impairments : Excessive alcohol can lead to optic neuropathy and retinopathy, especially in individuals with nutritional deficiencies or pre-existing conditions like diabetes.

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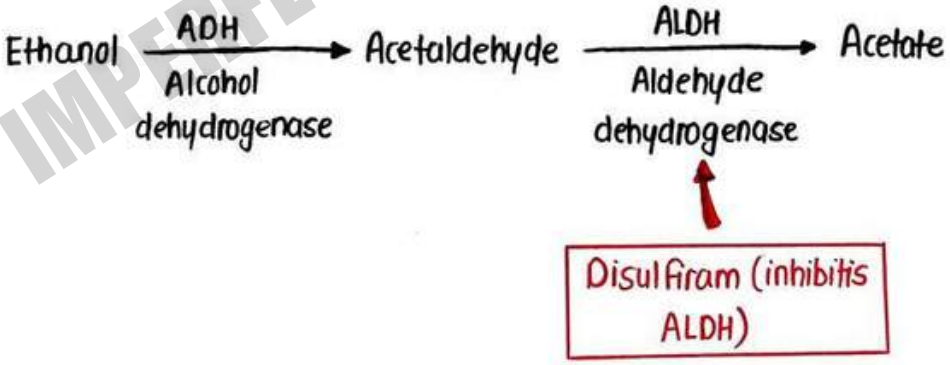
DISULFIRAM

- Disulfiram is a drug used in the management of chronic alcohol dependence.
- It is an aversion therapy agent that causes unpleasant effects when alcohol is consumed.

MECHANISM OF ACTION

- Disulfiram inhibits aldehyde dehydrogenase (ALDH), the enzyme that converts acetaldehyde ⟶ acetic acid in alcohol metabolism.

- This leads to accumulation of acetaldehyde



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This buildup causes toxic symptoms, producing unwanted effects:

- Throbbing headache
- Nause & Vomitting
- Chest pain
- Palpitations
- Hypotension
- Sweating & Anxiety etc.

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PHARMACOKINETICS

Absorption - Well absorbed orally.

Distribution - Widely distributed; crosses the blood-brain barrier.

Metabolism - Metabolized in the liver to active compounds; inhibits aldehyde dehydrogenase and dopamine β-hydroxylase.

Excretion - Excreted in urine and feces; effects may last up to 1-2 weeks after stopping.

USES

Main use: Treatment of chronic alcohol dependence.

Others (rare / investigational): Heavy metal chelation, cancer research.

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